Third Annual Comparative Medicine Resource Directors Meeting

Sponsored by: National Center for Research Resources, Bethesda, Maryland

> Hosted by: The Jackson Laboratory, Bar Harbor, Maine

> > June 7-8, 2001

AND

Summaries of Related Meetings:
Genetic Management Workshop - June 6, 2001
Mutant Mouse Regional Resource Centers Group - June 8, 2001
Specific Pathogen Free Macaque Resource Directors Meeting - June 8, 2001
Chimpanzee Management Program Resource Directors Meeting - June 8, 2001

Introduction

The National Center for Research Resources (NCRR), part of the National Institutes of Health (NIH), held its Third Annual Comparative Medicine Resource Directors Meeting on June 7-8, 2001, at The Jackson Laboratory (TJL), Bar Harbor, Maine. The meeting provided a forum to highlight activities of the NCRR-supported resource centers and to exchange other information. The Roster of invited attendees was expanded this year to include the principal investigators of new NCRR-supported centers funded by the P40 and U42 grant mechanisms, as well as grantees who have resource-related projects funded via the R24 mechanism. Additional attendees included members of various groups that held separate meetings in Bar Harbor during this same period. These groups include attendees from the Genetic Management Workshop, the Mutant Mouse Regional Resource Centers (MMRRC) Group, the Specific Pathogen Free (SPF) Macaque Resource Directors Meeting, and the NIH Chimpanzee Management Program (ChiMP) Resource Directors Meeting.

Meeting Agenda

June 7, 2001: Dr. Barbara Knowles, Associate Director and Director of Research at TJL and Dr. John Strandberg, NCRR Associate Director of Comparative Medicine, welcomed attendees and stated the purpose of the meeting.

Dr. Jeffrey Rogers of the Southwest Foundation for Biomedical Research, San Antonio, Texas, delivered the keynote address entitled *Comparative Genomics In Primates and Its Impact On*

Phenotype Analysis. Dr. Rogers described the efforts of many investigators to characterize the genetics, molecular biology, and genomics of nonhuman primates at many U.S. facilities. He said that providing the necessary bioinformatics support for these efforts is challenging, but necessary. He referenced the January 2001 conference on <u>Future Efforts in Primate Genomics</u>, held in Seattle, Washington.

Dr. Jeffrey Roberts of the California National Primate Research Center and Dr. Keith Mansfield of the New England National Primate Research Center jointly discussed *Zoonoses: Primate Facilities*. There is a variety of nonhuman primate species, and the panoply of infectious microorganisms possibly carried by these nonhuman primates presents a challenge to the research community. The Institute of Laboratory Animal Research of the National Research Council is currently revising a document entitled *Occupational Health and Safety in Nonhuman Primates*.

Dr. Lela Riley of the University of Missouri discussed *Zoonoses: Rodent Facilities*. There is a variety of known and unknown microorganisms that rodents may carry, and exposed humans (e.g., pregnant women) may exhibit differing susceptibilities.

Dr. Muriel Davisson of TJL and Dr. Christian Abee of the University of South Alabama informed meeting attendees of issues addressed during the previous day's **Genetic Management Workshop** and provided recommendations.

Dr. Jerry Robinson introduced the directors of the recently funded SPF Macaque Resources, which will help relieve the current shortage of SPF macaques. (See meeting summary below.)

Meeting attendees toured key areas of TJL, including the Induced Mutant Resource, the Mouse Mutant Resource, the cryopreservation laboratory, and the training laboratory.

June 8, 2001: For a portion of the day, attendees organized into four Working Groups:

- Group 1 <u>Value of Advisory Groups to Centers</u>
- Group 2 Self-Sufficiency/Cost Recovery of Resources
- Group 3 <u>International Affairs</u>
- Group 4 Microarrays

The proceedings of these working groups are described below.

In the full session, NCRR's Division of Comparative Medicine (DCM) staff and other NIH representatives provided information on recent events that affect NCRR-supported programs.

1. Dr. Franziska Grieder (DCM) reported on progress in establishing the MMRRCs and the associated Informatics Coordinating Center at TJL.

- 2. Dr. Ray O'Neill (DCM) reported on the NIH Chimpanzee Management Program Plan.
- 3. Dr. John Strandberg (DCM director) led a discussion of future comparative medicine initiatives that could be supported by the NCRR. He encouraged attendees to provide their ideas about resource needs of the biomedical research community.
- 4. Dr. Jerry Robinson (DCM) reported on a new NCRR Web-based database to be instituted in the near future for centers funded by the P40 mechanism to report their annual progress to NCRR.
- Dr. Nicole Leonard of the NIH National Heart, Lung, and Blood Institute reported on the progress of NCRR and the NIH Office of Technology Transfer to develop Intellectual Property Rights Guidelines. Attendees discussed the intent of the Bayh-Dole Act and the appropriate audience at individual universities for NIH to target regarding these issues.
- 6. Dr. Judith Blake of TJL talked about several bioinformatics activities underway at the laboratory as they relate to this topic. TJL's Web site provides an example of recent attempts to incorporate and annotate genotypic, phenotypic, computational, and literature-based information.

The meeting concluded with discussions of the next and Fourth Annual Comparative Medicine Resource Directors Meeting to be held at the Southwest Foundation for Biomedical Research, San Antonio, Texas, in 2002. Following adjournment of this meeting on June 8, three additional meetings were held: the MMRRC Group, the SPF Macaque Resource Directors Meeting, and the NIH Chimpanzee Management Program Resource Directors Meeting.

References:

- NCRR <u>Division of Comparative Medicine</u>
- NCRR Comparative Medicine Resources Directory 2001

Working Group 1 - Value of Advisory Groups to Centers Leader: Dr. Larry Mobraaten, TJL, Bar Harbor, Maine

The Working Group members described the Advisory Groups associated with their NCRR-supported resource centers. The method of member selection, how many members serve at once, the duration of service, the method used for rotating members, the roles of the Advisory Group, the means of governance, and the financial costs of the Advisory Group vary widely from resource to resource. The issues of greatest interest were how a resource can elicit the cooperation of the best potential advisors, what meeting format produces the best advice from the Advisory Group, and how this advice should be communicated and implemented within the organization.

Working Group 2 - Self-Sufficiency/Cost-Recovery of Resources Leader: Dr. Julia Hilliard, Georgia State University, Atlanta, Georgia

NCRR requires the centers supported through the P40 mechanism to strive for self-sufficiency. In addition, an NIH grants policy statement broadly outlines how grantees should attempt cost recovery for the products provided by NIH funding. The ability of any specific resource to achieve self-sufficiency is highly variable. Following a group discussion of numerous issues, the following conclusions evolved: Although tracking methods vary widely, all NCRR-supported resources should be able to identify the users of their resources and track how shipped specimens are used. This should include both purchasers and all associated research investigators. The lists of users and their funding sources could then be used to determine which NIH institutions benefitted from these resources and what publications resulted from the research projects.

References:

- NIH Grants Policy Statement
- <u>Division of Comparative Medicine Review Guidelines</u>

Working Group 3 -International Affairs Leader: Dr. William Morton, Washington National Primate Research Center, Seattle, Washington

Dr. William Morton described the International Program at the University of Washington regarding nonhuman primate programs, and he gave examples of how personal interaction, collaboration, and development of science programs in foreign countries led to its establishment. The program consists of four components: Resources, Research, Education-Training, and Conservation. Attendees discussed several concerns, including the need for better coordination among Federal regulatory agencies, such as the U.S. Department of Agriculture, the Fish and Wildlife Service, and the Centers for Disease Control and Prevention.

Working Group 4 - Microarrays Leader: Dr. Stuart Kim, Stanford University Medical School, Palo Alto, California

This Working Group discussed current technologies for performing micro- and macro-array experiments. Dr. Gary Churchill, TJL, discussed new approaches to the design and statistical analysis of microarray experiments. Dr. Andrew Cameron, California Institute of Technology, presented results using macroarrays of sea urchin cDNA and BAC clones, as synthesized and distributed by the Sea Urchin Genome Resource. Dr. Stuart Kim discussed the results obtained using microarrays containing *C. elegans* gene sequences, as synthesized, distributed, and hybridized at the microarray resource for *C. elegans*. Several different types of expertise (e.g., geneticists, statisticians, computer scientists,

engineers, and clinicians) are required to successfully develop array resources. It is a major challenge to integrate these disciplines, because they are not usually found within the same university department.

SUMMARIES OF RELATED MEETINGS

Genetic Management Workshop - June 6, 2001

Leaders: Dr. Christian Abee, University of South Alabama, Mobile, Alabama

Dr. Larry Mobraaten, TJL, Bar Harbor, Maine

Background

The need to hold this all-day workshop became evident during a session of the Second Annual Comparative Medicine Resource Directors meeting held in April 2000. To begin resolving the many issues associated with genetic and records management for colonies of nonhuman primates, a first Colony Records Analysis Workshop (CRAW I) meeting was held in January 2001 in San Antonio, Texas. Representatives of the eight National Primate Research Centers (NPRCs), plus another nonhuman primate resource center, attended this meeting. The workshop in Bar Harbor was intended to address issues relevant to animal colonies that are either purposely kept as inbred or genetically homogeneous as possible (such as mutant mice and zebrafish), as well as animal colonies that are kept as outbred or genetically heterogeneous as possible (such as almost all nonhuman primate colonies).

Agenda

In the morning session of this meeting, Drs. Muriel Davisson and Christian Abee welcomed the attendees and delivered opening remarks. Ms. Melissa Berry talked about "Genetic Management of Mutant Mouse Colonies" at TJL; Drs. Virginia Godfrey of the University of North Carolina and Cheryl Michels of Dataworks Development, Inc. talked about "Computer-based Management of Mouse Colonies;" Dr. Monte Westerfield of the University of Oregon presented "Zebrafish Genetic Management;" Dr. Bennett Dyke of the Southwest Foundation for Biomedical Research presented "Management of Outbred Primate Colonies: Issues and Preparation for Afternoon Working Group" and "Demonstration of PEDSYS Colony Management Program for Outbred (Primate) Colonies;" and Dr. Charles Donnelly of TJL concluded with "Demonstration of a Colony Management Program for Inbred (Rodent) Colonies."

In the afternoon, two working groups met concurrently, as follows:

- Dr. Muriel Davisson, TJL, led **Genetic Management of Inbred and Genetically Defined Colonies** (**Non-Primate**): Common Issues, Basic Information Needed, and Management
 Systems for Record Keeping.
- Dr. Jose Galvez, UC-Davis, delivered a presentation entitled *Telepathology: The Future of Pathology*. Real-time interactive telepathology acquisition is based on teleconsulting (i.e.,

consulting based on image transmission), which requires that multiple images be taken and transmitted (sometimes by e-mail or through Internet access). Improved dissemination of "genetic management information" to the scientific community that uses mutant mice is needed. Electronic-based management of resources should be shared among different systems.

Dr. Bennett Dyke, Southwest Foundation for Biomedical Research (SFBR), San Antonio, Texas, led the **Genetic Management of Outbred Colonies (Primate):** *Colony Records Analysis Workshop II.* Dr. Gerry Brush of the SFBR discussed some computer modeling done to assess "Avoidance of inbreeding vs. equalization of founder representation as strategies for maintaining genetic variability." Dr. Dyke presented model data sets. Reports on database queries and some general comments were provided by representatives of the California, New England, Oregon, Tulane, Washington, and Wisconsin NPRCs, the NIH Chimpanzee Database at ISIS, and the Squirrel Monkey Breeding and Research Resource. This working group recommended the following actions and future activities:

- 1. More complex model data should be developed.
- 2. Standardization is needed.
- 3. Software is needed for demographic/genetic management.
- 4. A technical database workshop (CRAW III) should be held.
- 5. A collated list of data checks that are performed at data entry at the various centers should be assembled and distributed to interested persons.
- 6. A consensus should be developed regarding what the minimal set of records should be for the purposes of management at any facility, and for export of a particular animal from center to center. Implicit in this is the need for uniform definitions, effective datachecking at data entry, and the ability to easily and accurately utilize the animal records database system for annual reporting to NCRR regarding grants funded through the P51 mechanism, as well as the upcoming need for reporting by P40 centers.
- 7. There is a need to continue computer modeling to devise optimal genetic management strategies at nonhuman primate centers, especially those with alternative reproductive management strategies.

References:

- CRAW I description
- Proceedings of Seattle Conference on Primate Genomics
- Proceedings of meeting: Genetic Typing and Breeding of Genetically Defined Nonhuman
 Primates for Immunological Studies of AIDS Vaccines

Mutant Mouse Regional Resource Centers (MMRRC) Group - June 8, 2001 Leader: Dr. Franziska Grieder, Division of Comparative Medicine, NCRR

Dr. Einhorn, TJL, led a discussion that centered on legal issues as they related to the operation of the MMRRCs. One such issue concerned the submission process that investigators would use to donate mice strains to the MMRRCs. One idea was to adopt the NIH National Cancer Institute (NCI) strain submission form developed for the Mouse Models of Human Cancers Consortium (MMHCC) located at the NCI-Frederick Cancer Research Center. The group also discussed the criteria by which the mice would be distributed, agreeing that the distribution process should be as streamlined as possible. For example, investigators who wish to submit or receive mice could apply via an MMRRC Web site. The group also tasked its Legal Subcommittee with investigating the patent policies of the NCI-supported MMHCC for possible application to the MMRRCs.

The group concluded its meeting with a discussion of issues related to reestablishing stocks from frozen germ-line materials that have been donated, a process that is not always successful. Therefore, both sperm and ovarian tissues should be frozen, and cryopreservation techniques should be improved. The MMRRC Cryobiology Subcommittee will develop policies regarding frozen materials.

Specific Pathogen Free Macaque Resource Directors Meeting - June 8, 2001 Leader: Dr. Jerry Robinson, Division of Comparative Medicine, NCRR

Dr. Keith Mansfield of the New England National Primate Resource Center (NENPRC) introduced the newest grantee from the Tulane NPRC. Subsequently, representatives from each NPRC provided brief background information and colony and activity updates for their centers. Attendees further discussed standardizing the request process used among the different Specific Pathogen Free (SPF) programs for investigators to request animals. Dr. Mansfield circulated the NENPRC request forms to all grantees; everyone agreed to use some adaptation of this sample form.

Grantees discussed the next meeting and agreed that it would take place in Puerto Rico, prior to the **Nonhuman Primate Models of AIDS Meeting** to be held November 7-11, 2002. The group also discussed the noncompeting renewal applications that are due on July 1, 2002.

There was further discussion regarding the potential impact of the proposed interpretation of the United States Department of Agriculture enrichment regulations on facility operation. Several directors expressed concern that their institutions would have to commit significant financial resources to satisfy an interpretation of regulations that have little or no scientific basis.

NIH Chimpanzee Management Program Resource Directors Meeting - June 8, 2001 Leader: Dr. Raymond O'Neill, Division of Comparative Medicine, NCRR During the NIH Chimpanzee Management Program Resource Directors Meeting, attendees reviewed the demographics of U.S. chimpanzees and their support/ownership; the status of the NCRR contract with the Alamogordo Primate Facility; the Interagency Animal Models Committee (led by committee chair Dr. Margaret Snyder of NIH). Attendees also received an update on activities related to Public Law 106-551, the CHIMP Sanctuary Act, and NIH's plans for its implementation. Further discussion was held regarding the need for a systematic method for designating a specific chimpanzee as surplus to National research needs; a questionnaire to be sent to all major U.S. chimpanzee research facilities to determine a preliminary estimate of how many chimpanzees are available for transfer to the planned sanctuary system. The group also considered a draft NIH policy as it applies to cases in which the same chimpanzee is needed by different groups of investigators. Finally, the group deliberated over animal records issues specific to chimpanzees (led by Mr. Rick Lukens of ISIS).

References:

Revised NIH Chimpanzee Management Program Plan

Roster

THE JACKSON LABORATORY / NCRR

Third Annual Comparative Medicine Resource Directors Meeting Genetic Management Workshop MMRRC Group

SPF Macaque Resource Directors Meeting Chimpanzee Management Program Resource Directors Meeting

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