Animal Models of Diabetic Complications Consortium
(U24 DK076169-01)

Annual Report
(2007)

"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/MMPC Infrastructure Re-Design

During this first funding period, we were focused on the re-design and creation of the infrastructure to support multiple consortia. This effort required that we re-write/create the AMDCC and MMPC websites, the object model and redesign the database schema. These design changes are technological advancements for the websites as a whole while others are more functional additions and enhancements. The following sections will describe these changes in more detail with example figures presented when appropriate.

.NET 1.1 to .NET 2.0 The most significant change we undertook during the last period was to convert the entire code base from the .NET 1.1 to .NET 2.0 frameworks. The previous website application was written using .NET 1.1. While this website was quite functional, there were a number of limitations of the .NET 1.1 application model that made maintenance and future enhancements of a multi-consortium system more cumbersome. The most significant advantages are the ability to use object factories and master pages (ASP.NET), which allows us to re-use code more efficiently. Figures 1 and 2 illustrate the changes and use of these technologies. The .NET framework is a high performance scalable programming paradigm that provides technologies to easily create web applications (ASP.NET) and Web Services (HTTP/SOAP). My laboratory exclusively writes our web applications in C#. The most significant advantage of C# and ASP.NET are that these technologies are strongly-typed fully object-oriented languages with full support for inheritance and polymorphism.

Software System Re-Design In order to implement this transition, we had to re-write the entire portal system for both consortia. This included the web portal, object model and database schema. Figure 1 presents both the old and new informatics design. As illustrated, we have developed a common object model base class that can be inherited by both consortium specific APIs. This is ideal since a large fraction of the objects and implementation are identical between the two consortia, allowing us to maintain one code base for both consortia. The common base class is inherited by each of the AMDCC and MMPC specific APIs, with the differences between the consortia being coded at level of these APIs. This object model covers the entire spectrum of objects from the previous AMDCC object model as well as new objects required for the MMPC. These include all the scientific objects (experiments, strains, models, protocols, assays, histology, etc.) as well as the administrative objects (members, clients, laboratories, meetings, security, privileges, etc.). The complete re-write of the object model to support multiple consortia required coding 188 total objects with more than 650 properties.

Database Schema The original AMDCC database did not have the concept of multiple consortia built into the schema. We have developed a unified database schema that can accommodate multiple consortia. This required a re-write of both the administrative data schema and the scientific data schema. The schema for the administrative database can maintain separate consortial memberships, meetings, security privileges, and security groups. With respect to the scientific data, we have unified the phenotypic assays, but allow consortium specific data for the experiments. This includes the measurements, mouse strains, laboratory animals, histology, protocols, and publications. For the MMPC, we added the data objects to support the creation of a dynamic catalog of tests available for the consortium as well as support for external clients of the MMPC. The newly completed schema required 183 tables, 746 stored procedures,160 views, 90 functions and 57 triggers.

Web Applications During this cycle, we have also re-written both the AMDCC and MMPC web portals. Because we are using .NET 2.0, we can take advantage of master pages. This allows us to create one page that contains the header and footer for the consortium and inject page specific code when needed. Because a good portion of the two web portals have similar content, we can unify the code execution using UserControls where the content display is the same. The advantage of this is we have to only maintain one code base for both web portals, so any change that is made will be inherited by both portals automatically. Consortium specific differences can be coded at the level of the UserControls. Figure 2 presents an example of the Experiments UserControl being rendered in both consortium. Because we pass a consortium ID during the rendering process, we can perform consortium specific rendering options if necessary. We have completed the entire re-write of each portal and are now in the testing and training phase. We expect to deploy the newly designed web portals in September. During this process, we decided to re-visit some of our design decisions and re-organized many of the pages based on user feedback.

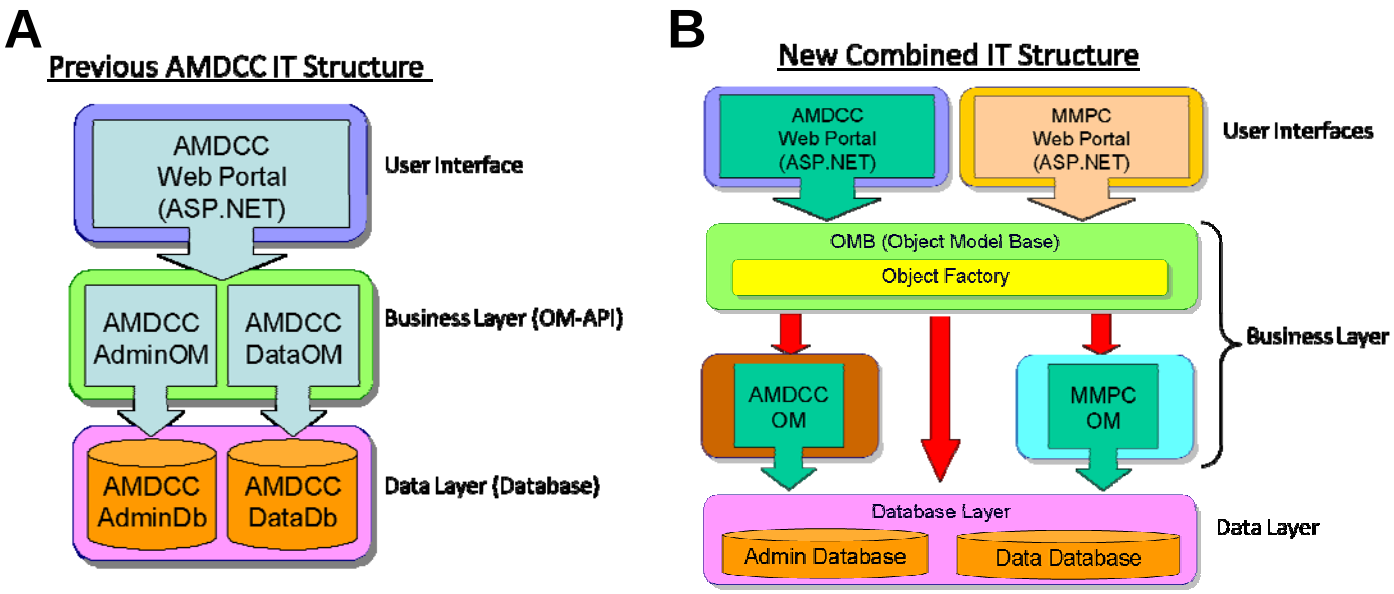
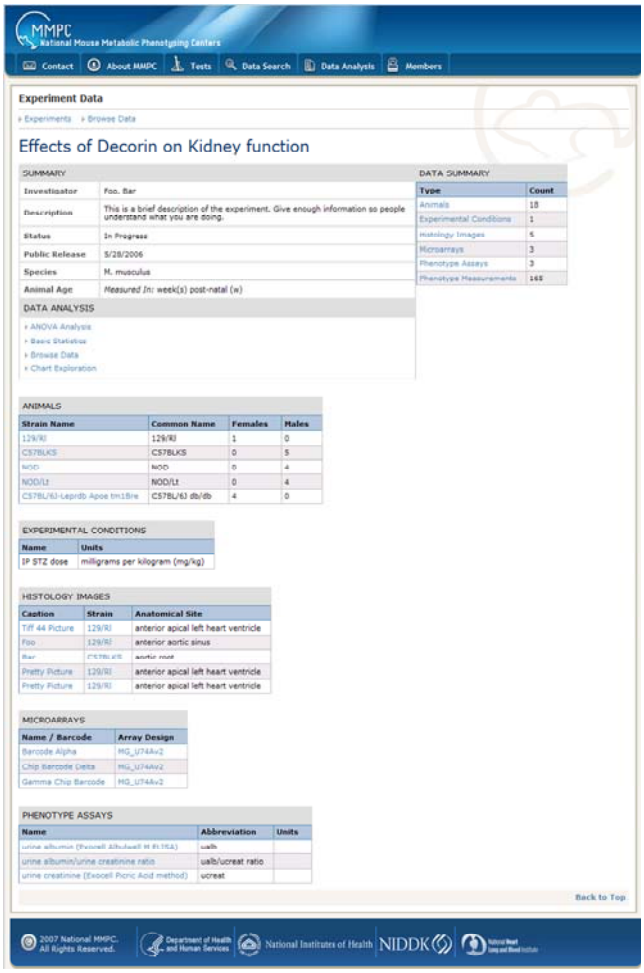


Figure 1. Infrastructure re-design. A) Previous IT structure used for the AMDCC. B) New infrastructure design for the support of multiple consortia. OMB provides the same interface and functionality to both portals. This allows for all common functionality to be implemented in the OMB code base and prevents code from having to be duplicated and separately maintained for each portal. OMB also allows its functionality to be overridden and/or customized through the concept of Object Factories.

MMPC Specific Information

During this last cycle, we conducted three separate RFPs for the MMPC. The first was a competitive Request for Proposals for 3 additional MMPC Centers, the second was the 2006 Pilot and Feasibility Program and the third was the 2007 Pilot and Feasibility program. With respect to the MMPC RFP, we received 8 grant submissions. The RFP applications were reviewed by 8 external reviewers chosen by the NIH program directors. The applications were reviewed and scored via teleconference on October 12th 2006. The scores and reviews were submitted to the NIH program directors where the funding decision was determined in consultation with the MMPC external advisors. Three centers were funded, Yale University, UT

A



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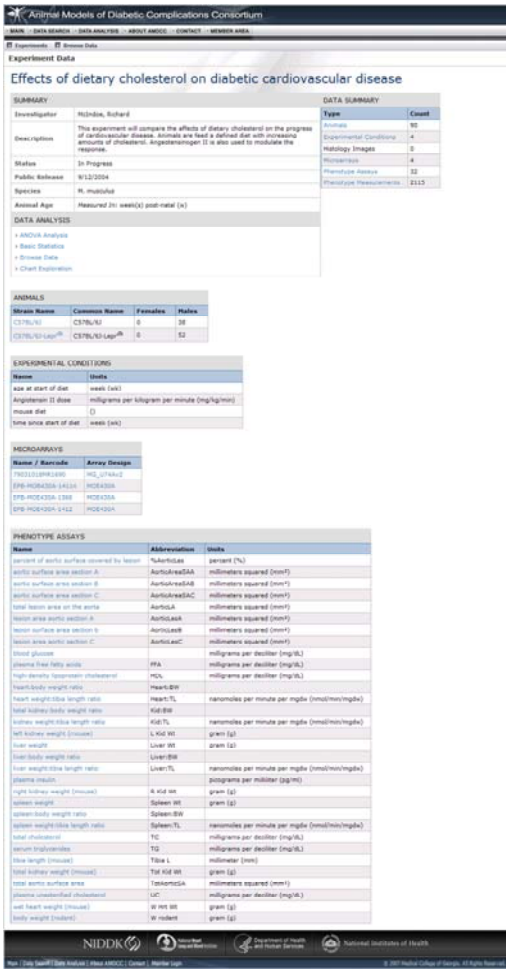

Figure 2. Example of using Master Pages and UserControls. A) The MMPC web portal using the Experiments UserControl with MMPC specific data. B) The AMDCC web portal using the same Experiments UserControl with AMDCC specific data. Before the UserControl is rendered a Consortium ID is passed to the control so we can render any consortium specific properties.

Southwestern and Case Western. With respect to the 2006 Pilot and Feasibility Program, three applications were received and reviewed by the NIH program directors and the MMPC external advisors. The three funded applications came from University of Washington, University of Cincinnati and Vanderbilt. The 2007 Pilot and Feasibility Program had 18 applications submitted on June 1st 2007 with one being returned for being non-responsive. The remaining 17 applications are currently under review by external reviewers and will be critiqued and scored by August.

Future Plans

We will continue the development of the web portals, increasing the functionality and accessibility of the data generated by the AMDCC and MMPC consortia. We will begin to develop the updated AMDCC web services and start to develop the MMPC web services. We will also develop a web based submission and review process for the MMPC Pilot and Feasibility program. In addition, we will be developing better data exploration and statistics tools as we talk to investigators to understand what needs they have. We will also work on developing the microarray analysis/visualization tools. We will also continue our work on the controlled vocabularies for histology and enhanced analytical tools.

2. Address previous EAC comments:

NOT APPLICABLE THIS YEAR

3. Publications:

ParaKMeans: Implementation of a Parallelized K-means algorithm Suitable for General Laboratory Use. Piotr Kraj, Robert Podolsky, Nikhil Garge, Ashok Sharma and Richard A McIndoe. Submitted to Bioinformatics

Hsueh, W, Abel, ED, Breslow, JL, Maeda,N, Davis,R, Fisher,EA, Dansky,H, McClain, DA, McIndoe,RA, Goldberg,IJ, and Rabadán-Diehl,C Recipes for Creating Animal Models of Diabetic Cardiovascular Disease 2007 Circulation (In Press)