Vanderbilt
Mouse Metabolic Phenotyping Center

http://www.mc.vanderbilt.edu/MMPC
twitter:@mousecentral

Staying Ahead of the Curve and Adding Value to the Program:

- Standardize
- “Brand”
- Innovate
- Education and Outreach

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MMPC Executive Committee

Director: David H. Wasserman, PhD

Associate Director: Owen P. McGuinness, PhD

Administrator and AP Guru: **Fran Tripp**

Executive Committee: Cone, Harris, Harrison, Magnuson, Peek, Powers

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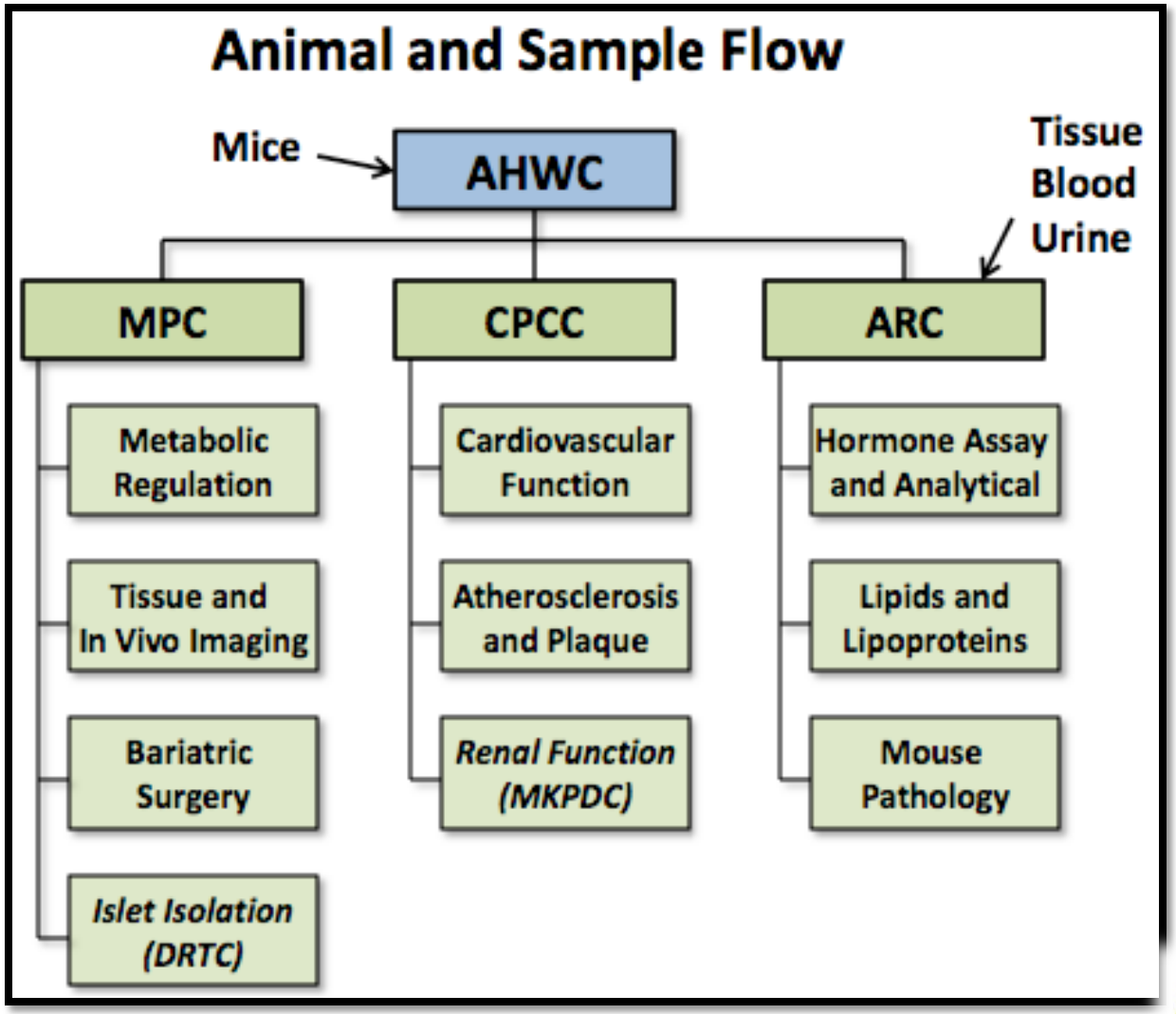
Cores and Subcores of the MMPC



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A New Policy

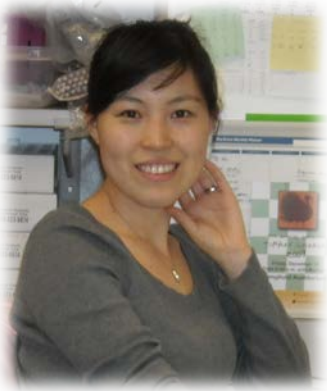
- Vandy now allows the MMPC to offset the added cost to outside investigators due to shipping, serology, quarantine.
- Outside investigators that request services that are of particular interest to our MMPC will be granted an “MMPC Scholarship”.

Metabolic Pathophysiology Core (MPC)

Director: Owen P. McGuinness, PhD

Associate Director: Kate Ellacott, PhD

Managing Director: Li Kang, PhD



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About Our New MMPC Laboratory…

One Important Step Closer

Procedures/services

- Telemetry (e.g. Temperature)
- **Energy balance (activity, food intake, EE)**
- **Urine and blood analysis**
- **Surgical procedures**
  - **Catheterizations**
  - Bariatric surgery

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Procedures

- **Glucose tolerance test**
- **Clamps**
- Metabolic flux during exercise
- Circadian rhythm cycles ****new****

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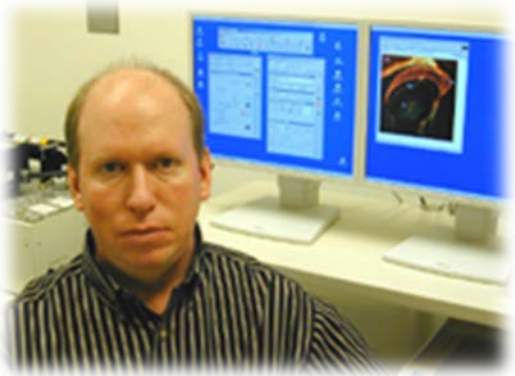
MPC Subcores



Imaging

- Director: Dave Piston PhD
- Associate Director: Sam Wells PhD

Islet Isolation (DRTC)

- Director: Marcella Brissova, PhD

Bariatric Surgery (DRTC, DDRC)

- Director: Dengping Yin, MD PhD

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Cardiovascular Pathophysiology and Complications Core

Director: Chee Lim, PhD

Consulting Director: Jeff Rottman, MD

Associate Director: MacRae Linton, MD

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Principal Services

- **Echocardiography**
- **Invasive and non-invasive measurements of BP**
- Exercise capacity
- **Telemetry and electrocardiography**
- **Myocardial infarct**
- Tissue O_2, N_2, diffusivity, blood flow ***new***
- Surgical models

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Analytical Core

Director: Sergio Fazio, MD

- Hormone Assay and Analytical Services (Edgerton/Snead)
- Lipids, Lipoproteins, and Atherosclerosis (Swift)
- Mouse Pathology (Boyd)

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Gross Income

Core	6/1/11 to 5/31/12	6/1/12 to 5/31/13	6/1/13 to 5/31/14**
	Dollars		
MPC	243,181	239,626	232,411
CPCC	201,390	239,845	231,077
ARC	196,692	185,360	210,648
Total	641,263	664,831	674,136

**Projected

Usage

Core	6/1/11 to 5/31/12	6/1/12 to 5/31/13	6/1/13 to 5/31/14**
	Local/Outside		
MPC Users	165/40	150/61	182/62
MPC Services	7608/2564	5949/2429	6143/2409
CPCC Users	120/22	75/12	87/17
CPCC Services	3523/265	3171/432	3213/773
ARC Users	150/105	108/164	104/99
ARC Services	30568/5396	9102/6762	11901/5979
Pharma/Biotech: Eli Lily, GSK, Pfizer, BMS, Halozyme, Imclone, Incyte, Genentech, Diamedica, Regeneron **annualized			

Necessity is the Mother of Invention

Metabolic Flux and Metabolomics

new

Wasserman/Young Laboratories

Clinton Hasenour PhD (expected Jan 2014)

Emerson Ridley

Martha Wall

Jamey Young PhD (Chem Eng)

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Analytical Core

Metabolic Flux and Metabolomics

new

<u>Developed by:</u>

Clinton Hasenour PhD (expected Jan 2014)

Emerson Ridley

Jamey Young PhD (Chem Eng)

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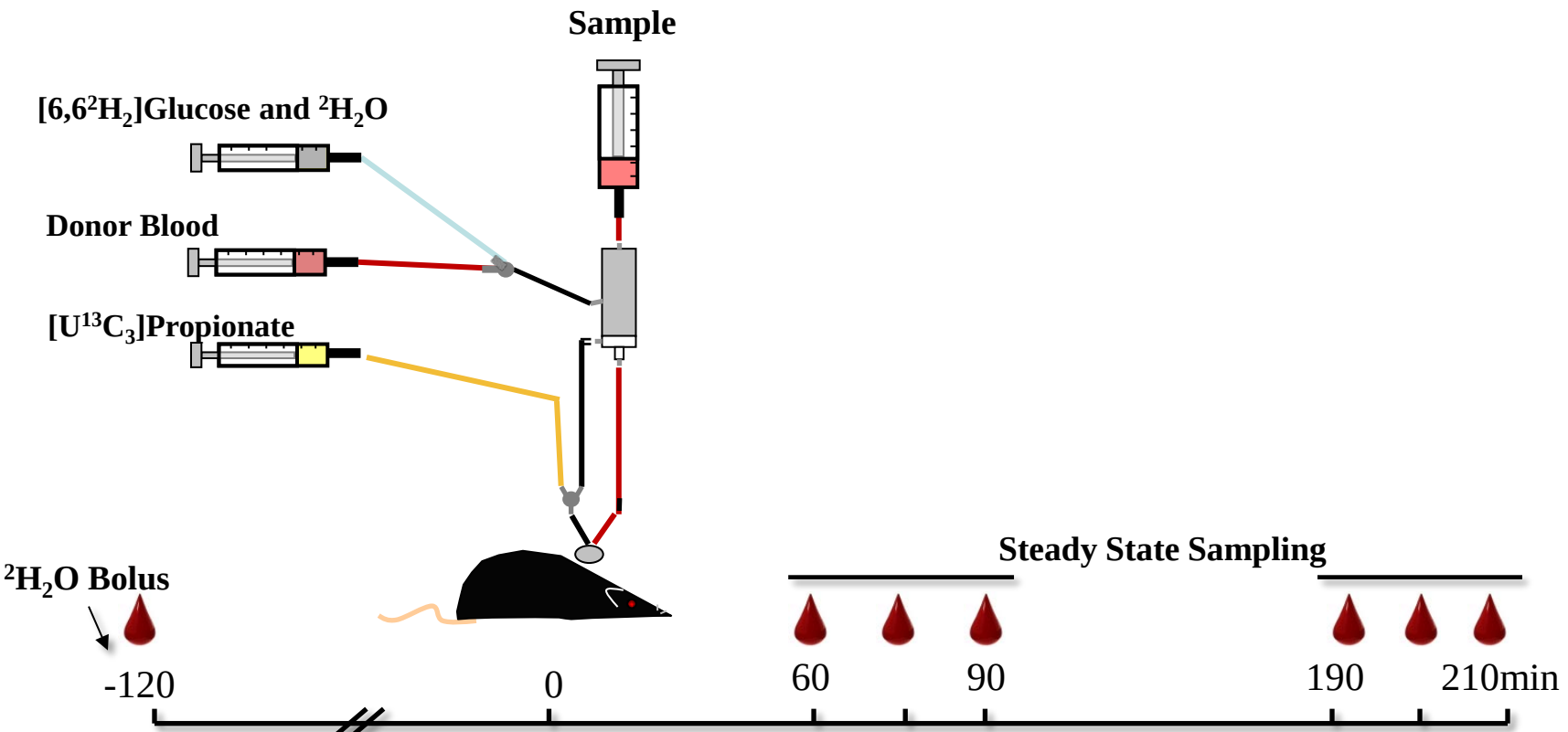
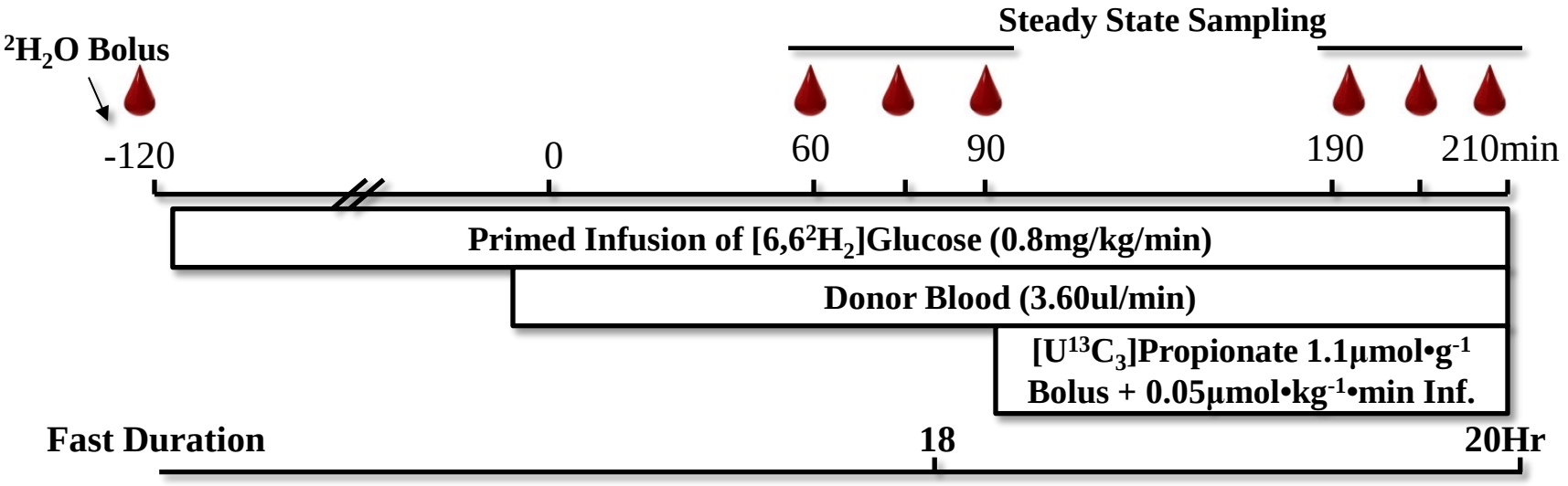
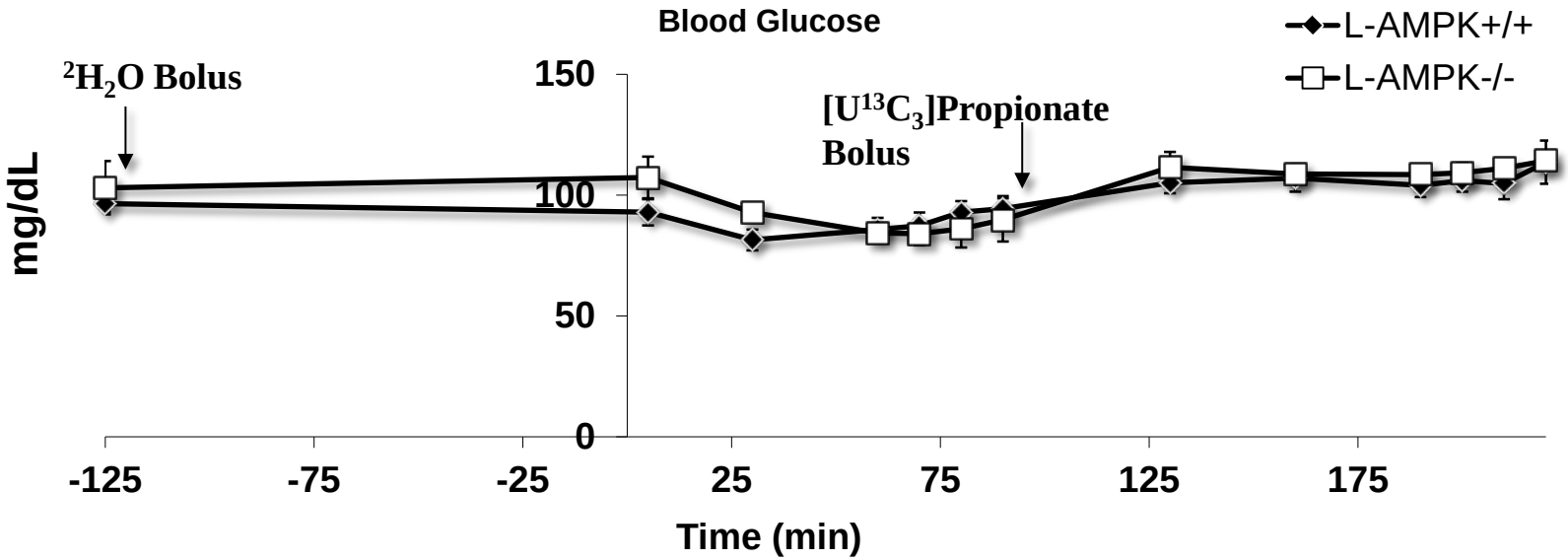
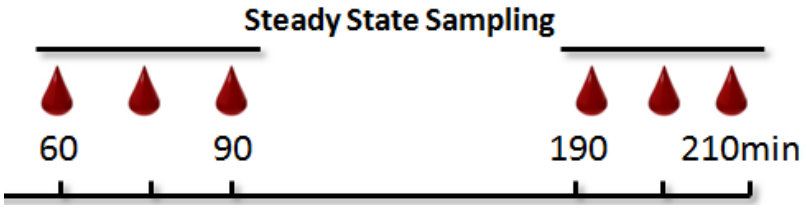
Experimental Approach for [U$^{13}C_3$]Propionate, [6,6$^2H_2$]Glucose and ^2H_2O studies

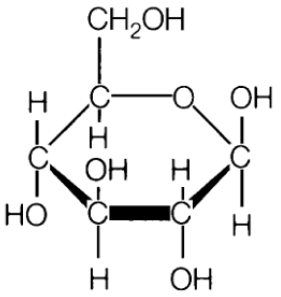


Experimental Approach for $[U^{13}C_3]$Propionate, $[6,6^2H_2]$Glucose and ^2H_2O studies







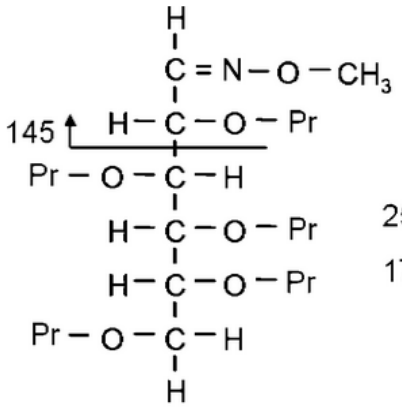


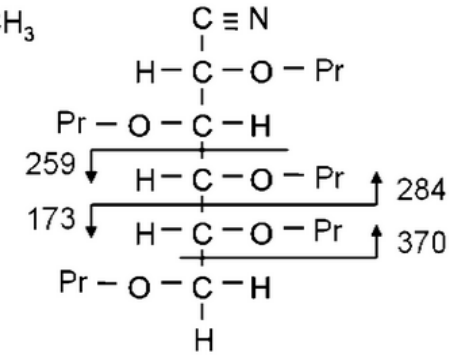
Measuring Deuterium Enrichment of Glucose Hydrogen Atoms by Gas Chromatography/Mass Spectrometry

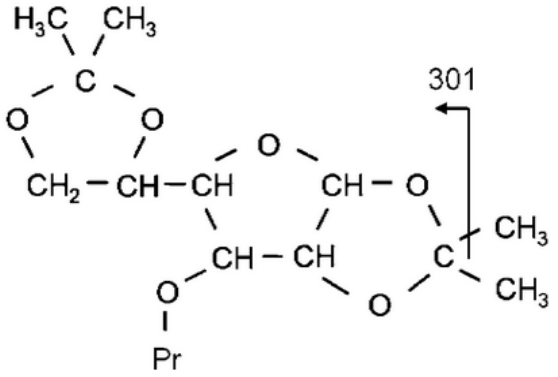
Maciek R. Antoniewicz,† Joanne K. Kelleher, and Gregory Stephanopoulos*

Department of Chemical Engineering, Bioinformatics and Metabolic Engineering Laboratory, Massachusetts Institute of Technology, Cambridge, Massachusetts 02139, United States

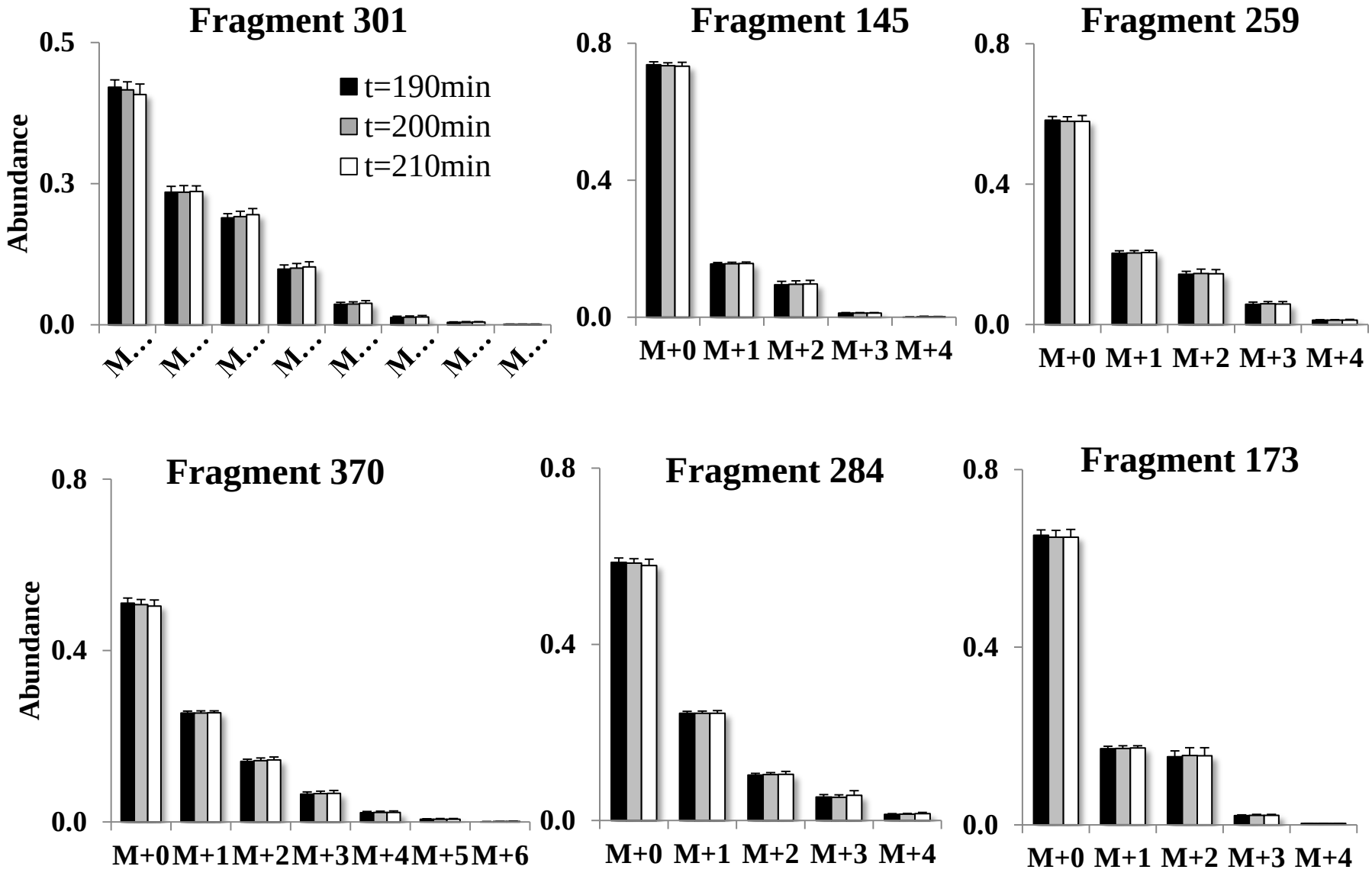
Supporting Information







Glucose Fragment Enrichment



Results are means ± SD

Results
Hasenour & Young Method

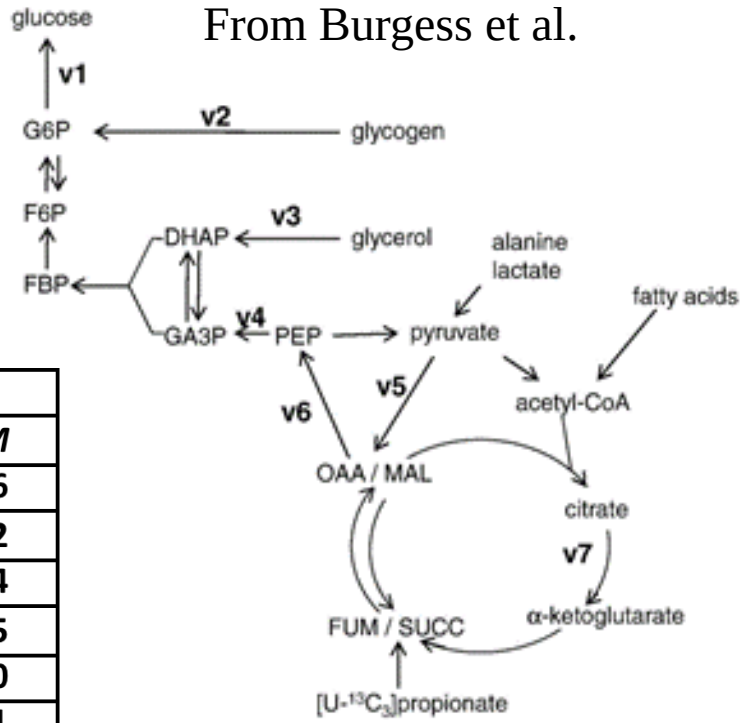
Modeling:		t=190, 200, 210 Time points				
Mouse	LA109-8		EndoRa	13.6	ng/kg/min	
Wt(kg)	0.0251			1.9	umol/min	
[6,6D2]Glucose Rate	0.8	mg/kg/min				

			Relative Fluxes		Absolute Flux Rates	
	Reaction	Equation	Value	StdE	umol/min	Error
Hinf	H.inf -> H		64.1	6.5	1.17	0.10
Hsink	H -> Sink		557.7	24.0	10.16	0.40

Absolute flux (μmol/min)	This study (n=5)	Satapati et al. (n=6-8)
EGP (v1)	1.79 ± 0.16	2.3 ± 0.1
Glycogenolysis (v2)	0.00 ± 0.00	0.02 ± 0.04
$GNG_{glycerol}$ (v3)	0.55 ± 0.06	0.68 ± 0.05
GNG_{PEP} (v4)	1.24 ± 0.10	1.61 ± 0.06
Pyruvate cycling (v5)	4.64 ± 0.61	5.31 ± 0.55
Cataplerosis (v6)	5.29 ± 0.65	8.54 ± 0.63
CAC flux (v7)	1.82 ± 0.24	1.95 ± 0.15

Results
Hasenour and Colleagues

From Burgess et al.



Fast Duration		9 hr		20 hr	
		Mean	*SEM*	*Mean*	*SEM*
EndoRa	*v1*	2.29	0.09	1.85	0.06
Glycogen	*v2*	0.73	0.06	0.06	0.02
Glycerol	*v3*	0.18	0.05	0.46	0.04
PEP	*v4*	1.38	0.06	1.33	0.05
Pyr Cycling	*v5*	4.99	0.46	5.23	0.40
Anaplerosis	*v6*	5.59	0.49	5.89	0.41
TCA	*v7*	2.27	0.16	1.80	0.12

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Big Advantages

1. Small blood volumes allowing for multiple measurements.
2. No requirement for ultra high-end equipment.
3. Shorter run time.
4. Flexible system.
5. Modeling Assumptions = NMR Method making results comparable.

Immediate Goals

1. Validate with liver specific PEPCK-C knockout (Young, MicroMouse).
2. Set up new GC/MS in Analytical Core
3. Turn key Calculations

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Vanderbilt Summer Research Education Program in Diabetes

- *Glucose Clamping the Conscious Mouse*
- *An Organ Systems Approach to Experimental Targeting of the Metabolic Syndrome***
- *Experimental Techniques in Mouse Kidney Injury Workshop*

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GCCM Class of 2013

<u>18 Registrants:</u>
1 NIH
2 Industry
15 Academic
(5 nonUS/13 US)

Coming Soon!!

Vanderbilt MMPC

Glucose Clamping the Conscious Mouse

September 2014

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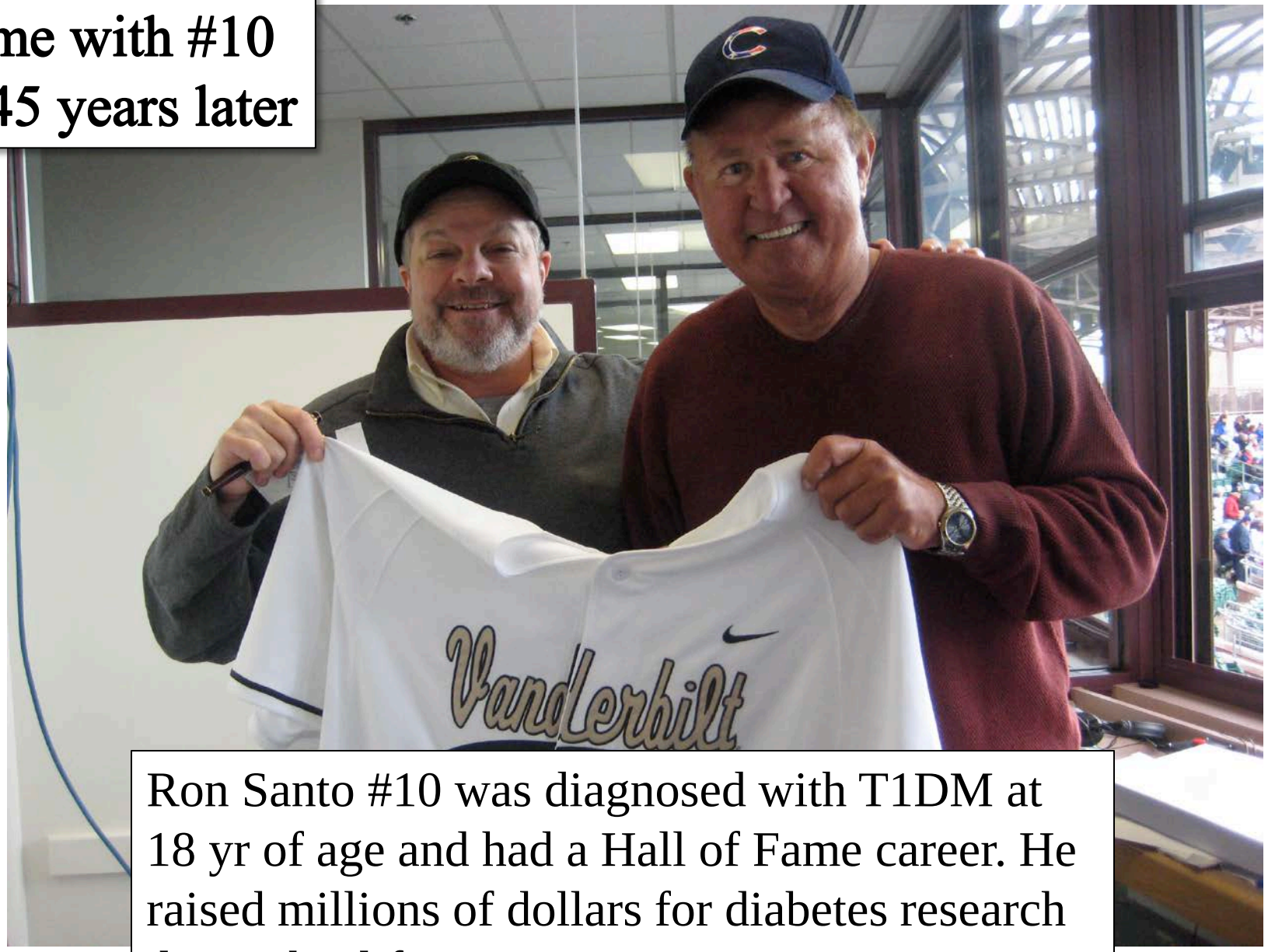
me with #10
45 years later



Ron Santo #10 was diagnosed with T1DM at 18 yr of age and had a Hall of Fame career. He raised millions of dollars for diabetes research during his life.