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

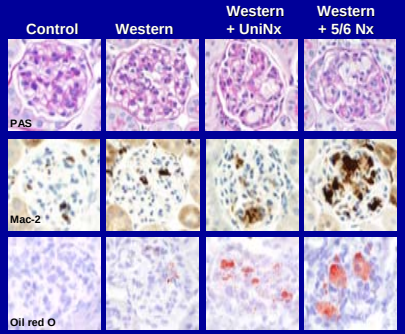
The Nephrology, Macrovascular and Microvascular Tissue core within the University of Washington MMPC provides a common facility and expertise for the broad spectrum of morphologic studies that are required for interpretation of kidney disease, with a particular but not exclusive emphasis on diabetes. 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

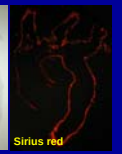
A Hyperlipidemic Mouse Model

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

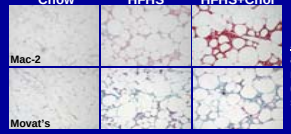


Vascular and Adipose Tissue Evaluation

Aortic Sinus: Sequential Oil Red O and Movat's Pentachrome staining on the SAME SECTION showing different localization of lipid and matrix components within atheromata. These differences are then quantitated morphometrically using computerized image analysis.

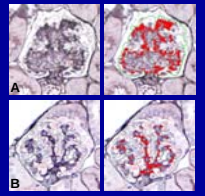


Aorta: Coronal ("Candy Cane") - New method of sectioning to evaluate atherosclerosis in multiple arterial branches.



Adipose Tissue: Macrophage accumulation and extracellular matrix expansion with Diabetogenic (Surwit) diet. HFHS: high fat high sucrose; Chol: cholesterol.

Morphometry Results: A Diabetic mouse "A" and control "B"



	A	B
Glomerular Area, μm²	5661.2 ± 178.4	2607.8 ± 142.3
Matrix Area, μm²	765.8 ±55.9	218.38.5 ± 20.5
% Matrix	13.6 ± 0.9	8.5 ± 0.8

We also evaluate morphometrically cell proliferation, apoptosis, glomerular size, matrix expansion, leukocyte infiltration (monocytes, lymphocytes, neutrophils and some subsets of these), and interstitial fibrosis (Sirius red and other matrix stains). Results shown are ± SEM.

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 measurements of whole mouse metabolism, and has developed resources to minimize the difficulties for investigators from institutions other than the University of Washington to send living mice for cardiac imaging 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 muring systems. Each site (UW, Vanderbilt, Univ. of Cincinnati, Case Western Univ. , UT Southwestern and Yale) offers a unique set of testing procedures based on the expertise available at that site. For a full description of each centers' offerings, please contact the overall MMPC website, www.mmpc.org.

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