The NIH Funded Mouse Metabolic Phenotyping Center (MMPC) at the University of Washington is a resource for investigators needing morphology support services

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Abstract

The Nephrology, Macrovascular and Microvascular Tissue core within the University of Washington MMPC provides a common facility and expertise for the broad spectrum of morphologic studies that are required for interpretation of kidney disease, with a particular but not exclusive emphasis on diabetes. The principal morphologic techniques provided by this Core, on a fee for service basis, include paraffin, cryostat, and electron microscopy tissue processing, routine histology including special histologic stains, immunohistochemistry, immunofluorescence microscopy, tissue enzyme histochemistry, photomicrography and computer imaging, quantitative morphometric analysis, electron microscopy, in situ hybridization, and ancillary techniques such as Western, Southern and Northern blotting and antibody binding and competitive inhibition assays needed to ensure the sensitivity and specificity of reagents and procedures. Additional major functions of this Core include development of antibodies and DNA and RNA probes that may be useful for the identification of cell types or localization of molecules in tissues from normal and diseased mice, and the development of enhancements to existing morphologic techniques that improve the ability of investigators to localize specific molecules in tissue sections. The directors and staff in this core and their collaborators bring unique expertise and experience in defining the role of growth factors, matrix proteins, inflammatory mediators, and lipid pathway molecules in renal and vascular diseases that serves the broad research community (both academic and corporate) currently utilizing this center. While the morphologic approaches are broadly applicable to studies of any organ, this core provides analytic expertise and specialized approaches to tissue preparation that are particularly applicable to studies of nephropathy and diabetic and hyperlipidemic macrovascular disease including atherosclerosis involving the aorta and other large arteries.

The University of Washington MMPC offers services to investigators including:

- Necropsy
- Tissue processing and sectioning
- Histology and Immunohistochemistry
- Morphometric quantification (variety of tissues, but with special expertise in kidney and atherosclerosis of the aorta and large arteries)
- In Situ hybridization
- Mouse blood pressure measurements

A Hyperlipidemic Mouse Model

Examples of morphologic studies – Special stains (PAS, Oil Red O) and Immunohistochemistry (Mac-2)

Control Western Western + UnNx Western + 5/6 Nx

Glomerular Morphometry Results: A Diabetic mouse “A” and control “B”

<table>
<thead>
<tr>
<th></th>
<th>A</th>
<th>B</th>
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</thead>
<tbody>
<tr>
<td>Glomerular Area, μm²</td>
<td>6411.2</td>
<td>2671.3</td>
</tr>
<tr>
<td>Matrix Area, μm²</td>
<td>2176.4</td>
<td>1423.2</td>
</tr>
<tr>
<td>% Matrix</td>
<td>33.5</td>
<td>25.0</td>
</tr>
<tr>
<td># Glomeruli</td>
<td>1.6</td>
<td>1.6</td>
</tr>
<tr>
<td># Intertubular Fibers</td>
<td>0.8</td>
<td>0.8</td>
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We also include morphometrically characterized glomeruli, tubules, glomerular size, matrix expansion, leukocyte infiltration (monocytes, lymphocytes, neutrophils, and rare or absent atherosclerotic lesions), and interstitial fibrosis (Sirius red and other matrix stains). Results shown are ± SEM.

Vascular and Adipose Tissue Evaluation

Aortic Injuries

Sequential Oil Red O and Movat Pentachrome staining on the SAME SECTION showing different localization of lipid and matrix components within atheromas. These differences are then correlated morphometrically using specialized image analysis.

Aortic Atherosclerosis (Candy Core): New method of sectioning to evaluate atheromas in multiple arterial branches.

Atherosclerosis Tissue: Morphology, immunohistochemistry, in situ hybridization, and ancillary techniques such as Western, Southern, and Northern blotting.

Summary

The Nephrology, Macrovascular and Microvascular Tissue Core works extensively with tissues provided by the client investigators. The UW MMPC center has additional cores focused on echocardiography and metabolic studies. The University of Washington MMPC is one of six MMPCs supported by the NIH to provide morphologic, physiologic, metabolic and biochemical research services to investigators using murine systems. Each site (UW, Vanderbilt, UN of Cincinnati, Case Western Reserve, UT Southwestern and Yale) offers a unique set of services that is particularly applicable to studies of diabetes and nephropathy and diabetic and hyperlipidemic macrovascular disease involving the aorta and other large arteries.

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