

## **ANIMAL MODELS OF DIABETIC COMPLICATIONS CONSORTIUM (AMDCC)**

<http://www.amdcc.org>

### **Description of Project**

- The AMDCC is an inter-disciplinary consortium designed to develop animal models that closely mimic the human complications of diabetes for the purpose of studying disease pathogenesis, prevention, and treatment.
- The consortium consists of eight model generation/validation sites, three phenotyping cores, and a bioinformatics/data coordinating center.
- The AMDCC generates mouse models by 3 different approaches (knock-in/knock-out of candidate genes, random mutagenesis, and genome tagging methods) and pig models by selective breeding and phenotypic screening.
- The AMDCC defines standards to validate each diabetic complication for its similarity to the human disease.
- The AMDCC tests the role of candidate genes or chromosomal regions that emerge from genetic studies of human diabetic complications.
- Finally, the AMDCC facilitates the sharing of animals, reagents, and expertise between members of the Consortium and the greater scientific community via its bioinformatics and data coordinating center.

### **Accomplishments**

- The AMDCC has defined validation criteria for diabetic nephropathy, cardiomyopathy, micro- and macro-vascular disease. The standards are written for both mouse and pig, but can apply to any animal (see <http://www.amdcc.org> for full details).
- The AMDCC has developed standardized assays for phenotyping diabetic complications to ensure that data can be easily compared between members of the consortium and the outside community. All protocols are freely available on the website (<http://www.amdcc.org/>). The validation criteria and standard assays for nephropathy have recently been published (Breyer MD, Bottinger E, Brosius FC 3rd, Coffman TM, Harris RC, Heilig CW, Sharma K; AMDCC. Mouse models of diabetic nephropathy. *J Am Soc Nephrol.* 16:27-45, 2005). Please see <http://www.amdcc.org/> for a full list of AMDCC publications).
- The Bioinformatics website has built an impressive and ever growing laboratory notebook that provides an interoperable phenotype database. Statistical and graphical modules within the database allow both AMDCC members and visitors (*i.e.* non-members) to view data and consolidate information across laboratories in order to perform meta-analyses. The AMDCC website currently receives about 1,200 “hits” per month from outside investigators.
- The AMDCC has identified several new animal models for diabetic complications. As of 10/26/04, the website lists 78 models under development and study – including a number of promising models for type 1 diabetic cardiomyopathy, nephropathy and neuropathy (please see <http://www.amdcc.org/> for a full list of models and resulting publications).

- The AMDCC provides the necessary infrastructure to facilitate sharing of information across the many scientific disciplines involved in complications research, and to ensure that animal models developed for one diabetic complication are screened for all relevant complications. This not only includes the sharing of mice and their tissues, but also includes the sharing of harvested pig tissues across the consortium.

### **Future Directions**

- The AMDCC will focus its efforts on fully phenotyping/characterizing the best animal models identified for each diabetic complication.
- Standardized protocols will continue to be developed and utilized by the established AMDCC phenotyping core facilities.
- The AMDCC will continue to add functionality to its bioinformatics website.
- Additional efforts will be made to publicize the AMDCC and its Bioinformatics website.

### **Research Resources Available to Researchers**

- Website: The AMDCC web-site (<http://www.amdcc.org/>) is a public portal providing access to the range of AMDCC activities including protocols, data, tools for data management and analysis, model characteristics, and publications.
- Validation Criteria: Standardized validation criteria have been established for diabetic nephropathy, cardiomyopathy, micro- and macro-vascular disease. The standards are written specifically for mouse and/or pig, but can apply to other species (see <http://www.amdcc.org/> for full details).
- Standard Methods for Phenotyping Organ-Specific Complications: Standardized assays for phenotyping diabetic complications in mouse and pig have been developed to ensure that data can be easily compared between members of the consortium and the outside community. The [website](#) lists more than 40 assays with protocols written to facilitate their use by the general scientific community. Consortium members recently published validation criteria and standard assays for nephropathy (*J Am Soc Neph* 16: 27-45; 2005).
- Model Development: Several new animal models for diabetic complications have been developed by the consortium. The website currently lists more than 70 models under development and study – including promising models for type 1 diabetic cardiomyopathy, nephropathy and neuropathy (see <http://www.amdcc.org/> for a full list of models and resulting publications).

### **Participants**

Sponsors:       National Institute of Diabetes and Digestive and Kidney Diseases  
                           National Heart, Lung, and Blood Institute

### **Participating Institutions**

Albert Einstein College of Medicine  
Brigham and Womens Hospital  
Columbia University  
Duke University Medical Center  
Jackson Laboratory  
JDRF  
Johns Hopkins University  
Medical College of Georgia  
Mount Sinai School of Medicine  
NCI  
NHLBI  
NIDDK  
Northwestern University  
Oregon Health Sciences University  
Rockefeller University  
Stanford University

The Cleveland Clinic Foundation  
Thomas Jefferson University  
University of Arizona  
University of California Los Angeles  
University of California San Diego  
University of Florida  
University of Miami  
University of Michigan  
University of Minnesota  
University of North Carolina  
University of Utah  
University of Washington  
University of Wisconsin  
Vanderbilt University  
Washington University St. Louis  
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