

**Animal Models of Diabetic Complications Consortium
(U24 DK076169)**

**Annual Report
(2010)**

**“Coordinating and Bioinformatics Unit for the AMDCC/MMPC”
Medical College of Georgia**

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Part A:

Principal Investigator's Summary

1. Program Accomplishments:

AMDCC Portal updates As part of the process we started last year, we have continued to re-designed the AMDCC web portal to make it easier to find data, protocols and model information for each of the covered diabetic complications. The updates and upgrades to the system have been done in consultation with the NIH program directors with the goal of making the site easier to find and analyze data.

Model Centric Web Portal One of the big changes we implemented was to make the AMDCC web site more model centric. Our first iteration of the website, while a good start, continues to need refinement and improvements. Over the last year we have developed and implemented dynamic data pulls using an Ajax based system design. For example, as one hovers over an assay from complication validation grids, the site pulls data for that strain and assay and displays trends over time. In addition, we have added a number of new features to the site, some of which are generated dynamically, some of which are more static in nature.

For example, we implemented scripts to automatically download publications from PubMed based on the grant numbers of the PIs. The script runs once a month and is used to keep the publications portal up to date. While the grant number is a good start, we need to continue to refine this process to capture publications of import for the AMDCC. A good example of this are the P&F recipients, because these are subcontracts associated with the CBU grant, it isn't always straightforward to capture these publications. We need to work on extracting and filtering based on name/institution combinations followed by hand curation to determine which publications are appropriate to add to the system.

We also created and implemented a system to allow the public to request tissue slides/blocks from the AMDCC. Some of the tissues captured during the primary screens are available to the public. The software we wrote provides a way to tag tissues from histology images as being available to the public and provides a semi-automated way for the individual to contact the AMDCC investigator responsible for the distribution of the tissue.

Another challenge for us was to develop a better way to present the metabolic data captured for each of the strains created and evaluated. Given the depth of the phenotyping, the numbers of assays are not always easy to display in a convenient single display. Our first attempt was to develop a tabbed usercontrol that presents the data in a logically partitioned form. The baseline information with respect to diabetic phenotyping (e.g. plasma glucose, plasma insulin, etc.) is partitioned from the complication specific data (e.g. EKG data). While this first interface iteration is good, it can be improved and we are in the process of making the data not only available but also in a more usable form to make comparison between strains easier.

During the last year the AMDCC investigators began to look more closely at the affects of the mouse diet on the complication phenotyping. After their discussions were concluded, a consensus was developed concerning what diets to use during phenotyping that represent a low, medium and high fat diet. As part of this process, the CBU developed a survey to collate the mouse diet information used by each of the laboratories. We have developed a mouse diet page that summarizes this data. In addition, while we developed the page we also modified the database model to allow us to associate each investigator with a list of diets used in their laboratory. We will use this now to help anticipate mouse diet information for the investigators during data upload.

Lastly, we have worked on making the Model Phenotyping page more user friendly so investigators can easily pick and choose the strains and data they want to evaluate. The grid on this page is dynamically generated and provides additional links to the reagents, histology and publications associated with the strains. The screen capture below is an example of the new design.

Jax Nomenclature	Metabolic	Cardiovascular	Nephropathy	Neuropathy
	Get Data ↓↓↓	Get Data ↓↓↓	Get Data ↓↓↓	Get Data ↓↓↓
129(B6)-Nos3 ^{tm1.1Rh} /J	Coming Soon	Coming Soon	Coming Soon	Coming Soon
B6.129-Ins2 ^{Akita} Bdkrb2 ^{tm1J^h} /SmiJ	Coming Soon	Coming Soon	Coming Soon	Coming Soon
B6.129-Tg(Tagln-cre/ESR1)1Feil/FdmdJ	Coming Soon	Coming Soon	Coming Soon	Coming Soon
B6.Cg-Ins2 ^{Akita} Gt(ROSA)26Sor ^{tm1.1(Ntn1)} Abel	Coming Soon	Coming Soon	Coming Soon	Coming Soon
B6.Cg-Sod2 ^{tm1Shs} /Elf J	Coming Soon	Coming Soon	Coming Soon	Coming Soon
B6.Cg-Sod2 ^{tm1Shs} Tg(Tagln-cre/ESR1)1Feil/J	Coming Soon	Coming Soon	Coming Soon	Coming Soon
B6;129-Gt(ROSA)26Sor ^{tm1(Ntn1)} Abel/J	Coming Soon	Coming Soon	Coming Soon	Coming Soon
BKS.Cg- Lepr ^{db} Sod2 ^{tm1Shs} Tg(Nes-cre)1Kln/J	Coming Soon	Coming Soon	Coming Soon	Coming Soon
BKS.Cg-Lepr ^{db} Sod2 ^{tm1Shs} /ElfJ	Coming Soon	Coming Soon	Coming Soon	Coming Soon
BKS.Cg-Lepr ^{db} Tg(Nes-cre)1Kln/J	Coming Soon	Coming Soon	Coming Soon	Coming Soon
BKS.Cq-m Lepr ^{db} /+ +	Get Data →	Coming Soon	Coming Soon	Coming Soon
C57BL/6-Ins2 ^{Akita} Bdkrb1/Bdkrb2 ^{tm2Mki} /J	Get Data →	Data Available <input type="checkbox"/>	Data Available <input type="checkbox"/>	Data Available <input type="checkbox"/>
C57BL/6J	Get Data →	Data Available <input type="checkbox"/>	Data Available <input type="checkbox"/>	Data Available <input type="checkbox"/>
C57BL/6J-Ins2 ^{Akita}	Get Data →	Data Available <input type="checkbox"/>	Data Available <input type="checkbox"/>	Data Available <input type="checkbox"/>
D2.129(B6)-Nos3 ^{tm1.1Rh} /J	Coming Soon	Coming Soon	Coming Soon	Coming Soon
D2.B6-Ins2 ^{Akita} /MatbJ	Get Data →	Data Available <input type="checkbox"/>	Data Available <input type="checkbox"/>	Data Available <input type="checkbox"/>
D2.Cg-Ins2 ^{Akita} Nr1h4 ^{tm1Gonz} /J	Coming Soon	Coming Soon	Coming Soon	Coming Soon
DBA/2J	Get Data →	Data Available <input type="checkbox"/>	Data Available <input type="checkbox"/>	Data Available <input type="checkbox"/>
FVB.B6-Ins2 ^{Akita} /MlnJ	Get Data →	Data Available <input type="checkbox"/>	Data Available <input type="checkbox"/>	Data Available <input type="checkbox"/>
FVB.BKS(D)-Lepr ^{db} /ChuaJ	Get Data →	Data Available <input type="checkbox"/>	Data Available <input type="checkbox"/>	Data Available <input type="checkbox"/>
FVB.Cg-Ins2 ^{Akita} Nr1h4 ^{tm1Gonz} /J	Coming Soon	Coming Soon	Coming Soon	Coming Soon
NOD	Coming Soon	Coming Soon	Coming Soon	Coming Soon
NOD/LtJ	Coming Soon	Coming Soon	Coming Soon	Coming Soon
NOD/Shi	Coming Soon	Coming Soon	Coming Soon	Coming Soon
SWR/J	Get Data →	Coming Soon	Coming Soon	Coming Soon
				Data Available <input type="checkbox"/>

AMDCC Pilot and Feasibility Program. The AMDCC P&F funding program system provides a complete workflow for both the review and management of P&F applications. Over this last year we conducted the 2009 AMDCC P&F solicitation. The program was very successful and we received 31 applications from investigators in the US (29), UK (1) and Greece (1). Applications from the US were spread across the 48 contiguous states and Hawaii. Based on the scores and critiques of the applications, the AMDCC funded 12 of these applications. The CBU has processed and executed the contracts for each of the funded awards.

MMPC Portal Updates

During the last year, we have been maintaining and augmenting the MMPC website. We have started to develop a different strategy for searching the data on the web portal. We have developed the software to search based on Measurement Category (carbohydrate metabolism, Hormone measurement, Lipid metabolism, protein), Research Area (e.g. Diabetes, Obesity, metabolism, endocrine deficiency, etc.) and Tests with Data. Below is a screen capture from the Measurement category carbohydrate metabolism followed by the basic statistics page that is generated with the data and plot of the glucose over time for one of the experiments.

Basic Statistics Results

Select a chart type to view the data.

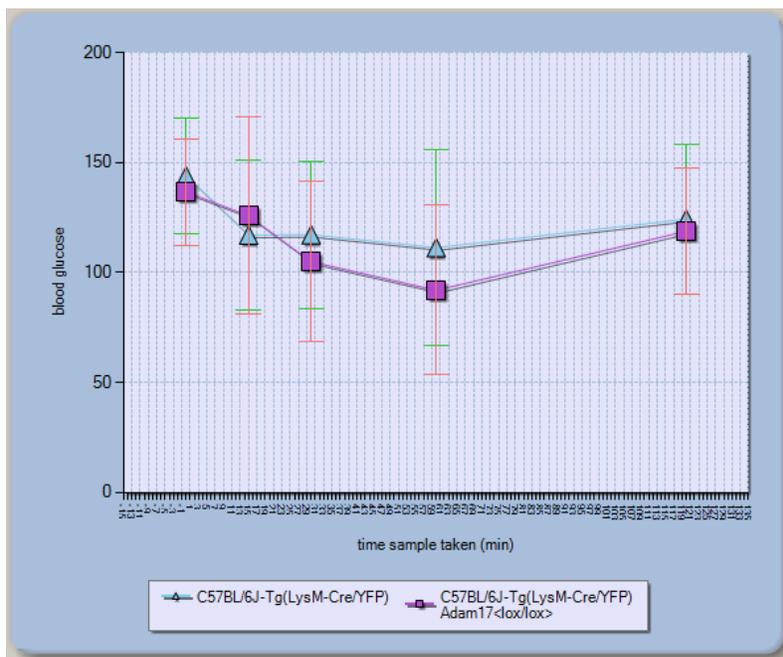
Column Chart
 Line Chart
 X-Y Chart

Y Axis: X Axis:

Data Filter Criteria:
 Sex: Males Only
 Age: No age filter given.

Experiment(s):
 Insulin Sensitivity Test

Assay	Strain	Group	Sex	Num	Avg	Stdev	Median	Min	Max	Var	Skewness	Kurtosis
blood glucose	C57BL/6J-Tg(LysM-Cre/YFP)	Control	Males	40	122.7	36.739	124.5	55	192	1349.76	-0.168	-0.901
	C57BL/6J-Tg(LysM-Cre/YFP) Adam17 ^{lox/lox}	Experiment	Males	35	115.543	38.654	111	32	192	1494.134	-0.059	-0.711



We also continue to update the site with respect to the funding program information, course information and work with the MMPC centers to add site specific data to the system.

MMPC Funding Programs

During this last cycle, we will have conducted 6 funding program solicitations. This was the yearly MMPC Pilot and Feasibility program followed by five quarters for the MMPC MICROMouse program. The 2009 MMPC P&F program had 3 applications with 2 being funded through the MMPC. These awarded applications will be completed in November of 2010. The MMPC MICROMouse program accepts applications throughout the year with reviews occurring quarterly. This last year we reviewed 8 applications over four quarters (2009) and funded 5 applications. We are in the process of completing the review of two applications during the first quarter of 2010 and soliciting applications for the second quarter. In addition, we are finishing the solicitations for the 2010 AMDCC and MMPC applications (May and June respectively).

ARRA Funding Supplement

The money requested for the ARRA supplement to this grant was used to purchase the new servers for the AMDCC/MMPC CBU, increased time to work on NIDDK integration activities (dkCOIN), 9 AMDCC Pilot & Feasibility program subcontracts and 3 MMPC Center initiatives (Case Western, Yale, UT Southwestern).

2. Address previous EAC comments:

We thank the EAC for the comments regarding the direction of the AMDCC web portal.

- With respect to data entry refresher course, the CBU has started to visit the AMDCC Pathobiology sites. Our first training session was in early May at the University of Colorado in the Levi laboratory since they were not familiar with the upload process. We will continue to hold these throughout the year as time and funds will allow. In addition, we continue to hold web conference training sessions *ad hoc* when investigators need a refresher or help. To accomplish this we use GotoMeeting. The investigators like this as it doesn't require a half day training session and they tend to be more focused on specific questions.
- To address the "thought experiment" question, the AMDCC/MMPC has set aside a small amount of money to fund summer students to design these thought experiments and use the AMDCC/MMPC websites to derive the data for their experiments. The solicitation went out in the last week of May and applications will be accepted and reviewed by the end of June. Each funded student will receive a \$3,000 stipend. The solicitation can be found here: <http://www.amdcc.org/shared/SummerStudentProgram.aspx>
- We are in the process of developing a strategy to allow the public to add comments regarding the histology images.

3. Publications:

Sharma A, Zhao J, Podolsky R, McIndoe RA. ParaSAM: A parallelized version of the significance analysis of microarrays algorithm. *Bioinformatics*. 2010 Apr 15. [Epub ahead of print] PubMed PMID: 20400455.

Brosius FC 3rd, Alpers CE, Bottinger EP, Breyer MD, Coffman TM, Gurley SB, Harris RC, Kakoki M, Kretzler M, Leiter EH, Levi M, McIndoe RA, Sharma K, Smithies O, Susztak K, Takahashi N, Takahashi T; Animal Models of Diabetic Complications Consortium. Mouse models of diabetic nephropathy. *J Am Soc Nephrol*. 2009 Dec;20(12):2503-12. Epub 2009 Sep 3. Review. PubMed PMID: 19729434.