



Catalog of Services

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MMPC Mission

Our mission is to advance medical and biological research by providing the scientific community with standardized, high quality metabolic and physiologic phenotyping services for mouse models of diabetes, diabetic complications, obesity and related disorders.

The six Centers are housed at outstanding academic institutions, staffed by experts in state-of-the-art technology. Researchers can ship mice to one of the Centers and obtain on a fee-for-service basis a range of complex exams used to characterize mouse metabolism, blood composition including hormones, energy balance and physical activity, eating and exercise, insulin resistance, organ function, metabolic fluxes and morphology, physiology, histology and measures of diabetic complications in heart, kidney, vasculature, eye, etc. Many tests are done in living animals and are designed to elucidate subtle to complex traits that would define models of metabolic disease.

The development of transgenic technology and gene targeting protocols has resulted in numerous mouse lines with specific phenotypes and well-defined DNA structural changes. Candidate genes for diabetes, obesity and other disorders of metabolism have been identified and transgenic mice are being generated using this technology. By broadening the availability of sophisticated metabolic phenotyping, we hope to help investigators identify and study new mouse models that will lead to an improved understanding of these complex diseases.

In 2006, the MMPC formed a collaboration with the NIH-sponsored Diabetic Complications Consortium (DCC) in order to more thoroughly phenotype putative new mouse models of disease for a range of complications including cardiovascular disease, nephropathy, neuropathy, retinopathy. The MMPC is committed to improving access to existing tests, and to developing new technologies for this purpose.

Goals

1. Broaden the scope of metabolic phenotyping tests for mice available to investigators.
2. Standardize key methodologies.
3. Expedite the completion of research.
4. Compile a database of information relevant to mouse models of diabetes, obesity, and diabetic complications.

Guidelines and Policies

The MMPC is sponsored by the National Institutes of Health as a resource to provide services to the community of scientists who use mice to study diabetes, obesity, diabetic complications, and other metabolic diseases. In order to accomplish this goal, the MMPC offers to researchers phenotyping tests that require specialized expertise or equipment. Modest fees for these tests are set at or below actual cost. Researchers can arrange to ship mice or murine tissues to the Centers for analysis. Complete information is available at www.mmmpc.org.

Center Structure & Steering Committees

Each Center has a structure that consists of an Executive Committee, an Administrative Core and Director, experimental and analytical Test Cores, an Animal Health and Welfare Core, and a Research & Development program. The MMPC program has a Coordinating and Bioinformatics Unit which houses the MMPC Pilot and Feasibility grant program, the MMPC website, and MMPC Database. This CBU is shared with the NIH-sponsored Diabetes Complications Consortium (DCC). Details for the structure and personnel at each MMPC can be obtained from the individual web sites. The six Centers share a National Steering Committee consisting of Center Directors, NIH personnel, and external advisors.

Application for Services

After identifying the appropriate Center(s) from the individual web pages or test catalog, www.mmmpc.org/shared/catalog.aspx, the applicant should first contact the Center Director or Core Director to discuss the mouse strain, determine the best set of tests to be conducted, and obtain an estimate of costs. The applicant then obtains a password protected account and completes an online request for services, www.mmmpc.org/shared/orderTest.aspx, which is targeted to the appropriate Center. The request is reviewed by the Center Executive Committee. Acceptance is based on Center workload, relevance of the available and/or requested tests to the mouse model, and the perceived value of the animal to diabetes, obesity, and metabolic disease research. The applicant will be contacted with the decision. Following consultation with the Center and/or Core Director(s), a written estimate for all tests agreed upon, including the number of mice required for each test and a timeline for receipt and testing of the mice at the MMPC, will be sent to the applicant for his/her approval.

Data

Tests will be conducted using the experimental protocols found on the individual MMPC web sites or in the catalog. Detailed descriptions will be provided upon request. Upon completion of the requested tests, data in an appropriate form will be stored in the MMPC database and posted on MMPC's password protected web site, www.mmmpc.org/secure/index.aspx, for viewing by the submitting investigator only. The Center personnel will be available to discuss experimental details, etc.

Data Ownership

All data generated from a submitted strain belongs to the submitting investigator and his/her institution.

Center personnel have no rights to use this data for personal or institutional research purposes unless a formal, documented arrangement of collaboration exists between Center personnel and the investigator.

The NIH strongly encourages the sharing of research data. NIH guidelines regarding data sharing can be found at <http://grants1.nih.gov/grants/guide/notice-files/NOT-OD-03-032.html>. This notice states,

We believe that data sharing is essential for expedited translation of research results into knowledge, products, and procedures to improve human health. The NIH endorses the sharing of final research data to serve these

and other important scientific goals. The NIH expects and supports the timely release and sharing of final research data from NIH-supported studies for use by other researchers... [The] definition of "the timely release and sharing" [is] to be no later than the acceptance for publication of the main findings from the final data set. NIH continues to expect that the initial investigators may benefit from first and continuing use but not from prolonged exclusive use.

All data collected at the Centers from background strains and standard disease models (i.e., those commercially available) will be stored in the publicly available MMPC database. It is anticipated that the complete set of data generated by the MMPCs on all newly generated strains, taken together in a database, will be valuable for understanding diabetes, obesity and other metabolic diseases.

Therefore, the NIH requests that investigators allow the data generated by an MMPC to be placed in a public MMPC database after the first of the following two conditions has been met:

- 1. The data have been published and are therefore in the public domain.**
- 2. Two years have passed since the investigator received the data from the Center.**

Because it is sometimes not possible to publish or even interpret data within a two-year timeframe, investigators may request that specific data be withheld from the public database for an additional period of time.

The Center personnel and the investigator must read and sign a Mouse / Tissue Transfer Agreement, www.mmhc.org/documents/MTA.pdf, which clearly states these rights and responsibilities.

Fees

Price information for each test is available on the individual Center web pages or by request from each MMPC. Applicants will receive a written estimate that must be acknowledged by the submitting investigator before animals can be shipped for testing. Fees are set as a fraction of the total costs incurred by the MMPC for that test, and are calculated based on the obtainment of revenue neutrality.

Animal Guidelines

Please see animal care and shipping section of this catalog or www.mmhc.org/shared/animalShipping.aspx. Specific instructions can be obtained from center personnel.

Acknowledgements

One index of success of the MMPC program is the contribution of data produced by the MMPC to publications and oral communications. Please acknowledge the MMPC when presenting data obtained using Center Services.

Animal Care and Shipping

Minimum testing required of mice received from other institutions

While each of the four institutions may require additional testing for mice received into their labs, below is an agreed upon list of the minimum testing that will be required prior to shipping. A health certificate, no older than 3 months, must be faxed/shipped to the receiving institution. This certificate must be received and reviewed before approval will be given to ship.

- Cilia-associated respiratory bacillus
- Clostridium piliforme (Tyzzer's disease)
- Ectromelia
- Lymphocytic choriomenengitis virus
- Mouse adenoviruses
- Mouse hepatitis virus
- Mouse parvoviruses
- Mouse rotavirus
- Mycoplasma pulmonis
- Pneumonia virus of mice
- Reovirus
- Sendai virus
- Theiler's virus (GD-7)
- Fur mites
- Pinworms

At this time, Vanderbilt routinely uses Fenbendazole medicated feed for four weeks and treats with Ivermectin as soon as the animals arrive. This center will continue to automatically treat their incoming animals. University of Cincinnati, and Yale will not treat unless testing indicates it is necessary.

Quarantine Testing

Below is an agreed upon list of tests to be performed while the mice are in quarantine. While each center will have additional tests that may vary, this is a list of the minimum testing to be performed for this program. As standard procedure, testing of incoming animals will include the storage of an aliquot of serum for retesting at a different lab in the case of positive test results. All researchers sending animals from a non-commercial source should attempt to send two additional animals, one to be tested upon arrival and the second to be tested in 3-4 weeks.

- **Serology:**
 - Cilia-associated respiratory bacillus
 - Clostridium piliforme (Tyzzer's disease)
 - Ectromelia
 - Lymphocytic choriomenengitis virus
 - Mouse adenoviruses
 - Mouse cytomegalovirus
 - Mouse hepatitis virus
 - Mouse parvoviruses
 - Mouse rotavirus
 - Mouse thymic virus
 - Mycoplasma pulmonis
 - Pneumonia virus of mice
 - Reovirus
 - Sendai virus

- Theiler's virus (GD-7)
- **Subgross examination of the pelt:**
 - Fur Mites
- **Subgross examination of the cecal and colon contents:**
 - Pinworms

Length of quarantine time for animals

Three to four weeks is the minimum amount of time required to release the animals into regular colonies. A one-week minimum period is appropriate for animals to recover from the stress of traveling and new environment prior to phenotyping. Vanderbilt does not allow researchers access to their animals before the 3-4 week quarantine period. After that time, they can remove the animals for terminal procedures only. University of Cincinnati and Yale University will allow researchers access to the animals during the 3-4 week minimum quarantine, but the animals cannot be taken out of the facility except for terminal procedures.

Cages

- **Bedding:**
 - Bed-O-Cob bedding will be used, changed every two weeks.
- **Ventilation:**
 - Ventilated cages will be used.
- **Watering Systems:**
 - Not standardized.
- **Cage Capacity:**
 - Female: maximum 5/cage & minimum 2/cage
 - Male: maximum 2/cage (monitor for signs of stress)
- **Diet:**
 - Harland Teklad irradiated chow will be used at all centers. The product code is #7912, Tekland LM-485 Mouse/Rat Sterilizable Diet. In the cases of feeding studies, a semi-purified diet with defined composition will be used instead of the chow.

Shipping

- **Bax Global**
 - 1-800 CALL BAX
 - www.baxworld.com
- **World Courier**
 - 1-800-221-6600
 - www.worldcourier.com

Release of Protocol Information

All animal care protocols developed during the planning of this project will be shared with NIH.

- **Required Approvals:**
 - All phenotyping tests carried out at the Centers must be done using protocols that have been previously approved by the University IACUC.

- **Current Center Capacities:**

- University of Cincinnati Medical Center: 1,000 cages
- Vanderbilt University Medical Center: 120 cages
- Yale University School of Medicine: 120 cages (anticipates increase)

Committee on Animal Husbandry Issues

- Greg Hanley, DVM, Ph.D. Dipl. ACLAM Vanderbilt University
- Phil Howles, Ph.D. University of Cincinnati
- Todd Jackson, DVM, Dipl. ACLAM University of Cincinnati
- Robert Jacoby, DVM, Ph.D. Yale University
- James Macy, DVM, Dipl. ACLAM Yale University (11/02/01 meeting only)
- Patrick Tso, Ph.D. University of Cincinnati

Tests Listed by General Subject

The first letter of each Test No. denotes the center:

CA = Case Western Reserve University
 D = University of California Davis
 C = University of Cincinnati Medical Center
 M = University of Massachusetts Medical School
 V = Vanderbilt University School of Medicine
 Y = Yale University School of Medicine

Amino Acid Metabolism

| Test No. | Test Name | Keywords |
|----------|---|--|
| V3090 | Full amino acid profiles by HPLC / PITC or HLPC / OPA | amino acids, HPLC |
| T2001 | Sources of plasma glucose using 2H NMR | gluconeogenesis, glucose production, glycogenesis, hepatic, liver, metabolism, NMR, spectroscopy |
| T2011 | Intermediary metabolism in the isolated liver using NMR | hepatic, liver, metabolism, NMR, spectroscopy |
| V3009 | Amino acid kinetics | amino acid flux, amino acid kinetics, isotopes |
| V3091 | Specific selected amino acid profiles | amino acids, HPLC |
| V3092 | Radioactivity of specific individual amino acids | amino acids, chromatography, protein synthesis, proteolysis, specific activity |
| V3093 | Specific activities for gluconeogenic and glycogenic assessment | amino acids, chromatography, protein synthesis, proteolysis, specific activity |
| CA2017 | Tissue-specific protein synthesis using 2H-labeled water | amino acids, metabolism, protein synthesis |

Body Composition

| Test No. | Test Name | Keywords |
|----------|---|---|
| C1041 | Body Composition | body composition, carcass analysis, obesity, QMR, total body fat |
| CA2000 | Body composition using 2H-labeled water | body composition, body weight, fat |
| CA2002 | Body Weight | body composition, body weight, food intake |
| S6101 | Body Composition | body composition, energy balance, fat, fat mass, obesity, water |
| V4004 | Urine pH | pH, urine |
| Y4087 | Blood Electrolytes-Na/Cl/K | electrolytes, metabolism, muscle, pH, plasma, potassium, serum chemicals, serum metabolic panel, sodium |
| Y5004 | Blood or Urine Calcium | serum chemicals |
| Y5005 | Blood Inorganic Phosphorous | inorganic phosphate, phosphate, serum chemicals |
| Y5007 | Magnesium | serum chemicals |
| Y5006 | Urine Inorganic Phosphorous | inorganic phosphate, phosphate, urine |
| Y5010 | Apolipoprotein C3 | lipids, lipoproteins, serum chemicals |
| Y4088 | Urine Electrolytes-Na/K/Cl | electrolytes, muscle, potassium, urine |

| Test No. | Test Name | Keywords |
|----------|-----------------------------------|-------------------------------------|
| D4001 | Gross Body Composition | body composition, imaging |
| D4002 | Adiposity (adipose depot weights) | adipose, body composition |
| M1012 | Body composition (whole body) | fat mass, lean muscle mass, obesity |
| M1013 | Body composition (organs) | fat mass, lean muscle mass, obesity |

Carbohydrate Metabolism

| Test No. | Test Name | Keywords |
|----------|---|---|
| C1070 | Glucose tolerance tests (intraperitoneal glucose tolerance, oral glucose tolerance) | glucose disposal, glucose metabolism, glucose tolerance, insulin secretion, intraperitoneal glucose tolerance |
| C1088 | Plasma Glucose-dependent insulintropic peptide (GIP) concentration | gut, hormone, lipids, metabolism |
| C1072 | Insulin Sensitivity Test | diabetes, insulin action, insulin sensitivity, metabolism |
| C1087 | Glucose enrichment and concentration | carbohydrate metabolism, diabetes |
| T2001 | Sources of plasma glucose using 2H NMR | gluconeogenesis, glucose production, glycogenesis, hepatic, liver, metabolism, NMR, spectroscopy |
| T2002 | Gluconeogenic and citric acid cycle pathways (relative fluxes using 2H, 13C and J-HSQC NMR) | citric acid cycle, gluconeogenesis, hepatic, Krebs's cycle, liver, spectroscopy, TCA cycle |
| T2003 | Absolute gluconeogenic flux rates | gluconeogenesis, glucose production, glycogenolysis, hepatic, liver, metabolism |
| V3003 | Glucose Tolerance Test (Oral and Intravenous) | glucose intolerance, glucose tolerance, insulin action |
| V3004 | Glucose turnover | endogenous glucose production, glucose flux, glucose kinetics, glucose turnover, isotopes, tracers |
| V3005 | Hyperinsulinemic clamp | hyperinsulinemic clamp, insulin action, insulin resistance |
| V3006 | Hyperglycemic clamp | hyperglycemic clamp, insulin secretion, pancreas |
| V3007 | Gluconeogenesis & glycogenolysis (from hepatic 14C-UDPglucose and PEP) | gluconeogenesis, glucose production, glycogenolysis, liver |
| V3008 | Glycogen synthesis | glycogen synthesis, liver, muscle |
| V3010 | Tissue specific glucose uptake | 2-deoxyglucose, glucose metabolic index, tissue specific glucose uptake |
| Y4001 | Hyperinsulinemic-euglycemic clamp experiments | insulin action, insulin resistance |
| CA2004 | Glucose tolerance tests (GTT) | carbohydrate metabolism, diabetes, glucose |
| CA2005 | Insulin concentrations at fasting and post intraperitoneal glucose administration | insulin, insulin secretion |
| CA2006 | Plasma insulin measurement by ELISA | carbohydrate metabolism, insulin, insulin action |
| CA2007 | Insulin concentrations at fasting and post intraperitoneal insulin administration | |
| CA2008 | Glucose concentrations at fasting and post intraperitoneal insulin administration - insulin | carbohydrate metabolism, diabetes, insulin sensitivity |

| Test No. | Test Name | Keywords |
|----------|---|---|
| | tolerance test (ITT) | |
| CA2013 | Hyperinsulinemic Clamp (Hypoglycemic or Euglycemic) using stable isotopes | |
| CA2024 | Metabolomic profile of citric acid cycle and gluconeogenic intermediates | |
| C1071 | Plasma glucose levels | carbohydrate, diabetes, metabolism |
| S6120 | Intraperitoneal Glucose Tolerance Test | carbohydrate metabolism, diabetes, glucose intolerance, glucose tolerance, insulin action |
| S6121 | Insulin Sensitivity Test | carbohydrate metabolism, diabetes, glucose tolerance, insulin action, insulin resistance, insulin sensitivity |
| Y4002 | Hyperglycemic clamp experiments | insulin secretion, pancreas |
| V4005 | Glycemic Control using Minimed | glucose |
| Y4083 | Blood Glucose | carbohydrate, diabetes, glucose, plasma, serum chemicals, serum metabolic panel |

Cardiac Function

| Test No. | Test Name | Keywords |
|----------|---|--|
| C1003 | Arterial baroreflex responses | cardiac function, vascular tone |
| C1010 | Cardiac output | contractility, ejection fraction, heart, stroke volume |
| C1020 | Cardiac contractility (left ventricular function in the isolated heart) | cardiac, heart, pressure, ventricular |
| C1021 | Echocardiography | cardiac, heart, morphology |
| C1022 | Left ventricular pressure measurements in intact mice | cardiac, heart, pressure, ventricular |
| T2010 | Substrate oxidation and anaplerosis in the isolated heart | anaplerosis, cardiac, heart, metabolism, NMR, spectroscopy, substrate oxidation |
| T2013 | TCA cycle flux (VTCA) and alpha-ketoglutarate-glutamate exchange flux (Vx) in the isolated mouse heart using ¹ H NMR | citric acid cycle, heart, Krebs' cycle, metabolism, NMR, spectroscopy, TCA cycle |
| T2012 | Intracellular sodium or high-energy phosphates in the isolated perfused mouse liver or heart | heart, high-energy phosphates, liver, NMR, sodium, spectroscopy |
| V3030 | In vitro Morphology, Morphometrics and Histology (isolated heart) | cardiac function, heart, morphology |
| V3031 | Echocardiography, in vivo morphology, systolic and diastolic function; Stress echocardiography | diastolic, echocardiography, morphology, stress, systolic |
| V3032 | Electrocardiography and telemetry | cardiac, ECG, EKG, electrocardiography, heart, telemetry |
| V3095 | Heart Rate Open Variability | |
| V3096 | Ventricular Hemodynamics | |
| S6200 | Echocardiography (non-invasive) | cardiac function, echocardiography, heart, morphology |
| S6201 | Electrocardiography - ECG (non-invasive) | echocardiography, heart |

| Test No. | Test Name | Keywords |
|----------|---|--|
| S6202 | Invasive Hemodynamics - Left Ventricular Catheterization/Millar | cardiac function, cardiac output, contractility, echocardiography, heart, pressure, stroke volume, ventricular |
| S6204 | Telemetry (invasive) | cardiac, ECG, EKG, electrocardiography, heart, telemetry |
| S6205 | Blood Pressure (non-invasive) | blood flow, blood pressure, hypertension, hypotension, vascular |
| S6206 | Carotid Stenosis - Arterial response to injury | blood vessel, endothelial denudation, histology, neointimal hyperplasia, smooth muscle, vascular |
| Y4091 | Blood Albumin | liver, plasma, serum albumin, serum chemicals |
| Y5007 | Magnesium | serum chemicals |
| S6207 | Myocardial Infarction | cardiac, heart |
| S6208 | Hindlimb Ischemia | blood vessel, cardiac, cardiac function, heart, hypertension, hypotension, restenosis, vascular |
| S6209 | Open Thoracotomy | surgery |
| S6210 | Vein Catheter Insertion | catheterization, surgery, vascular, vein |
| S6211 | Bone Marrow Transplantation | |
| S6212 | Drug Treatment | |
| S6213 | Ultrasound Imaging - Aortic | cardiac function, heart |
| C1106 | Telemetry - Cardiac parameters (BP, HR, Pulse Pressure, Activity) | blood pressure, telemetry |
| D5001 | Macrovascular permeability & lipoprotein flux | cardiac function, imaging, immunohistochemistry, lipids, vascular function |
| D5002 | Microvascular permeability & lipoprotein flux | cardiac function, imaging, immunohistochemistry, lipids, vascular function |
| D5004 | Atheroma quantification | cardiac function, imaging, vascular function |
| D5005 | BP measurement by tail cuff | blood pressure, cardiac function, vascular function |
| D5006 | BP & heart rate variability measurements by telemetry | blood pressure, cardiac function, telemetry, vascular function |
| D5007 | Aortic & mesenteric reactivity & vascular stiffening | aortic reactivity, mesenteric reactivity, vascular stiffening |
| D5009 | Cardiac electrophysiology | cardiac, electrocardiography |
| D5010 | Echocardiography | cardiac function, echocardiography, vascular function |
| D5011 | CT, MRI, PET, & combinations | cardiac function, central nervous system, CT, imaging, MRI, PET, spectroscopy, vascular function |

Central Nervous System

| Test No. | Test Name | Keywords |
|----------|------------------------------|---|
| C1043 | Hypothalamic Gene Expression | central nervous system, hormone, hypothalamus, neuroendocrine |

| Test No. | Test Name | Keywords |
|----------|------------------------------|--|
| D5011 | CT, MRI, PET, & combinations | cardiac function, central nervous system, CT, imaging, MRI, PET, spectroscopy, vascular function |

Circulation

| Test No. | Test Name | Keywords |
|----------|---|--|
| C1002 | Inter-arterial pressure | blood pressure, blood vessel, hypertension, hypotension, vascular |
| C1001 | Tail Cuff Blood pressure | blood pressure, blood vessel, hypertension, hypotension, vascular |
| C1003 | Arterial baroreflex responses | cardiac function, vascular tone |
| C1010 | Cardiac output | contractility, ejection fraction, heart, stroke volume |
| C1011 | Regional Blood Flow Measurements | blood flow, blood pressure, smooth muscle, vascular |
| C1013 | Arterial response to injury (neointimal hyperplasia) | angioplasty, endothelial denudation, neointimal hyperplasia, restenosis |
| C1014 | Vascular contractility measurements | aortic ring, contractility, vascular function |
| C1020 | Cardiac contractility (left ventricular function in the isolated heart) | cardiac, heart, pressure, ventricular |
| C1021 | Echocardiography | cardiac, heart, morphology |
| C1022 | Left ventricular pressure measurements in intact mice | cardiac, heart, pressure, ventricular |
| V3033 | Blood pressure measurements | blood pressure, blood vessel, hypertension, hypotension, vascular |
| V3034 | Vascular morphology | blood vessel, histology, intima, smooth muscle, vascular |
| C1012 | Renal blood flow regulation (free flow measurements) | blood flow, kidney, renal, vascular |
| Y5007 | Magnesium | serum chemicals |
| S6230 | Myography - basic | |
| S6231 | Myography - additional | |
| D5005 | BP measurement by tail cuff | blood pressure, cardiac function, vascular function |
| D5006 | BP & heart rate variability measurements by telemetry | blood pressure, cardiac function, telemetry, vascular function |
| D5011 | CT, MRI, PET, & combinations | cardiac function, central nervous system, CT, imaging, MRI, PET, spectroscopy, vascular function |

Diabetes

| Test No. | Test Name | Keywords |
|----------|---|---|
| C1070 | Glucose tolerance tests (intraperitoneal glucose tolerance, oral glucose tolerance) | glucose disposal, glucose metabolism, glucose tolerance, insulin secretion, intraperitoneal glucose tolerance |
| C1072 | Insulin Sensitivity Test | diabetes, insulin action, insulin sensitivity, metabolism |

| Test No. | Test Name | Keywords |
|----------|--|---|
| C1087 | Glucose enrichment and concentration | carbohydrate metabolism, diabetes |
| T2001 | Sources of plasma glucose using 2H NMR | gluconeogenesis, glucose production, glycogenesis, hepatic, liver, metabolism, NMR, spectroscopy |
| T2002 | Gluconeogenic and citric acid cycle pathways (relative fluxes using 2H, 13C and J-HSQC NMR) | citric acid cycle, gluconeogenesis, hepatic, Krebs's cycle, liver, spectroscopy, TCA cycle |
| T2003 | Absolute gluconeogenic flux rates | gluconeogenesis, glucose production, glycogenolysis, hepatic, liver, metabolism |
| V3002 | Jugular vein and carotid artery catheterization | blood vessel, chronic, surgery |
| V3004 | Glucose turnover | endogenous glucose production, glucose flux, glucose kinetics, glucose turnover, isotopes, tracers |
| V3005 | Hyperinsulinemic clamp | hyperinsulinemic clamp, insulin action, insulin resistance |
| V3006 | Hyperglycemic clamp | hyperglycemic clamp, insulin secretion, pancreas |
| V3007 | Gluconeogenesis & glycogenolysis (from hepatic 14C-UDPglucose and PEP) | gluconeogenesis, glucose production, glycogenolysis, liver |
| V3008 | Glycogen synthesis | glycogen synthesis, liver, muscle |
| V3010 | Tissue specific glucose uptake | 2-deoxyglucose, glucose metabolic index, tissue specific glucose uptake |
| V3082 | Tissue microdissection | laser microdissection, pancreas |
| Y4001 | Hyperinsulinemic-euglycemic clamp experiments | insulin action, insulin resistance |
| CA2004 | Glucose tolerance tests (GTT) | carbohydrate metabolism, diabetes, glucose |
| CA2005 | Insulin concentrations at fasting and post intraperitoneal glucose administration | insulin, insulin secretion |
| CA2006 | Plasma insulin measurement by ELISA | carbohydrate metabolism, insulin, insulin action |
| CA2007 | Insulin concentrations at fasting and post intraperitoneal insulin administration | |
| CA2008 | Glucose concentrations at fasting and post intraperitoneal insulin administration - insulin tolerance test (ITT) | carbohydrate metabolism, diabetes, insulin sensitivity |
| CA2013 | Hyperinsulinemic Clamp (Hypoglycemic or Euglycemic) using stable isotopes | |
| C1071 | Plasma glucose levels | carbohydrate, diabetes, metabolism |
| S6120 | Intraperitoneal Glucose Tolerance Test | carbohydrate metabolism, diabetes, glucose intolerance, glucose tolerance, insulin action |
| S6121 | Insulin Sensitivity Test | carbohydrate metabolism, diabetes, glucose tolerance, insulin action, insulin resistance, insulin sensitivity |
| S6122 | Drug treatment (Streptozotocin; other) | |
| Y4002 | Hyperglycemic clamp experiments | insulin secretion, pancreas |
| Y4083 | Blood Glucose | carbohydrate, diabetes, glucose, plasma, serum chemicals, serum metabolic panel |
| Y4098 | HDL Cholesterol | cholesterol, lipids, lipoproteins |

| Test No. | Test Name | Keywords |
|----------|---|--|
| Y4099 | LDL Cholesterol | cholesterol, lipids, plasma, serum chemicals |
| Y5000 | Cholesterol | cholesterol, lipids, plasma, serum chemicals |
| Y5003 | Beta-Hydroxybutyrate (COBAS) | diabetes, ketones, plasma, serum chemicals |
| S6230 | Myography - basic | |
| S6231 | Myography - additional | |
| S6105 | Running Wheels Activity | |
| S6140 | General Chemistry - Glucose | |
| S6141 | Lipids - Lipid Extraction | |
| S6142 | Lipids - Free Fatty Acids | |
| S6143 | Lipids - HDL | |
| S6144 | Lipids - Triglyceride TG | |
| S6145 | Lipids - Cholesterol TC | |
| S6146 | Lipids - FPLC | |
| S6147 | Cytokines & Hormones - TNF Alpha | |
| S6148 | Cytokines & Hormones - IL-6 | |
| S6149 | Cytokines & Hormones - IL-4 | |
| S6150 | Cytokines & Hormones - Leptin | |
| S6151 | Cytokines & Hormones - Insulin | |
| S6152 | Cytokines & Hormones - PAI-1 and others | |
| S6153 | Cytokines & Hormones - Glucagon | |
| S6154 | Cytokines & Hormones - Adiponectin | |
| S6155 | Cytokines & Hormones - Urine Albumin | |
| S6156 | Cytokines & Hormones - Urine Creatinine | |
| S6157 | Cytokines & Hormones - BUN | |
| S6158 | Cytokines & Hormones - Insulin (by Eliza) | |
| S6159 | Cytokines & Hormones - Taqman PCR Quantification | |
| D3101 | Intravenous Glucose Tolerance Test | diabetes, insulin, insulin action, insulin secretion |
| D3102 | Hyperinsulinemic, Euglycemic Clamp | diabetes, hyperinsulinemic clamp, insulin, insulin action |
| D3103 | IN VIVO Insulin Tolerance Tests | diabetes, insulin, insulin action |
| D3104 | IN VIVO GlucoseTolerance Tests | diabetes, glucose, glucose metabolism, glucose tolerance |
| D3105 | IN VIVO Glucose-stimulates Insulin Secretion Test | diabetes, glucose, glucose metabolism, insulin, insulin action |
| D3106 | Positron emission tomography (microPET) | diabetes, glucose, glucose metabolism, imaging |
| D3401 | Glucose (urine/plasma) | glucose, plasma, urine |
| D3403 | beta-OH butyrate | diabetes, insulin, liver, metabolism |
| D3490 | Triglyceride | metabolism, triglycerides |
| D3405 | Total Cholesterol | cholesterol, liver, metabolism, total cholesterol |

| Test No. | Test Name | Keywords |
|----------|--|--|
| D3406 | HDL cholesterol | cholesterol, lipids, liver, metabolism |
| D3407 | Direct LDL cholesterol | cholesterol, lipids, metabolism |
| D3408 | Non esterified fatty acids | lipids, liver, metabolism, non-esterified fatty acid |
| D3409 | Apolipoprotein profiling (A-1, AII, B, E, CII, CIII) | apolipoproteins, lipids, liver, metabolism |
| D3410 | Apolipoprotein profiling | apolipoproteins, lipids, liver, metabolism |
| D3411 | Lipoprotein Particle Size | hormone, lipids, lipoproteins, liver, metabolism |
| D3412 | Metabolomics | diabetes, hormone, lipids, liver, metabolism, metabolite |
| D3413 | Complex lipid ratios | diabetes, lipids, liver |
| D3431 | Hormones - Generic ELISA Assay | hormone, liver |
| D3432 | Insulin | diabetes, hormone, insulin, liver |
| D3433 | C-Peptide | hormone, insulin, liver |
| D3434 | Proinsulin | hormone, insulin, liver |
| D3435 | Leptin | hormone, leptin, leptin measurement, liver |
| D3436 | Adiponectin (total) | adiponectin, hormone, lipids, liver |
| D3437 | Adiponectin (HMW) | adiponectin, hormone, lipids, liver |
| D3438 | Glucagon | glucagon, hormone, lipids, liver |
| D3439 | Glucagon-like peptide 1 (active) | glucagon, hormone, lipids, liver |
| D3440 | Glucagon-like peptide 1 (total) | glucagon, hormone, lipids, liver |
| D3441 | Ghrelin | hormone, liver |
| M1001 | Hyperinsulinemic-euglycemic clamp | glucose metabolism, insulin action, insulin resistance |
| M1002 | Basal glucose metabolism | glucose turnover |
| M1003 | Organ-specific glucose uptake | glucose uptake |
| M1004 | Hyperglycemic clamp | beta cell, insulin secretion, pancreas |
| M1005 | Insulin clearance | insulin |
| M1006 | Glucose tolerance test | glucose clearance, glucose tolerance |
| M1007 | Glucose tolerance test with insulin secretion | glucose tolerance, insulin |
| M1008 | Insulin tolerance test | insulin sensitivity |
| M1009 | Hepatic gluconeogenesis | pyruvate tolerance test |
| M1015 | Chronic high-fat feeding | diet-induced obesity, high-fat diet, obesity |
| M1017 | STZ-induced type 1 diabetes model | hyperglycemia, streptozotocin, type 1 diabetes |
| M1019 | Chronic/acute phloridzin treatment | glucose clearance, renal |
| M2001 | Glucose | diabetes, glucose, hyperglycemia, hypoglycemia, metabolite |
| M2002 | Hemoglobin A1c | diabetes, glucose, hyperglycemia, metabolite |
| M2003 | Lactate | diabetes, glucose, metabolite |
| M2004 | Insulin | diabetes, hormone, hyperinsulinemic clamp, insulin, pancreas |
| M2005 | C-peptide | hormone, insulin, insulin secretion, pancreas |

| Test No. | Test Name | Keywords |
|----------|--------------------------------|--|
| M2006 | Glucagon | glucose, hepatic, hormone, pancreas |
| M2007 | Leptin | adipokine, feeding behavior, hormone |
| M2010 | Triglyceride | lipids, metabolite, obesity |
| M2011 | Non-esterified fatty acids | insulin resistance, lipids, metabolite, obesity |
| M2032 | Cytokines Panel I - multiplex | chemokines, complications, cytokines, diabetes, inflammation, insulin resistance, monokines, obesity |
| M2033 | Cytokines Panel II - multiplex | chemokines, complications, cytokines, diabetes, inflammation, insulin resistance, monokines, obesity |
| M2034 | Islet histology | beta cell, diabetes, insulin |
| M2035 | Molecular islet analysis | beta cell, diabetes, insulin |

Energetics

| Test No. | Test Name | Keywords |
|----------|---|--|
| T2002 | Gluconeogenic and citric acid cycle pathways (relative fluxes using 2H, 13C and J-HSQC NMR) | citric acid cycle, gluconeogenesis, hepatic, Krebs's cycle, liver, spectroscopy, TCA cycle |
| T2010 | Substrate oxidation and anaplerosis in the isolated heart | anaplerosis, cardiac, heart, metabolism, NMR, spectroscopy, substrate oxidation |
| T2013 | TCA cycle flux (VTCA) and alpha-ketoglutarate-glutamate exchange flux (Vx) in the isolated mouse heart using 1H NMR | citric acid cycle, heart, Krebs's cycle, metabolism, NMR, spectroscopy, TCA cycle |
| T2012 | Intracellular sodium or high-energy phosphates in the isolated perfused mouse liver or heart | heart, high-energy phosphates, liver, NMR, sodium, spectroscopy |
| CA2015 | Turnover of glucose, lipid and/or protein | |
| CA2022 | 13C-Labeling pattern of acetyl moiety of citrate (substrate oxidation) | |
| CA2046 | Indirect Calorimetry : First 36-hr measurement (for 8 mice) | |
| CA2047 | Treadmill Training/Endurance Study PLUS Indirect Calorimetry (for 8 mice) | |
| D4005 | Digestible Energy | energetics, food intake, gastrointestinal tract |
| D4006 | Gut Microbiome Analysis | energetics, gastrointestinal tract, gut, microbiome |
| D4007 | Standard Fed & Postabsorptive Energy Expenditure | energy balance, energy expenditure, food intake, indirect calorimetry |
| D4009 | Brown Adipose Tissue Thermogenic Activation | adipose, energetics, energy expenditure |

Energy Expenditure & Exercise

| Test No. | Test Name | Keywords |
|----------|--|---|
| C1042 | Energy Expenditure Measurements | basal metabolic rate, CO2 production, obesity, oxygen consumption, respiratory quotient |
| V3012 | Indirect calorimetry /energy expenditure | carbon dioxide, energy expenditure, gas exchange, indirect calorimetry, oxygen |

| Test No. | Test Name | Keywords |
|----------|---|---|
| V3013 | Exercise capacity (metabolic response to exercise) | endurance, exercise capacity, exercise tolerance |
| V3014 | Spontaneous exercise activity | spontaneous exercise activity, wheel running |
| V3016 | Exploratory locomotor activity | energy expenditure, exploratory locomotor activity |
| CA2003 | Measurement of body temperature (by probe) | energy expenditure, exercise |
| CA2011 | Total Energy expenditure using doubly-labeled water | energy expenditure, water |
| S6102 | Energy Expenditure | body weight, energy balance, energy expenditure |
| S6104 | Body Temperature | |
| Y5003 | Beta-Hydroxybutyrate (COBAS) | diabetes, ketones, plasma, serum chemicals |
| S6105 | Running Wheels Activity | |
| CA2046 | Indirect Calorimetry : First 36-hr measurement (for 8 mice) | |
| CA2047 | Treadmill Training/Endurance Study PLUS Indirect Calorimetry (for 8 mice) | |
| CA2049 | Additional 24-hr measurement (for 8 mice) | |
| C1107 | Telemetry - Activity and Temperature measurements | telemetry |
| D4003 | Meal Pattern Analysis | energy expenditure, exercise, food intake, meal pattern |
| D4007 | Standard Fed & Postabsorptive Energy Expenditure | energy balance, energy expenditure, food intake, indirect calorimetry |
| D4009 | Brown Adipose Tissue Thermogenic Activation | adipose, energetics, energy expenditure |
| D4010 | Comprehensive Longitudinal Metabolic Profile | energy expenditure, food intake, glucose, hormone, insulin |
| M1014 | Energy balance – food intake, energy expenditure, physical activity | indirect calorimetry, metabolism |
| M1020 | Exercise model | Activity, Cage Activity, exercise |

Enzymatic Activity

| Test No. | Test Name | Keywords |
|----------|---|--|
| Y5008 | Creatine Kinase | creatine kinase, serum chemicals |
| D3402 | Hemoglobin A1C | Hemoglobin A1C, liver, metabolism |
| D3481 | 8-Isoprostane (urinary) | enzyme activity |
| D3482 | Protein Carbonyl (plasma, cell lysates, tissue homogenates) | enzyme activity |
| D3483 | Catalase (plasma, cell lysates, tissue homogenates) | diabetes, inflammation |
| D3484 | Glutathione | enzyme activity, oxidative stress |
| D3485 | Glutathione Peroxidase | enzyme activity, oxidative stress |
| D3486 | Glutathione Reductase | enzyme activity, oxidative stress |
| D3487 | Hydrogen Peroxide (urinary) | hydrogen peroxide, oxidative stress |
| D3488 | Superoxide Dismutase | oxidative stress, superoxide dismutase |

| Test No. | Test Name | Keywords |
|----------|---------------------------------------|-------------------|
| D3489 | Myeloperoxidase (cell lysate, plasma) | oxidative stress |
| M2017 | Amylase | enzyme activity |
| M2018 | Creatine kinase | enzyme activity |
| M2019 | Alkaline phosphatase | enzyme activity |
| M2020 | Lactate dehydrogenase | enzyme activity |
| M2021 | Albumin | liver, metabolite |
| M2022 | Alanine transferase | liver, metabolite |
| M2023 | Aspartate transferase | liver, metabolite |

Food Intake

| Test No. | Test Name | Keywords |
|----------|--|--|
| C1040 | Food intake and body weight measurements | energy balance, energy expenditure, nutrition |
| C1041 | Body Composition | body composition, carcass analysis, obesity, QMR, total body fat |
| C1043 | Hypothalamic Gene Expression | central nervous system, hormone, hypothalamus, neuroendocrine |
| V3015 | Food Consumption | spontaneous exercise activity, wheel running |
| CA2001 | Food Consumption | food intake |
| CA2002 | Body Weight | body composition, body weight, food intake |
| C1044 | DietMax Meal Pattern Analysis | food intake, meal pattern |
| S6103 | Meal Pattern Analysis | food intake |
| D4003 | Meal Pattern Analysis | energy expenditure, exercise, food intake, meal pattern |
| D4004 | Gastric Emptying | food intake, gastrointestinal tract |
| D4005 | Digestible Energy | energetics, food intake, gastrointestinal tract |
| D4006 | Gut Microbiome Analysis | energetics, gastrointestinal tract, gut, microbiome |
| D4010 | Comprehensive Longitudinal Metabolic Profile | energy expenditure, food intake, glucose, hormone, insulin |
| M1015 | Chronic high-fat feeding | diet-induced obesity, high-fat diet, obesity |
| M2007 | Leptin | adipokine, feeding behavior, hormone |

Hormone Measurements

| Test No. | Test Name | Keywords |
|----------|---|--------------------------------------|
| V3090 | Full amino acid profiles by HPLC / PITC or HLPC / OPA | amino acids, HPLC |
| C1088 | Plasma Glucose-dependent insulinotropic peptide (GIP) concentration | gut, hormone, lipids, metabolism |
| C1081 | C-Peptide | diabetes, hormone, insulin |
| C1082 | Cholecystokinin (CCK) | CCK, gut, hormone, intestine |
| C1085 | Plasma/serum concentrations glucagon | counterregulatory, hormone, pancreas |
| C1086 | Plasma Glucagon-like peptide 1 (GLP-1) concentration | counterregulatory, hormone, pancreas |

| Test No. | Test Name | Keywords |
|----------|--|--|
| C1089 | Insulin concentrations in plasma/serum/lymph/cerebrospinal fluid | diabetes, hormone, pancreas |
| C1090 | Plasma/serum concentrations of leptin | eating behaviour, fat, hormone, lipids |
| C1091 | Somatostatin in plasma or tissue extracts | diabetes, hormone, pancreas |
| V3050 | Insulin | hormone |
| V3051 | Glucagon | hormone |
| V3052 | Corticosterone | hormone |
| V3053 | Catecholamines | hormone |
| V3054 | Leptin | hormone |
| V3055 | C-Peptide | hormone |
| V3056 | Growth Hormone (GH) | hormone |
| V3058 | TSH | hormone |
| V3059 | PRL | hormone |
| V3060 | ACTH | hormone |
| V3061 | Insulin-like growth hormone-1 (IGF-1) | hormone |
| Y4080 | Insulin | hormone |
| Y4081 | Glucagon | hormone |
| Y4082 | Leptin | hormone |
| V3062 | Aldosterone | hormone |
| V3064 | Resistin | hormone |
| V3065 | Adiponectin | hormone |
| V3066 | Estradiol | hormone |
| V3067 | Testosterone | hormone |
| C1108 | Multiplexing assays | |
| C1109 | Euglycemic-hyperinsulinemic clamp | hyperinsulinemic clamp |
| D3201 | Adipocyte metabolism/hormone production - Isolation/cell size/# | hormone, insulin, insulin action, lipid extraction, lipids |
| D3202 | Adipocyte metabolism/hormone production - 96h culture/glucose utilization/lactate production | hormone, insulin, insulin action |
| D3203 | Adipocyte metabolism/hormone production - leptin secretion at 96 hour | hormone, leptin, leptin measurement |
| D3204 | Adipocyte metabolism/hormone production - adiponectin secretion at 96 hour | adiponectin |
| D3205 | Adipocyte metabolism/hormone production - lipolysis (glycerol baseline and 96h) | glycerol, lipid extraction, lipids |
| D3206 | Adipocyte metabolism/hormone production - lipogenesis from labeled glucose | adipose, glucose, glucose turnover, triglycerides |
| D3207 | Adipocyte metabolism/hormone production - glucose/FA oxidation from labeled glucose/FA | glucose, hormone |
| D3250 | In vitro pancreatic islet insulin secretion | insulin, insulin secretion |
| D3412 | Metabolomics | diabetes, hormone, lipids, liver, metabolism, metabolite |
| D3431 | Hormones - Generic ELISA Assay | hormone, liver |

| Test No. | Test Name | Keywords |
|----------|--|---|
| D3432 | Insulin | diabetes, hormone, insulin, liver |
| D3433 | C-Peptide | hormone, insulin, liver |
| D3434 | Proinsulin | hormone, insulin, liver |
| D3435 | Leptin | hormone, leptin, leptin measurement, liver |
| D3436 | Adiponectin (total) | adiponectin, hormone, lipids, liver |
| D3437 | Adiponectin (HMW) | adiponectin, hormone, lipids, liver |
| D3438 | Glucagon | glucagon, hormone, lipids, liver |
| D3439 | Glucagon-like peptide 1 (active) | glucagon, hormone, lipids, liver |
| D3440 | Glucagon-like peptide 1 (total) | glucagon, hormone, lipids, liver |
| D3441 | Ghrelin | hormone, liver |
| D3467 | sE-Selectin | diabetes, inflammation |
| D3468 | sP-Selectin | diabetes, inflammation |
| D3491 | Insulin Signalling pathway | diabetes, inflammation, insulin, leptin, obesity, stress |
| D3492 | Endoplasmic reticulum stress pathway | diabetes, hormone, immunology, insulin, insulin action, obesity, stress |
| D3493 | Inflammation pathway | diabetes, hormone, immunology, inflammation, insulin |
| D3494 | Leptin Signaling pathway | diabetes, hormone, leptin, obesity |
| D4010 | Comprehensive Longitudinal Metabolic Profile | energy expenditure, food intake, glucose, hormone, insulin |
| D5012 | Luminex / multiplex | hormone, immunology, kidney, lipids, liver, metabolite |
| M2004 | Insulin | diabetes, hormone, hyperinsulinemic clamp, insulin, pancreas |
| M2007 | Leptin | adipokine, feeding behavior, hormone |
| M2008 | Adiponectin | adipokine, hormone, insulin resistance |
| M2009 | Resistin | adipokine, hormone, insulin resistance |

Imaging

| Test No. | Test Name | Keywords |
|----------|---|--|
| V3090 | Full amino acid profiles by HPLC / PITC or HLPC / OPA | amino acids, HPLC |
| V3017 | Assess real time imaging of cellular metabolic events | islets, metabolism, microcirculation, muscle, real time imaging |
| V3018 | In vivo optical imaging of gene expression | gene expression, GFP, luciferase |
| CA2048 | Whole Body Fixation (PFA)+ Tissue Collection | |
| D3106 | Positron emission tomography (microPET) | diabetes, glucose, glucose metabolism, imaging |
| D4001 | Gross Body Composition | body composition, imaging |
| D5001 | Macrovascular permeability & lipoprotein flux | cardiac function, imaging, immunohistochemistry, lipids, vascular function |
| D5002 | Microvascular permeability & lipoprotein flux | cardiac function, imaging, |

| Test No. | Test Name | Keywords |
|----------|--|--|
| | | immunohistochemistry, lipids, vascular function |
| D5004 | Atheroma quantification | cardiac function, imaging, vascular function |
| D5007 | Aortic & mesenteric reactivity & vascular stiffening | aortic reactivity, mesenteric reactivity, vascular stiffening |
| D5011 | CT, MRI, PET, & combinations | cardiac function, central nervous system, CT, imaging, MRI, PET, spectroscopy, vascular function |
| D5013 | MMPC mouse gross necropsy with histology | histology, morphology, necropsy |
| D5014 | UC Davis Comparative Pathology Laboratory services | hematology, histology, morphometry, necropsy, serum chemicals, urinalysis |

Immunology of Diabetes

| Test No. | Test Name | Keywords |
|----------|---|--|
| V3082 | Tissue microdissection | laser microdissection, pancreas |
| D3461 | Markers of Inflammation - full panel | diabetes, growth factors, immunology, inflammation, interleukins |
| D3462 | Markers of Inflammation - limited panel | diabetes, growth factors, immunology, inflammation, interleukins |
| D3463 | HS CRP | diabetes, inflammation |
| D3464 | Serum Amyloid A3 | diabetes, inflammation, serum metabolic panel |
| D3465 | sICAM | diabetes, inflammation |
| D3466 | sVCAM | diabetes, inflammation |
| D3467 | sE-Selectin | diabetes, inflammation |
| D3468 | sP-Selectin | diabetes, inflammation |
| D3491 | Insulin Signalling pathway | diabetes, inflammation, insulin, leptin, obesity, stress |
| D3492 | Endoplasmic reticulum stress pathway | diabetes, hormone, immunology, insulin, insulin action, obesity, stress |
| D3493 | Inflammation pathway | diabetes, hormone, immunology, inflammation, insulin |
| D3494 | Leptin Signaling pathway | diabetes, hormone, leptin, obesity |
| M2032 | Cytokines Panel I - multiplex | chemokines, complications, cytokines, diabetes, inflammation, insulin resistance, monokines, obesity |
| M2033 | Cytokines Panel II - multiplex | chemokines, complications, cytokines, diabetes, inflammation, insulin resistance, monokines, obesity |
| M2034 | Islet histology | beta cell, diabetes, insulin |
| M2035 | Molecular islet analysis | beta cell, diabetes, insulin |

Insulin and Insulin Function

| Test No. | Test Name | Keywords |
|----------|---|---|
| C1070 | Glucose tolerance tests (intraperitoneal glucose tolerance, oral glucose tolerance) | glucose disposal, glucose metabolism, glucose tolerance, insulin secretion, intraperitoneal glucose tolerance |

| Test No. | Test Name | Keywords |
|----------|--|---|
| C1072 | Insulin Sensitivity Test | diabetes, insulin action, insulin sensitivity, metabolism |
| V3002 | Jugular vein and carotid artery catheterization | blood vessel, chronic, surgery |
| V3005 | Hyperinsulinemic clamp | hyperinsulinemic clamp, insulin action, insulin resistance |
| V3006 | Hyperglycemic clamp | hyperglycemic clamp, insulin secretion, pancreas |
| V3082 | Tissue microdissection | laser microdissection, pancreas |
| Y4001 | Hyperinsulinemic-euglycemic clamp experiments | insulin action, insulin resistance |
| CA2004 | Glucose tolerance tests (GTT) | carbohydrate metabolism, diabetes, glucose |
| CA2005 | Insulin concentrations at fasting and post intraperitoneal glucose administration | insulin, insulin secretion |
| CA2006 | Plasma insulin measurement by ELISA | carbohydrate metabolism, insulin, insulin action |
| CA2007 | Insulin concentrations at fasting and post intraperitoneal insulin administration | |
| CA2008 | Glucose concentrations at fasting and post intraperitoneal insulin administration - insulin tolerance test (ITT) | carbohydrate metabolism, diabetes, insulin sensitivity |
| CA2013 | Hyperinsulinemic Clamp (Hypoglycemic or Euglycemic) using stable isotopes | |
| S6120 | Intraperitoneal Glucose Tolerance Test | carbohydrate metabolism, diabetes, glucose intolerance, glucose tolerance, insulin action |
| S6121 | Insulin Sensitivity Test | carbohydrate metabolism, diabetes, glucose tolerance, insulin action, insulin resistance, insulin sensitivity |
| Y4002 | Hyperglycemic clamp experiments | insulin secretion, pancreas |
| D3101 | Intravenous Glucose Tolerance Test | diabetes, insulin, insulin action, insulin secretion |
| D3102 | Hyperinsulinemic, Euglycemic Clamp | diabetes, hyperinsulinemic clamp, insulin, insulin action |
| D3103 | IN VIVO Insulin Tolerance Tests | diabetes, insulin, insulin action |
| D3104 | IN VIVO Glucose Tolerance Tests | diabetes, glucose, glucose metabolism, glucose tolerance |
| D3105 | IN VIVO Glucose-stimulates Insulin Secretion Test | diabetes, glucose, glucose metabolism, insulin, insulin action |
| D3201 | Adipocyte metabolism/hormone production - Isolation/cell size/# | hormone, insulin, insulin action, lipid extraction, lipids |
| D3202 | Adipocyte metabolism/hormone production - 96h culture/glucose utilization/lactate production | hormone, insulin, insulin action |
| D3207 | Adipocyte metabolism/hormone production - glucose/FA oxidation from labeled glucose/FA | glucose, hormone |
| D3250 | In vitro pancreatic islet insulin secretion | insulin, insulin secretion |
| D3401 | Glucose (urine/plasma) | glucose, plasma, urine |
| D3403 | beta-OH butyrate | diabetes, insulin, liver, metabolism |
| D3432 | Insulin | diabetes, hormone, insulin, liver |

| Test No. | Test Name | Keywords |
|----------|---|---|
| D3433 | C-Peptide | hormone, insulin, liver |
| D3434 | Proinsulin | hormone, insulin, liver |
| D3491 | Insulin Signalling pathway | diabetes, inflammation, insulin, leptin, obesity, stress |
| D3492 | Endoplasmic reticulum stress pathway | diabetes, hormone, immunology, insulin, insulin action, obesity, stress |
| D3493 | Inflammation pathway | diabetes, hormone, immunology, inflammation, insulin |
| D3494 | Leptin Signaling pathway | diabetes, hormone, leptin, obesity |
| M1001 | Hyperinsulinemic-euglycemic clamp | glucose metabolism, insulin action, insulin resistance |
| M1002 | Basal glucose metabolism | glucose turnover |
| M1003 | Organ-specific glucose uptake | glucose uptake |
| M1004 | Hyperglycemic clamp | beta cell, insulin secretion, pancreas |
| M1005 | Insulin clearance | insulin |
| M1006 | Glucose tolerance test | glucose clearance, glucose tolerance |
| M1007 | Glucose tolerance test with insulin secretion | glucose tolerance, insulin |
| M1008 | Insulin tolerance test | insulin sensitivity |
| M1017 | STZ-induced type 1 diabetes model | hyperglycemia, streptozotocin, type 1 diabetes |
| M1019 | Chronic/acute phloridzin treatment | glucose clearance, renal |
| M2001 | Glucose | diabetes, glucose, hyperglycemia, hypoglycemia, metabolite |
| M2002 | Hemoglobin A1c | diabetes, glucose, hyperglycemia, metabolite |
| M2003 | Lactate | diabetes, glucose, metabolite |
| M2004 | Insulin | diabetes, hormone, hyperinsulinemic clamp, insulin, pancreas |
| M2005 | C-peptide | hormone, insulin, insulin secretion, pancreas |
| M2008 | Adiponectin | adipokine, hormone, insulin resistance |
| M2009 | Resistin | adipokine, hormone, insulin resistance |

Isolated Organ and Cell Perfusion

| Test No. | Test Name | Keywords |
|----------|---|--|
| C1020 | Cardiac contractility (left ventricular function in the isolated heart) | cardiac, heart, pressure, ventricular |
| T2010 | Substrate oxidation and anaplerosis in the isolated heart | anaplerosis, cardiac, heart, metabolism, NMR, spectroscopy, substrate oxidation |
| T2013 | TCA cycle flux (VTCA) and alpha-ketoglutarate-glutamate exchange flux (Vx) in the isolated mouse heart using 1H NMR | citric acid cycle, heart, Kreb's cycle, metabolism, NMR, spectroscopy, TCA cycle |
| T2012 | Intracellular sodium or high-energy phosphates in the isolated perfused mouse liver or heart | heart, high-energy phosphates, liver, NMR, sodium, spectroscopy |
| T2011 | Intermediary metabolism in the isolated liver using NMR | hepatic, liver, metabolism, NMR, spectroscopy |

| Test No. | Test Name | Keywords |
|----------|---|--|
| V3030 | In vitro Morphology, Morphometrics and Histology (isolated heart) | cardiac function, heart, morphology |
| V3094 | Perfusion-Fixation/Heart Dimension | |
| CA2048 | Whole Body Fixation (PFA)+ Tissue Collection | |
| CA2052 | Isolated mouse HEART perfusion | heart |
| CA2053 | Isolated mouse LIVER perfusion | liver |
| D3250 | In vitro pancreatic islet insulin secretion | insulin, insulin secretion |
| D5001 | Macrovascular permeability & lipoprotein flux | cardiac function, imaging, immunohistochemistry, lipids, vascular function |
| D5002 | Microvascular permeability & lipoprotein flux | cardiac function, imaging, immunohistochemistry, lipids, vascular function |
| D5004 | Atheroma quantification | cardiac function, imaging, vascular function |
| D5007 | Aortic & mesenteric reactivity & vascular stiffening | aortic reactivity, mesenteric reactivity, vascular stiffening |

Kidney Function

| Test No. | Test Name | Keywords |
|----------|--|---|
| C1030 | Micropuncture measurements | blood flow, kidney, renal, vascular |
| C1032 | In situ microperfusion | kidney, renal, vascular |
| C1033 | Control of Renal Perfusion Pressure | glomerular filtration, kidney, renal, vascular |
| C1034 | Whole kidney clearance | glomerular filtration, kidney, renal, vascular |
| V3036 | Metabolic panel | |
| C1031 | Renal Blood Flow Regulation | blood flow, kidney, renal, vascular |
| C1012 | Renal blood flow regulation (free flow measurements) | blood flow, kidney, renal, vascular |
| V3098 | GFR-FITC-Inulin; HPLC Cr | glomerular filtration, HPLC, kidney |
| V3099 | Albuminuria | kidney, urine |
| V4000 | Renal Blood Flow (Doppler) | blood flow, blood pressure, kidney |
| Y4084 | Blood Urea Nitrogen | renal, serum chemicals, serum metabolic panel |
| Y4085 | Blood Creatinine-HPLC | kidney, muscle, renal, serum chemicals, serum metabolic panel |
| Y4086 | Urine Creatinine-HPLC | kidney, muscle, renal, serum chemicals, serum metabolic panel, urine |
| Y4087 | Blood Electrolytes-Na/Cl/K | electrolytes, metabolism, muscle, pH, plasma, potassium, serum chemicals, serum metabolic panel, sodium |
| Y5009 | Lactate Dehydrogenase | serum chemicals |
| D3451 | Urinary Albumin Excretion | albumin, kidney, renal, urine |
| D3452 | Creatinine | creatinine, kidney, renal, urine |
| D3453 | Urea | kidney, renal, urea |
| D5012 | Luminex / multiplex | hormone, immunology, kidney, lipids, liver, metabolite |

| Test No. | Test Name | Keywords |
|----------|------------|--------------------|
| M2026 | Creatinine | kidney, metabolite |
| M2029 | Urea/BUN | kidney, metabolite |
| M2030 | Uric acid | kidney, metabolite |

Lipid Metabolism

| Test No. | Test Name | Keywords |
|----------|--|---|
| C1051 | Intestinal lipid absorption in the conscious mouse | absorption, fistula, gastrointestinal tract, lipids, lymph |
| C1052 | Plasma lipid profiles | non-esterified fatty acid, phospholipids, total cholesterol, triglycerides |
| C1053 | Lipoprotein profiles | agarose, agarose gel electrophoresis, electrophoresis, lipids, lipoproteins |
| C1054 | Lipoprotein fractionation by FPLC | apolipoproteins, FPLC, lipids, lipoproteins |
| C1055 | Chylomicron metabolism (lymph) | apolipoproteins, chylomicron, chylomicron remnants, intestine, lipids |
| C1056 | Cholesterol synthetic rate | cholesterol, fatty acids, lipids, sterol, synthesis |
| C1057 | Plasma Free fatty Acid Levels | free fatty acids, non-esterified fatty acid |
| V3011 | Tissue specific fatty acid uptake | 125I-BMIPP, tissue specific fatty acid uptake |
| V3070 | Plasma lipids | fat, lipids, metabolism |
| V3071 | Lipid extraction, separation, quantitation | fat, lipids, metabolism |
| V3072 | Fatty acid profiles of lipid esters by gas liquid chromatography | fat, GCMS, lipids, metabolism |
| V3073 | Quantitation of individual phospholipid classes | cholesterol, fat, lipids, metabolism, phospholipids |
| V3074 | Short chain fatty acid analysis by gas liquid chromatography | fat, GCMS, lipids, metabolism, short chain fatty acid |
| V3075 | Lipoprotein fractionation and characterization | fat, lipids, lipoproteins, metabolism |
| Y4060 | Diacylglycerol concentration | fat, lipids, metabolism, signaling |
| Y4072 | Lipid Panel | serum chemicals, serum metabolic panel |
| CA2010 | Plasma triglycerides | plasma |
| CA2016 | Fatty acid and cholesterol synthesis using 2H-labeled water | |
| CA2018 | Profile of acylcarnitines in plasma/urine or tissue samples | |
| CA2019 | Profile of long chain acyl-CoAs in tissue | |
| CA2020 | Measurement of acetyl-CoA, propionyl-CoA and/or succinyl-CoA in tissue | |
| C1059 | Non-invasive measurement of fat absorption | fecal fat absorption |
| C1060 | Chemical determination of phospholipid | fat, fatty acids, lipids, phospholipids |
| C1061 | Serum/Plasma Adiponectin | adiponectin, gut hormones, peptides |
| C1062 | Serum/Plasma Resistin | resistin |
| Y4061 | Lysophosphatidic Acid | lipids |
| Y4098 | HDL Cholesterol | cholesterol, lipids, lipoproteins |
| Y4099 | LDL Cholesterol | cholesterol, lipids, plasma, serum chemicals |

| Test No. | Test Name | Keywords |
|----------|---|--|
| Y5000 | Cholesterol | cholesterol, lipids, plasma, serum chemicals |
| Y5001 | Triglycerides | lipids, plasma, serum chemicals |
| Y5002 | Non-Esterified Fatty Acids | fatty acids, lipids, non-esterified fatty acid, serum chemicals |
| Y5003 | Beta-Hydroxybutyrate (COBAS) | diabetes, ketones, plasma, serum chemicals |
| Y5010 | Apolipoprotein C3 | lipids, lipoproteins, serum chemicals |
| C1104 | Lipid extraction via folch | folch, lipid extraction |
| C1105 | Fatty Acid analysis via GC | |
| D3201 | Adipocyte metabolism/hormone production - Isolation/cell size/# | hormone, insulin, insulin action, lipid extraction, lipids |
| D3205 | Adipocyte metabolism/hormone production - lipolysis (glycerol baseline and 96h) | glycerol, lipid extraction, lipids |
| D3206 | Adipocyte metabolism/hormone production - lipogenesis from labeled glucose | adipose, glucose, glucose turnover, triglycerides |
| D3301 | Lipid extraction from liver or muscle - Tissue Cholesterol | cholesterol, liver, muscle, total cholesterol |
| D3302 | Lipid extraction from liver or muscle - Tissue Triglyceride | liver, muscle, triglycerides |
| D3403 | beta-OH butyrate | diabetes, insulin, liver, metabolism |
| D3490 | Triglyceride | metabolism, triglycerides |
| D3405 | Total Cholesterol | cholesterol, liver, metabolism, total cholesterol |
| D3406 | HDL cholesterol | cholesterol, lipids, liver, metabolism |
| D3407 | Direct LDL cholesterol | cholesterol, lipids, metabolism |
| D3408 | Non esterified fatty acids | lipids, liver, metabolism, non-esterified fatty acid |
| D3409 | Apolipoprotein profiling (A-1, AII, B, E, CII, CIII) | apolipoproteins, lipids, liver, metabolism |
| D3410 | Apolipoprotein profiling | apolipoproteins, lipids, liver, metabolism |
| D3411 | Lipoprotein Particle Size | hormone, lipids, lipoproteins, liver, metabolism |
| D3412 | Metabolomics | diabetes, hormone, lipids, liver, metabolism, metabolite |
| D3413 | Complex lipid ratios | diabetes, lipids, liver |
| D3431 | Hormones - Generic ELISA Assay | hormone, liver |
| D3435 | Leptin | hormone, leptin, leptin measurement, liver |
| D3436 | Adiponectin (total) | adiponectin, hormone, lipids, liver |
| D3437 | Adiponectin (HMW) | adiponectin, hormone, lipids, liver |
| D3438 | Glucagon | glucagon, hormone, lipids, liver |
| D5001 | Macrovascular permeability & lipoprotein flux | cardiac function, imaging, immunohistochemistry, lipids, vascular function |
| D5002 | Microvascular permeability & lipoprotein flux | cardiac function, imaging, immunohistochemistry, lipids, vascular function |
| D5003 | Lipoprotein analysis by LTRS | imaging, lipids, lipoproteins |

| Test No. | Test Name | Keywords |
|----------|----------------------------|--|
| D5012 | Luminex / multiplex | hormone, immunology, kidney, lipids, liver, metabolite |
| M1010 | Lipid metabolism | palmitate, triglycerides |
| M1018 | Acute lipid infusion | fatty acids, lipids |
| M2010 | Triglyceride | lipids, metabolite, obesity |
| M2011 | Non-esterified fatty acids | insulin resistance, lipids, metabolite, obesity |
| M2012 | Cholesterol (total) | atherosclerosis, lipids, liver, metabolite, obesity |
| M2013 | Cholesterol (HDL) | atherosclerosis, lipids, liver, metabolite, obesity |
| M2014 | Cholesterol (LDL) | atherosclerosis, lipids, liver, metabolite, obesity |
| M2015 | Ammonia | lipids, metabolite |
| M2016 | Lipase | lipids, metabolite, obesity |

Liver Function

| Test No. | Test Name | Keywords |
|----------|--|--|
| T2001 | Sources of plasma glucose using 2H NMR | gluconeogenesis, glucose production, glycogenesis, hepatic, liver, metabolism, NMR, spectroscopy |
| T2002 | Gluconeogenic and citric acid cycle pathways (relative fluxes using 2H, 13C and J-HSQC NMR) | citric acid cycle, gluconeogenesis, hepatic, Krebs's cycle, liver, spectroscopy, TCA cycle |
| T2003 | Absolute gluconeogenic flux rates | gluconeogenesis, glucose production, glycogenolysis, hepatic, liver, metabolism |
| T2012 | Intracellular sodium or high-energy phosphates in the isolated perfused mouse liver or heart | heart, high-energy phosphates, liver, NMR, sodium, spectroscopy |
| T2011 | Intermediary metabolism in the isolated liver using NMR | hepatic, liver, metabolism, NMR, spectroscopy |
| V3004 | Glucose turnover | endogenous glucose production, glucose flux, glucose kinetics, glucose turnover, isotopes, tracers |
| V3007 | Gluconeogenesis & glycogenolysis (from hepatic 14C-UDPglucose and PEP) | gluconeogenesis, glucose production, glycogenolysis, liver |
| V3008 | Glycogen synthesis | glycogen synthesis, liver, muscle |
| Y4091 | Blood Albumin | liver, plasma, serum albumin, serum chemicals |
| Y4092 | Alanine Aminotransferase | ALT, liver, plasma, serum chemicals |
| Y4093 | Aspartate Aminotransferase | liver, plasma, serum chemicals |
| Y4094 | Alkaline Phosphatase | liver, plasma, serum chemicals |
| Y4095 | Total Bilirubin | bilirubin, liver, serum chemicals |
| Y4097 | Total Protein | liver, plasma, serum chemicals |
| Y5000 | Cholesterol | cholesterol, lipids, plasma, serum chemicals |
| Y5009 | Lactate Dehydrogenase | serum chemicals |
| CA2053 | Isolated mouse LIVER perfusion | liver |

| Test No. | Test Name | Keywords |
|----------|---|--|
| D3301 | Lipid extraction from liver or muscle - Tissue Cholesterol | cholesterol, liver, muscle, total cholesterol |
| D3302 | Lipid extraction from liver or muscle - Tissue Triglyceride | liver, muscle, triglycerides |
| D3401 | Glucose (urine/plasma) | glucose, plasma, urine |
| D3402 | Hemoglobin A1C | Hemoglobin A1C, liver, metabolism |
| D3403 | beta-OH butyrate | diabetes, insulin, liver, metabolism |
| D3490 | Triglyceride | metabolism, triglycerides |
| D3405 | Total Cholesterol | cholesterol, liver, metabolism, total cholesterol |
| D3406 | HDL cholesterol | cholesterol, lipids, liver, metabolism |
| D3407 | Direct LDL cholesterol | cholesterol, lipids, metabolism |
| D3408 | Non esterified fatty acids | lipids, liver, metabolism, non-esterified fatty acid |
| D3409 | Apolipoprotein profiling (A-1, AII, B, E, CII, CIII) | apolipoproteins, lipids, liver, metabolism |
| D3410 | Apolipoprotein profiling | apolipoproteins, lipids, liver, metabolism |
| D3411 | Lipoprotein Particle Size | hormone, lipids, lipoproteins, liver, metabolism |
| D3412 | Metabolomics | diabetes, hormone, lipids, liver, metabolism, metabolite |
| D3413 | Complex lipid ratios | diabetes, lipids, liver |
| D3431 | Hormones - Generic ELISA Assay | hormone, liver |
| D3432 | Insulin | diabetes, hormone, insulin, liver |
| D3433 | C-Peptide | hormone, insulin, liver |
| D3434 | Proinsulin | hormone, insulin, liver |
| D3435 | Leptin | hormone, leptin, leptin measurement, liver |
| D3436 | Adiponectin (total) | adiponectin, hormone, lipids, liver |
| D3437 | Adiponectin (HMW) | adiponectin, hormone, lipids, liver |
| D3438 | Glucagon | glucagon, hormone, lipids, liver |
| D3439 | Glucagon-like peptide 1 (active) | glucagon, hormone, lipids, liver |
| D3440 | Glucagon-like peptide 1 (total) | glucagon, hormone, lipids, liver |
| D3441 | Ghrelin | hormone, liver |
| D5012 | Luminex / multiplex | hormone, immunology, kidney, lipids, liver, metabolite |
| M1009 | Hepatic gluconeogenesis | pyruvate tolerance test |
| M2013 | Cholesterol (HDL) | atherosclerosis, lipids, liver, metabolite, obesity |
| M2021 | Albumin | liver, metabolite |
| M2022 | Alanine transferase | liver, metabolite |
| M2023 | Aspartate transferase | liver, metabolite |
| M2024 | Bilirubin | liver, metabolite |
| M2025 | Gamma-glutamyl Transferase | liver, metabolite |
| M2027 | C-reactive peptide | inflammation, liver, metabolite |

Metabolite Concentration and Enrichment

| Test No. | Test Name | Keywords |
|----------|---|---|
| V3090 | Full amino acid profiles by HPLC / PITC or HLPC / OPA | amino acids, HPLC |
| C1057 | Plasma Free fatty Acid Levels | free fatty acids, non-esterified fatty acid |
| C1087 | Glucose enrichment and concentration | carbohydrate metabolism, diabetes |
| C1092 | Plasma/Organ Triglycerides | fat, lipids, metabolism |
| T2010 | Substrate oxidation and anaplerosis in the isolated heart | anaplerosis, cardiac, heart, metabolism, NMR, spectroscopy, substrate oxidation |
| V3036 | Metabolic panel | |
| V3070 | Plasma lipids | fat, lipids, metabolism |
| V3075 | Lipoprotein fractionation and characterization | fat, lipids, lipoproteins, metabolism |
| V3091 | Specific selected amino acid profiles | amino acids, HPLC |
| V3092 | Radioactivity of specific individual amino acids | amino acids, chromatography, protein synthesis, proteolysis, specific activity |
| V3093 | Specific activities for gluconeogenic and glycogenic assessment | amino acids, chromatography, protein synthesis, proteolysis, specific activity |
| Y4050 | Amino Acids | amino acids, enrichment, isotopes, metabolite |
| Y4051 | Beta-hydroxybutyrate | diabetes, enrichment, ketones, metabolite |
| Y4052 | Free fatty acid | diabetes, enrichment, fat, lipids, metabolite |
| Y4053 | Glucose | carbohydrate, diabetes, metabolite |
| Y4054 | Glycerol | diabetes, enrichment, lipids, metabolite |
| Y4055 | Glycogen | carbohydrate, diabetes, metabolite |
| Y4057 | Long-chain fatty acyl CoA esters | fat, lipids, metabolism |
| Y4059 | ADP, ATP | energetics, high-energy phosphates, mitochondria |
| Y4070 | Chem 7 | serum chemicals, serum metabolic panel |
| Y4071 | Liver Function Tests | serum chemicals, serum metabolic panel |
| Y4072 | Lipid Panel | serum chemicals, serum metabolic panel |
| Y4073 | Divalent Ions | serum chemicals |
| CA2009 | Triglycerides in liver | lipids, liver |
| CA2010 | Plasma triglycerides | plasma |
| C1058 | Plasma beta-hydroxybutyrate levels | beta-hydroxybutyrate |
| C1083 | Cholesterol (Total, HDL, LDL) | cholesterol, fat, lipids, metabolism |
| V4001 | Urine Na/K | plasma, potassium, sodium, urine |
| V4002 | Osmometer Plasma/Urine | osmolality, plasma, urine |
| V4003 | Urine Ca/Phosphorus Excretion | urine |
| CA2025 | Chronic arterial and jugular vein catherization | catheterization, surgery |
| CA2026 | Chronic arterial or jugular vein catherization | catheterization, surgery |
| CA2028 | Acute arterial or jugular vein catherization | catheterization, surgery |
| CA2029 | Acute portal vein catherization | catheterization, surgery |
| CA2030 | Implant [G2 E – Mitters™] | surgery |
| CA2040 | Metabolomic profile of Free Fatty Acids/sterols | fatty acids, metabolism, tissue |

| Test No. | Test Name | Keywords |
|----------|--|--|
| | in Plasma, Urine or Tissue | |
| CA2045 | Measurement of ATP/ADP | ATP, tissue |
| CA2016A | Measurement of 2H-enrichment of a body fluid | |
| CA2024CT | Custom Designed Tracer Experiment | |
| CA2049 | Additional 24-hr measurement (for 8 mice) | |
| D5012 | Luminex / multiplex | hormone, immunology, kidney, lipids, liver, metabolite |
| M2015 | Ammonia | lipids, metabolite |
| M2016 | Lipase | lipids, metabolite, obesity |
| M2021 | Albumin | liver, metabolite |
| M2022 | Alanine transferase | liver, metabolite |
| M2024 | Bilirubin | liver, metabolite |
| M2025 | Gamma-glutamyl Transferase | liver, metabolite |
| M2026 | Creatinine | kidney, metabolite |
| M2027 | C-reactive peptide | inflammation, liver, metabolite |
| M2028 | Total protein | metabolite |
| M2029 | Urea/BUN | kidney, metabolite |
| M2030 | Uric acid | kidney, metabolite |
| M2031 | Electrolytes | electrolyte panel |

Modeling and Simulation

| Test No. | Test Name | Keywords |
|----------|---|--------------------------------|
| V3090 | Full amino acid profiles by HPLC / PITC or HLPC / OPA | amino acids, HPLC |
| T2020 | Simulating the consequences of genetic manipulations | model, simulation |
| D2005 | Mouse Model Purchase | animal husbandry, mouse models |
| D2006 | Mouse Model Creation | animal husbandry, mouse models |

Magnetic Resonance Spectroscopy & Imaging

| Test No. | Test Name | Keywords |
|----------|---|--|
| T2001 | Sources of plasma glucose using 2H NMR | gluconeogenesis, glucose production, glycogenesis, hepatic, liver, metabolism, NMR, spectroscopy |
| T2002 | Gluconeogenic and citric acid cycle pathways (relative fluxes using 2H, 13C and J-HSQC NMR) | citric acid cycle, gluconeogenesis, hepatic, Krebs's cycle, liver, spectroscopy, TCA cycle |
| T2003 | Absolute gluconeogenic flux rates | gluconeogenesis, glucose production, glycogenolysis, hepatic, liver, metabolism |
| T2013 | TCA cycle flux (VTCA) and alpha-ketoglutarate-glutamate exchange flux (Vx) in the isolated mouse heart using 1H NMR | citric acid cycle, heart, Krebs's cycle, metabolism, NMR, spectroscopy, TCA cycle |
| T2012 | Intracellular sodium or high-energy | heart, high-energy phosphates, liver, NMR, |

| Test No. | Test Name | Keywords |
|----------|--|--|
| | phosphates in the isolated perfused mouse liver or heart | sodium, spectroscopy |
| T2011 | Intermediary metabolism in the isolated liver using NMR | hepatic, liver, metabolism, NMR, spectroscopy |
| T2020 | Simulating the consequences of genetic manipulations | model, simulation |
| D5011 | CT, MRI, PET, & combinations | cardiac function, central nervous system, CT, imaging, MRI, PET, spectroscopy, vascular function |

Pancreas, Islets and Beta Cells

| Test No. | Test Name | Keywords |
|----------|---|---------------------------------|
| V3082 | Tissue microdissection | laser microdissection, pancreas |
| D3250 | In vitro pancreatic islet insulin secretion | insulin, insulin secretion |

Pathology & Immunohistochemistry

| Test No. | Test Name | Keywords |
|----------|--|---|
| V3080 | Gross examinations and necropsy | gross examination, necropsy |
| V3081 | Tissue preparation, embedding, sectioning and routine staining | embedding, sectioning, staining, tissue preparation |
| V3082 | Tissue microdissection | laser microdissection, pancreas |
| V3083 | Screen/optimize immunohistochemical protocols for mouse-specific commercial and custom-designed antisera | histology, immunohistochemistry |
| V3097 | Perfusion-Fixation/Histopathology/Quantify Sclerosis | |
| CA2041 | Tissue processing by Pathology Core | histology, tissue preparation |
| CA2042 | Plasma panel Triglycerides, CHOL, β -OH, NEFA (Marshfield labs) | histology, staining, tissue preparation |
| CA2043 | Portal vein injection and tissue collection (at 0 min. & 5 min.) | tissue preparation |
| S6300 | Tissue Processing & Sectioning - Trim & Cassette Tissue | |
| S6301 | Tissue Processing & Sectioning - Process & Embed Tissue, Paraffin | |
| S6302 | Tissue Processing & Sectioning - Section Paraffin Block | |
| S6303 | Tissue Processing & Sectioning - Section Frozen Block | |
| S6304 | Tissue Processing & Sectioning - Additional Unstained Slides Sections | |
| S6305 | Tissue Processing & Sectioning - Decalcification | |
| S6306 | Tissue Processing & Sectioning - Serial Sections/fat tissue | |
| S6307 | Histology - H&E | |

| Test No. | Test Name | Keywords |
|----------|---|--|
| S6308 | Histology - PAS | |
| S6309 | Histology - Picrosirius Red | |
| S6310 | Histology - Masson's Trichrome | |
| S6311 | Histology - von Kossa | |
| S6312 | Histology - Silver Methenamine | |
| S6313 | Histology - MOVATS Pentachrome | |
| S6314 | Histology - Oil Red O | |
| S6315 | Histology - Other Stains | |
| S6316 | Immunohistochemistry - IHC/FITC Staining | |
| S6317 | Immunohistochemistry - Batch Staining | |
| S6318 | Immunohistochemistry - New Antibody Workup | |
| S6319 | Immunohistochemistry - TUNEL (Apoptag Plus) | |
| S6320 | Electron Microscopy - Process & Embed | |
| S6321 | Electron Microscopy - Thick Section | |
| S6322 | Electron Microscopy - Thin Section | |
| S6323 | Electron Microscopy - Scope Time | |
| S6324 | In Situ Hybridization - Probe Labelling, Radioactive | |
| S6325 | In Situ Hybridization - Plasmid Linearization | |
| S6326 | In Situ Hybridization | |
| S6327 | Morphometric Analysis - Atherosclerosis, Aortic Root w/MOVATS | |
| S6328 | Morphometric Analysis - Atherosclerosis, Aortic Root w/Oil Red O | |
| S6329 | Morphometric Analysis - Atherosclerosis, Aortic Root w/Oil Red O and MOVATS | |
| S6330 | Morphometric Analysis - Atherosclerosis, Whole Aorta, En Face | |
| S6331 | Morphometric Analysis - Atherosclerosis, Inominates | |
| S6332 | Morphometric Analysis - Kidney, Glomerular Size & Percent Matrix | |
| S6333 | Morphometric Analysis - Kidney, Interstitial Fibrosis | |
| S6334 | Morphometric Analysis - Other | |
| CA2048 | Whole Body Fixation (PFA)+ Tissue Collection | |
| CA2051 | Excise Tissues, Blood Serum/Plasma | |
| D5001 | Macrovascular permeability & lipoprotein flux | cardiac function, imaging, immunohistochemistry, lipids, vascular function |
| D5002 | Microvascular permeability & lipoprotein flux | cardiac function, imaging, immunohistochemistry, lipids, vascular function |

| Test No. | Test Name | Keywords |
|----------|--|--|
| D5004 | Atheroma quantification | cardiac function, imaging, vascular function |
| D5007 | Aortic & mesenteric reactivity & vascular stiffening | aortic reactivity, mesenteric reactivity, vascular stiffening |
| D5013 | MMPC mouse gross necropsy with histology | histology, morphology, necropsy |
| D5014 | UC Davis Comparative Pathology Laboratory services | hematology, histology, morphometry, necropsy, serum chemicals, urinalysis |
| M2032 | Cytokines Panel I - multiplex | chemokines, complications, cytokines, diabetes, inflammation, insulin resistance, monokines, obesity |
| M2033 | Cytokines Panel II - multiplex | chemokines, complications, cytokines, diabetes, inflammation, insulin resistance, monokines, obesity |
| M2034 | Islet histology | beta cell, diabetes, insulin |
| M2035 | Molecular islet analysis | beta cell, diabetes, insulin |

Surgery

| Test No. | Test Name | Keywords |
|----------|---|--|
| C1051 | Intestinal lipid absorption in the conscious mouse | absorption, fistula, gastrointestinal tract, lipids, lymph |
| V3001 | Cannulation of cerebral ventricle | brain, central control, CSF |
| V3002 | Jugular vein and carotid artery catheterization | blood vessel, chronic, surgery |
| S6123 | Necropsy | necropsy, surgery |
| Y4089 | Blood Bicarbonate/CO2 | carbon dioxide, metabolism, serum chemicals, serum metabolic panel |
| CA2027 | Acute arterial and jugular vein catheterization | catheterization, surgery |
| CA2028 | Acute arterial or jugular vein catheterization | catheterization, surgery |
| CA2029 | Acute portal vein catheterization | catheterization, surgery |
| CA2030 | Implant [G2 E - Mitters™] | surgery |
| CA2031 | Long-term analysis of surgery implantation on Min-Mitter™ | surgery |
| CA2041 | Tissue processing by Pathology Core | histology, tissue preparation |
| CA2042 | Plasma panel Triglycerides, CHOL, β -OH, NEFA (Marshfield labs) | histology, staining, tissue preparation |
| CA2044 | Brain uptake and blood flow | blood flow, brain |
| M1021 | Surgery – jugular vein cannulation | surgery |
| M1022 | M1022 Surgery – tail vein injection | surgery |
| M1023 | Surgery – carotid artery cannulation | surgery |

Vascular Function

| Test No. | Test Name | Keywords |
|----------|--------------------------|---|
| C1002 | Inter-arterial pressure | blood pressure, blood vessel, hypertension, hypotension, vascular |
| C1001 | Tail Cuff Blood pressure | blood pressure, blood vessel, hypertension, hypotension, vascular |

| Test No. | Test Name | Keywords |
|----------|---|--|
| C1003 | Arterial baroreflex responses | cardiac function, vascular tone |
| C1013 | Arterial response to injury (neointimal hyperplasia) | angioplasty, endothelial denudation, neointimal hyperplasia, restenosis |
| C1014 | Vascular contractility measurements | aortic ring, contractility, vascular function |
| V3033 | Blood pressure measurements | blood pressure, blood vessel, hypertension, hypotension, vascular |
| V3034 | Vascular morphology | blood vessel, histology, intima, smooth muscle, vascular |
| V3076 | Morphometric determinations (aorta) | blood vessel, histology, intima, smooth muscle, vascular |
| S6206 | Carotid Stenosis - Arterial response to injury | blood vessel, endothelial denudation, histology, neointimal hyperplasia, smooth muscle, vascular |
| S6230 | Myography - basic | |
| S6231 | Myography - additional | |
| D5001 | Macrovascular permeability & lipoprotein flux | cardiac function, imaging, immunohistochemistry, lipids, vascular function |
| D5002 | Microvascular permeability & lipoprotein flux | cardiac function, imaging, immunohistochemistry, lipids, vascular function |
| D5004 | Atheroma quantification | cardiac function, imaging, vascular function |
| D5005 | BP measurement by tail cuff | blood pressure, cardiac function, vascular function |
| D5006 | BP & heart rate variability measurements by telemetry | blood pressure, cardiac function, telemetry, vascular function |
| D5007 | Aortic & mesenteric reactivity & vascular stiffening | aortic reactivity, mesenteric reactivity, vascular stiffening |
| D5008 | Erectile dysfunction | vascular function |
| D5009 | Cardiac electrophysiology | cardiac, electrocardiography |
| D5010 | Echocardiography | cardiac function, echocardiography, vascular function |
| D5011 | CT, MRI, PET, & combinations | cardiac function, central nervous system, CT, imaging, MRI, PET, spectroscopy, vascular function |

Miscellaneous

| Test No. | Test Name | Keywords |
|----------|--|--------------------|
| V3000A | Miscellaneous Tissue and Body Fluid Collection | tissue |
| V3000B | Miscellaneous Implantation of Catheters, Sensors and Pellets | catheterization |
| V3000C | Equipment Usage | |
| V3000D | Personnel Training | |
| V3000E | Cerebral Ventricle Cannulation | cerebral ventricle |
| V3000F | Jugular Vein and Carotid Artery Catheterization | catheterization |
| CA2050 | Data summary Interpretation | |

| Test No. | Test Name | Keywords |
|----------|---|--|
| CA2053B | Custom Designed Biological Experiment | |
| CA2055 | Quarantine (4 weeks) mice imported to Case | |
| CA2056 | Housing mice 1 to 14 days | |
| C1103 | Necropsy (tissue collection) | necropsy |
| D2001 | Importation of Mice and Material | animal husbandry, mouse models |
| D2002 | Per Diem (4 cages/line X 14 days) | animal husbandry |
| D2003 | Colony Management (if needed) | animal husbandry |
| D2004 | Genotyping (if needed) | genotyping, mouse models |
| D2005 | Mouse Model Purchase | animal husbandry, mouse models |
| D2006 | Mouse Model Creation | animal husbandry, mouse models |
| D3402 | Hemoglobin A1C | Hemoglobin A1C, liver, metabolism |
| D3412 | Metabolomics | diabetes, hormone, lipids, liver, metabolism, metabolite |
| D3431 | Hormones - Generic ELISA Assay | hormone, liver |
| D3432 | Insulin | diabetes, hormone, insulin, liver |
| D3433 | C-Peptide | hormone, insulin, liver |
| D3434 | Proinsulin | hormone, insulin, liver |
| D3481 | 8-Isoprostane (urinary) | enzyme activity |
| D3482 | Protein Carbonyl (plasma, cell lysates, tissue homogenates) | enzyme activity |
| D3483 | Catalase (plasma, cell lysates, tissue homogenates) | diabetes, inflammation |
| D3484 | Glutathione | enzyme activity, oxidative stress |
| D3485 | Glutathione Peroxidase | enzyme activity, oxidative stress |
| D3486 | Glutathione Reductase | enzyme activity, oxidative stress |
| D3487 | Hydrogen Peroxide (urinary) | hydrogen peroxide, oxidative stress |
| D3488 | Superoxide Dismutase | oxidative stress, superoxide dismutase |
| D3489 | Myeloperoxidase (cell lysate, plasma) | oxidative stress |
| D4003 | Meal Pattern Analysis | energy expenditure, exercise, food intake, meal pattern |
| D4004 | Gastric Emptying | food intake, gastrointestinal tract |
| D4005 | Digestible Energy | energetics, food intake, gastrointestinal tract |
| D4006 | Gut Microbiome Analysis | energetics, gastrointestinal tract, gut, microbiome |
| D4009 | Brown Adipose Tissue Thermogenic Activation | adipose, energetics, energy expenditure |
| D4010 | Comprehensive Longitudinal Metabolic Profile | energy expenditure, food intake, glucose, hormone, insulin |
| D5001 | Macrovascular permeability & lipoprotein flux | cardiac function, imaging, immunohistochemistry, lipids, vascular function |
| D5002 | Microvascular permeability & lipoprotein flux | cardiac function, imaging, immunohistochemistry, lipids, vascular function |
| D5004 | Atheroma quantification | cardiac function, imaging, vascular function |

| Test No. | Test Name | Keywords |
|----------|---|--|
| D5005 | BP measurement by tail cuff | blood pressure, cardiac function, vascular function |
| D5006 | BP & heart rate variability measurements by telemetry | blood pressure, cardiac function, telemetry, vascular function |
| D5007 | Aortic & mesenteric reactivity & vascular stiffening | aortic reactivity, mesenteric reactivity, vascular stiffening |
| D5008 | Erectile dysfunction | vascular function |
| D5009 | Cardiac electrophysiology | cardiac, electrocardiography |
| D5010 | Echocardiography | cardiac function, echocardiography, vascular function |
| D5011 | CT, MRI, PET, & combinations | cardiac function, central nervous system, CT, imaging, MRI, PET, spectroscopy, vascular function |
| D5012 | Luminex / multiplex | hormone, immunology, kidney, lipids, liver, metabolite |
| D5013 | MMPC mouse gross necropsy with histology | histology, morphology, necropsy |
| D5014 | UC Davis Comparative Pathology Laboratory services | hematology, histology, morphometry, necropsy, serum chemicals, urinalysis |
| M1011 | Protein metabolism | phenylalanine, protein synthesis |
| M1016 | Chronic drug delivery | infusion, osmotic pump |
| M1018 | Acute lipid infusion | fatty acids, lipids |
| M2006 | Glucagon | glucose, hepatic, hormone, pancreas |

Protein

| Test No. | Test Name | Keywords |
|----------|--|--|
| C1041 | Body Composition | body composition, carcass analysis, obesity, QMR, total body fat |
| T2020 | Simulating the consequences of genetic manipulations | model, simulation |
| V3009 | Amino acid kinetics | amino acid flux, amino acid kinetics, isotopes |
| S6101 | Body Composition | body composition, energy balance, fat, fat mass, obesity, water |
| D3409 | Apolipoprotein profiling (A-1, AII, B, E, CII, CIII) | apolipoproteins, lipids, liver, metabolism |
| D3410 | Apolipoprotein profiling | apolipoproteins, lipids, liver, metabolism |
| D3411 | Lipoprotein Particle Size | hormone, lipids, lipoproteins, liver, metabolism |
| D3431 | Hormones - Generic ELISA Assay | hormone, liver |
| D3432 | Insulin | diabetes, hormone, insulin, liver |
| D3433 | C-Peptide | hormone, insulin, liver |
| D3434 | Proinsulin | hormone, insulin, liver |
| D3435 | Leptin | hormone, leptin, leptin measurement, liver |
| D3436 | Adiponectin (total) | adiponectin, hormone, lipids, liver |
| D3437 | Adiponectin (HMW) | adiponectin, hormone, lipids, liver |
| D3438 | Glucagon | glucagon, hormone, lipids, liver |

| Test No. | Test Name | Keywords |
|----------|---|--|
| D3439 | Glucagon-like peptide 1 (active) | glucagon, hormone, lipids, liver |
| D3440 | Glucagon-like peptide 1 (total) | glucagon, hormone, lipids, liver |
| D3441 | Ghrelin | hormone, liver |
| D3451 | Urinary Albumin Excretion | albumin, kidney, renal, urine |
| D3452 | Creatinine | creatinine, kidney, renal, urine |
| D3453 | Urea | kidney, renal, urea |
| D3481 | 8-Isoprostane (urinary) | enzyme activity |
| D3482 | Protein Carbonyl (plasma, cell lysates, tissue homogenates) | enzyme activity |
| D3483 | Catalase (plasma, cell lysates, tissue homogenates) | diabetes, inflammation |
| D3484 | Glutathione | enzyme activity, oxidative stress |
| D3485 | Glutathione Peroxidase | enzyme activity, oxidative stress |
| D3486 | Glutathione Reductase | enzyme activity, oxidative stress |
| D3487 | Hydrogen Peroxide (urinary) | hydrogen peroxide, oxidative stress |
| D3488 | Superoxide Dismutase | oxidative stress, superoxide dismutase |
| D3489 | Myeloperoxidase (cell lysate, plasma) | oxidative stress |
| M1011 | Protein metabolism | phenylalanine, protein synthesis |
| M2026 | Creatinine | kidney, metabolite |
| M2027 | C-reactive peptide | inflammation, liver, metabolite |
| M2028 | Total protein | metabolite |
| M2029 | Urea/BUN | kidney, metabolite |
| M2030 | Uric acid | kidney, metabolite |

Tests Listed by Center

CASE WESTERN RESERVE UNIVERSITY

Analytical Core

Director: Colleen Croniger, Personnel: Michelle Puchowicz

The analytical Core conducts all assays involving the determination of isotope labeling and concentration profiles of metabolites including

- (i) the 2H-labeling of water, lipids and amino acids,
- (ii) the 18O-labeling of water,
- (iii) the concentration profile of acyl-CoAs (e.g. short, medium and long-chain species), and
- (iv) metabolic profiles of citric acid cycle intermediates, amino acids and fatty acids.

| Test No. | Test Name | Keywords |
|----------|--|--|
| CA2011 | Total Energy expenditure using doubly-labeled water | energy expenditure, water |
| CA2015 | Turnover of glucose, lipid and/or protein | |
| CA2016 | Fatty acid and cholesterol synthesis using 2H-labeled water | |
| CA2017 | Tissue-specific protein synthesis using 2H-labeled water | amino acids, metabolism, protein synthesis |
| CA2018 | Profile of acylcarnitines in plasma/urine or tissue samples | |
| CA2019 | Profile of long chain acyl-CoAs in tissue | |
| CA2020 | Measurement of acetyl-CoA, propionyl-CoA and/or succinyl-CoA in tissue | |
| CA2022 | ¹³ C-Labeling pattern of acetyl moiety of citrate (substrate oxidation) | |
| CA2024 | Metabolomic profile of citric acid cycle and gluconeogenic intermediates | |
| CA2041 | Tissue processing by Pathology Core | histology, tissue preparation |
| CA2042 | Plasma panel Triglycerides, CHOL, β -OH, NEFA (Marshfield labs) | histology, staining, tissue preparation |
| CA2043 | Protal vein injection and tissue collection (at 0 min. & 5 min.) | tissue preparation |
| CA2044 | Brain uptake and blood flow | blood flow, brain |
| CA2045 | Measurement of ATP/ADP | ATP, tissue |
| CA2016A | Measurement of 2H-enrichment of a body fluid | |
| CA2024CT | Custom Designed Tracer Experiment | |
| CA2046 | Indirect Calorimetry : First 36-hr measurement (for 8 mice) | |
| CA2047 | Treadmill Training/Endurance Study PLUS Indirect Calorimetry (for 8 mice) | |
| CA2048 | Whole Body Fixation (PFA)+ Tissue Collection | |
| CA2049 | Additional 24-hr measurement (for 8 mice) | |
| CA2050 | Data summary Interpretation | |

| Test No. | Test Name | Keywords |
|----------|--|----------|
| CA2051 | Excise Tissues, Blood Serum/Plasma | |
| CA2052 | Isolated mouse HEART perfusion | heart |
| CA2053 | Isolated mouse LIVER perfusion | liver |
| CA2053B | Custom Designed Biological Experiment | |
| CA2055 | Quarantine (4 weeks) mice imported to Case | |
| CA2056 | Housing mice 1 to 14 days | |

Metabolic Core

Director: Colleen Croniger, Associate Director: Michelle Puchowicz

The Metabolic Core conducts in vivo and ex vivo metabolic experiments on mice shipped to the Case MMPC. This core focuses on the following techniques and measurements:

- 1) Chronic or acute arterial, jugular and/or gastric catheterization
- 2) Acute catheterization of portal vein or urinary bladder
- 3) Energy expenditure integrated over four days by the "doubly-labeled water" method
- 4) Rates of fatty acid, cholesterol, triglycerides, or protein synthesis measured using 2H₂O
- 5) Insulin clamp, pancreatic clamp
- 6) Food intake
- 7) Body temperature
- 8) Urine and blood chemistry analysis
- 9) Glycosylated hemoglobin
- 10) Liver perfusion and heart perfusion
- 11) Tissue perfusion and fixation

| Test No. | Test Name | Keywords |
|----------|--|--|
| CA2000 | Body composition using 2H-labeled water | body composition, body weight, fat |
| CA2001 | Food Consumption | food intake |
| CA2002 | Body Weight | body composition, body weight, food intake |
| CA2003 | Measurement of body temperature (by probe) | energy expenditure, exercise |
| CA2004 | Glucose tolerance tests (GTT) | carbohydrate metabolism, diabetes, glucose |
| CA2005 | Insulin concentrations at fasting and post intraperitoneal glucose administration | insulin, insulin secretion |
| CA2006 | Plasma insulin measurement by ELISA | carbohydrate metabolism, insulin, insulin action |
| CA2007 | Insulin concentrations at fasting and post intraperitoneal insulin administration | |
| CA2008 | Glucose concentrations at fasting and post intraperitoneal insulin administration - insulin tolerance test (ITT) | carbohydrate metabolism, diabetes, insulin sensitivity |
| CA2009 | Triglycerides in liver | lipids, liver |
| CA2010 | Plasma triglycerides | plasma |

| Test No. | Test Name | Keywords |
|----------|--|---------------------------------|
| CA2013 | Hyperinsulinemic Clamp (Hypoglycemic or Euglycemic) using stable isotopes | |
| CA2025 | Chronic arterial and jugular vein catherization | catheterization, surgery |
| CA2026 | Chronic arterial or jugular vein catherization | catheterization, surgery |
| CA2027 | Acute arterial and jugular vein catherization | catheterization, surgery |
| CA2028 | Acute arterial or jugular vein catherization | catheterization, surgery |
| CA2029 | Acute portal vein catherization | catheterization, surgery |
| CA2030 | Implant [G2 E – Mitters™] | surgery |
| CA2031 | Long-term analysis of surgery implantation on Min-Mitter™ | surgery |
| CA2040 | Metabolomic profile of Free Fatty Acids/sterols in Plasma, Urine or Tissue | fatty acids, metabolism, tissue |

UNIVERSITY OF CALIFORNIA DAVIS

Animal Care Core

Director: Katherine Wasson, Co-Director: Stephen Griffey

The Animal Core for the Mouse Metabolic Phenotyping Center (MMPC) at UCD (MMPC-UCD) is comprised of space, resources, and personnel within the UCD Mouse Biology Program (MBP). The Core imports and acclimatizes investigator's mice into the MMPC for phenotypic analysis with minimal delay. This process increases throughput of mice into the MMPC, reduces wait times for investigators, broadens the availability of metabolic phenotyping tests, and expedites data generation and project completion. For investigators that do not specific mutant mice, the Core can arrange for purchase from any number of public repositories, including the KOMP and MMRRC repositories at UCD. In addition, the Core can make genetically-altered mutant mice for investigators and enter them directly and immediately entered into the MMPC for analysis.

| Test No. | Test Name | Keywords |
|----------|-----------------------------------|--------------------------------|
| D2001 | Importation of Mice and Material | animal husbandry, mouse models |
| D2002 | Per Diem (4 cages/line X 14 days) | animal husbandry |
| D2003 | Colony Management (if needed) | animal husbandry |
| D2004 | Genotyping (if needed) | genotyping, mouse models |
| D2005 | Mouse Model Purchase | animal husbandry, mouse models |
| D2006 | Mouse Model Creation | animal husbandry, mouse models |

Metabolism and Endocrinology Core

Director: Peter Havel, Co-Director: Fawaz Haj

The Metabolism and Endocrinology Core provides expertise, technical resources, and instrumentation necessary to characterize perturbations in metabolism in murine models potentially useful for understanding diabetes, its complications, obesity, and related metabolic disorders. The Core conducts in vivo and in vitro metabolic procedures to assess insulin secretion, insulin sensitivity, and glucose tolerance and offers an extensive list of assays of metabolic substrates, endocrine hormones, and indices of renal function, insulin signaling, inflammation and endoplasmic reticulum stress. In addition, the Core provides assay management services for the analysis of samples generated by other Cores of the MMPC-UCD

| Test No. | Test Name | Keywords |
|----------|------------------------------------|--|
| D3101 | Intravenous Glucose Tolerance Test | diabetes, insulin, insulin action, insulin secretion |

| Test No. | Test Name | Keywords |
|----------|--|--|
| D3102 | Hyperinsulinemic, Euglycemic Clamp | diabetes, hyperinsulinemic clamp, insulin, insulin action |
| D3103 | IN VIVO Insulin Tolerance Tests | diabetes, insulin, insulin action |
| D3104 | IN VIVO GlucoseTolerance Tests | diabetes, glucose, glucose metabolism, glucose tolerance |
| D3105 | IN VIVO Glucose-stimulates Insulin Secretion Test | diabetes, glucose, glucose metabolism, insulin, insulin action |
| D3106 | Positron emission tomography (microPET) | diabetes, glucose, glucose metabolism, imaging |
| D3201 | Adipocyte metabolism/hormone production - Isolation/cell size/# | hormone, insulin, insulin action, lipid extraction, lipids |
| D3202 | Adipocyte metabolism/hormone production - 96h culture/glucose utilization/lactate production | hormone, insulin, insulin action |
| D3203 | Adipocyte metabolism/hormone production - leptin secretion at 96 hour | hormone, leptin, leptin measurement |
| D3204 | Adipocyte metabolism/hormone production - adiponectin secretion at 96 hour | adiponectin |
| D3205 | Adipocyte metabolism/hormone production - lipolysis (glycerol baseline and 96h) | glycerol, lipid extraction, lipids |
| D3206 | Adipocyte metabolism/hormone production - lipogenesis from labeled glucose | adipose, glucose, glucose turnover, triglycerides |
| D3207 | Adipocyte metabolism/hormone production - glucose/FA oxidation from labeled glucose/FA | glucose, hormone |
| D3250 | In vitro pancreatic islet insulin secretion | insulin, insulin secretion |
| D3301 | Lipid extraction from liver or muscle - Tissue Cholesterol | cholesterol, liver, muscle, total cholesterol |
| D3302 | Lipid extraction from liver or muscle - Tissue Triglyceride | liver, muscle, triglycerides |
| D3401 | Glucose (urine/plasma) | glucose, plasma, urine |
| D3402 | Hemoglobin A1C | Hemoglobin A1C, liver, metabolism |
| D3403 | beta-OH butyrate | diabetes, insulin, liver, metabolism |
| D3490 | Triglyceride | metabolism, triglycerides |
| D3405 | Total Cholesterol | cholesterol, liver, metabolism, total cholesterol |
| D3406 | HDL cholesterol | cholesterol, lipids, liver, metabolism |
| D3407 | Direct LDL cholesterol | cholesterol, lipids, metabolism |
| D3408 | Non esterified fatty acids | lipids, liver, metabolism, non-esterified fatty acid |
| D3409 | Apolipoprotein profiling (A-1, AII, B, E, CII, CIII) | apolipoproteins, lipids, liver, metabolism |
| D3410 | Apolipoprotein profiling | apolipoproteins, lipids, liver, metabolism |
| D3411 | Lipoprotein Particle Size | hormone, lipids, lipoproteins, liver, metabolism |
| D3412 | Metabolomics | diabetes, hormone, lipids, liver, metabolism, metabolite |
| D3413 | Complex lipid ratios | diabetes, lipids, liver |
| D3431 | Hormones - Generic ELISA Assay | hormone, liver |

| Test No. | Test Name | Keywords |
|----------|---|---|
| D3432 | Insulin | diabetes, hormone, insulin, liver |
| D3433 | C-Peptide | hormone, insulin, liver |
| D3434 | Proinsulin | hormone, insulin, liver |
| D3435 | Leptin | hormone, leptin, leptin measurement, liver |
| D3436 | Adiponectin (total) | adiponectin, hormone, lipids, liver |
| D3437 | Adiponectin (HMW) | adiponectin, hormone, lipids, liver |
| D3438 | Glucagon | glucagon, hormone, lipids, liver |
| D3439 | Glucagon-like peptide 1 (active) | glucagon, hormone, lipids, liver |
| D3440 | Glucagon-like peptide 1 (total) | glucagon, hormone, lipids, liver |
| D3441 | Ghrelin | hormone, liver |
| D3451 | Urinary Albumin Excretion | albumin, kidney, renal, urine |
| D3452 | Creatinine | creatinine, kidney, renal, urine |
| D3453 | Urea | kidney, renal, urea |
| D3461 | Markers of Inflammation - full panel | diabetes, growth factors, immunology, inflammation, interleukins |
| D3462 | Markers of Inflammation - limited panel | diabetes, growth factors, immunology, inflammation, interleukins |
| D3463 | HS CRP | diabetes, inflammation |
| D3464 | Serum Amyloid A3 | diabetes, inflammation, serum metabolic panel |
| D3465 | sICAM | diabetes, inflammation |
| D3466 | sVCAM | diabetes, inflammation |
| D3467 | sE-Selectin | diabetes, inflammation |
| D3468 | sP-Selectin | diabetes, inflammation |
| D3481 | 8-Isoprostane (urinary) | enzyme activity |
| D3482 | Protein Carbonyl (plasma, cell lysates, tissue homogenates) | enzyme activity |
| D3483 | Catalase (plasma, cell lysates, tissue homogenates) | diabetes, inflammation |
| D3484 | Glutathione | enzyme activity, oxidative stress |
| D3485 | Glutathione Peroxidase | enzyme activity, oxidative stress |
| D3486 | Glutathione Reductase | enzyme activity, oxidative stress |
| D3487 | Hydrogen Peroxide (urinary) | hydrogen peroxide, oxidative stress |
| D3488 | Superoxide Dismutase | oxidative stress, superoxide dismutase |
| D3489 | Myeloperoxidase (cell lysate, plasma) | oxidative stress |
| D3491 | Insulin Signalling pathway | diabetes, inflammation, insulin, leptin, obesity, stress |
| D3492 | Endoplasmic reticulum stress pathway | diabetes, hormone, immunology, insulin, insulin action, obesity, stress |
| D3493 | Inflammation pathway | diabetes, hormone, immunology, inflammation, insulin |
| D3494 | Leptin Signaling pathway | diabetes, hormone, leptin, obesity |

Body Composition, Thermoregulation, and Food Intake Behavior Core

Director: Sean Adams, Co-Director: Jon Ramsey, Personnel: Trina Knotts

The Body Composition, Thermoregulation, and Food Intake Behavior Core provides clients with in-depth assessments of molecular and whole-animal phenomena relevant to body weight regulation and metabolism. This Core has a unique strength in the application of dietary and thermoregulatory challenge tests designed to unmask subtle phenotypes associated with energy balance and gut function. Core personnel have proven capabilities in studying mouse energetic, adipose tissue biology, and energy balance regulators including gut signals. The Core employs state-of-the-art approaches and a unique perspective that includes an appreciation of the roles of gut physiology and peripheral neuron function.

| Test No. | Test Name | Keywords |
|----------|--|---|
| D4001 | Gross Body Composition | body composition, imaging |
| D4002 | Adiposity (adipose depot weights) | adipose, body composition |
| D4003 | Meal Pattern Analysis | energy expenditure, exercise, food intake, meal pattern |
| D4004 | Gastric Emptying | food intake, gastrointestinal tract |
| D4005 | Digestible Energy | energetics, food intake, gastrointestinal tract |
| D4006 | Gut Microbiome Analysis | energetics, gastrointestinal tract, gut, microbiome |
| D4007 | Standard Fed & Postabsorptive Energy Expenditure | energy balance, energy expenditure, food intake, indirect calorimetry |
| D4009 | Brown Adipose Tissue Thermogenic Activation | adipose, energetics, energy expenditure |
| D4010 | Comprehensive Longitudinal Metabolic Profile | energy expenditure, food intake, glucose, hormone, insulin |

Cardiovascular Biology and Pathology Core

Director: John Rutledge

The Complications and Pathology Core provides detailed metabolic and cardiovascular phenotyping of mice for macrovascular and microvascular complications of diabetes and obesity using new state-of-the-art approaches. Core expertise includes monocyte and endothelial cell biology, cerebrovascular and cardiac structure and function, and mouse cardiovascular anatomy, physiology, pathology, and micro imaging.

| Test No. | Test Name | Keywords |
|----------|---|--|
| D5001 | Macrovascular permeability & lipoprotein flux | cardiac function, imaging, immunohistochemistry, lipids, vascular function |
| D5002 | Microvascular permeability & lipoprotein flux | cardiac function, imaging, immunohistochemistry, lipids, vascular function |
| D5003 | Lipoprotein analysis by LTRS | imaging, lipids, lipoproteins |
| D5004 | Atheroma quantification | cardiac function, imaging, vascular function |
| D5005 | BP measurement by tail cuff | blood pressure, cardiac function, vascular function |
| D5006 | BP & heart rate variability measurements by telemetry | blood pressure, cardiac function, telemetry, vascular function |
| D5007 | Aortic & mesenteric reactivity & vascular stiffening | aortic reactivity, mesenteric reactivity, vascular stiffening |
| D5008 | Erectile dysfunction | vascular function |
| D5009 | Cardiac electrophysiology | cardiac, electrocardiography |
| D5010 | Echocardiography | cardiac function, echocardiography, vascular function |

| Test No. | Test Name | Keywords |
|----------|--|--|
| D5011 | CT, MRI, PET, & combinations | cardiac function, central nervous system, CT, imaging, MRI, PET, spectroscopy, vascular function |
| D5012 | Luminex / multiplex | hormone, immunology, kidney, lipids, liver, metabolite |
| D5013 | MMPC mouse gross necropsy with histology | histology, morphology, necropsy |
| D5014 | UC Davis Comparative Pathology Laboratory services | hematology, histology, morphometry, necropsy, serum chemicals, urinalysis |

UNIVERSITY OF CINCINNATI MEDICAL CENTER

Lipid, Lipoprotein and Glucose Metabolism Core

Director: Patrick Tso

Diabetes is defined by abnormalities in circulating metabolites; obviously glucose metabolism is impaired, but the presence of certain dyslipidemias can also lead to a predisposition for cardiovascular disease in diabetic patients.

This core is capable of measuring numerous metabolic parameters in mouse models pertaining to serum lipid profiles, glucose metabolism and plasma hormones.

| Test No. | Test Name | Keywords |
|----------|---|---|
| C1070 | Glucose tolerance tests (intraperitoneal glucose tolerance, oral glucose tolerance) | glucose disposal, glucose metabolism, glucose tolerance, insulin secretion, intraperitoneal glucose tolerance |
| C1088 | Plasma Glucose-dependent insulintropic peptide (GIP) concentration | gut, hormone, lipids, metabolism |
| C1051 | Intestinal lipid absorption in the conscious mouse | absorption, fistula, gastrointestinal tract, lipids, lymph |
| C1052 | Plasma lipid profiles | non-esterified fatty acid, phospholipids, total cholesterol, triglycerides |
| C1053 | Lipoprotein profiles | agarose, agarose gel electrophoresis, electrophoresis, lipids, lipoproteins |
| C1054 | Lipoprotein fractionation by FPLC | apolipoproteins, FPLC, lipids, lipoproteins |
| C1055 | Chylomicron metabolism (lymph) | apolipoproteins, chylomicron, chylomicron remnants, intestine, lipids |
| C1056 | Cholesterol synthetic rate | cholesterol, fatty acids, lipids, sterol, synthesis |
| C1057 | Plasma Free fatty Acid Levels | free fatty acids, non-esterified fatty acid |
| C1072 | Insulin Sensitivity Test | diabetes, insulin action, insulin sensitivity, metabolism |
| C1081 | C-Peptide | diabetes, hormone, insulin |
| C1085 | Plasma/serum concentrations glucagon | counterregulatory, hormone, pancreas |
| C1086 | Plasma Glucagon-like peptide 1 (GLP-1) concentration | counterregulatory, hormone, pancreas |
| C1087 | Glucose enrichment and concentration | carbohydrate metabolism, diabetes |
| C1089 | Insulin concentrations in plasma/serum/lymph/cerebrospinal fluid | diabetes, hormone, pancreas |
| C1090 | Plasma/serum concentrations of leptin | eating behaviour, fat, hormone, lipids |
| C1091 | Somatostatin in plasma or tissue extracts | diabetes, hormone, pancreas |

| Test No. | Test Name | Keywords |
|----------|---|---|
| C1092 | Plasma/Organ Triglycerides | fat, lipids, metabolism |
| C1058 | Plasma beta-hydroxybutyrate levels | beta-hydroxybutyrate |
| C1059 | Non-invasive measurement of fat absorption | fecal fat absorption |
| C1060 | Chemical determination of phospholipid | fat, fatty acids, lipids, phospholipids |
| C1061 | Serum/Plasma Adiponectin | adiponectin, gut hormones, peptides |
| C1062 | Serum/Plasma Resistin | resistin |
| C1071 | Plasma glucose levels | carbohydrate, diabetes, metabolism |
| C1083 | Cholesterol (Total, HDL, LDL) | cholesterol, fat, lipids, metabolism |
| C1103 | Necropsy (tissue collection) | necropsy |
| C1104 | Lipid extraction via folch | folch, lipid extraction |
| C1105 | Fatty Acid analysis via GC | |
| C1106 | Telemetry - Cardiac parameters (BP, HR, Pulse Pressure, Activity) | blood pressure, telemetry |
| C1107 | Telemetry - Activity and Temperature measurements | telemetry |
| C1108 | Multiplexing assays | |
| C1109 | Euglycemic-hyperinsulinemic clamp | hyperinsulinemic clamp |

Energy Metabolism, Food Intake & Body Weight Regulation Core

Co-Director: Randy Seeley, Co-Director: Steve Woods

Obesity is the major predisposing risk factor for type II diabetes. This core provides comprehensive set of measurements of food intake, energy expenditure (including use of indirect calorimetry) and body fat composition.

| Test No. | Test Name | Keywords |
|----------|---------------------------------|---|
| C1041 | Body Composition | body composition, carcass analysis, obesity, QMR, total body fat |
| C1042 | Energy Expenditure Measurements | basal metabolic rate, CO2 production, obesity, oxygen consumption, respiratory quotient |
| C1044 | DietMax Meal Pattern Analysis | food intake, meal pattern |

UNIVERSITY OF MASSACHUSETTS MEDICAL SCHOOL

Metabolism Core

Director: Jason Kim, Co-Director: Dae Young Jung

The Metabolism Core conducts non-invasive, in vivo, and physiological experiments to identify metabolic phenotypes in awake mice. The Core services are highlighted by hyperinsulinemic-euglycemic clamps to measure insulin sensitivity and glucose metabolism, hyperglycemic clamps to assess pancreatic β -cell function, ^3H -MRS to determine body composition, and metabolic cage analysis to examine food intake, physical activity, and energy expenditure.

| Test No. | Test Name | Keywords |
|----------|-----------------------------------|--|
| M1001 | Hyperinsulinemic-euglycemic clamp | glucose metabolism, insulin action, insulin resistance |
| M1002 | Basal glucose metabolism | glucose turnover |
| M1003 | Organ-specific glucose uptake | glucose uptake |

| Test No. | Test Name | Keywords |
|----------|---|--|
| M1004 | Hyperglycemic clamp | beta cell, insulin secretion, pancreas |
| M1005 | Insulin clearance | insulin |
| M1006 | Glucose tolerance test | glucose clearance, glucose tolerance |
| M1007 | Glucose tolerance test with insulin secretion | glucose tolerance, insulin |
| M1008 | Insulin tolerance test | insulin sensitivity |
| M1009 | Hepatic gluconeogenesis | pyruvate tolerance test |
| M1010 | Lipid metabolism | palmitate, triglycerides |
| M1011 | Protein metabolism | phenylalanine, protein synthesis |
| M1012 | Body composition (whole body) | fat mass, lean muscle mass, obesity |
| M1013 | Body composition (organs) | fat mass, lean muscle mass, obesity |
| M1014 | Energy balance – food intake, energy expenditure, physical activity | indirect calorimetry, metabolism |
| M1015 | Chronic high-fat feeding | diet-induced obesity, high-fat diet, obesity |
| M1016 | Chronic drug delivery | infusion, osmotic pump |
| M1017 | STZ-induced type 1 diabetes model | hyperglycemia, streptozotocin, type 1 diabetes |
| M1018 | Acute lipid infusion | fatty acids, lipids |
| M1019 | Chronic/acute phloridzin treatment | glucose clearance, renal |
| M1020 | Exercise model | Activity, Cage Activity, exercise |
| M1021 | Surgery – jugular vein cannulation | surgery |
| M1022 | M1022 Surgery – tail vein injection | surgery |
| M1023 | Surgery – carotid artery cannulation | surgery |
| M2002 | Hemoglobin A1c | diabetes, glucose, hyperglycemia, metabolite |

Analytical Core

Director: David Harlan, Co-Director: Randall Friedline, Co-Director: Klaus Pechold

The Analytical Core utilizes high-throughput instrumentations to provide standardized measurements of hormones, metabolites, and cytokines in serum/tissue samples obtained from mice. Leading expertise in islet biology offers histological and molecular analysis of pancreatic islet cells.

| Test No. | Test Name | Keywords |
|----------|----------------------------|--|
| M2001 | Glucose | diabetes, glucose, hyperglycemia, hypoglycemia, metabolite |
| M2003 | Lactate | diabetes, glucose, metabolite |
| M2004 | Insulin | diabetes, hormone, hyperinsulinemic clamp, insulin, pancreas |
| M2005 | C-peptide | hormone, insulin, insulin secretion, pancreas |
| M2006 | Glucagon | glucose, hepatic, hormone, pancreas |
| M2007 | Leptin | adipokine, feeding behavior, hormone |
| M2008 | Adiponectin | adipokine, hormone, insulin resistance |
| M2009 | Resistin | adipokine, hormone, insulin resistance |
| M2010 | Triglyceride | lipids, metabolite, obesity |
| M2011 | Non-esterified fatty acids | insulin resistance, lipids, metabolite, obesity |

| Test No. | Test Name | Keywords |
|----------|--------------------------------|--|
| M2012 | Cholesterol (total) | atherosclerosis, lipids, liver, metabolite, obesity |
| M2013 | Cholesterol (HDL) | atherosclerosis, lipids, liver, metabolite, obesity |
| M2014 | Cholesterol (LDL) | atherosclerosis, lipids, liver, metabolite, obesity |
| M2015 | Ammonia | lipids, metabolite |
| M2016 | Lipase | lipids, metabolite, obesity |
| M2017 | Amylase | enzyme activity |
| M2018 | Creatine kinase | enzyme activity |
| M2019 | Alkaline phosphatase | enzyme activity |
| M2020 | Lactate dehydrogenase | enzyme activity |
| M2021 | Albumin | liver, metabolite |
| M2022 | Alanine transferase | liver, metabolite |
| M2023 | Aspartate transferase | liver, metabolite |
| M2024 | Bilirubin | liver, metabolite |
| M2025 | Gamma-glutamyl Transferase | liver, metabolite |
| M2026 | Creatinine | kidney, metabolite |
| M2027 | C-reactive peptide | inflammation, liver, metabolite |
| M2028 | Total protein | metabolite |
| M2029 | Urea/BUN | kidney, metabolite |
| M2030 | Uric acid | kidney, metabolite |
| M2031 | Electrolytes | electrolyte panel |
| M2032 | Cytokines Panel I - multiplex | chemokines, complications, cytokines, diabetes, inflammation, insulin resistance, monokines, obesity |
| M2033 | Cytokines Panel II - multiplex | chemokines, complications, cytokines, diabetes, inflammation, insulin resistance, monokines, obesity |
| M2034 | Islet histology | beta cell, diabetes, insulin |
| M2035 | Molecular islet analysis | beta cell, diabetes, insulin |

VANDERBILT UNIVERSITY SCHOOL OF MEDICINE

Metabolic Pathophysiology Core

Director: Owen McGuinness, Co-Director: Li Kang, Associate Director: Kate Ellacott, Personnel: Emily Born

The Metabolic Pathophysiology conducts these major tests: vein/artery cannulations, glucose and insulin clamps, glucose tolerance test, tissue specific glucose/fatty acid uptake, calorimetry, exercise, gluconeogenesis/glycogenolysis, body composition, food consumption, optical imaging of gene expression/cellular events, isolation of pancreatic islets /insulin secretion.

| Test No. | Test Name | Keywords |
|----------|---|--------------------------------|
| V3001 | Cannulation of cerebral ventricle | brain, central control, CSF |
| V3002 | Jugular vein and carotid artery catheterization | blood vessel, chronic, surgery |

| Test No. | Test Name | Keywords |
|----------|--|--|
| V3003 | Glucose Tolerance Test (Oral and Intravenous) | glucose intolerance, glucose tolerance, insulin action |
| V3004 | Glucose turnover | endogenous glucose production, glucose flux, glucose kinetics, glucose turnover, isotopes, tracers |
| V3005 | Hyperinsulinemic clamp | hyperinsulinemic clamp, insulin action, insulin resistance |
| V3006 | Hyperglycemic clamp | hyperglycemic clamp, insulin secretion, pancreas |
| V3007 | Gluconeogenesis & glycogenolysis (from hepatic 14C-UDPglucose and PEP) | gluconeogenesis, glucose production, glycogenolysis, liver |
| V3008 | Glycogen synthesis | glycogen synthesis, liver, muscle |
| V3009 | Amino acid kinetics | amino acid flux, amino acid kinetics, isotopes |
| V3010 | Tissue specific glucose uptake | 2-deoxyglucose, glucose metabolic index, tissue specific glucose uptake |
| V3011 | Tissue specific fatty acid uptake | 125I-BMIPP, tissue specific fatty acid uptake |
| V3012 | Indirect calorimetry /energy expenditure | carbon dioxide, energy expenditure, gas exchange, indirect calorimetry, oxygen |
| V3013 | Exercise capacity (metabolic response to exercise) | endurance, exercise capacity, exercise tolerance |
| V3014 | Spontaneous exercise activity | spontaneous exercise activity, wheel running |
| V3015 | Food Consumption | spontaneous exercise activity, wheel running |
| V3016 | Exploratory locomotor activity | energy expenditure, exploratory locomotor activity |
| V3017 | Assess real time imaging of cellular metabolic events | islets, metabolism, microcirculation, muscle, real time imaging |
| V3018 | In vivo optical imaging of gene expression | gene expression, GFP, luciferase |
| V3000A | Miscellaneous Tissue and Body Fluid Collection | tissue |
| V3000B | Miscellaneous Implantation of Catheters, Sensors and Pellets | catheterization |
| V3000C | Equipment Usage | |
| V3000D | Personnel Training | |
| V3000E | Cerebral Ventricle Cannulation | cerebral ventricle |
| V3000F | Jugular Vein and Carotid Artery Catheterization | catheterization |

Cardiovascular Pathophysiology & Complications Core

Director: Douglas Vaughan, Associate Director: Jeff Rottman

The Cardiovascular Pathophysiology and Complications Core conducts these major tests: morphology and histology, echocardiography, electrocardiography, blood pressure, vascular morphology, renal function, metabolic panel in state-of-the-art facilities.

| Test No. | Test Name | Keywords |
|----------|---|--|
| V3030 | In vitro Morphology, Morphometrics and Histology (isolated heart) | cardiac function, heart, morphology |
| V3031 | Echocardiography, in vivo morphology, systolic | diastolic, echocardiography, morphology, |

| Test No. | Test Name | Keywords |
|----------|--|---|
| | and diastolic function; Stress echocardiography | stress, systolic |
| V3032 | Electrocardiography and telemetry | cardiac, ECG, EKG, electrocardiography, heart, telemetry |
| V3033 | Blood pressure measurements | blood pressure, blood vessel, hypertension, hypotension, vascular |
| V3034 | Vascular morphology | blood vessel, histology, intima, smooth muscle, vascular |
| V3035 | Electrolytes, indices of renal function | |
| V3036 | Metabolic panel | |
| V3094 | Perfusion-Fixation/Heart Dimension | |
| V3095 | Heart Rate Open Variability | |
| V3096 | Ventricular Hemodynamics | |
| V3097 | Perfusion-Fixation/Histopathology/Quantify Sclerosis | |
| V3098 | GFR-FITC-Inulin; HPLC Cr | glomerular filtration, HPLC, kidney |
| V3099 | Albuminuria | kidney, urine |
| V4000 | Renal Blood Flow (Doppler) | blood flow, blood pressure, kidney |
| V4001 | Urine Na/K | plasma, potassium, sodium, urine |
| V4002 | Osmometer Plasma/Urine | osmolality, plasma, urine |
| V4003 | Urine Ca/Phosphorus Excretion | urine |
| V4004 | Urine pH | pH, urine |
| V4005 | Glycemic Control using Minimed | glucose |

Analytical Resources Core

Director: Sergio Fazio

The Analytical Resources Core performs these major tests: plasma hormones, amino acids, lipids and lipoproteins, pathology and immunohistochemistry.

| Test No. | Test Name | Keywords |
|----------|---|-------------------|
| V3090 | Full amino acid profiles by HPLC / PITC or HLPC / OPA | amino acids, HPLC |
| V3050 | Insulin | hormone |
| V3051 | Glucagon | hormone |
| V3052 | Corticosterone | hormone |
| V3053 | Catecholamines | hormone |
| V3054 | Leptin | hormone |
| V3055 | C-Peptide | hormone |
| V3056 | Growth Hormone (GH) | hormone |
| V3058 | TSH | hormone |
| V3059 | PRL | hormone |
| V3060 | ACTH | hormone |
| V3061 | Insulin-like growth hormone-1 (IGF-1) | hormone |

| Test No. | Test Name | Keywords |
|----------|--|--|
| V3070 | Plasma lipids | fat, lipids, metabolism |
| V3071 | Lipid extraction, separation, quantitation | fat, lipids, metabolism |
| V3072 | Fatty acid profiles of lipid esters by gas liquid chromatography | fat, GCMS, lipids, metabolism |
| V3073 | Quantitation of individual phospholipid classes | cholesterol, fat, lipids, metabolism, phospholipids |
| V3074 | Short chain fatty acid analysis by gas liquid chromatography | fat, GCMS, lipids, metabolism, short chain fatty acid |
| V3075 | Lipoprotein fractionation and characterization | fat, lipids, lipoproteins, metabolism |
| V3076 | Morphometric determinations (aorta) | blood vessel, histology, intima, smooth muscle, vascular |
| V3080 | Gross examinations and necropsy | gross examination, necropsy |
| V3081 | Tissue preparation, embedding, sectioning and routine staining | embedding, sectioning, staining, tissue preparation |
| V3082 | Tissue microdissection | laser microdissection, pancreas |
| V3083 | Screen/optimize immunohistochemical protocols for mouse-specific commercial and custom-designed antisera | histology, immunohistochemistry |
| V3091 | Specific selected amino acid profiles | amino acids, HPLC |
| V3092 | Radioactivity of specific individual amino acids | amino acids, chromatography, protein synthesis, proteolysis, specific activity |
| V3093 | Specific activities for gluconeogenic and glycogenic assessment | amino acids, chromatography, protein synthesis, proteolysis, specific activity |
| V3062 | Aldosterone | hormone |
| V3064 | Resistin | hormone |
| V3065 | Adiponectin | hormone |
| V3066 | Estradiol | hormone |
| V3067 | Testosterone | hormone |

YALE UNIVERSITY SCHOOL OF MEDICINE

In Vivo Metabolism Core

Director: Michael Jurczak, Co-Director: Cheol Soo Choi, Personnel: David Frederick, Personnel: Andreas Birkenfeld, Personnel: Lara Thomas

The In Vivo Metabolism Core at the Yale Mouse Metabolic Phenotyping Center is designed to conduct in vivo experiments and analytical assays to characterize the metabolic phenotype of transgenic/knockout mouse models potentially useful for understanding diabetes, its complications, obesity, and related metabolic disorders.

| Test No. | Test Name | Keywords |
|----------|---|------------------------------------|
| Y4001 | Hyperinsulinemic-euglycemic clamp experiments | insulin action, insulin resistance |
| Y4002 | Hyperglycemic clamp experiments | insulin secretion, pancreas |

Analytical Core

Director: Gary Cline, Personnel: Mario Kahn, Personnel: Xian-Man Zhang, Personnel: Lara Thomas

Metabolic phenotyping of transgenic mice requires the ability to determine whole body, tissue specific, and cellular metabolic fluxes, and to delineate cellular mechanisms of signal transduction. The Analytical Core provides the expertise, technical resources, and instrumentation necessary to characterize perturbations in metabolism in transgenic mice strains, and serves as a resource lab for the analysis of samples generated during the course of experiments undertaken by the in vivo, in vitro, and NMR cores.

| Test No. | Test Name | Keywords |
|----------|----------------------------------|---|
| Y4060 | Diacylglycerol concentration | fat, lipids, metabolism, signaling |
| Y4050 | Amino Acids | amino acids, enrichment, isotopes, metabolite |
| Y4051 | Beta-hydroxybutyrate | diabetes, enrichment, ketones, metabolite |
| Y4052 | Free fatty acid | diabetes, enrichment, fat, lipids, metabolite |
| Y4053 | Glucose | carbohydrate, diabetes, metabolite |
| Y4054 | Glycerol | diabetes, enrichment, lipids, metabolite |
| Y4055 | Glycogen | carbohydrate, diabetes, metabolite |
| Y4057 | Long-chain fatty acyl CoA esters | fat, lipids, metabolism |
| Y4059 | ADP, ATP | energetics, high-energy phosphates, mitochondria |
| Y4070 | Chem 7 | serum chemicals, serum metabolic panel |
| Y4071 | Liver Function Tests | serum chemicals, serum metabolic panel |
| Y4072 | Lipid Panel | serum chemicals, serum metabolic panel |
| Y4073 | Divalent Ions | serum chemicals |
| Y4080 | Insulin | hormone |
| Y4081 | Glucagon | hormone |
| Y4082 | Leptin | hormone |
| Y4061 | Lysophosphatidic Acid | lipids |
| Y4083 | Blood Glucose | carbohydrate, diabetes, glucose, plasma, serum chemicals, serum metabolic panel |
| Y4084 | Blood Urea Nitrogen | renal, serum chemicals, serum metabolic panel |
| Y4085 | Blood Creatinine-HPLC | kidney, muscle, renal, serum chemicals, serum metabolic panel |
| Y4086 | Urine Creatinine-HPLC | kidney, muscle, renal, serum chemicals, serum metabolic panel, urine |
| Y4087 | Blood Electrolytes-Na/Cl/K | electrolytes, metabolism, muscle, pH, plasma, potassium, serum chemicals, serum metabolic panel, sodium |
| Y4089 | Blood Bicarbonate/CO2 | carbon dioxide, metabolism, serum chemicals, serum metabolic panel |
| Y4091 | Blood Albumin | liver, plasma, serum albumin, serum chemicals |
| Y4092 | Alanine Aminotransferase | ALT, liver, plasma, serum chemicals |
| Y4093 | Aspartate Aminotransferase | liver, plasma, serum chemicals |
| Y4094 | Alkaline Phosphatase | liver, plasma, serum chemicals |
| Y4095 | Total Bilirubin | bilirubin, liver, serum chemicals |
| Y4097 | Total Protein | liver, plasma, serum chemicals |
| Y4098 | HDL Cholesterol | cholesterol, lipids, lipoproteins |
| Y4099 | LDL Cholesterol | cholesterol, lipids, plasma, serum chemicals |

| Test No. | Test Name | Keywords |
|----------|------------------------------|---|
| Y5000 | Cholesterol | cholesterol, lipids, plasma, serum chemicals |
| Y5001 | Triglycerides | lipids, plasma, serum chemicals |
| Y5002 | Non-Esterified Fatty Acids | fatty acids, lipids, non-esterified fatty acid, serum chemicals |
| Y5003 | Beta-Hydroxybutyrate (COBAS) | diabetes, ketones, plasma, serum chemicals |
| Y5004 | Blood or Urine Calcium | serum chemicals |
| Y5005 | Blood Inorganic Phosphorous | inorganic phosphate, phosphate, serum chemicals |
| Y5007 | Magnesium | serum chemicals |
| Y5006 | Urine Inorganic Phosphorous | inorganic phosphate, phosphate, urine |
| Y5008 | Creatine Kinase | creatine kinase, serum chemicals |
| Y5009 | Lactate Dehydrogenase | serum chemicals |
| Y5010 | Apolipoprotein C3 | lipids, lipoproteins, serum chemicals |
| Y4088 | Urine Electrolytes-Na/K/Cl | electrolytes, muscle, potassium, urine |

Test Descriptions by Center

CASE WESTERN RESERVE UNIVERSITY

Analytical Core

CA2011 Total Energy expenditure using doubly-labeled water

Keywords: energy expenditure, water

TEE is equal to the sum of basal metabolic metabolic, thermic effect of eating and physical activity. Following a single bolus injection of 2H and 18O-labeled water one can determine TEE via the elimination of 2H and 18O from body water. This test requires serial measurements of the labeling of body water over approximately 1 week, which necessitates the collection of blood or urine samples.

Note: This test does not require catheterized mice, nor does it require that mice be shipped to the MMPC. The isotopes are non-radioactive and no special safety precautions are required, the tracers will be shipped from the MMPC to the investigator. Investigators will be instructed on how to administer the isotopes, collect samples and then ship them back to the MMPC.

CA2015 Turnover of glucose, lipid and/or protein

Keywords:

During a constant tracer infusion, the dilution of the infused tracer yields a measure of that molecule's rate of appearance. One can measure the turnover of numerous molecules using this strategy. One can determine the kinetics glucose, glycerol and protein using [6,6-2H₂]glucose, [2H₅]glycerol and [2H₅]phenylalanine.

This test requires a catheterized animal.

CA2016 Fatty acid and cholesterol synthesis using 2H-labeled water

Keywords:

Rates of fatty acid and cholesterol synthesis can be determined in tissues via the incorporation of 2H or 13C-labeled precursors. For example, following a bolus injection of 2H-labeled water one can collect samples (e.g. blood, liver and/or adipose tissue). The respective lipids are isolated and their 2H-labeling is determined. This test can be performed in 2 modes, short term vs long term. In a short term study, the tracer is administered and samples are collected within hours to determine the synthesis of lipids in plasma and/or liver. In a long term study, the tracer is continuously administered over several days. Samples of adipose tissue are collected. The difference in time scale is necessary since the pool of lipids in adipose tissue is relatively large and requires more time for label to appear.

Note: This test does not require catheterized mice, nor does it require that mice be shipped to the MMPC. The isotopes are non-radioactive and no special safety precautions are required, the tracers will be shipped from the MMPC to the investigator. Investigators will be instructed on how to administer the isotopes, collect samples and then ship them back to the MMPC.

CA2017 Tissue-specific protein synthesis using 2H-labeled water

Keywords: amino acids, metabolism, protein synthesis

Rates of protein synthesis can be determined from the incorporation of 2H-labeled water. For example, following a bolus injection of 2H-labeled water one can collect samples (e.g. blood, liver, muscle, etc). Total proteins are isolated and their 2H-labeling is determined. This test can be performed in 2 modes, short term vs long term. In a short term study, the tracer is administered and samples are collected within hours to determine the synthesis of proteins in plasma, liver, etc. This mode is well-suited for examining the acute response of protein synthesis to a perturbation (e.g. food intake). In a long term study, the tracer is continuously administered over several days. Samples are collected and the assays are performed. The long term design yields an integrative measure of protein synthesis, i.e. the isotope is present during the fed and the fasted state and accounts for all protein synthesis over such a transition.

Note: This test does not require catheterized mice, nor does it require that mice be shipped to the MMPC. The isotopes are non-radioactive and no special safety precautions are required, the tracers will be shipped from the MMPC to the investigator. Investigators will be instructed on how to administer the isotopes, collect samples and then ship them back to the MMPC.

CA2018 Profile of acylcarnitines in plasma/urine or tissue samples

Keywords:

These LC-MS-MS assays are routinely run in which acylcarnitines are identified as C_x, where x is the number of carbons in the acyl group. Samples are spiked with unlabeled and labeled internal standards. The mass isotopomer distribution of each peak is determined to characterize its labeling pattern.

This test, coupled with the assay of the profile of urinary organic acids helps in the characterization of a number of metabolic defects, such as inborn errors of fatty acid oxidation disorders.

CA2019 Profile of long chain acyl-CoAs in tissue

Keywords:

Commercial preparations of CoA and acyl-CoA contain an unnatural analog of CoA, iso-CoA, in which the 3' phosphate has been moved to the 2' position of ribose. We can use the acyl-iso-CoA esters as internal standards to calculate the concentration and mass isotopomer distribution of acyl-CoAs from LC-MS data.

CA2020 Measurement of acetyl-CoA, propionyl-CoA and/or succinyl-CoA in tissue

Keywords:

Commercial preparations of CoA and acyl-CoA contain an unnatural analog of CoA, iso-CoA, in which the 3' phosphate has been moved to the 2' position of ribose. We can use the acyl-iso-CoA esters as internal standards to calculate the concentration and mass isotopomer distribution of acyl-CoAs from LC-MS data.

CA2022 ¹³C-Labeling pattern of acetyl moiety of citrate (substrate oxidation)

Keywords:

A number of investigators, who use ¹³C-labeled precursors of acetyl-CoA -in vivo- in isolated organs or in cell incubations, have attempted to estimate the labeling of mitochondrial acetyl-CoA to calculate the contribution of the substrate to the acetyl-CoA oxidized in the citric acid cycle (CAC). The best proxy for mitochondrial acetyl-CoA is the acetyl moiety of citrate.

We developed an assay of the labeling of the acetyl moiety of citrate which involves (i) tissue extraction, (ii) alkaline hydrolysis of extant acetyl-CoA, (iii) after pH adjustment, cleavage of citrate with CoA + ATP-citrate lyase which we isolated from rat liver.

The acetyl-CoA formed is either assayed as such by LC-MS, or reacted with thiophenol, followed by GC-MS assay of acetylthiophenol. This assay allows one to calculate the contribution of two or three substrates to mitochondrial acetyl-CoA in the same experiment.

For example, consider a mouse heart perfused with unlabeled glucose + [1-¹³C]palmitate + [U-¹³C₄]acetoacetate.

These substrates yield acetyl-CoA that is unlabeled (M), singly labeled (M₁), or doubly labeled (M₂), respectively. So, the percent abundances of the M, M₁, and M₂ mass isotopomers of the acetyl moiety of citrate yield the contribution of each of the substrates to mitochondrial energy production.

CA2024 Metabolomic profile of citric acid cycle and gluconeogenic intermediates

Keywords:

We will assay the relative concentration of citric acid cycle intermediates and those in the gluconeogenic pathway. Assays can be run using samples from mice/organs that have also been infused with a ¹³C-labeled tracer, e.g. ¹³C-lactate. This strategy allows one to determine flux rates (via the ¹³C-labeling patterns) and identify points of control of a pathway, e.g. gluconeogenesis (via the relative concentration profiles).

CA2041 Tissue processing by Pathology Core

Keywords: histology, tissue preparation

Tissue processing by Pathology Core (embedded in paraffin)

CA2042 Plasma panel Triglycerides, CHOL, β-OH, NEFA (Marshfield labs)

Keywords: histology, staining, tissue preparation

Plasma panel Triglycerides, CHOL, β-OH, NEFA (Marshfield labs)

CA2043 Portal vein injection and tissue collection (at 0 min. & 5 min.)

Keywords: tissue preparation

Portal vein injection and tissue collection (at 0 min. & 5 min.)

CA2044 Brain uptake and blood flow

Keywords: blood flow, brain

Brain uptake and blood flow

CA2045 Measurement of ATP/ADP

Keywords: ATP, tissue

ATP tissue concentrations will be analyzed enzymatically from 25-30 mg of tissue and reported as nmol/mg wet tissue weight.

CA2016A Measurement of 2H-enrichment of a body fluid

Keywords:

Measurement of 2H-enrichment of a body fluid

CA2024CT Custom Designed Tracer Experiment

Keywords:

Custom Designed Tracer Experiment

CA2046 Indirect Calorimetry : First 36-hr measurement (for 8 mice)

Keywords:

Both total energy expenditure and relative rates of carbohydrate versus fat oxidation will be determined via indirect calorimetry measured by CO₂ production in specially designed chambers for mice.

CA2047 Treadmill Training/Endurance Study PLUS Indirect Calorimetry (for 8 mice)

Keywords:

Both total energy expenditure and relative rates of carbohydrate versus fat oxidation will be determined via indirect calorimetry measured by CO₂ production in specially designed treadmill chambers for mice.

CA2048 Whole Body Fixation (PFA)+ Tissue Collection

Keywords:

CA2049 Additional 24-hr measurement (for 8 mice)

Keywords:

Additional 24-hr measurement (for 8 mice)

CA2050 Data summary Interpretation

Keywords:

Data summary Interpretation

CA2051 Excise Tissues, Blood Serum/Plasma

Keywords:

Excise Tissues, Blood Serum/Plasma

CA2052 Isolated mouse HEART perfusion

Keywords: heart

Isolated mouse HEART perfusion

CA2053 Isolated mouse LIVER perfusion

Keywords: liver

Isolated mouse LIVER perfusion

CA2053B Custom Designed Biological Experiment

Keywords:

Custom Designed Biological Experiment

CA2055 Quarantine (4 weeks) mice imported to Case

Keywords:

Quarantine (4 weeks) mice imported to Case

CA2056 Housing mice 1 to 14 days

Keywords:

Housing mice 1 to 14 days

Metabolic Core

CA2000 Body composition using 2H-labeled water

Keywords: body composition, body weight, fat

The body is composed of 2 major compartments, fat and fat-free mass. Fat-free mass consists of water, inorganic matter (e.g. minerals) and organic matter (e.g. protein, DNA). One can determine total body water via the initial dilution of 2H-labeled water. Fat mass can be calculated assuming a constant relationship between water and inorganic and organic matter in fat-free mass.

This test requires a single injection of 2H-labeled water and the collection of 1 blood sample 2.5 hours post-injection.

Note: This test does not require catheterized mice, nor does it require that mice be shipped to the MMPC. The isotopes are non-radioactive and no special safety precautions are required, the tracers will be shipped from the MMPC to the investigator. Investigators will be instructed on how to administer the isotopes, collect samples and then ship them back to the MMPC.

CA2001 Food Consumption

Keywords: food intake

CA2002 Body Weight

Keywords: body composition, body weight, food intake

CA2003 Measurement of body temperature (by probe)

Keywords: energy expenditure, exercise

Body temperature will be measured by anal probe for a short period of time. This can be done at room temperature or under cold challenge conditions.

CA2004 Glucose tolerance tests (GTT)

Keywords: carbohydrate metabolism, diabetes, glucose

Mice will be fasted for 5 hours. A fasting blood sample will be removed from the tail vein and a concentrated solution of glucose injected into the abdominal cavity of the mice through a needle passed through the abdominal skin. Blood samples (~ 5ul) will be removed from the tail vein 15, 30, 60 and 120 minutes later and glucose will be measured by

glucometer.

CA2005 Insulin concentrations at fasting and post intraperitoneal glucose administration

Keywords: insulin, insulin secretion

Mice will be fasted for 5 hours. A fasting blood sample will be removed from the tail vein and a concentrated solution of glucose injected into the abdominal cavity of the mice through a needle passed through the abdominal skin. Thirty minutes later, another blood sample will be taken. Insulin in plasma at time 0 and 30 min will be measured by ELISA (CA2006).

CA2006 Plasma insulin measurement by ELISA

Keywords: carbohydrate metabolism, insulin, insulin action

We will measure insulin concentration in plasma from mice (~25ul/mouse in duplicate) by commercially available ELISA.

CA2007 Insulin concentrations at fasting and post intraperitoneal insulin administration

Keywords:

Insulin concentrations at fasting and post intraperitoneal insulin administration.

CA2008 Glucose concentrations at fasting and post intraperitoneal insulin administration - insulin tolerance test (ITT)

Keywords: carbohydrate metabolism, diabetes, insulin sensitivity

Mice will be fasted for 5 hours and anesthetized. A fasting blood sample will be removed from the tail vein and insulin (0.5mU/g) will be injected into the abdominal cavity. Blood samples will be removed from the tail vein 15, 30, 45 and 60 minutes later. Samples of plasma obtained during the test will be measured for concentrations of glucose and insulin.

CA2009 Triglycerides in liver

Keywords: lipids, liver

A small piece of liver tissue will be homogenized and liver triglycerides will be saponified in KOH. Glycerol will be measured against glycerol standards using a commercially available reagent set.

CA2010 Plasma triglycerides

Keywords: plasma

Plasma triglycerides will be saponified in KOH. Glycerol will be measured against glycerol standards using a commercially available reagent set.

CA2013 Hyperinsulinemic Clamp (Hypoglycemic or Euglycemic) using stable isotopes

Keywords:

The euglycemic-hyperinsulinemic clamp is used to investigate insulin action and glucose metabolism in the intact, conscious mouse. The use of different glucose or glucose analog tracers with the option of using dual tracers (3-H or 14-C labeled) allows the determination of tissue-specific glucose uptake in addition to whole body glucose production and disposal. We can also use stable isotopes for the glucose clamp studies

A chronic indwelling catheter is surgically implanted into the right jugular vein of the mouse. After a minimum of 4 days recovery, the mice are fasted the morning of the experiment. The 120 minute protocol begins with a prime-continuous infusion of glucose tracer and a prime-continuous infusion of insulin, at a rate dependant on the goals and conditions of the experiment. Glucose is infused at a rate that maintains euglycemia and is a measure of insulin sensitivity. Tissues can be collected at the conclusion of the clamp for later assessment of tissue-specific glucose uptake as well as other biochemical assays as desired.

CA2025 Chronic arterial and jugular vein catheterization

Keywords: catheterization, surgery

Chronic arterial and jugular vein catheterization

CA2026 Chronic arterial or jugular vein catheterization

Keywords: catheterization, surgery

Chronic arterial or jugular vein catheterization

CA2027 Acute arterial and jugular vein catheterization

Keywords: catheterization, surgery

Acute arterial and jugular vein catheterization

CA2028 Acute arterial or jugular vein catheterization

Keywords: catheterization, surgery

Acute arterial or jugular vein catheterization

CA2029 Acute portal vein catheterization

Keywords: catheterization, surgery

Acute portal vein catheterization

CA2030 Implant [G2 E – Mitters™]

Keywords: surgery

Implant [G2 E – Mitters™]

CA2031 Long-term analysis of surgery implantation on Min-Mitter™

Keywords: surgery

Long-term analysis of surgery implantation on Min-Mitter™

CA2040 Metabolomic profile of Free Fatty Acids/sterols in Plasma, Urine or Tissue

Keywords: fatty acids, metabolism, tissue

Metabolomic profile of free fatty acids in tissue

UNIVERSITY OF CALIFORNIA DAVIS

Animal Care Core

D2001 Importation of Mice and Material

Keywords: animal husbandry, mouse models

Assume 10 experimental mice {5M, 5F} and 10 WT controls {5M, 5F}

Importation of 1 crate of mice

D2002 Per Diem (4 cages/line X 14 days)

Keywords: animal husbandry

Assume 10 experimental mice {5M, 5F} and 10 wt controls {5M, 5F}

Husbandry for 56 total days

D2003 Colony Management (if needed)

Keywords: animal husbandry

Assume 10 experimental mice {5M, 5F} and 10 wt controls {5M, 5F}

Colony management per cage day of mice

D2004 Genotyping (if needed)

Keywords: genotyping, mouse models

Assume 10 experimental mice {5M, 5F} and 10 wt controls {5M, 5F}

PCR-based genotyping to confirm mouse identification

D2005 Mouse Model Purchase

Keywords: animal husbandry, mouse models

Access mutant mouse models from the MMRRC or the KOMP Repositories and submit to MMPC for phenotyping

D2006 Mouse Model Creation

Keywords: animal husbandry, mouse models

Create mutant mouse models de novo and submit to MMPC for phenotyping

Metabolism and Endocrinology Core

D3101 Intravenous Glucose Tolerance Test

Keywords: diabetes, insulin, insulin action, insulin secretion

Assessment of insulin sensitivity, glucose tolerance, and insulin secretion in vivo.

Price include insulin/glucose assay costs.

Mice from an inbred strain with low inter-animal variability in insulin sensitivity will be run with each group of animals undergoing the IVGTTs/clamps as an internal standard.

D3102 Hyperinsulinemic, Euglycemic Clamp

Keywords: diabetes, hyperinsulinemic clamp, insulin, insulin action

Determine hepatic glucose production and insulin mediated glucose disposal

Prices include insulin/glucose assay costs.

Mice from an inbred strain with low inter-animal variability in insulin sensitivity will be run with each group of animals undergoing the IVGTTs/clamps as an internal standard.

D3103 IN VIVO Insulin Tolerance Tests

Keywords: diabetes, insulin, insulin action

Mice will be injected IP with 1mU/g of insulin. Samples will be collected at 0,15,30,45,60,90,120 min for the measurement of glucose. Plumpton, 1969

Includes housing, surgery, biochemical assays to measure glucose/insulin level.

Mice from an inbred strain with low inter-animal variability will be run with each group of animals undergoing the same procedure

D3104 IN VIVO Glucose Tolerance Tests

Keywords: diabetes, glucose, glucose metabolism, glucose tolerance

Mice will be injected IP with 2mg/g of glucose. Samples will be collected at 0,15,30,60,120 min for the measurement of glucose.

Includes housing, surgery, biochemical assays to measure glucose/insulin level.

Mice from an inbred strain with low inter-animal variability will be run with each group of animals undergoing the same procedure.

D3105 IN VIVO Glucose-stimulates Insulin Secretion Test

Keywords: diabetes, glucose, glucose metabolism, insulin, insulin action

Mice will be injected IP with 2mg/g of glucose. Samples will be collected at 0,2,5,15,30 min for the measurement of glucose and insulin.

Includes housing, surgery, biochemical assays to measure glucose/insulin level.

Mice from an inbred strain with low inter-animal variability will be run with each group of animals undergoing the same procedure

D3106 Positron emission tomography (microPET)

Keywords: diabetes, glucose, glucose metabolism, imaging

Noninvasive longitudinal analysis of changes in glucose metabolism.

Mice from an inbred strain with low inter-animal variability will be run with each group of animals undergoing the same procedure.

D3201 Adipocyte metabolism/hormone production - Isolation/cell size/#

Keywords: hormone, insulin, insulin action, lipid extraction, lipids

Adipocyte hypertrophy, adipocyte insulin insensitivity, and FFA release are important factors in the onset and progression of insulin resistance. Adipocyte metabolism and hormone secretion are determinants of whole body energy homeostasis and insulin action.

Adipocytes will be isolated by collagenase digestion according to the method of Rodbell as modified (Mueller et al, Endocrinology, 1998). Adipocytes will be maintained in culture for 96 h to assess metabolism and hormone secretion.

D3202 Adipocyte metabolism/hormone production - 96h culture/glucose utilization/lactate production

Keywords: hormone, insulin, insulin action

Adipocyte hypertrophy, adipocyte insulin insensitivity, and FFA release are important factors in the onset and progression of insulin resistance. Adipocyte metabolism and hormone secretion are determinants of whole body energy homeostasis and insulin action.

Measured enzymatically with a YSI analyzer

D3203 Adipocyte metabolism/hormone production - leptin secretion at 96 hour

Keywords: hormone, leptin, leptin measurement

Adipocyte hypertrophy, adipocyte insulin insensitivity, and FFA release are important factors in the onset and progression of insulin resistance. Adipocyte metabolism and hormone secretion are determinants of whole body energy homeostasis and insulin action.

Determine leptin concentrations in culture media with Millipore RIA

D3204 Adipocyte metabolism/hormone production - adiponectin secretion at 96 hour

Keywords: adiponectin

Adipocyte hypertrophy, adipocyte insulin insensitivity, and FFA release are important factors in the onset and progression of insulin resistance. Adipocyte metabolism and hormone secretion are determinants of whole body energy homeostasis and insulin action.

Determine adiponectin concentrations in media with B Bridge ELISA

D3205 Adipocyte metabolism/hormone production - lipolysis (glycerol baseline and 96h)

Keywords: glycerol, lipid extraction, lipids

Adipocyte hypertrophy, adipocyte insulin insensitivity, and FFA release are important factors in the onset and progression of insulin resistance. Adipocyte metabolism and hormone secretion are determinants of whole body energy homeostasis and insulin action.

Determine glycerol concentrations in media with with Analox GM17 instrument

D3206 Adipocyte metabolism/hormone production - lipogenesis from labeled glucose

Keywords: adipose, glucose, glucose turnover, triglycerides

Adipocyte hypertrophy, adipocyte insulin insensitivity, and FFA release are important factors in the onset and progression of insulin resistance. Adipocyte metabolism and hormone secretion are determinants of whole body energy homeostasis and insulin action.

Measured as ¹⁴C-labeled glucose carbon incorporation into the triglyceride fraction of adipocytes

D3207 Adipocyte metabolism/hormone production - glucose/FA oxidation from labeled glucose/FA

Keywords: glucose, hormone

Adipocyte hypertrophy, adipocyte insulin insensitivity, and FFA release are important factors in the onset and progression of insulin resistance. Adipocyte metabolism and hormone secretion are determinants of whole body energy homeostasis and insulin action.

Measured as ¹⁴C release into CO₂ captured in whatcom paper containing vials.

D3250 In vitro pancreatic islet insulin secretion

Keywords: insulin, insulin secretion

Measures islet insulin secretion independent of neural signals and incretin hormones.

Measure insulin secretion levels in cultured Min6 cells

D3301 Lipid extraction from liver or muscle - Tissue Cholesterol

Keywords: cholesterol, liver, muscle, total cholesterol

Cholesterol content in liver and muscle tissue will be determined by the Folch method (Folch, 1957). Weighed tissue samples are homogenized in methanol:chloroform. After overnight extraction, 0.7% sodium chloride is added. The aqueous layer is aspirated and duplicate aliquots of the chloroform/lipid layer are dried under nitrogen gas. The lipid is reconstituted in isopropyl alcohol and assayed for TG spectrophotometrically with enzymatic reagents from Thermo DMA (Arlington, TX).

D3302 Lipid extraction from liver or muscle - Tissue Triglyceride

Keywords: liver, muscle, triglycerides

Triglyceride content in liver and muscle tissue will be determined by the Folch method (Folch, 1957). Weighed tissue samples are homogenized in methanol:chloroform. After overnight extraction, 0.7% sodium chloride is added. The aqueous layer is aspirated and duplicate aliquots of the chloroform/lipid layer are dried under nitrogen gas. The lipid is reconstituted in isopropyl alcohol and assayed for TG spectrophotometrically with enzymatic reagents from Thermo DMA (Arlington, TX).

D3401 Glucose (urine/plasma)

Keywords: glucose, plasma, urine

Hyperglycemia/ glycosuria

Thermo microplate (5ul) enzymatic assay

D3402 Hemoglobin A1C

Keywords: Hemoglobin A1C, liver, metabolism

Index of long-term glycemic control.

Diazyme (20ul whole blood) enzymatic assay.

D3403 beta-OH butyrate

Keywords: diabetes, insulin, liver, metabolism

Markers of ketosis.

WAKO microplate (5ul) enzymatic assay.

D3490 Triglyceride

Keywords: metabolism, triglycerides

PolyChem Analyzer (2ul) with standard reagents from PolyMedCo

D3405 Total Cholesterol

Keywords: cholesterol, liver, metabolism, total cholesterol

PolyChem Analyzer (2ul) with standard reagents from PolyMedCo

D3406 HDL cholesterol

Keywords: cholesterol, lipids, liver, metabolism

PolyChem Analyzer (2ul) with standard reagents from PolyMedCo

D3407 Direct LDL cholesterol

Keywords: cholesterol, lipids, metabolism

PolyChem Analyzer (2ul) with standard reagents from PolyMedCo

D3408 Non esterified fatty acids

Keywords: lipids, liver, metabolism, non-esterified fatty acid

WAKO microplate (5ul) with standard reagents from PolyMedCo

D3409 Apolipoprotein profiling (A-1, AII, B, E, CII, CIII)

Keywords: apolipoproteins, lipids, liver, metabolism

Initial low volume screening.

PolyChem Analyzer (<75ul total) with standard reagents from PolyMedCo

D3410 Apolipoprotein profiling

Keywords: apolipoproteins, lipids, liver, metabolism

Altered plasma apoLP levels associated with atherosclerosis/renal dysfunction.

Differential centrifugation, HPLC time of flight mass spectrometry (1000ul); Analysis done by Liposearch

D3411 Lipoprotein Particle Size

Keywords: hormone, lipids, lipoproteins, liver, metabolism

Lipoprotein particle size influences atherosclerotic risk associated with increased TRLPs.

Dynamic Light Scattering (100ul); Analysis done by Liposearch

D3412 Metabolomics

Keywords: diabetes, hormone, lipids, liver, metabolism, metabolite

Multiple metabolite levels measured. Intensity values normalized to total metabolome content. Gass Chromatograph

(GC)-Time of Flight (TOF) mass spectrometry. MS deconvolution, BinBase DB processing. compounds.

D3413 Complex lipid ratios

Keywords: diabetes, lipids, liver

Multiple metabolite levels measured. Intensity values normalized to total metabolome content. UPLC/QTOF mass spectrometry. MZmine data processing. Identification on accurate mass and MS/MS databases.

D3431 Hormones - Generic ELISA Assay

Keywords: hormone, liver

Any hormone can be measured if it is offered in an assay format without extraction (for example IGF1, Corticosterone, Resistin, etc).

D3432 Insulin

Keywords: diabetes, hormone, insulin, liver

Fasting insulin is an index of IR. Also measured for functional tests ALPCO ELISA (5ul)

D3433 C-Peptide

Keywords: hormone, insulin, liver

Proinsulin cleavage product. ALPCO ELISA (10ul)

D3434 Proinsulin

Keywords: hormone, insulin, liver

Precursor to insulin. ALPCO ELISA (10ul)

D3435 Leptin

Keywords: hormone, leptin, leptin measurement, liver

Adipocyte hormone involved in energy balance/anti-steatotic ALPCO ELISA (5ul)

D3436 Adiponectin (total)

Keywords: adiponectin, hormone, lipids, liver

Insulin-sensitizing/anti-steatotic/anti-atherogenic adipocyte hormone

Millipore RIA (5ul)

D3437 Adiponectin (HMW)

Keywords: adiponectin, hormone, lipids, liver

Insulin-sensitizing/anti-steatotic/anti-atherogenic adipocyte hormone. ALPCO ELISA (5ul)

D3438 Glucagon

Keywords: glucagon, hormone, lipids, liver

Counterregulatory hormone. Millipore RIA (100ul)

D3439 Glucagon-like peptide 1 (active)

Keywords: glucagon, hormone, lipids, liver

Incretin hormone. MSD ELISA (25ul)

D3440 Glucagon-like peptide 1 (total)

Keywords: glucagon, hormone, lipids, liver

Incretin hormone. MSD ELISA (25ul)

D3441 Ghrelin

Keywords: hormone, liver

Orexigenic GI hormone. Millipore ELISA (50ul)

D3451 Urinary Albumin Excretion

Keywords: albumin, kidney, renal, urine

Index of renal damage/Impaired glomerular function. 24 hour urine samples are collected from animals in a metabolic cage and albumin is measured with a standard assay kit, using Albumin Blue 580 Fluorescence

D3452 Creatinine

Keywords: creatinine, kidney, renal, urine

Uremia products. Uses Cayman ELISA (20ul)

D3453 Urea

Keywords: kidney, renal, urea

Uremia products. Uses Cayman ELISA (20ul)

D3461 Markers of Inflammation - full panel

Keywords: diabetes, growth factors, immunology, inflammation, interleukins

Inflammation plays a crucial role in atherosclerosis and contributes to insulin resistance. Molecules tested: IL-1a, IL-1b, IL-2, IL-4, IL-5, IL-6, IL-7, IL-9, IL-10, IL-12(p70), IL-13, IL-15, IL-17, IFNg, IP-10, G-CSF, GMCSF, TNFa, KC, MCP-1, MIP-1a, and RANTES using BioPlex (25ul) in Multiplex platform

D3462 Markers of Inflammation - limited panel

Keywords: diabetes, growth factors, immunology, inflammation, interleukins

Inflammation plays a crucial role in atherosclerosis and contributes to insulin

resistance. Molecules tested: IL-2, IL-4, IL-6, IL-10, TNF, IFN-g using BioPlex (25ul) in Multiplex platform

D3463 HS CRP

Keywords: diabetes, inflammation

Associated with insulin resistance and dyslipidemia. ALPCO ELISA (10ul)

D3464 Serum Amyloid A3

Keywords: diabetes, inflammation, serum metabolic panel

Displaces apo A1 from HDL. Millipore ELISA (10ul)

D3465 sICAM

Keywords: diabetes, inflammation

Soluble intercellular adhesion molecule-1. Increased levels associated with increased risk of vascular disease. R&D ELISA (10ul)

D3466 sVCAM

Keywords: diabetes, inflammation

Vascular cell adhesion molecule-1. Increased levels associated with increased risk of vascular disease. R&D ELISA (10ul)

D3467 sE-Selectin

Keywords: diabetes, inflammation

Soluble E-selectin. Increased levels associated with increased risk of vascular disease. R&D ELISA (10ul)

D3468 sP-Selectin

Keywords: diabetes, inflammation

Soluble P-selectin. Increased levels associated with increased risk of vascular disease. R&D ELISA (10ul)

D3481 8-Isoprostane (urinary)

Keywords: enzyme activity

Oxidative stress is associated with obese and diabetic phenotypes and with insulin resistance and cardiovascular risk. Cayman ELISA (50ul)

D3482 Protein Carbonyl (plasma, cell lysates, tissue homogenates)

Keywords: enzyme activity

Oxidative stress is associated with obese and diabetic phenotypes and with insulin resistance and cardiovascular risk. Cayman ELISA (400ul)

D3483 Catalase (plasma, cell lysates, tissue homogenates)

Keywords: diabetes, inflammation

Oxidative stress is associated with obese and diabetic phenotypes and with insulin resistance and cardiovascular risk. Cayman ELISA (200ul)

D3484 Glutathione

Keywords: enzyme activity, oxidative stress

Oxidative stress is associated with obese and diabetic phenotypes and with insulin resistance and cardiovascular risk. Samples can come from plasma, cell lysates, tissue homogenates.

Cayman ELISA (50ul deproteinized sample)

D3485 Glutathione Peroxidase

Keywords: enzyme activity, oxidative stress

Oxidative stress is associated with obese and diabetic phenotypes and with insulin resistance and cardiovascular risk.

Cayman ELISA (20ul)

D3486 Glutathione Reductase

Keywords: enzyme activity, oxidative stress

Oxidative stress is associated with obese and diabetic phenotypes and with insulin resistance and cardiovascular risk. Samples from plasma, cell lysates, tissue homogenates.

Cayman ELISA (20ul)

D3487 Hydrogen Peroxide (urinary)

Keywords: hydrogen peroxide, oxidative stress

Oxidative stress is associated with obese and diabetic phenotypes and with insulin resistance and cardiovascular risk.

Cayman ELISA (10ul)

D3488 Superoxide Dismutase

Keywords: oxidative stress, superoxide dismutase

Oxidative stress is associated with obese and diabetic phenotypes and with insulin resistance and cardiovascular risk.

Cayman ELISA (20ul)

D3489 Myeloperoxidase (cell lysate, plasma)

Keywords: oxidative stress

Oxidative stress is associated with obese and diabetic phenotypes and with insulin resistance and cardiovascular risk.

Cayman ELISA (100ul)

D3491 Insulin Signalling pathway

Keywords: diabetes, inflammation, insulin, leptin, obesity, stress

Inflammation and ER stress associated with obese and diabetic phenotypes and with insulin/leptin resistance and cardiovascular risk; assessment by Western Immunoblotting for Akt, Erk1, Erk2, IR, IRS1

Includes assessment of activation of component of Insulin signaling pathway, markers of insulin Resistance and Inflammation

D3492 Endoplasmic reticulum stress pathway

Keywords: diabetes, hormone, immunology, insulin, insulin action, obesity, stress

Immunoblotting for PERK ,BiP, eIF2a, IRE1, XBP1s ,ATF6

D3493 Inflammation pathway

Keywords: diabetes, hormone, immunology, inflammation, insulin

Immunoblotting for TNFa, MCP1, JNK, p38

D3494 Leptin Signaling pathway

Keywords: diabetes, hormone, leptin, obesity

Immunoblotting for Jak, STAT3

Body Composition, Thermoregulation, and Food Intake Behavior Core

D4001 Gross Body Composition

Keywords: body composition, imaging

Measures adiposity and lean mass using DEXA (PixiMus)

D4002 Adiposity (adipose depot weights)

Keywords: adipose, body composition

Measures adiposity and lean mass, by manual tissue dissection.

D4003 Meal Pattern Analysis

Keywords: energy expenditure, exercise, food intake, meal pattern

Detects gross cumulative food intake with meal size analysis, inter-meal interval, subtle food intake phenotypes. CLAMS automated detection of food intake for up to 1 wk; operator summarization of results of meal patterns for 72 hr.

D4004 Gastric Emptying

Keywords: food intake, gastrointestinal tract

Measures rate of GE to assess phenotypes of GI function; Radiolabeled protein intake monitored in vivo.

D4005 Digestible Energy

Keywords: energetics, food intake, gastrointestinal tract

Assesses efficiency of gut energy uptake; Fecal collection followed by proximate analysis and bomb calorimetry.

D4006 Gut Microbiome Analysis

Keywords: energetics, gastrointestinal tract, gut, microbiome

Determines differences in gut microbe population prevalence; Fecal collection followed by rRNA analysis in high throughput 454 instrument; correlation of results with metabolic phenotype variables.

D4007 Standard Fed & Postabsorptive Energy Expenditure

Keywords: energy balance, energy expenditure, food intake, indirect calorimetry

Measures energy utilization and fuel preference by indirect calorimetry; gross 24 hour food and water intake; body composition by DEXA

D4009 Brown Adipose Tissue Thermogenic Activation

Keywords: adipose, energetics, energy expenditure

Secondary Assay measures if energetic phenotypes are related to changes in BAT activation; UCP1 protein/gene expression and thermogenic mRNA marker panel.

D4010 Comprehensive Longitudinal Metabolic Profile

Keywords: energy expenditure, food intake, glucose, hormone, insulin

Full metabolic phenotyping protocol; 8 wk long analysis of energy balance parameters, glucose and insulin homeostasis, endocrine and tissue profiling.

Cardiovascular Biology and Pathology Core

D5001 Macrovascular permeability & lipoprotein flux

Keywords: cardiac function, imaging, immunohistochemistry, lipids, vascular function

Can measure permeability &/or lipoprotein flux of carotid arteries or aorta.

D5002 Microvascular permeability & lipoprotein flux

Keywords: cardiac function, imaging, immunohistochemistry, lipids, vascular function

Can measure permeability &/or lipoprotein flux of brain, heart, & mesentary.

D5003 Lipoprotein analysis by LTRS

Keywords: imaging, lipids, lipoproteins

Will take measurement of 100 lipoproteins per mice. Collect blood in streptokinase.

D5004 Atheroma quantification

Keywords: cardiac function, imaging, vascular function

Atheroma quantification. Depends on the specificity of the analyses.

D5005 BP measurement by tail cuff

Keywords: blood pressure, cardiac function, vascular function

BP measurement by tail cuff (Jin). Mice must be acclimated to procedure

D5006 BP & heart rate variability measurements by telemetry

Keywords: blood pressure, cardiac function, telemetry, vascular function

BP & heart rate variability measurements by telemetry (Jin)

D5007 Aortic & mesenteric reactivity & vascular stiffening

Keywords: aortic reactivity, mesenteric reactivity, vascular stiffening

Aortic & mesenteric reactivity is measured ex vivo. Vascular stiffening is measured in vivo. (Jin & Rutledge)

D5008 Erectile dysfunction

Keywords: vascular function

Measurement of intracavernosal / mean arterial pressure

D5009 Cardiac electrophysiology

Keywords: cardiac, electrocardiography

Cardiac electrophysiology. Baseline & after provocation will be assessed.

D5010 Echocardiography

Keywords: cardiac function, echocardiography, vascular function

Echocardiography. Cardiac chamber dimensions, valvular abnormalities, & cardiac output.

D5011 CT, MRI, PET, & combinations

Keywords: cardiac function, central nervous system, CT, imaging, MRI, PET, spectroscopy, vascular function

CT, MRI, PET, & combinations. Cardiac or brain are assessed.

<http://imaging.bme.ucdavis.edu/faqs/recharge-rates/>

D5012 Luminex / multiplex

Keywords: hormone, immunology, kidney, lipids, liver, metabolite

50 uL blood needed. This supposes that all analytes can be run simultaneously on one plate. The analytes to be measured will determine the ultimate cost and design of the analysis.

D5013 MMPC mouse gross necropsy with histology

Keywords: histology, morphology, necropsy

Assessment of gross and histologic changes to complement other MMPC assays; Gross necropsy with documentation of changes present. Collection and histologic processing (paraffin blocks/H&E slides) and interpretation of kidneys, liver, spleen, pancreas, heart, lungs, esophagus, trachea, thymus, mesenteric lymph nodes, GI Tract, cerebrum, cerebellum, urinary bladder, and reproductive tract and additional tissues with gross changes. This includes photodocumentation of significant findings. This assay can be customized to include other target organs based on findings from other MMPC assays.

D5014 UC Davis Comparative Pathology Laboratory services

Keywords: hematology, histology, morphometry, necropsy, serum chemicals, urinalysis

The CPL can provide additional ancillary testing to support MMPC studies that are not included as part of the MMPC assays. For information please go to <http://cpl.ucdavis.edu>; Services include serum/plasma/urine chemistry, hematology analysis, urinalysis, mutant mouse anatomic pathology phenotyping, diagnostic gross necropsy examinations with tissue characterizations and recording of organ weights, diagnostic histological examinations with interpretations, research project dissections, tissue collections, and special preparations or staining. CPL specializes in performing assays optimized for the micro-sample volumes commonly encountered in rodent biology.

Lipid, Lipoprotein and Glucose Metabolism Core

C1070 Glucose tolerance tests (intraperitoneal glucose tolerance, oral glucose tolerance)

Keywords: glucose disposal, glucose metabolism, glucose tolerance, insulin secretion, intraperitoneal glucose tolerance

Mice will be fasted for 4 hours and anesthetized. A fasting blood sample will be removed from the tail vein and a concentrated solution of glucose injected into the abdominal cavity of the mice through a needle passed through the abdominal skin. Blood samples will be removed from the tail vein 5, 10, 15, 20, 25 and 30 minutes later. Samples of plasma obtained during the test will be measured for concentrations of glucose and insulin.

C1088 Plasma Glucose-dependent insulinotropic peptide (GIP) concentration

Keywords: gut, hormone, lipids, metabolism

Glucose-dependent insulinotropic polypeptide (GIP) is measured by radioimmunoassay.

C1051 Intestinal lipid absorption in the conscious mouse

Keywords: absorption, fistula, gastrointestinal tract, lipids, lymph

This procedure enables the study of the intestinal digestion, absorption and lymphatic transport of dietary lipid in the conscious mouse. By infusing the lipid test meal intraduodenally at a constant rate, the lymphatic lipid output usually reaches a steady rate by the 3rd or 4th hour. Thus, lymphatic lipid output during the 5th or 6th hour represents the amount of lipid transported by the small intestine under steady-state conditions. At the end of the study, both luminal as well as mucosal radioactive lipids can be collected. Thus one can obtain a considerable amount of information regarding the digestion, uptake and mucosal esterification and the lymphatic transport of lipids.

C1052 Plasma lipid profiles

Keywords: non-esterified fatty acid, phospholipids, total cholesterol, triglycerides

Plasma lipid profiles

C1053 Lipoprotein profiles

Keywords: agarose, agarose gel electrophoresis, electrophoresis, lipids, lipoproteins

As part of the standard lipoprotein determination, plasma lipoproteins will be analyzed using agarose gel electrophoresis. Small aliquots of lymph or plasma can be used for the assay. It is particularly useful for identifying beta-VLDL and the analysis of lipoprotein classes when plasma triglycerides are high (>300 mg/dl)

C1054 Lipoprotein fractionation by FPLC

Keywords: apolipoproteins, FPLC, lipids, lipoproteins

To obtain a more precise determination of lipids and apolipoproteins in the different lipoprotein fractions, the lipoproteins of plasma or lymph can be separated using Fast Protein Liquid Chromatography. This method is sometimes preferred over ultracentrifugation as the amount of blood required is much lower. The lipoproteins in each column fraction will be separated by agarose electrophoresis and stained to identify VLDL remnants, LDL, apo E-containing large HDL particles, small alpha migrating HDL and pre-beta HDL.

C1055 Chylomicron metabolism (lymph)

Keywords: apolipoproteins, chylomicron, chylomicron remnants, intestine, lipids

The intestinal lymph duct and duodenum will be surgically cannulated. Chylomicrons are harvested and sized by negative staining. A small sample will be delipidated, and the apoprotein composition will be analyzed by polyacrylamide gel electrophoresis. Labeled CM is injected into mice and the plasma clearance rate is calculated as well as a determination of the uptake by the liver.

C1056 Cholesterol synthetic rate

Keywords: cholesterol, fatty acids, lipids, sterol, synthesis

To measure sterol synthesis rates, mice will be injected with deuterated water i.p. One hour later, the animals are anesthetized and exsanguinated. Tissues are removed and saponified. The amount of digitonin-precipitable sterols will be determined and cholesterol synthesis can then be calculated.

C1057 Plasma Free fatty Acid Levels

Keywords: free fatty acids, non-esterified fatty acid

Determinations of substrates (free fatty acids) in blood will be made using specific biochemical reactions that generate a specific color in proportion to their concentration. Reactions will be run in microtiter plates and analyzed on a plate reader. Using this method assays can be performed on small (5-25ul) samples of plasma or serum.

C1072 Insulin Sensitivity Test

Keywords: diabetes, insulin action, insulin sensitivity, metabolism

Mice will be fasted for 4 hours and anesthetized. A fasting blood sample will be removed from the tail vein and insulin (0.5mU/g) will be injected into the abdominal cavity. Blood samples will be removed from the tail vein 5, 10, 15, 20, 25 and 30 minutes later. samples of plasma obtained during the test will be measured for concentrations of glucose and insulin.

C1081 C-Peptide

Keywords: diabetes, hormone, insulin

Plasma concentrations of C-peptide are determined using radioimmunoassay kits available fro Linco Inc. (St. Louis, MO)

C1085 Plasma/serum concentrations glucagon

Keywords: counterregulatory, hormone, pancreas

Plasma concentrations of glucagon are determined using radioimmunoassay kits available fro Linco Inc. (St. Louis, MO)

C1086 Plasma Glucagon-like peptide 1 (GLP-1) concentration

Keywords: counterregulatory, hormone, pancreas

Glucagon-like peptide 1 (GLP-1) concentrations are measured using a specific radioimmunoassay.

C1087 Glucose enrichment and concentration

Keywords: carbohydrate metabolism, diabetes

Glucose enrichment and concentration

C1089 Insulin concentrations in plasma/serum/lymph/cerebrospinal fluid

Keywords: diabetes, hormone, pancreas

Concentrations of insulin in plasma or serum are determined using a sensitive radioimmunoassay that is specific for insulin but also reacts with proinsulin. The assay has been sensitized such that concentrations of insulin can be determined in small (10-25 ul) aliquots of serum/plasma. The assay has been used to detect insulin concentrations in other body fluids such as lymph and cerebrospinal fluid.

C1090 Plasma/serum concentrations of leptin

Keywords: eating behaviour, fat, hormone, lipids

Plasma concentrations of leptin are determined using radioimmunoassay kits available fro Linco Inc. (St. Louis, MO)

C1091 Somatostatin in plasma or tissue extracts

Keywords: diabetes, hormone, pancreas

Somatostatin is measured with a radioimmunoassay that detects all of the prosomatostatin peptides.

C1092 Plasma/Organ Triglycerides

Keywords: fat, lipids, metabolism

Triglyceride concentrations in plasma or organs (including liver).

Blood samples will be collected in EDTA-containing tubes from the tails of mice after a 4 hour fast. Plasma will be prepared from these samples using centrifugation and the lipid levels will be determined using enzymatic methods.

C1058 Plasma beta-hydroxybutyrate levels

Keywords: beta-hydroxybutyrate

Determinations of substrates (B-hydroxybutyrate) in blood will be made using specific biochemical reactions that generate a specific color in proportion to their concentration. Reactions will be run in microtiter plates and analyzed on a plate reader. Using this method assays can be performed on small (5-25ul) samples of plasma or serum.

C1059 Non-invasive measurement of fat absorption

Keywords: fecal fat absorption

Non-invasive measurement of fat absorption

C1060 Chemical determination of phospholipid

Keywords: fat, fatty acids, lipids, phospholipids

Chemical determination of phospholipid

C1061 Serum/Plasma Adiponectin

Keywords: adiponectin, gut hormones, peptides

Serum/Plasma Adiponectin

C1062 Serum/Plasma Resistin

Keywords: resistin

Serum/Plasma Resistin

C1071 Plasma glucose levels

Keywords: carbohydrate, diabetes, metabolism

Determinations of substrates (glucose) in blood will be made using specific biochemical reactions that generate a specific color in proportion to their concentration. Reactions will be run in microtiter plates and analyzed on a plate reader. Using this method assays can be performed on small (5-25ul) samples of plasma or serum.

C1083 Cholesterol (Total, HDL, LDL)

Keywords: cholesterol, fat, lipids, metabolism

Blood samples will be collected in EDTA-containing tubes from the tails of mice after a 4 hour fast. Plasma will be prepared from these samples using centrifugation and the lipid levels will be determined using enzymatic methods. The LDL-cholesterol will be estimated using the equation: $(VLDL+LDL\text{-cholesterol}) - (VLDL\text{-triglycerides})/5$.

C1103 Necropsy (tissue collection)

Keywords: necropsy

Animals will be anesthetized and tissues harvested as requested. These tissue will be frozen in liquid nitrogen or fixed.

C1104 Lipid extraction via folch

Keywords: folch, lipid extraction

Lipids will be extracted from tissues using the Folch extraction method.

Folch et al., J Biol Chem 1957, 226, 497

C1105 Fatty Acid analysis via GC

Keywords:

Samples are saponified and methylated for GC analysis. The extracted solution is injected into the GC and retention times are compared to known standards.

C1106 Telemetry - Cardiac parameters (BP, HR, Pulse Pressure, Activity)

Keywords: blood pressure, telemetry

Adult mice will be anesthetized and the PA-C10 telemetry device (available from Data Sciences International) will be placed SQ and anchored with suture to the abdominal muscle wall in a location that will not hinder the animal's mobility. The catheter tip will be inserted into the animal's left carotid artery and advanced so that it enters the aorta. Animals will be allowed to recover for at least seven days before the onset of testing. The PA-C10 device will measure physiological variables such as blood pressure, heart rate, pulse pressure and activity.

C1107 Telemetry - Activity and Temperature measurements

Keywords: telemetry

Adult mice will be anesthetized and the TA-F20 device (available from Data Sciences International) will be inserted through an incision in the animal's right or left flank into the abdominal cavity. Animals will be allowed to recover for at least seven days before the onset of testing. The TA-F20 device will measure temperature and activity.

C1108 Multiplexing assays

Keywords:

Multiplexing assays can be analyzed on the LUMINEX 200 box. These specific assays can be designed and ordered through Millipore, Biosource, and BioRad.

C1109 Euglycemic-hyperinsulinemic clamp

Keywords: hyperinsulinemic clamp

The euglycemic-hyperinsulinemic clamp is used to investigate insulin action and glucose metabolism in the intact, conscious mouse. The use of different glucose or glucose analog tracers with the option of using dual tracers (3-H or 14-C labeled) allows the determination of tissue-specific glucose uptake in addition to whole body glucose production and disposal.

A chronic indwelling catheter is surgically implanted into the right jugular vein of the mouse. After a minimum of 4 days recovery, the mice are fasted the morning of the experiment. The 120 minute protocol begins with a prime-continuous infusion of glucose tracer and a prime-continuous infusion of insulin, at a rate dependant on the goals and conditions of the experiment. Glucose is infused at a rate that maintains euglycemia and is a measure of insulin sensitivity. Tissues can be collected at the conclusion of the clamp for later assessment of tissue-specific glucose uptake as well as other biochemical assays as desired.

Energy Metabolism, Food Intake & Body Weight Regulation Core

C1041 Body Composition

Keywords: body composition, carcass analysis, obesity, QMR, total body fat

Total body composition in live, un-anesthetized small animals and carcasses will reveal absolute amounts of body fat, lean tissue and body water via quantitative magnetic resonance (QMR).

References:

Tinsley FC, Taicher GZ, Heiman ML. Evaluation of a quantitative magnetic resonance method for mouse whole body composition analysis. *Obes Res.* 2004 Jan;12(1):150-60.

C1042 Energy Expenditure Measurements

Keywords: basal metabolic rate, CO₂ production, obesity, oxygen consumption, respiratory quotient

Both total energy expenditure and relative rates of carbohydrate versus fat oxidation will be determined via indirect calorimetry.

C1044 DietMax Meal Pattern Analysis

Keywords: food intake, meal pattern

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Metabolism Core

M1001 Hyperinsulinemic-euglycemic clamp

Keywords: glucose metabolism, insulin action, insulin resistance

A survival surgery with anesthesia is performed at 4~5 days prior to the clamp to establish a chronic indwelling catheter in the right jugular vein for intravenous infusion during the clamp. On the day of experiment, a mouse fasted for overnight (14-hr; 18:00-08:00) or 5 hrs (07:00-12:00) is placed in an over-sized restrainer (i.e., rat-sized) for the experiment to be conducted in fully conscious and minimally-stressed state. The tail is tape-tethered at one end to obtain blood samples from the tail vessel during the clamp. This procedure is applied for 2 hours before the clamp (basal period) for acclimatization in this partially-restrained state and recovery from the initial handling. Intravenous catheter is connected to a microdialysis infusion pump via a 3-way connector. During the basal period, D-[3-3H]glucose is infused at 0.05 μ Ci/min to assess basal glucose turnover. A blood sample (40 μ l) is collected at the end for the basal measurement of plasma glucose, insulin, and [3H]glucose concentrations.

Following the basal period, a 2-hr hyperinsulinemic-euglycemic clamp begins with a primed (150 mU per kg body weight) and continuous infusion of human insulin at a rate of 15 pmol/kg/min to raise plasma insulin within a physiological range (\sim 300 pM). Blood samples (10 μ l) are collected at 10~20 min intervals for the immediate measurement of plasma glucose using glucose analyzer, and 20% dextrose is infused at variable rates to maintain basal glucose levels (\sim 7 mM). Insulin-stimulated whole body glucose turnover rate is measured with a continuous infusion of [3H]glucose throughout the clamp (0.1 μ Ci/min).

To estimate glucose uptake in individual organs, 2-[1-14C]deoxy-D-glucose (2-[14C]DG) is administered as a bolus (10 μ Ci) at 75 min after the start of clamp. Blood samples (20 μ l) are taken at 80, 85, 90, 100, 110, and 120 min of clamp for the measurement of plasma [3H]glucose, 3H₂O, and 2-[14C]DG concentrations. Additional blood sample (20 μ l) is taken at 120 min to measure clamp plasma insulin levels. At the end of clamp, the mouse is anesthetized using sodium pentobarbital, and tissue samples (gastrocnemius and quadriceps from both hindlimbs, epididymal white adipose tissue, interscapular brown adipose tissue, liver, and heart) are taken for biochemical analyses. Serum and tissue samples may be transferred to the Analytical Core for analytical measurements (e.g., insulin, adipokines).

The hyperinsulinemic-euglycemic clamp is a "gold-standard" method of measuring insulin sensitivity and generates the following metabolic data:

- Insulin-stimulated whole body glucose turnover, glycolysis, and glycogen synthesis
- Basal and insulin-stimulated rates of hepatic glucose production
- Insulin-stimulated glucose uptake, glycogen synthesis, and glycolysis in individual organs

Further details of the clamp experiment and calculation of clamp-derived parameters can be found in the following references: Diabetes 53:1060-1067 (2004), Stocker (ed.), Type 2 Diabetes, Methods in Molecular Biology, Vol. 560:221-238 (2009)

M1002 Basal glucose metabolism

Keywords: glucose turnover

Following overnight fast or in fed state (5 hours after food removal), basal glucose metabolism is assessed using an intravenous infusion of [3-3H]glucose (0.05 μ Ci/min) for 2 hours in conscious mice. Blood samples are taken at 110 and 120 min for the measurement of plasma glucose and [3H]glucose concentrations. During basal state, whole body glucose turnover is estimated to be the basal rate of hepatic glucose production.

M1003 Organ-specific glucose uptake

Keywords: glucose uptake

Following overnight fast or in fed state (5 hours after food removal), basal glucose uptake in individual organs is determined using a bolus intravenous injection of 2-[1-14C]deoxy-D-glucose (2-[14C]DG; 20 μ Ci) in conscious mice and collecting tissues after 30 min to measure intracellular 2-[14C]DG-6-P concentrations using ion-exchange columns.

M1004 Hyperglycemic clamp

Keywords: beta cell, insulin secretion, pancreas

A survival surgery with anesthesia is performed at 4~5 days prior to the clamp to establish a chronic indwelling catheter in the right jugular vein for intravenous infusion during the clamp. On the day of experiment, a mouse fasted for overnight (14-hr; 18:00-08:00) or 5 hrs (07:00-12:00) is placed in an over-sized restrainer (i.e., rat-sized) for the experiment to be conducted in fully conscious and minimally-stressed state. The tail is tape-tethered at one end to obtain blood samples from the tail vessel during the clamp. Intravenous catheter is connected to a microdialysis infusion pump, and a blood sample (20 μ l) is collected to measure basal glucose and insulin concentrations.

A 2-hr hyperglycemic clamp begins with a variable infusion of 20% dextrose to raise and maintain plasma glucose concentration at \sim 300 mg/dl. Blood samples (20 μ l) are collected at 0, 10, 20, 30, 45, 60, 80, 100, and 120 min to measure plasma glucose and insulin concentrations using glucose analyzer and Luminex, respectively. At the end of clamp, the mouse may be anesthetized, and pancreas may be collected for islet isolation and histology/molecular analyses by the Analytical Core.

The area-under-curve of plasma insulin levels indicates glucose-induced insulin secretion or in vivo pancreatic β -cell function. In addition to insulin, c-peptide levels may be measured using additional blood samples for direct assessment of glucose-induced insulin secretion in mouse models potentially affected by altered hepatic insulin clearance.

M1005 Insulin clearance

Keywords: insulin

Hepatic insulin clearance is assessed in conscious mice by administering an intraperitoneal bolus injection of human insulin (1 U/kg of body weight) and collecting blood samples at 5, 10, 15, 20, 30, 45, and 60 min for the measurement of plasma insulin levels.

M1006 Glucose tolerance test

Keywords: glucose clearance, glucose tolerance

Intraperitoneal (IP) or intravenous (IV) glucose tolerance tests (GTTs) are performed in conscious mice following overnight fast (\sim 14 hours). Glucose is administered as a bolus at 1 or 2 g/kg body weight, and blood samples (20 μ l) are taken from tail vessels at 0, 10, 20, 30, 60, 90, and 120 min following a glucose bolus. Plasma glucose concentrations are determined using a glucose analyzer, and glucose clearance or area-under-curve of GTT reflects insulin sensitivity, assuming normal pancreatic β -cell function.

M1007 Glucose tolerance test with insulin secretion

Keywords: glucose tolerance, insulin

During IP or IV GTTs, additional blood samples (20~40 μ l) are taken to measure plasma insulin and/or C-peptide levels using Luminex. Insulin or C-peptide levels in response to a bolus glucose load reflect pancreatic beta-cell function.

M1008 Insulin tolerance test

Keywords: insulin sensitivity

Intraperitoneal (IP) or intravenous (IV) insulin tolerance tests (ITTs) are performed in conscious mice at fed state (at least 5 hours after food removal). Insulin is administered as a bolus at 0.25 or 0.5 U/kg body weight, and blood samples (20 μ l) are taken from tail vessels at 0, 10, 20, 30, 60, 90, and 120 min following a glucose bolus. Plasma glucose concentrations are determined using a glucose analyzer, and glucose

M1009 Hepatic gluconeogenesis

Keywords: pyruvate tolerance test

Pyruvate tolerance test indirectly measures hepatic gluconeogenesis in conscious mice following overnight fast (\sim 14 hours). Pyruvate is intraperitoneally administered as a bolus at 1 g/kg body weight, and blood samples (20 μ l) are taken from tail vessels at 0, 15, 30, 45, 60, 90, and 120 min following a pyruvate bolus. Plasma glucose concentrations are determined using a glucose analyzer, and glucose derived from pyruvate reflects hepatic gluconeogenesis.

M1010 Lipid metabolism

Keywords: palmitate, triglycerides

Lipid metabolism is measured in conscious mice using labeled palmitate or glucose incorporation into tissue-specific triglyceride. The experiment begins with an intravenous bolus injection of [¹⁴C]palmitate (20 uCi), and blood samples (20 ul) are collected at 0, 0.5, 1, 2, 3, 4, and 5 min following a bolus injection. At the end of experiment, mice are euthanized, and tissue samples are rapidly taken for biochemical assays to measure [¹⁴C]palmitate incorporation into [¹⁴C]-labeled triglyceride in individual organs. Plasma [¹⁴C]palmitate concentrations are measured using liquid scintillation counter to assess systemic clearance of [¹⁴C]palmitate.

Alternatively, [³-³H]glucose (20 uCi) is intraperitoneally administered as a bolus, and mice are euthanized after 1 hour for tissue collection. Biochemical assays are performed to measure [³-³H]glucose incorporation into [³H]-labeled triglyceride in individual organs.

M1011 Protein metabolism

Keywords: phenylalanine, protein synthesis

Protein metabolism is assessed using the flooding-dose method previously described by Dr. Thomas C. Vary (Am. J. Physiol. 262:C445-452, 1992; Am. J. Physiol. 262:C1513-1519, 1992). The experiment begins with an intraperitoneal bolus injection of [³H]-L-phenylalanine (0.2 uCi/ml/umol, 30uCi/100 g/body weight; 1 ml/100 g/body weight) in conscious mice. After 15 min, mice are euthanized, and blood and tissue samples are rapidly taken for biochemical analyses. Blood samples are used to measure plasma phenylalanine and [³H]-L-phenylalanine concentrations. The phenylalanine levels are measured by HPLC analysis of supernatants from trichloroacetic acid extracts of plasma samples. The assumption in using this technique to estimate the rate of protein synthesis in vivo is that the tissue phenylalanine concentration is elevated to a high level thereby limiting any dilution effect of non-radioactive phenylalanine derived from proteolysis on the intracellular specific radioactivity. Under the condition of elevated plasma phenylalanine level (~1.2 mM), the specific radioactivity of the plasma phenylalanine is assumed to be equal to the specific radioactivity of the tRNA-bound phenylalanine.

M1012 Body composition (whole body)

Keywords: fat mass, lean muscle mass, obesity

Whole body composition of fat/lean/water mass is non-invasively measured in conscious mice using 1H-MRS developed by Echo Medical Systems (EchoMRI 3-in-1). This instrument has an important advantage over commonly used mouse densitometer (PIXImus), which applies dual energy x-ray technology for analysis of body composition in anesthetized mice. In contrast, 1H-MRS can be applied in studies requiring multiple measurement in individual mice, such as chronic changes in adiposity in response to a high-fat diet, without the risk of anesthesia-associated complications.

M1013 Body composition (organs)

Keywords: fat mass, lean muscle mass, obesity

Organ-specific composition of fat/lean/water mass is non-invasively measured in conscious mice using 1H-MRS developed by Echo Medical Systems (EchoMRI 3-in-1).

M1014 Energy balance – food intake, energy expenditure, physical activity

Keywords: indirect calorimetry, metabolism

Metabolic cages (TSE Systems) are used to perform indirect calorimetry and simultaneously measure food/water intake, energy expenditure, and physical activity in conscious mice. The experiment non-invasively measures VO₂ consumption and VCO₂ production in individual mice using metabolic chambers and calculates the respiratory exchange ratio (RER) to reflect energy expenditure. RER values close to 1.0 reflects carbohydrate utilization, and RER values close to 0.7 reflects lipid utilization. The metabolic cages are also used for the quantitative measurement of horizontal and vertical movement (XYZ-axis) as an index of physical activity and food/water intake over a given period of time (typically 3 days). TSE metabolic cages provide natural food intake setting with cage-lid location of food, and mice tend to quickly acclimate to the TSE metabolic cages with natural cage setting during the 3-day measurements.

M1015 Chronic high-fat feeding

Keywords: diet-induced obesity, high-fat diet, obesity

An experimental mouse model of obesity can be generated by feeding a high-fat diet (HFD) ad libitum for select duration. Quality control studies indicate that a short-term (3-4 weeks) of HFD feeding increases whole body fat mass by more than 2-fold and causes insulin resistance in male C57BL/6 mice. Most of the mice fed short-term HFD develop compensatory hyperinsulinemia but do not develop hyperglycemia. Chronic HFD feeding of longer term (2-6 months) further increases obesity and exacerbates insulin resistance in skeletal muscle, liver, adipose tissue, and heart. Most of

the mice fed chronic HFD develop hyperglycemia, a hallmark of type 2 diabetes. The Metabolism Core works with the users in designing a study with appropriate feeding duration and selection of HFD with respect to percent and composition of fat in the diet.

M1016 Chronic drug delivery

Keywords: infusion, osmotic pump

Alzet mini-osmotic pump (Alza) is subcutaneously implanted for chronic delivery of drugs. For this procedure, mice are anesthetized with ketamine/xylazine, and osmotic pumps containing drug or placebo are subcutaneously inserted to the mice prior to the metabolic experiments. Alternatively, drug or placebo may be administered using subcutaneous injection or oral gavage.

M1017 STZ-induced type 1 diabetes model

Keywords: hyperglycemia, streptozotocin, type 1 diabetes

An experimental mouse model of hyperglycemia and type 1 diabetes can be generated by intraperitoneal injection of streptozotocin (STZ; 50 mg/kg daily for 5 days), which selectively destroys the pancreatic beta-cells with rapid and irreversible necrosis. STZ-injected mice develop hypoinsulinemia within several days and thereby, hyperglycemia. Following STZ injection, blood glucose levels are monitored for the onset and maintenance of hyperglycemia. For selected mouse models, other STZ doses may be required to maintain chronic hyperglycemia. With onset of hyperglycemia and significant urinary loss of glucose, mice are closely monitored for proper hydration with adequate water supply and frequent change of cage bedding.

M1018 Acute lipid infusion

Keywords: fatty acids, lipids

An experimental model of acute hyperlipidemia can be generated by an intravenous infusion of lipid emulsion at a rate of 2.5 ml/kg body weight/hour and heparin (6 U/hour). A 2-hour hyperinsulinemic-euglycemic clamp experiment may follow acute lipid infusion to measure insulin sensitivity in conscious mice exposed to acute hyperlipidemia. Quality control studies indicate that an acute lipid infusion for 5 hours increases serum fatty acids levels to 3~4 mM and causes insulin resistance in skeletal muscle. Lipid emulsion may be infused at different rates to raise serum fatty acids to different levels. This study allows users to investigate acute and direct effects of fatty acids without altering obesity or adipokines that may affect glucose metabolism.

M1019 Chronic/acute phloridzin treatment

Keywords: glucose clearance, renal

Acute hypoglycemia in normal mice or acute/chronic glucose reduction in hyperglycemic mice may be achieved by acute or chronic treatment of phloridzin (PHZ; 100 ug/kg body weight/min for acute treatment, 0.4 mg/kg body weight twice daily for chronic treatment). This procedure can be used prior to in vivo experiments.

M1020 Exercise model

Keywords: Activity, Cage Activity, exercise

Cage wheels, designed to fit into the home cages, are used to induce exercise in mice. This procedure can be used prior to in vivo experiments to examine exercise-mediated metabolic effects and metabolic phenotypes secondary to exercise-induced weight loss.

M1021 Surgery – jugular vein cannulation

Keywords: surgery

At 4-5 days prior to metabolic experiments requiring intravenous infusion, a survival surgery is performed to place an indwelling intravenous catheter in anesthetized mice. Experiments are performed 4-5 days after the surgery in order for the mice to fully recuperate from surgery/anesthesia stress, which is measured by a regain of body weight to pre-operative level.

Mice are anesthetized with an intraperitoneal injection of ketamine (100 mg/kg body weight) and xylazine (10 mg/kg body weight). A transverse incision (~0.5 cm) is made over the trachea, and the right jugular vein is isolated. A silastic catheter (PE 10) is inserted into the vessel. The catheter is filled with a saline solution containing heparin (10 U/ml) and plugged. The catheter is then tunneled to the back of the neck, and placed under the back skin to prevent its accessibility from the mouse. A silk is tied to the catheter, and a small opening is made at the back of neck. This

silk, which is partially exposed, is used on the day of metabolic experiment to expose and connect the catheter. The catheter requires no other care until the experiment day when it is flushed with a heparinized saline solution to reopen. This surgery requires ~15 minutes to complete. All surgical procedures are performed using standardized aseptic techniques, and all surgical tools are autoclaved following the surgery.

In order to prevent hypothermia, a heating pad is used during the surgery, while a heating lamp and/or heating pad is used during the post-operative recovery period. After surgery, the mice are monitored closely in a post-operative cage with gauze bedding. Mice are monitored until they are awake and about which is usually within 1-2 hours. Mice are then housed in individual cages and monitored for post-operative recovery and weight gain on a daily basis for 48 hours for evidence of catheter infection.

M1022 M1022 Surgery – tail vein injection

Keywords: surgery

Intravenous injection via tail vein is used for acute delivery of drugs, hormones, and adeno-associated virus.

M1023 Surgery – carotid artery cannulation

Keywords: surgery

Carotid artery is cannulated and indwelling catheter is placed in order to obtain rapid blood samples from mice during select experiments.

M2002 Hemoglobin A1c

Keywords: diabetes, glucose, hyperglycemia, metabolite

Hemoglobin A1c levels rise in response to chronic hyperglycemia and can be measured using Cobas Clinical Chemistry Analyzer (Roche).

Analytical Core

M2001 Glucose

Keywords: diabetes, glucose, hyperglycemia, hypoglycemia, metabolite

Plasma glucose concentrations are determined for a variety of metabolic experiments (e.g., hyperinsulinemic-euglycemic clamp, hyperglycemic clamp, GTT, ITT) performed by the Metabolism Core and for stand-alone measurements as a marker of perturbed glucose homeostasis in mice. Plasma glucose concentrations are measured by the glucose oxidase method using Analox GM7 Micro-stat Rapid Multi-assay Analyzer (Analox Instruments, Holliston, MA). This instrument requires 5 ul of plasma for rapid (~5 seconds) and accurate measure of glucose concentrations, which is important for select metabolic experiments such as hyperinsulinemic-euglycemic clamp and hyperglycemic clamp.

Alternatively, blood glucose concentrations are measured using a glucometer for those metabolic experiments (e.g., GTT, ITT) that may be repeated in individual mouse.

Plasma and tissue concentrations of labeled-glucose ([³H]glucose and 2-[¹⁴C]deoxyglucose) are measured using liquid scintillation counter (Beckman-Coulter).

M2003 Lactate

Keywords: diabetes, glucose, metabolite

Lactate levels are altered in metabolic syndrome and can be measured using Cobas Clinical Chemistry Analyzer (Roche).

M2004 Insulin

Keywords: diabetes, hormone, hyperinsulinemic clamp, insulin, pancreas

Insulin is a critical metabolic hormone synthesized by pancreatic beta-cells to regulate glucose homeostasis. Plasma insulin concentrations are determined for a variety of metabolic experiments (e.g., hyperinsulinemic-euglycemic clamp, hyperglycemic clamp) performed by the Metabolism Core and for stand-alone measurements as a marker of insulin resistance in mice. Plasma insulin concentrations are measured using Bio-Plex 200 Luminex System, which requires 5~25 ul of plasma samples for multiplex, high-throughput, and accurate determination of insulin.

Alternatively, plasma insulin concentrations are determined by ELISA using ultra-sensitive or sensitive antibody kits.

M2005 C-peptide

Keywords: hormone, insulin, insulin secretion, pancreas

C-peptide is synthesized by pancreatic beta-cells when proinsulin is cleaved to form an active insulin and C-peptide. Since a large fraction of insulin secreted by pancreatic beta-cells is cleared and metabolized by liver, systemic levels of insulin may not accurately reflect insulin secretion by beta-cells. For direct assessment of islet insulin secretion, plasma C-peptide concentrations are measured using Bio-Plex 200 Luminex System.

M2006 Glucagon

Keywords: glucose, hepatic, hormone, pancreas

Glucagon is a key hormone synthesized by pancreatic alpha-cells to regulate hepatic glucose production and glucose homeostasis in post-absorptive state. Glucagon further regulates insulin secretion via paracrine effects. Plasma glucagon concentrations are measured using Bio-Plex 200 Luminex System

M2007 Leptin

Keywords: adipokine, feeding behavior, hormone

Leptin is an adipocyte-derived hormone that plays an important role in regulating feeding behavior. Since alterations in food intake affect energy balance, leptin levels are important factors in obesity. Plasma leptin concentrations are measured using Bio-Plex 200 Luminex System.

M2008 Adiponectin

Keywords: adipokine, hormone, insulin resistance

Adiponectin is an adipocyte-derived hormone that affects multiple systems in our body including metabolism, vascular biology, and inflammation. Plasma adiponectin concentrations are measured using Bio-Plex 200 Luminex System.

M2009 Resistin

Keywords: adipokine, hormone, insulin resistance

Resistin is an adipocyte-derived hormone that affects insulin action and hepatic glucose metabolism. Plasma resistin concentrations are measured using Bio-Plex 200 Luminex System.

M2010 Triglyceride

Keywords: lipids, metabolite, obesity

Serum triglyceride levels are elevated in obesity and type 2 diabetes. Tissue triglyceride levels are also associated with insulin resistance. Plasma and tissue triglyceride concentrations are determined using chloroform-methanol lipid extraction assay and Cobas Clinical Chemistry Analyzer (Roche).

M2011 Non-esterified fatty acids

Keywords: insulin resistance, lipids, metabolite, obesity

Serum fatty acids levels are elevated in obesity and type 2 diabetes. Fatty acids and their metabolites are shown affect insulin action, glucose metabolism, and oxidative stress. Plasma fatty acids concentrations are measured using Cobas Clinical Chemistry Analyzer (Roche).

M2012 Cholesterol (total)

Keywords: atherosclerosis, lipids, liver, metabolite, obesity

Alterations in cholesterol metabolism and circulating cholesterol levels are known to affect cardiovascular system and diabetic complications. Plasma total cholesterol levels are measured using Cobas Clinical Chemistry Analyzer (Roche).

M2013 Cholesterol (HDL)

Keywords: atherosclerosis, lipids, liver, metabolite, obesity

Alterations in cholesterol metabolism and circulating HDL-cholesterol levels are known to affect cardiovascular system and diabetic complications. Plasma HDL-cholesterol levels are measured using Cobas Clinical Chemistry Analyzer (Roche).

M2014 Cholesterol (LDL)

Keywords: atherosclerosis, lipids, liver, metabolite, obesity

Alterations in cholesterol metabolism and circulating LDL-cholesterol levels are known to affect cardiovascular system and diabetic complications. Plasma LDL-cholesterol levels are measured using Cobas Clinical Chemistry Analyzer (Roche).

M2015 Ammonia

Keywords: lipids, metabolite

Plasma ammonia levels are measured using Cobas Clinical Chemistry Analyzer (Roche).

M2016 Lipase

Keywords: lipids, metabolite, obesity

Lipase is an important enzyme that hydrolyzes circulating triglyceride and breaks down triglyceride into free fatty acids and glycerol. Plasma lipase levels are measured using Cobas Clinical Chemistry Analyzer (Roche).

M2017 Amylase

Keywords: enzyme activity

Amylase is an important enzyme that breaks down complex carbohydrates into glucose molecules. Plasma amylase levels are measured using Cobas Clinical Chemistry Analyzer (Roche).

M2018 Creatine kinase

Keywords: enzyme activity

Plasma creatine kinase levels are measured using Cobas Clinical Chemistry Analyzer (Roche).

M2019 Alkaline phosphatase

Keywords: enzyme activity

Plasma ALP levels are measured using Cobas Clinical Chemistry Analyzer (Roche).

M2020 Lactate dehydrogenase

Keywords: enzyme activity

Plasma LDH (lactate dehydrogenase) levels are measured using Cobas Clinical Chemistry Analyzer (Roche).

M2021 Albumin

Keywords: liver, metabolite

Albumin is a major circulating protein, and altered albumin levels reflect liver dysfunction. Plasma albumin levels are measured using Cobas Clinical Chemistry Analyzer (Roche).

M2022 Alanine transferase

Keywords: liver, metabolite

ALT (alanine transferase) is a major liver enzyme that regulates amino acid flux into hepatic gluconeogenesis. Thereby, serum ALT levels reflect liver function. Plasma ALT levels are measured using Cobas Clinical Chemistry Analyzer (Roche).

M2023 Aspartate transferase

Keywords: liver, metabolite

AST (aspartate transferase) is a major liver enzyme that regulates amino acid flux into hepatic gluconeogenesis. Thereby, serum AST levels reflect liver function. Plasma ALT levels are measured using Cobas Clinical Chemistry Analyzer (Roche).

M2024 Bilirubin

Keywords: liver, metabolite

Bilirubin is primarily synthesized by liver as a component of liver bile that plays an important role in intestinal digestion and absorption of lipid. Plasma bilirubin levels are measured using Cobas Clinical Chemistry Analyzer (Roche).

M2025 Gamma-glutamyl Transferase

Keywords: liver, metabolite

GGT is a major liver enzyme that reflects liver function. Plasma GGT levels are measured using Cobas Clinical Chemistry Analyzer (Roche).

M2026 Creatinine

Keywords: kidney, metabolite

Creatinine is a product of muscle breakdown and is cleared by the renal system. Thereby, serum creatinine levels reflect protein metabolism and renal function. Plasma creatinine levels are measured using Cobas Clinical Chemistry Analyzer (Roche).

M2027 C-reactive peptide

Keywords: inflammation, liver, metabolite

CRP (c-reactive peptide) is primarily produced by liver in response to IL-6 stimulation of hepatocytes, and serum CRP levels reflect systemic inflammatory state. Plasma CRP levels are measured using Cobas Clinical Chemistry Analyzer (Roche).

M2028 Total protein

Keywords: metabolite

Serum total protein levels are measured using Cobas Clinical Chemistry Analyzer (Roche).

M2029 Urea/BUN

Keywords: kidney, metabolite

Circulating and urine levels of urea/BUN reflect renal function. Urea/BUN levels are measured using Cobas Clinical Chemistry Analyzer (Roche).

M2030 Uric acid

Keywords: kidney, metabolite

Serum and urine levels of uric acid are measured using Cobas Clinical Chemistry Analyzer (Roche).

M2031 Electrolytes

Keywords: electrolyte panel

Serum levels of bicarbonate, calcium, iron, magnesium, phosphorus, potassium, and sodium are measured using Cobas Clinical Chemistry Analyzer (Roche).

M2032 Cytokines Panel I - multiplex

Keywords: chemokines, complications, cytokines, diabetes, inflammation, insulin resistance, monokines, obesity

Chronic and local inflammation is characterized by obesity and type 2 diabetes. Increased levels of cytokines and chemokines are known to affect insulin resistance and diabetic complications. Plasma and tissue lysate concentrations of IL-1, IL-2, IL-3, IL-4, IL-5, IL-6, IL-7, IL-9, IL-12 (p40), IL-12 (p70), IL-13,, IL-17, TNF-alpha, IFN-gamma G-CSF,

GM-CSF, KC, MCP-1, MiP-z,, MiP-1b, RANTES, and Eotaxin are measured in multiplexed format using Bio-Plex 200 Luminex System.

M2033 Cytokines Panel II - multiplex

Keywords: chemokines, complications, cytokines, diabetes, inflammation, insulin resistance, monokines, obesity

Chronic and local inflammation is characterized by obesity and type 2 diabetes. Increased levels of cytokines and chemokines are known to affect insulin resistance and diabetic complications. Plasma and tissue lysate concentrations of IL-15, IL-18, LIF, MIP-2, M-CSF, MIG, VEGF, PDGF-BB, and Basic FGF are measured in multiplexed format using Bio-Plex 200 Luminex System.

M2034 Islet histology

Keywords: beta cell, diabetes, insulin

Altered structure and size of pancreatic islets are characterized in obesity and during the development of insulin resistance and type 2 diabetes. Whole pancreas are processed from anesthetized mice using microscopy, and tissue sections are analyzed according to standard operating procedures. Inflammation, hyperplasia, and hypertrophy are assessed on H&E stains from sections of FFPE tissue blocks. Further spatial insights and prominent alterations of cellularity among endocrine islet cell subsets are obtained by confocal microscopy of fluorescently-labeled sections from FFPE tissue.

M2035 Molecular islet analysis

Keywords: beta cell, diabetes, insulin

Alterations in islets structure and function are major events in obesity and insulin resistance and causally associated with the onset of type 2 diabetes. A leading islet expertise of Analytical Core provides the following cellular and molecular analyses of mouse pancreatic islets:

Quantitative Nuclease Protection Assay (qNPA): FACS-purified cells are subjected to customized qNPA tests using manufacturer SOPs with supplies exclusively distributed by High Throughput Genomics (HTG) Inc. Raw data from digital images are evaluated using Vuescript 6.7 software, and results on individual gene transcription are determined per 1,000 cell input by default. Presently, genes already covered by our qNPA arrays include: insulin, Iapp, Glp1r, pro-hormone convertases Pcsk1 and 2, Zn-transporter Slc30a8 (beta cell function); Pdx1, Mafa (function-associated transcription factors); Nkx2.2 and -6.1, Pax4 and -6, Neurod1 (lineage development); Ngn3, cyclin D2, Mafk, Ki-67 (regeneration). In addition, several gene-probes have been added to control for lineage purity (distinction between endocrine islet cell subsets) of cell input and/or are "housekeeping" controls.

Flow Cytometry: Stained single cell islet suspensions are prepared and run on a Flow Cytometer Analyzer (to obtain phenotypic data), or submitted to fluorescence-activated cell sorting for transcriptional studies.

Changes in cellular composition, abundance and properties of individual endocrine islet cell subpopulations: Islet isolation followed by dissociating into single cell suspension, standard intracytoplasmic staining techniques involving formaldehyde-fixation and detergent-facilitated membrane permeabilization, and analysis by multi-parameter flow cytometry have become an established approach to examine pancreatic islet cell subpopulations. The Analytical Core applies a set of analytical FACS staining protocols to endocrine islet cell subsets such as β -cells, designed to determine for instance the relative frequencies (e.g. hyperplasia or deficiency), average hormone content per cells (based on staining intensity), proliferative activity assessed from incorporating a nucleoside analogs (BrdU, EdU), detecting cell cycle associated nuclear proteins (Ki-67), or performing cell cycle analysis (DNA quantification per cell), and apoptosis (TUNEL-staining).

Gene transcription profiling of FACS-purified endocrine islet subsets - qNPA methodology: We have previously demonstrated that unlike RT-PCR based approaches, qNPA does not require RNA extraction and is unaffected by and compatible with previous cell fixation. It is also very sensitive, and that the major endocrine islet cell subsets, namely β - and δ -cells that can typically be recovered by FACS from a single healthy mouse are sufficient to perform one or more qNPAs quantifying 16 or 47 genes each. We are currently developing protocols to sequentially hybridize samples to expand on the number of genes that can be quantified. Nuclease protection uses 50mer cDNA probes which hybridize to mRNA in a complementary manner. The single nucleic acid strand ribonuclease (S1) is then added to degrade those RNA domains that were not hybridized ("protected") by cDNA probes, and any unbound probes. Finally, nuclease removal, denaturation and RNA hydrolyzation leave only "protected" cDNA probes which can be quantified using sandwich hybridization protocol and detected by chemiluminescence in a manner proportional to the abundance of "protected" cDNA probes.

Metabolic Pathophysiology Core

V3001 Cannulation of cerebral ventricle

Keywords: brain, central control, CSF

Implantation of a cerebral ventricle cannula allows investigators to evaluate physiological responses following central administration of various compounds. Anesthetized mice are placed in a digital stereotaxic apparatus (0.001 mm accuracy, Cartesian Instruments) specifically designed for mice. The dorsal scalp will be shaved, wiped with a betadine solution, and then a small midline incision over the dorsal surface is made to allow access to the cranium. After the affixed centering scope is used to "zero" lambda and bregma landmarks, a single guide cannula (2.5 mm length, 26-gauge, Plastics One) is positioned 1.0 mm above the lateral ventricle (coordinates: 0.6 mm posterior to bregma, 1.5 mm lateral to midline, 1.4 mm below the surface of the skull) and fixed to the skull using two stainless steel screws and dental cement. The incision in the scalp is then closed with surgical thread. Animals are removed to a post-surgical warming bed, and then individually housed for several hours until fully awake. Animals will be allowed to recover from surgery for a minimum of 7 days prior to testing, during which time a 30-gauge dummy cannula is left inside the guide cannula to prevent blockage.

V3002 Jugular vein and carotid artery catheterization

Keywords: blood vessel, chronic, surgery

Arterial catheterization allows investigators to sample arterial blood as required for adequate glucose clamping (Niswender et al. J. Biol. Chem, 1997, Halseth et al. Am. J. Physiol. 1999) or other infusion/sampling purposes (Rottman et al. Am. J. Physiol. 1999) Catheterization of the right jugular vein allows the infusion of hormones, substrates, and tracers into the systemic circulation. The jugular venous catheter can be used to sample venous blood in long-term experiments because the jugular vein catheter will work for almost a month.

Arterial catheters are made from polyethylene tubing (PE-10) that is connected to silicone tubing (0.3 mm I.D., and 0.64 mm O.D.), 25 mm long. Jugular vein catheters are made from silicone tubing (0.3 mm I.D., and 0.64 mm O.D.). These catheters are connected to stainless steel tubes (0.3 mm I.D., 0.41 mm O.D., 15 mm) bent into an L shape. On the free end of the L shaped stainless steel tube a 20 mm piece of micro-renathane tubing (0.36 mm I.D., and 0.84 mm O.D.) is attached. The L shaped stainless steel tubes, attached to an arterial and a jugular vein catheter, are bundled together with silicone tubing (0.76 mm I.D. and 1.65 mm O.D.) and anchored with silastic medical adhesive (Silicone Type A). The catheters and the micro-renathane-stainless steel tubing will be heat sterilized.

The mouse is anesthetized and its skin on the interscapula and ventral surface of the neck is depilated by plucking. The depilated area is sterilized with 10% povidone-iodine. A small longitudinal incision (about 5 mm) is made in the skin over where the anterior jugular, acromiodeltoid, and cephalic veins join together. The connective tissues surrounding this junction are carefully removed. Two thin threads of silk (6-0 Silk, Davis+Geck) are passed under the jugular vein below the level of the junction. They are separated by about 3 mm. The cephalic thread, placed just below the joint, is tied to prevent bleeding. A small incision is then made just below the ligature, and the catheter is pushed 13 mm into the lumen. The catheter is fixed with the second thread and the thread previously used to tie the jugular vein. The common carotid artery is separated from the vagus nerve and muscle, and then two thin threads of silk (6-0 Silk, Davis+Geck) are passed under the artery. The cephalic thread is tied to prevent bleeding and then the artery is clamped by small bulldog clamp. A small incision is made just below the ligature, and the catheter is inserted into the lumen. The clamp is taken off and the catheter is pushed in 10 mm. The catheter is fixed with a second thread and the thread previously used to prevent bleeding. A blunt needle (16 gauge) is carefully inserted through the incision on the interscapula and pushed subcutaneously until the end comes out through the incision in the neck. The catheters will be carefully seized and pulled slowly through the needle. The incisions in the skin are then sutured. The catheters are connected to the stainless steel tubes. The bent portion of the stainless steel tubing is implanted under the skin and the incision is sutured. The implanted catheter is flushed with saline containing 200 U heparin/ml and 1 mg ampicillin/ml. Then the micro-renathane tubing is closed with a stainless steel wire. The mouse is injected subcutaneously with 150 mg/kg ampicillin. The total duration of the operation is about 50 min. Animals are removed to a post-surgical warming bed, and monitored until fully awake. Postoperative body weight and food intake are measured daily.

V3003 Glucose Tolerance Test (Oral and Intravenous)

Keywords: glucose intolerance, glucose tolerance, insulin action

Oral glucose tolerance tests are performed on conscious mice with catheters chronically implanted directly in the stomach and the carotid artery. Intravenous glucose tolerance tests are performed on conscious mice with catheters chronically implanted in the jugular vein and carotid artery. Glucose will be given at 1g/kg or 2g/kg. These doses lead to peak blood glucose levels of approximately 250 mg/dl and 400 mg/dl in wild type C57/bl/6 mice.

V3004 Glucose turnover

Keywords: endogenous glucose production, glucose flux, glucose kinetics, glucose turnover, isotopes, tracers

A primed (2 μCi) continuous infusion of [3-3H]glucose (0.4 $\mu\text{Ci}/\text{min}$) is used to assess the rates of glucose appearance (R_a) and disappearance (R_d). Tracer is infused to allow a steady state to be reached then blood samples are taken to assess arterial glucose specific activity. R_a will be estimated as the ratio of the rate of infusion of [3-3H]glucose and the steady state plasma [3H] glucose specific activity (dpm/mg). Under steady state conditions, the rate of glucose disappearance (R_d) equals the rate of glucose appearance. The rate of glucose clearance is calculated by dividing the R_d by the arterial glucose concentration. Application of this technique is described by Niswender et al. J. Biol. Chem. 1997, and She et al. Mol. Cell. Biol. 2000.

V3005 Hyperinsulinemic clamp

Keywords: hyperinsulinemic clamp, insulin action, insulin resistance

The hyperinsulinemic clamp is used to measure insulin action in vivo. Hyperinsulinemic clamps are performed on conscious mice with catheters chronically implanted in the jugular vein and carotid artery. A continuous infusion of insulin is given. Glucose levels are monitored in arterial samples every 5-10 min using a Hemocue glucose analyzer that allows the analysis of glucose with only 8 μl of blood. Glucose is infused in the jugular vein catheter at rates necessary to achieve the desired glucose level, based on feedback from arterial glucose measurements. These methods allow assessment of the responsiveness of the body to insulin (Halseth et al. Am. J. Physiol. 1999). By combining this technique with the tracer method one can also examine the impact of insulin on suppression of endogenous glucose production.

V3006 Hyperglycemic clamp

Keywords: hyperglycemic clamp, insulin secretion, pancreas

The responsiveness of the pancreas to glucose is assessed using the hyperglycemic clamp. Hyperglycemic clamps are performed on conscious mice with catheters chronically implanted in the jugular vein and carotid artery. A defined hyperglycemic stimulus is created using a primed variable glucose infusion to raise the glucose level to twice basal for 120 min. An established priming algorithm is used to elevate glucose quickly. Mice with extra copies of the glucokinase gene locus were demonstrated to have a blunted insulin response to hyperglycemia using this technique (Niswender et al. J. Biol. Chem. 1997).

V3007 Gluconeogenesis & glycogenolysis (from hepatic 14C-UDPglucose and PEP)

Keywords: gluconeogenesis, glucose production, glycogenolysis, liver

The contribution of gluconeogenesis to the rate of glucose appearance is estimated from the specific activities of 14C-labeled hepatic uridine diphosphoglucose (this is assumed to reflect the specific activity of hepatic glucose 6-phosphate), and hepatic phosphoenolpyruvate (PEP) following the infusion of [U-14C]lactate. [3-3H]glucose is used to measure the rate of glucose appearance. Gluconeogenesis is equal to the rate of glucose appearance \times [14C]UDP-glucose specific activity/[14C]PEP specific activity \times 2. Glycogenolysis is equal to the difference between rates of glucose appearance and gluconeogenesis. The contribution of the kidney to these measurements is assumed to be small.

V3008 Glycogen synthesis

Keywords: glycogen synthesis, liver, muscle

Using [U-14C]glucose, the incorporation of the carbon of glucose into glycogen can be measured. If the ratio of [14C]UDP-glucose to blood glucose specific activity is assessed the fraction of glycogen formation from direct and indirect pathways can be calculated.

V3009 Amino acid kinetics

Keywords: amino acid flux, amino acid kinetics, isotopes

The turnover of phenylalanine (3H ring 2,3,4,5,6 phenylalanine), glutamine (U-14C-glutamine) and leucine (1-14C-leucine) is assessed by a primed continuous infusion of their respective isotopes for 2 hours (0.2-0.4 $\mu\text{Ci}/\text{min}$). Blood samples (20 μl) are taken after a steady state is reached to assess plasma amino acid specific activity. Blood samples are mixed with an equal volume of 6% sulfosalicylic acid. Incorporation of tracer in tissue protein is used to assess tissue specific protein synthesis.

V3010 Tissue specific glucose uptake

Keywords: 2-deoxyglucose, glucose metabolic index, tissue specific glucose uptake

Tissue specific glucose uptake is assessed by measuring the tissue specific uptake of [2-3H]-deoxyglucose([2-3H]DG). [2-3H]DG is infused (0.2 μ Ci/min) for 40 minutes or injected (12 μ Ci) . Arterial plasma samples are taken to determine the time course of [2-3H]DG during the 40 min period. [2-3H]DG is transported into cells and phosphorylated to yield [2-3H]DG-6-phosphate which is trapped in muscle. After 40 min mice are anesthetized with an intravenous infusion of pentobarbital and tissues of interest are rapidly removed and frozen in liquid nitrogen. This method has been applied during insulin- and exercise-stimulated conditions (Halseth et al. Am. J. Physiol. 1999).

V3011 Tissue specific fatty acid uptake

Keywords: 125I-BMIPP, tissue specific fatty acid uptake

Tissue fatty acid uptake is assessed by measuring tissue-specific incorporation of circulating 125I-BMIPP (Rottman et al. Am. J. Physiol. 2002). The beta-methyl modification of the long-chain fatty acid BMIPP (beta-methyl-p-iodophenylpentadecanoic acid) causes terminal trapping in the TCA cycle. Studies in man and a variety of small animal models, including rodents, have shown that BMIPP uptake and metabolism closely tracks that of endogenous long-chain fatty acids in a variety of normal and pathophysiologic states.

BMIPP is dissolved in propionic acid, and incorporation of 125I is catalyzed with CuSO₄. After extraction, the purified 125I-BMIPP is dissolved in ursodeoxycholic acid, filtered, and adjusted to defined activity. This stable compound is suitable for direct intravascular injection. Serum levels are stable in tracer amounts after injection, and tissue incorporation is measured by gamma counting of freeze-clamped samples in protocols compatible with the simultaneous assay of, for example, [2-3H]DG.

V3012 Indirect calorimetry /energy expenditure

Keywords: carbon dioxide, energy expenditure, gas exchange, indirect calorimetry, oxygen

Whole body VO₂ and VCO₂ is measured continuously in conscious mice using a very flexible system. The core of this system is the Oxymax Deluxe System. Oxymax software allows for calibration, experiment execution and the review of obtained data. Data can be exported or reviewed within the Oxymax System.

The system used is flexible and sensitive enough to measure small changes in VO₂ and VCO₂. It can be used to measure resting or exercising gas exchange and energy expenditure.

V3013 Exercise capacity (metabolic response to exercise)

Keywords: endurance, exercise capacity, exercise tolerance

Exercise is an integrated measure of fitness. Abnormal exercise capacity and decreased activity are a hallmark of most severe cardiovascular and metabolic diseases, and changes in exercise capacity are sensitive and early markers of cardiac and metabolic dysfunction. Thus abnormalities can be revealed with exercise that may not otherwise be manifested. Gas exchange techniques can be used during treadmill exercise in the mouse to describe the metabolic cost of exercise. Substrate fluxes and metabolism can be assessed isotopically during exercise in chronically catheterized mice (Halseth et al. Am. J. Physiol. 1999).

Treadmill exercise can be used to quantify the capacity of a mouse for either endurance or high intensity exercise. Peak exercise capacity and VO₂ max will be measured using a closed gas exchange treadmill. Acclimated mice will exercise at 3.5 m/min, 0° grade, increased to 5 m/min, 2° grade 3 minutes later and then increased by 2.5 m/min and 2° grade every 3 min thereafter up to 20 m/min and 14° grade.

V3014 Spontaneous exercise activity

Keywords: spontaneous exercise activity, wheel running

Spontaneous exercise activity is measured using a recording wheel placed in the cage during a 48 h period. The light dark cycle will be stringently controlled to minimize diurnal variations and training effects will be minimized by placing an identical wheel in the cage for the 24 hrs preceding the test measurement. Variables recorded include total distance traveled, peak speed and exercise duration.

V3015 Food Consumption

Keywords: spontaneous exercise activity, wheel running

Food consumption is assessed using an automated feeding apparatus that continually measure feeding behavior in an unobtrusive manner by allowing animals free access to food cups that are mounted on balances. The apparatus currently is capable of measuring and time-stamping individual weights from 16 balances simultaneously every 30

seconds and downloading the data directly to a computer for subsequent analysis. Therefore, cumulative food consumed and the time at which feeding bouts occur are continuously monitored. All feeding studies are done after the animal has acclimatized to the facility for at least 24 hours.

V3016 Exploratory locomotor activity

Keywords: energy expenditure, exploratory locomotor activity

Exploratory locomotor activity

V3017 Assess real time imaging of cellular metabolic events

Keywords: islets, metabolism, microcirculation, muscle, real time imaging

V3018 In vivo optical imaging of gene expression

Keywords: gene expression, GFP, luciferase

V3000A Miscellaneous Tissue and Body Fluid Collection

Keywords: tissue

Miscellaneous Tissue and Body Fluid Collection

V3000B Miscellaneous Implantation of Catheters, Sensors and Pellets

Keywords: catheterization

Miscellaneous Implantation of Catheters, Sensors and Pellets

V3000C Equipment Usage

Keywords:

Equipment Usage

V3000D Personnel Training

Keywords:

Personnel Training

V3000E Cerebral Ventricle Cannulation

Keywords: cerebral ventricle

Cerebral Ventricle Cannulation

V3000F Jugular Vein and Carotid Artery Catheterization

Keywords: catheterization

Jugular Vein and Carotid Artery Catheterization

Cardiovascular Pathophysiology & Complications Core

V3030 In vitro Morphology, Morphometrics and Histology (isolated heart)

Keywords: cardiac function, heart, morphology

A limited necropsy is conducted, noting gross observations, and removing and weighing the heart and lungs separately. After fixation, the heart is sectioned in a standard four-chamber view. Digital photographs on each heart is recorded and archived in a web-accessible format. Chamber and mural dimensions will be measured. The fixed hearts will be maintained in a physical archive, while one slice will be paraffin embedded. 4-5 sections will be cut and prepared for H& E and Masson trichrome. Digital photomicrographs will be recorded and archived together with summary evaluations. A cardiologist with special expertise in mouse cardiac development and histology reviews all gross and microscopic sections.

V3031 Echocardiography, in vivo morphology, systolic and diastolic function; Stress echocardiography

Keywords: diastolic, echocardiography, morphology, stress, systolic

Echocardiography can detect the presence of localized or generalized hypertrophy or thinning of the myocardium of the left ventricle and the presence of regional or global wall motion abnormalities. In addition to assessment of left ventricular systolic dysfunction, the application of transmitral Doppler analysis allows the detection of abnormal filling patterns associated with left ventricular diastolic dysfunction. The presence of congenital or acquired structural abnormalities of the mitral valve, as well as obstructions of left ventricular outflow (at the muscular, subvalvular, valvular or supra-valvular level) can also be evident on echocardiographic screening.

Mice are maintained at an ambient temperature of 37°C prior to imaging. Electrodes are adhered to mice using Redux creme™ to help with conductivity. Mice are imaged with transducers of at least 12 MHz using a standoff generated with Aquasonic gel™ (that is pre-centrifuged to remove air bubbles) placed in the tip of a late glove finger pulled over the tip of the transducer. The transducer is pressed gently against the mouse.

Mice are placed in a left lateral decubitus position. They are imaged initially in a parasternal long axis view to study the septum, posterior wall, apex and left ventricular outflow tract. Short axis views at the chordal level to study symmetry of wall thickness and contraction and from the supraclavicular window to examine the aortic arch and the ascending and descending aorta is obtained subsequently. For Doppler studies a mid-precordial long-axis view of the heart is acquired for color-flow and pulsed-Doppler recording. Two-dimensional and Doppler images are recorded on video tape; M-mode images are recorded on a strip chart at a speed of 100 mm/sec. Stress echocardiography is assessed following the administration of dobutamine 1.0 to 1.5 µg/g body weight by intraperitoneal injection.

The process of acclimation of the mouse to the desired temperature and imaging will take a total of 2-3 hours per mouse, though total technician attention is not required throughout this period. The stress component of the study following the administration of dobutamine is additional 10-30 minutes per mouse. All data are recorded on videotape, indexed by animal code number. A summary interpretation, as well as dimensions from the M-mode tracings, is entered in the database. A trained echocardiographer reviews data quality, raw data, and interpretation on each mouse.

V3032 Electrocardiography and telemetry

Keywords: cardiac, ECG, EKG, electrocardiography, heart, telemetry

Because of difficulties in detecting arrhythmias in anesthetized mice, a commercially-available system for recording ECG data in unanesthetized, unrestrained animals is used. Small (< 4 gm) telemetry devices (Data Sciences, Inc.) are implanted under anesthesia in the peritoneum and the wires tunneled to appropriate locations (generally left shoulder and right leg). The animals recover within a day, and ECG data can then be obtained for many hours via a telemetry receiver placed under the cage. The system has been adapted to allow detection of periods of irregular heart beat (as is seen with ventricular ectopic activity or atrial fibrillation), and analysis of heart rate variability. Data acquisition procedure consists of recording ECG data for 30 minutes from each animal typically followed by intra-peritoneal administration of isoproterenol (100 µg). An electrophysiologist examines raw and analyzed data and insures quality control.

V3033 Blood pressure measurements

Keywords: blood pressure, blood vessel, hypertension, hypotension, vascular

Blood pressure represents an integrated measure of overall cardiovascular function, and is affected by stroke volume, heart rate, inotropic state, and vascular tone. Abnormalities of blood pressure regulation (primarily hypertension, but also hypotension) are associated with major cardiovascular morbidity and mortality, and are epidemiologically associated with diabetes. Basal measurements of blood pressure are performed after mice are acclimated to the tail cuff apparatus during 3 sessions on successive days. This regimen has been shown to reduce stress-related perturbations and artifacts in measurement. Systolic and diastolic pressures are then measured over 3 sequential determinations. To mimic a particularly important human stress, we can also apply a vascular pathology model in which we induce a hypertrophic phenotype. Measurements can also be made in a model of vascular pathology in which a hypertrophic phenotype is induced dissolving 1 mg/ml of L-NAME in drinking water for 30 days. The systolic arterial pressure and heart rate of each mouse is measured before treatment and after the second and fourth weeks of treatment.

V3034 Vascular morphology

Keywords: blood vessel, histology, intima, smooth muscle, vascular

A variety of tissues (heart, aorta, kidney, brain) can be processed in four µm sections. Aortic sections are examined for wall thickening, perivascular fibrosis, and fibrin deposition. The inner border, the lumen outer border, the tunica media are traced in each arterial image with Masson's trichrome stain and imaged at a magnification of 200X. The

lumen ratio (the medial thickness to internal diameter and the area fibrosis (collagen deposition stained with aniline blue) surrounding blood vessels are calculated and compared. Perivascular fibrosis is determined as the ratio of the area of fibrosis surrounding the vessel wall to the total vessel area.

V3035 Electrolytes, indices of renal function

Keywords:

V3036 Metabolic panel

Keywords:

V3094 Perfusion-Fixation/Heart Dimension

Keywords:

Perfusion-Fixation/Heart Dimension

V3095 Heart Rate Open Variability

Keywords:

Heart Rate Open Variability

V3096 Ventricular Hemodynamics

Keywords:

Ventricular Hemodynamics

V3097 Perfusion-Fixation/Histopathology/Quantify Sclerosis

Keywords:

Anesthetized mouse will be perfused with phosphate buffered saline (PBS) at 150-160 mmHg via a butterfly 23G needle inserted into left ventricle. One kidney can be harvested and the other kidney can be further perfused with 4% paraformaldehyde.

Mouse kidney perfused with 4% paraformaldehyde will be embedded in parafine. Four-micrometer section can be processed and stained with hematoxylin-eosin (HE) or periodic acid Schiff (PAS).

Glomerulosclerotic score can be calculated in PAS stained section. Mesangial matrix expansion occupying <25, 25-50, 50-75, or >75% of tuft is scored 1, 2, 3, and 4+, respectively, and no mesangial expansion was scored as 0.

V3098 GFR-FITC-Inulin; HPLC Cr

Keywords: glomerular filtration, HPLC, kidney

GFR will be measured in conscious mice based on the decay rate of plasma FITC-inulin following a single bolus intravenous injection of FITC-inulin. This method does not require urine collection, and GFR can be periodically measured in same mouse.

Additional approach for determining GFR in conscious mouse is based on creatinine clearance rate. Mouse 24-hour urine will be collected using metabolic cage. Plasma and urinary creatinine concentration will be determined using HPLC approach.

V3099 Albuminuria

Keywords: kidney, urine

Mouse urinary albumin excretion rate can be determined by two methods: (1) measuring the albumin to creatinine ratio in spot urine sample; (2) measuring albumin concentration in urine collected over 24 hours using metabolic cage. Urinary albumin and creatinine concentration will be determined using cartridge-based DCA2000 (Bayer Diagnostics) or ELISA kits (Exocell Inc).

V4000 Renal Blood Flow (Doppler)

Keywords: blood flow, blood pressure, kidney

Mouse renal cortical and medullary blood flow can be measured using a laser-doppler flowmeter (Tansonic Systems Inc). This system will also monitor blood pressure and heart rate. Renal function including urinary electrolyte excretion can be studied.

V4001 Urine Na/K

Keywords: plasma, potassium, sodium, urine

Sodium and potassium concentration in mouse plasma and urine will be determined using an automatic flame photometer (Instrumentation laboratory Inc). This measurement requires 20 μ l of plasma or urine.

V4002 Osmometer Plasma/Urine

Keywords: osmolality, plasma, urine

Plasma and urine osmolality will be determined using a freezing point osmometer (Precision System Osmette). This measurement requires 50 μ l of plasma or urine.

V4003 Urine Ca/Phosphorus Excretion

Keywords: urine

Calcium and phosphorus are two important electrolytes in the urine. The concentration of urinary calcium and phosphorus will be determined using colorimetric assay (BioAssay Systems). The measurement for calcium and phosphorus requires 5 μ l and 50 μ l of urine, respectively.

V4004 Urine pH

Keywords: pH, urine

The pH can be determined in as little as 5 μ l of urine (or other body fluid) using a Mini Combo pH Electrode (World Precision Instruments).

V4005 Glycemic Control using Minimed

Keywords: glucose

Blood glucose levels over 72 hours can be monitored in conscious mice using Medtronic MiniMed CGMS System (Medtronic). In this system, blood glucose level is determined based on glucose concentration in interstitial fluid. A correlation between glucose levels in the blood and interstitial fluid in mice has been previously demonstrated. A fiber probe will be implanted subcutaneously. This probe will detect interstitial glucose levels every ten seconds over three days and the signals will be stored in a glucose monitor. The probe will be removed after the experiment and the mice can be sent back to the researcher.

Analytical Resources Core

V3090 Full amino acid profiles by HPLC / PITC or HLPC / OPA

Keywords: amino acids, HPLC

The laboratory primarily measures full amino acid profiles using reverse-phase, HPLC and either derivatized with phenylisothiocyanate (PITC) or orthophthalaldehyde (OPA). The minimal sample requirement is 5 μ l injection volume.

V3050 Insulin

Keywords: hormone

The insulin assay is a double-antibody/PEG RIA. The lower limit of detection is 0.02 ng/ml. Ten μ l of sample are required for a single analysis.

V3051 Glucagon

Keywords: hormone

The glucagon assay is a double-antibody/PEG RIA. The lower limit of detection is 5 pg/ml. The volume of sample required for a single analysis is 10 μ l.

V3052 Corticosterone

Keywords: hormone

The mouse corticosterone is a solid phase RIA procedure. The lower limit of detection is 20 ng/ml. The volume of sample for a single analysis is 10 µl.

V3053 Catecholamines

Keywords: hormone

The method employed is an HPLC procedure. The lower limits of detection for norepinephrine and epinephrine are 20 pg/ml. The volume of sample required for a single analysis is 100 µl.

V3054 Leptin

Keywords: hormone

Mouse leptin is assayed using a double antibody/PEG RIA. The lower limit of detection is 0.5 ng/ml. The volume required a single measurement is 20 µl.

V3055 C-Peptide

Keywords: hormone

C-Peptide is a five-day double antibody procedure. Requires 25 micro liters of plasma for duplicate analysis.

V3056 Growth Hormone (GH)

Keywords: hormone

Growth hormone is assayed in a duplicate analysis five-day double antibody procedure using 25 micro liters.

V3058 TSH

Keywords: hormone

TSH is assayed in a double-antibody RIA format. 55 micro liters of plasma is required for duplicate analysis. It involves a dilution step and is a 5-day double antibody procedure. The lower limit of the assay is 0.4ng/ml.

V3059 PRL

Keywords: hormone

Prolactin is assayed in a double-antibody RIA format. 25 micro liters of plasma is required for the assay. A dilution step is required and is 5-day double antibody assay. The lower limit of detection if 1.5ng/ml.

V3060 ACTH

Keywords: hormone

ACTH is assayed in a duplicate analysis five-day double antibody procedure using 55 micro liters of plasma.

V3061 Insulin-like growth hormone-1 (IGF-1)

Keywords: hormone

IGF-1 is a five-day double antibody procedure. 30 micro liters of plasma is used for extraction and duplicate analysis.

V3070 Plasma lipids

Keywords: fat, lipids, metabolism

Total plasma cholesterol and triglyceride are measured by standard enzymatic assays. HDL cholesterol is measured with the enzymatic method after precipitation of VLDL and LDL using dextran sulfate and Mg⁺⁺. Using these data LDL cholesterol can be calculated using the Friedewald equation, if triglyceride levels are below 400 mg/dl. Investigators may request a total plasma lipid profile or specific plasma lipid measurements.

Free fatty acids are extracted from plasma using heptane/isopropanol. The heptane layer containing FFA is removed,

plated on silica gel plates and developed in petroleum ether, ethyl ether, and acetic acid. The FFA band is scraped from the plate and FFAs are eluted with heptane /isopropanol. The solvent is removed, and the FFAs are methylated. Methylated fatty acids are analyzed by gas chromatography. Depending on the assay a variety of chromatograph conditions and columns are utilized. A computer identifies each fatty acid peak and can provide data in a number of different ways including quantitation of mass of fatty acid, percent distribution of fatty acids present, quantitation of total lipid in the sample.

V3071 Lipid extraction, separation, quantitation

Keywords: fat, lipids, metabolism

Lipids are extracted from tissue, cells, or plasma. Individual lipid classes are separated by thin layer chromatography. Lipid classes are visualized by either iodine vapors or rhodamine 6G, scraped from the plates and eluted from the silica gel. For colorimetric analysis of lipid classes, the individual lipids are eluted from the TLC silica gel. Phospholipids are analyzed either in total lipid extract or on phospholipid fraction eluted from TLC plates. Cholesterol esters and unesterified cholesterol are analyzed by the method of Babson. Alternatively, cholesterol is analyzed by gas chromatography. Lipid classes containing fatty acids are also quantitated by gas chromatography.

V3072 Fatty acid profiles of lipid esters by gas liquid chromatography

Keywords: fat, GCMS, lipids, metabolism

Total lipids are extracted and lipid classes separated by TLC as described above. Lipid ester spots are scraped from the plates and methylated. Fatty acids of lipid esters can be methylated without removal of the lipid from the silica gel. However, in some applications, we have found it advantageous to elute the lipid from the silica gel prior to methylation. The fatty acid profile of the lipid class is also determined. By this method total lipid mass and fatty acid profile for each lipid is determined.

V3073 Quantitation of individual phospholipid classes

Keywords: cholesterol, fat, lipids, metabolism, phospholipids

Individual phospholipid classes are isolated by one dimensional TLC. A total lipid extract is applied to high performance TLC plates. To quantitate the individual classes, the spots are scraped from the plate, eluted and phosphorus is determined. To determine the fatty acid composition of the individual phospholipid classes, the spots are scraped from the plates and fatty acids methylated.

V3074 Short chain fatty acid analysis by gas liquid chromatography

Keywords: fat, GCMS, lipids, metabolism, short chain fatty acid

Plasma short chain fatty acids are analyzed by the following procedure: to 200 ul of EDTA plasma in a 1.5 ml Eppendorf microfuge tube is added 20 μ l of internal standard and 1 ml of absolute ethanol. The sample is mixed thoroughly, centrifuged, and the supernatant is recovered. The sample is evaporated using a Speed Vac and dissolved in 15 μ l water, and prior to injection 5 μ l of orthophosphoric acid (25%) is added. The short chain fatty acids are separated on a 6' x 2 mm glass column packed with SP-1200/1%H₃PO₄ on 80/100 Chromosorb W AW.

V3075 Lipoprotein fractionation and characterization

Keywords: fat, lipids, lipoproteins, metabolism

Lipoprotein fractions are isolated using columns arranged in tandem to achieve complete resolution of the major lipoprotein classes from 1-2 ml of plasma. The columns are equilibrated in 50 mM phosphate-buffered saline and calibrated using lipoprotein fractions isolated by ultracentrifugation. Fractions (0.5 ml) are collected and the appropriate tubes containing the desired lipoprotein fraction(s) combined. The position of the major lipoprotein classes are determined by cholesterol (or triglyceride) assay on the column fractions using a microtiter plate enzyme-based assay. As an alternative method lipoproteins can be isolated by fast protein liquid chromatography.

This includes analysis of the composition of the fraction (protein and lipid) as well as morphologic analysis (sizing) by negative stain electron microscopy. For compositional analysis the lipoprotein fractions protein is analyzed using the BCA method with a modification to eliminate lipid interference. The samples are then lyophilized and delipidated using ethanol and ether. Lipid components are separated by TLC and analyzed by GLC and/or colorimetric assays.

V3076 Morphometric determinations (aorta)

Keywords: blood vessel, histology, intima, smooth muscle, vascular

Mice are sacrificed and flushed with 30 ml saline. The heart with ascending aorta is embedded and snap-frozen in liquid N₂. Cryosections of 10 µm thickness are taken from the region of the proximal aorta. Cryosections are stained with Oil Red O and counterstained with hematoxylin. In addition to the aortic cross-sections, whole aortas will be analyzed in "en face" preparations to evaluate the distribution and characteristics of atherosclerotic lesions in the distal aorta. After the removal of the heart and the aortic arch, the entire remainder of the thoracic and abdominal aorta is dissected from the carcass. An incision is then performed longitudinally and for the total length of the specimen, so to expose the inside face. The open face aorta is pinned out on a black cardboard submerged in saline, and then stained with Oil Red O.

V3080 Gross examinations and necropsy

Keywords: gross examination, necropsy

The standard necropsy procedure for diabetic mice includes an examination of the pancreas, heart, liver, eyes, peripheral nerves, peripheral vasculature, fat, and kidneys. Complete, intermediate, or limited necropsies will be performed with or without the aid of a dissecting microscope. Gross pathologic findings will be described, documented by digital photography and organs will be weighed.

V3081 Tissue preparation, embedding, sectioning and routine staining

Keywords: embedding, sectioning, staining, tissue preparation

The default fixative will be 4% paraformaldehyde. This offers investigators the option of later performing in situ hybridization or laser microdissection and capture of protein, DNA or RNA from select populations. This fixative provides a minimal degree of cross-linking of the proteins, thereby rendering antigenic sites more accessible. Other fixatives are used as appropriate. If frozen sections are needed, tissues will be snap frozen in liquid nitrogen and sectioned on a cryostat. When molecular analyses are required, tissue samples can also be rapidly placed in Trizol or RNA extraction solutions and stored at -80°C until investigators retrieve their samples.

V3082 Tissue microdissection

Keywords: laser microdissection, pancreas

Potential applications of laser dissection include the selective microdissection of islet cells for gene expression studies, harvesting and analysis of specific glomerular cells in diabetic nephropathy, and harvesting endothelial cells from diseased microvasculature. This Core has available a PixCell II™ laser capture microdissection device (Arcturus Engineering) and a PALM microdissection scope. These workstations perform laser capture microdissection simply, quickly and precisely. They are capable of locating single cells or large groups of cells and, using a simple aim-and-shoot method to extract them for subsequent molecular analysis (DNA, RNA, or protein).

V3083 Screen/optimize immunohistochemical protocols for mouse-specific commercial and custom-designed antisera

Keywords: histology, immunohistochemistry

To stain mouse tissues with mouse monoclonal antisera we utilize Mouse-on-Mouse (MOM) kits (Vector Labs), Ark kits (DAKO Corp) or HistoMouse Kits. Although peroxidase-based protocols will be the mainstay of the Subcore with visualization by brown DAB or red AEC chromagens, staff is familiar with the alkaline phosphatase-based kit and its detection with the fuschin chromagen. Fluorescently-tagged primary, secondary, or tertiary antibodies in frozen sections, cultured cells, or for co-localization studies will be used as required to tailor protocols to address investigator needs. Non-fluorescent double immunostaining will also be performed in the Pathology Subcore using the Double Label Kit provided by DAKO. When prospective antisera fail to recognize antigenic sites in paraffin embedded sections or produce non-specific staining patterns, we advise investigators to proceed with frozen sectioning.

V3091 Specific selected amino acid profiles

Keywords: amino acids, HPLC

BCAA and phenylalanine, gluconeogenic amino acids, and glutamate and GABA are measured using OPA derivatization and reverse-phase HPLC. These methods offer the advantages of speed, small sample sizes (<20 µl) and high sensitivity.

V3092 Radioactivity of specific individual amino acids

Keywords: amino acids, chromatography, protein synthesis, proteolysis, specific activity

a. Alanine and glutamine: Deproteinized blood will be injected onto a cation exchange column; separating the amino

acids. As the amino acids elute, a portion of the eluent is diverted to a fraction collector for counting of radioactivity. A portion of the eluent is derivatized with ninhydrin. The color complex produced is measured to determine amino acid concentrations.

b. Leucine and phenylalanine: An HPLC method, requiring 20 μ l of blood is used to measure specific activities in blood and tissue in tissues.

V3093 Specific activities for gluconeogenic and glycogenic assessment

Keywords: amino acids, chromatography, protein synthesis, proteolysis, specific activity

UDP glucose, UDP -galactose and PEP specific activities in perchloric acid extracts of liver will be obtained by sequential chromatographic separations as described by Rossetti.

V3062 Aldosterone

Keywords: hormone

The aldosterone assay is a non-extraction double-antibody RIA. The lower limit of detection is 2 pg/ml. 45 micro liters of plasma for duplicate analysis. Involves a dilution step and is a 2-day double antibody procedure.

V3064 Resistin

Keywords: hormone

Resistin may be analyzed in a double - antibody RIA format. It is a two day assay at room temperature. Sample volume: 50 μ L Plasma, serum or tissue culture medium. The lower limit of detection is 0.78 ng/mL. Can also be run as single-plexed assays using luminex instrumentation. A dilution step is required for the adiponectin requiring a minimum of 5 ul of sample. The resistin does not require a dilution and may be multiplexed with other adipokines with a required sample volume of 25 ul for duplicate analysis.

V3065 Adiponectin

Keywords: hormone

Adiponectin may be analyzed in a double-antibody RIA format. It requires an overnight incubation at room temperature. Sample volume < 2 μ L serum or plasma, or < 100 μ L tissue culture media. A 1:400 x dilution is required. The lower limit of detection is 1.56 pg/mL. Can also be run as single-plexed assays using luminex instrumentation. A dilution step is required for the adiponectin requiring a minimum of 5 ul of sample. The resistin does not require a dilution and may be multiplexed with other adipokines with a required sample volume of 25 ul for duplicate analysis.

V3066 Estradiol

Keywords: hormone

Estradiol is assayed in a double- antibody RIA in an overnight incubation at 37C + 15-20 minutes at room temperature. Fifty micro liters of sample are required for duplicate analysis. The lower limit of detection is 4.7 pg/ml.

V3067 Testosterone

Keywords: hormone

Testosterone is assayed in a Double Antibody RIA. Fifty μ L of serum or plasma is required for duplicate analysis. An overnight incubation at 37C + 10-15 minutes at room temperature are required. The lower limit of detection is 0.05ng/ml.

YALE UNIVERSITY SCHOOL OF MEDICINE

In Vivo Metabolism Core

Y4001 Hyperinsulinemic-euglycemic clamp experiments

Keywords: insulin action, insulin resistance

The surgery is performed at 4-5 days prior to the hyperinsulinemic-euglycemic clamp to establish a chronic catheter for intravenous infusion of substances (e.g., glucose, insulin) during the clamp. For this, a mouse is anesthetized with

an intraperitoneal injection of ketamine and xylazine, and a catheter is inserted in the right jugular vein. On the day of clamp experiment, an overnight-fasted mouse is placed in an over-sized restrainer (i.e., rat-sized) for the experiment to be conducted in awake and minimally-stressed state. The tail is tethered using a tape for 2 hours prior to the start of experiment for acclimatization. A 3-way connector is attached to the jugular vein catheter for intravenous infusion, and the blood samples are obtained from the tail vessels requiring a small tail cut. A 2-hour hyperinsulinemic-euglycemic clamp is conducted with a primed-continuous infusion of human insulin at a rate of 15 pmol/kg/min to raise plasma insulin within a physiological range (~300 pM). Blood samples (20 ml) are collected at 10-20 min intervals for the immediate measurement of plasma glucose concentration, and 20% glucose is infused at variable rates to maintain glucose at basal concentrations (~6 mM). Insulin-stimulated whole body glucose metabolism is assessed with a continuous infusion of [3-3H]glucose (0.1 mCi/min) throughout the clamps. Basal rates of whole body glucose turnover are assessed using a primed-continuous infusion of [3-3H]glucose for 2 hours prior to the start of clamp. All infusions are performed using the microdialysis pumps, and all procedures are approved by Yale University Animal Care and Use Committee. To estimate insulin-stimulated glucose uptake in individual tissues, 2-deoxy-D-[1-14C]glucose (2-[14C]DG) is administered as a bolus (10 mCi) at 75 min after the start of clamp. Blood samples (20 ml) are taken at -5, 80, 85, 90, 100, 110, and 120 min of clamp for the measurement of plasma [3H]glucose, 3H₂O, and/or 2-[14C]DG concentrations. Additional blood samples (20 ml) are collected before and at the end of clamp for the measurement of plasma insulin concentrations. At the end of clamp, mouse is anesthetized with sodium pentobarbital injection, and tissues are taken and stored for biochemical/molecular analysis. The clamp experiment measures tissue-specific insulin action and glucose metabolism and includes the following measurements: 1) basal and insulin-stimulated hepatic glucose production, 2) insulin-stimulated whole body glucose uptake, glycolysis, and glycogen plus lipid synthesis, and 3) insulin-stimulated glucose uptake, glycolysis, and glycogen synthesis in individual tissues (e.g., skeletal muscle, adipose tissue, heart). Additionally, biochemical/molecular assays may be performed to assess tissue-specific insulin signaling activities (e.g., insulin-stimulated tyrosine phosphorylation of IRS, PI 3-kinase activity) and tissue-specific triglyceride contents. Further details of the clamp experiment can be found in the following references: Diabetes 53:1060 (2004), J. Clin. Invest. 114:823 (2004).

Y4002 Hyperglycemic clamp experiments

Keywords: insulin secretion, pancreas

The procedure involves chronic cannulation of the jugular vein which is necessary for The surgery is performed at 4-5 days prior to the hyperglycemic clamp to establish a chronic catheter for intravenous infusion of substances (e.g., glucose, insulin) during the clamp. For this, a mouse is anesthetized with an intraperitoneal injection of ketamine and xylazine, and a catheter is inserted in the right jugular vein. On the day of clamp experiment, an overnight-fasted mouse is placed in an over-sized restrainer (i.e., rat-sized) for the experiment to be conducted in awake and minimally-stressed state. The tail is tethered using a tape for 2 hours prior to the start of experiment for acclimatization. A 3-way connector is attached to the jugular vein catheter for intravenous infusion, and the blood samples are obtained from the tail vessels requiring a small tail cut. A 2-hour hyperglycemic clamp is conducted with a variable infusion of 20% glucose to raise and maintain plasma glucose concentrations at ~16 mM. Blood samples (20 ml) are collected at 10-20 min intervals for the immediate measurement of plasma glucose concentrations using Beckman Glucose Analyzer. The area under curve of plasma glucose and insulin profiles is assessed to determine glucose-induced insulin secretion in vivo (i.e., pancreatic β -cell function).

Analytical Core

Y4060 Diacylglycerol concentration

Keywords: fat, lipids, metabolism, signaling

Diacylglycerols (DAGs) are extracted from 100mg frozen tissue with chloroform/methanol (2:1, vol/vol) containing 0.01% BHT (butylated hydroxytoluene). Prior to the extraction, known amount of 1,3-dipentadecanoin and triheptadecanoin are added as internal standard. Extracted samples were evaporate to dryness and redissolved in 1ml of hexane:ethyl acetate (85:15, vol/vol). DAGs were isolated from triglycerides (TGs) by use of a diol bonded phase SPE column (Waters, Inc., Milford, MA) under vacuum. The SPE column was preconditioned with 4 ml hexane, the lipid extract was placed on the column and TGs eluted with 8 ml of hexane-methylene chloride-ethyl ether (89:10:1, vol/vol/vol). DAGs were eluted with 8 ml of hexane-ethyl acetate (85:15, vol/vol) into a second set of collection tubes. The solvent were evaporated to dryness under vacuum and redissolved in 0.5 ml of hexane:ethyl acetate (85:15, vol/vol) for LC/MS/MS analysis. Separation of TGs from DAGs was assessed by monitoring for the presence of triheptadecanoin in the DAG fraction. Analysis is performed on a bench top tandem mass spectrometer API3000 (Perkin- Elmer Sciex) interfaced with an APCI (Atmospheric Pressure Chemical Ionization) source in flow injection mode. DAG species are readily ionized in APCI mode, and are quantified by monitoring $_M+H-18_+$ /product ions from corresponding fatty acid moiety.

Y4050 Amino Acids

Keywords: amino acids, enrichment, isotopes, metabolite

BCAA and phenylalanine, gluconeogenic amino acids, and glutamate and GABA concentration, and ^{13}C or ^2H isotopic enrichments, are measured (as the trifluoro-acetamide n-butyl ester derivatives) using GC-MS (HP 5973MSD, Hewlett-Packard Instrument Corp., Palo Alto, CA). These measurements can be made in 20 μl plasma, or 50 mg tissue.

Y4051 Beta-hydroxybutyrate

Keywords: diabetes, enrichment, ketones, metabolite

Plasma beta-hydroxybutyrate concentration, and ^{13}C or ^2H isotopic enrichments, are measured (as the TMS derivative) using GC-MS (HP 5973MSD, Hewlett-Packard Instrument Corp., Palo Alto, CA). These measurements can be made in 20 μl plasma.

Y4052 Free fatty acid

Keywords: diabetes, enrichment, fat, lipids, metabolite

Total serum non-esterified fatty acid concentrations are measured using an acyl-CoA oxidase-based colorimetric kit (Wako NEFA-C, Wako Pure Chemical Industries, Osaka, Japan). For measurements of free fatty acid profiles, and isotopic enrichments, ^{13}C , or ^2H , the lipids are extracted from plasma with heptane/isopropanol. This solvent is evaporated and the free fatty acids are methylated using diazomethane, and analyzed by GC-MS (HP 5973MSD, Hewlett-Packard Instrument Corp., Palo Alto, CA). These measurements can be made in 20 μl plasma.

Y4053 Glucose

Keywords: carbohydrate, diabetes, metabolite

Plasma glucose concentrations are measured by the glucose oxidase method (Glucose Analyzer II; Beckman Instruments, Fullerton, CA). ^{13}C , or ^2H , isotopic enrichments, are measured (as the penta-acetate derivative) using GC-MS (HP 5973MSD, Hewlett-Packard Instrument Corp., Palo Alto, CA). These measurements can be made in 20 μl plasma.

Y4054 Glycerol

Keywords: diabetes, enrichment, lipids, metabolite

Plasma glycerol concentrations, ^{13}C , or ^2H , isotopic enrichments, are measured (as the tri-acetate derivative) using GC-MS (HP 5973MSD, Hewlett-Packard Instrument Corp., Palo Alto, CA). These measurements can be made in 20 μl plasma.

Y4055 Glycogen

Keywords: carbohydrate, diabetes, metabolite

Liver, and muscle glycogen is extracted with 0.9 N perchloric acid and 99% ethanol to precipitate glycogen. The glycogen from the pellet is dialysed, and digested to free glucose with amyloglucosidase. Concentrations are determined as described above for glucose. These measurements can be made in 10 mg tissue. Specific carbon labeling is determined by ^{13}C -NMR (Avance 500, Bruker, Inc. Billerica, MA). Total ^{13}C , or ^2H , isotopic enrichments are determined (as the penta-acetate derivative) using GC-MS (HP 5973MSD, Hewlett-Packard Instrument Corp., Palo Alto, CA). These measurements can be made in 100 mg tissue.

Y4057 Long-chain fatty acyl CoA esters

Keywords: fat, lipids, metabolism

Frozen tissue (~100mg), liver or muscle, is ground under liquid nitrogen and homogenized in 100mM KH_2PO_4 , pH 4.9 and 2-propanol. Heptadecanoyl CoA was added as internal standard. Saturated $(\text{NH}_4)_2\text{SO}_4$ and acetonitrile are added for phase separation solid phase extraction using Oligonucleotide Purification Cartridges (Applied Biosystems, Singapore). The cartridges are washed with distilled water, and then long-chain fatty acyl CoA esters (LCACoAs) are eluted slowly with 0.5ml of 60% acetonitrile. The eluent is dried, then reconstituted in 100 μl of methanol/ H_2O for ESI/MS/MS analysis. Analysis is performed on a bench top tandem mass spectrometer API3000 (Perkin-Elmer Sciex) interfaced with a TurboIonspray ionization source in flow injection mode. Using negative electrospray ionization mode, LCACoAs are ionized predominantly to doubly charged form and yields abundant specific product ions from CID (collision induced dissociation). LCACoAs are quantified by monitoring $[\text{M}-2\text{H}]^{2-}/[\text{M}-\text{H}-80]^{-}$.

Y4059 ADP, ATP

Keywords: energetics, high-energy phosphates, mitochondria

Tissues (50 to 100 mg) are extracted with 0.9N ice-cold perchloric acid. The concentrations of nucleotides, ATP, ADP, and AMP, in the supernatant are then determined by HPLC using a Supelcosil SAX1 (25cm x 4.6 mm x 0.5 μ m) column using a gradient of 5 mM ammonium phosphate, pH2.8 (buffer A) and 750 mM ammonium phosphate, pH 3.9 (buffer B) at a flow rate of 1 ml/min. A linear gradient is developed over 14 minutes at 0% buffer B to 9% buffer B, then from 14 to 32 minutes from 9% buffer B to 100% buffer B. A Rainin HPXL solvent delivery system (2 pumps) with a Rainin Dynamax UV-1 absorbance detector (254 nm) controlled by Rainin Dynamax HPLC Method Manager is used for solvent programming and data collection. Peak identification was assigned by comparison of retention times to known external standards (AMP: \sim 5.5 min, ADP: \sim 25.7 min, ATP: \sim 29.0 min). Nucleotide concentrations were calculated from the concentration standard curves of absorbance for the external standards

Y4070 Chem 7

Keywords: serum chemicals, serum metabolic panel

A complete panel consists of five analytical tests. The cost for a complete Chem 7 Panel is 5 times the price indicated for each analysis. Each of these tests can be individually chosen from the catalog.

The serum metabolic panel is obtained using the COBAS MIRA system (Roche Diagnostics, Indianapolis, IN).

The serum chemicals are as follows:

- 1) BUN (blood urea nitrogen)
- 2) Chloride
- 3) CO₂ (carbon dioxide)
- 4) Creatinine
- 5) Glucose
- 6) Potassium
- 7) Sodium

Y4071 Liver Function Tests

Keywords: serum chemicals, serum metabolic panel

A complete panel consists of seven analytical tests. The cost for a complete Liver Function Test panel is 7 times the price indicated for each analysis. For a subset of this panel, select each desired test individually from the catalog.

The serum metabolic panel is obtained using the COBAS MIRA system (Roche Diagnostics, Indianapolis, IN).

The serum chemicals, and enzyme activities, measured are as follows:

- 1) Albumin
- 2) ALT: Alanine Transferase
- 3) ALP: Alkaline Phosphatase
- 4) AST: Aspartate Aminotransferase
- 5) Total Bilirubin
- 6) Total Protein

Y4072 Lipid Panel

Keywords: serum chemicals, serum metabolic panel

A complete panel consists of six analytical tests. The cost for a complete Lipid Panel is 6 times the price indicated for each analysis. A subset of the complete panel can be chosen.

A serum metabolic panel is obtained using the COBAS MIRA system (Roche Diagnostics, Indianapolis, IN).

The serum chemicals, and enzyme activities, measured are as follows:

- 1) Non-esterified fatty acids
- 2) β -Hydroxybutyrate
- 3) Cholesterol
- 4) HDL-cholesterol direct
- 5) LDL-cholesterol direct
- 6) Triglycerides

Y4073 Divalent Ions

Keywords: serum chemicals

A complete panel consists of three analytical tests. The cost for a complete panel is 3 times the price indicated for each analysis. A subset of the complete panel can be chosen.

A serum metabolic panel is obtained using the COBAS MIRA system (Roche Diagnostics, Indianapolis, IN).

The serum divalent ions measured are as follows:

- 1) Calcium
- 2) Inorganic Phosphorus
- 3) Magnesium

Y4080 Insulin

Keywords: hormone

Plasma immunoreactive insulin is assayed using a double-antibody immunoassay kit and rat insulin standards (Linco Research, St. Louis, MO).

Y4081 Glucagon

Keywords: hormone

Plasma immunoreactive glucagon is assayed using a double-antibody immunoassay kit (Linco Research, St. Louis, MO).

Y4082 Leptin

Keywords: hormone

Plasma immunoreactive leptin is assayed using a double-antibody immunoassay kit (Linco Research, St. Louis, MO)

Y4061 Lysophosphatidic Acid

Keywords: lipids

Y4083 Blood Glucose

Keywords: carbohydrate, diabetes, glucose, plasma, serum chemicals, serum metabolic panel

Measures serum or plasma glucose levels by the Hexokinase (HK) Glucose-6-phosphate dehydrogenase (G-6-P-DH) reactions. The test is performed on a Roche COBAS Mira Plus automated chemistry analyzer.

Y4084 Blood Urea Nitrogen

Keywords: renal, serum chemicals, serum metabolic panel

Determination of "blood" urea nitrogen (BUN) is used as a test for renal function, usually in conjunction with other tests such as creatinine. The test is performed on serum or plasma using the Roche COBAS Mira Plus automated

chemistry analyzer.

Y4085 Blood Creatinine-HPLC

Keywords: kidney, muscle, renal, serum chemicals, serum metabolic panel

The quantitation of creatinine in serum or plasma can be useful in determining renal function, particularly in combination with the BUN assay. Creatinine is quantified by HPLC/MS/MS.

Y4086 Urine Creatinine-HPLC

Keywords: kidney, muscle, renal, serum chemicals, serum metabolic panel, urine

The quantitation of creatinine in urine can be useful in determining renal function, particularly in combination with the BUN assay. Creatinine is quantified by HPLC/MS/MS.

Y4087 Blood Electrolytes-Na/Cl/K

Keywords: electrolytes, metabolism, muscle, pH, plasma, potassium, serum chemicals, serum metabolic panel, sodium

For the determination of plasma or serum electrolyte levels (chloride, potassium, and sodium) using ion-selective electrodes on the Roche COBAS Mira Plus automated chemistry analyzer. All three analytes are measured simultaneously, and are therefore ordered and reported as a group.

Y4089 Blood Bicarbonate/CO₂

Keywords: carbon dioxide, metabolism, serum chemicals, serum metabolic panel

Approximately 90% of carbon dioxide present in serum or plasma is in the form of bicarbonate. The remainder is in the form of dissolved gas and as carbamino-bound CO₂. The measurement of serum or plasma CO₂ content, when performed in conjunction with the determination of pH, is useful in the assessment of disturbances acid-base balance in respirator or metabolic acidosis and alkalosis. The enzymatic assay is performed on blood serum or plasma with a Roche COBAS Mira Plus automated chemistry analyzer.

Y4091 Blood Albumin

Keywords: liver, plasma, serum albumin, serum chemicals

Elevated serum albumin is seldom encountered, and it is usually a result of dehydration. Main causes are malnutrition, decreased synthesis in liver diseases, proteinuria in the nephrotic syndrome, losses or decreased absorption in gastrointestinal diseases, carcinomatosis, congestive heart failure, and/or losses from extensive skin lesions such as diffuse dermatitis and burns. Determinations of blood albumin levels are conducted on the Roche COBAS Mira Plus automated chemistry analyzer, using the albumin-bromocresol green reaction.

Y4092 Alanine Aminotransferase

Keywords: ALT, liver, plasma, serum chemicals

The ALT test can be used for the diagnosis of acute hepatic diseases. The determination of ALT activity in serum or plasma is conducted on the Roche COBAS Mira Plus automated chemistry analyzer.

Y4093 Aspartate Aminotransferase

Keywords: liver, plasma, serum chemicals

This test is used for the quantitative determination of aspartate aminotransferase activity in serum or plasma on the Roche COBAS Mira Plus automated chemistry analyzer.

Y4094 Alkaline Phosphatase

Keywords: liver, plasma, serum chemicals

Alkaline phosphatase is found in almost every tissue in the body. Most of the ALP in normal adult serum is from the liver or biliary tract. Elevation of alkaline phosphatase values occurs in liver diseases such as hepatitis, cirrhosis, malignancy, chemical toxicity, and in bone diseases such as metastatic carcinoma, rickets, Paget's disease, and

osteomalacia. This test is for the quantitative determination of alkaline phosphatase (E.C. 3.1.3.1) activity in serum or plasma and uses the Roche COBAS Mira Plus automated chemistry analyzer.

Y4095 Total Bilirubin

Keywords: bilirubin, liver, serum chemicals

This test is intended for the quantitative determination of total bilirubin in serum using the Roche COBAS Mira Plus automated chemistry analyzer

Y4097 Total Protein

Keywords: liver, plasma, serum chemicals

This test is intended for the quantitative determination of total protein in serum or plasma using the Roche COBAS Mira Plus automated chemistry analyzer.

Y4098 HDL Cholesterol

Keywords: cholesterol, lipids, lipoproteins

This test is intended for the quantitative determination of HDL cholesterol in serum or plasma using the Roche COBAS Mira Plus automated chemistry analyzer.

Y4099 LDL Cholesterol

Keywords: cholesterol, lipids, plasma, serum chemicals

This test is intended for the quantitative determination of LDL cholesterol in serum or plasma using the Roche COBAS Mira Plus automated chemistry analyzer.

Y5000 Cholesterol

Keywords: cholesterol, lipids, plasma, serum chemicals

This test is intended for the quantitative in vitro measurement of total serum or plasma cholesterol concentrations, utilizing the Roche COBAS Mira Plus automated chemistry analyzer.

Y5001 Triglycerides

Keywords: lipids, plasma, serum chemicals

This test is intended for the quantitative determination of triglycerides in serum or plasma, utilizing the Roche COBAS Mira Plus automated chemistry analyzer.

Y5002 Non-Esterified Fatty Acids

Keywords: fatty acids, lipids, non-esterified fatty acid, serum chemicals

This test is an in vitro enzymatic colorimetric method for the quantitative determination of non-esterified fatty acids (NEFA) in serum, utilizing the Roche COBAS Mira Plus automated chemistry analyzer.

Specimens that are noticeably icteric, hemolyzed, or lipemic will require a sample blank in order to yield accurate results. A sample blank requires a minimum serum volume equal to that of the normal assay, and will be billed as a separate assay.

Y5003 Beta-Hydroxybutyrate (COBAS)

Keywords: diabetes, ketones, plasma, serum chemicals

This test is intended for the quantitative determination of beta-hydroxybutyrate in serum or plasma, utilizing the Roche COBAS Mira Plus automated chemistry analyzer.

Y5004 Blood or Urine Calcium

Keywords: serum chemicals

This is intended for the quantitative determination of calcium in serum, utilizing the Roche COBAS Mira Plus automated

chemistry analyzer.

Y5005 Blood Inorganic Phosphorous

Keywords: inorganic phosphate, phosphate, serum chemicals

This test is intended for the quantitative determination of inorganic phosphorous in serum using the Roche COBAS Mira Plus automated chemistry analyzer.

Y5007 Magnesium

Keywords: serum chemicals

This test is intended for the quantitative determination of serum magnesium, utilizing the Roche COBAS Mira Plus automated chemistry analyzer.

Y5006 Urine Inorganic Phosphorous

Keywords: inorganic phosphate, phosphate, urine

This test is intended for the quantitative determination of inorganic phosphorous in urine, utilizing the Roche COBAS Mira Plus automated chemistry analyzer.

Y5008 Creatine Kinase

Keywords: creatine kinase, serum chemicals

This test is intended for the quantitative determination of creatine kinase in serum, utilizing the Roche COBAS Mira Plus automated chemistry analyzer.

Y5009 Lactate Dehydrogenase

Keywords: serum chemicals

This test is intended for the quantitative determination of lactate dehydrogenase activity in serum, utilizing the Roche COBAS Mira Plus automated chemistry analyzer.

Y5010 Apolipoprotein C3

Keywords: lipids, lipoproteins, serum chemicals

This test is intended for the quantitative determination of human apolipoprotein (ApoC3) in serum by immunoturbidimetric assay, utilizing the Roche COBAS Mira Plus automated chemistry analyzer.

Y4088 Urine Electrolytes-Na/K/Cl

Keywords: electrolytes, muscle, potassium, urine

For the determination of urine electrolyte levels (chloride, potassium, and sodium) using ion-selective electrodes on the Roche COBAS Mira Plus automated chemistry analyzer. All three analytes are measured simultaneously, and are therefore ordered and reported as a group.