Ninth International Mouse Genome Conference (November 1995)

Sessions at last November's Ninth International Mouse Genome Conference in Ann Arbor, Michigan, focused on mutant gene isolation, comparative mapping, informatics, complex traits, mutagenesis, gene identification, and genetic and physical mapping. Informal discussions among the more than 300 registrants also involved future directions for research on ESTs, mutagenesis, and electronic database development.

Recent cloning successes were described for the eed mutant genes required for mesoderm formation, the mouse homolog of the Drosophila locus Extra sex combs (Armin Schumacher, Case Western Reserve University); tight skin caused by duplication of the fibrillin 1 gene (Linda Siracusa, Jefferson Cancer Institute); Snell's waltzer, a deafness gene encoding the unconventional myosin VI (Nancy Jenkins, ABL); a novel voltage-gated sodium channel responsible for the neurological disorder motor endplate disease [David Kohrman, University of Michigan, Ann Arbor (UMAA)]; and a potassium channel responsible for the cerebellar mutant weaver (Nila Patel, Stanford University Medical Center). Mutation of a transcription factor has been associated with the limb disorder hypodactyly (Jeffrey Innis, UMAA), and the cell growth and proliferation defect in the pygmy mouse is associated with mutations of the high-mobility-group protein HMGIC (Kiran Chada, UMDNJ).

Identification of the T2Bob gene adjacent to Brachury (T) provided an example of nonallelic noncomplementation in the mouse (Karen Artzt, University of Texas, Austin), and a transporter defect was described in the osteosclerosis mutant [Kevin Brady, Brigham and Women's Hospital (BWH)].

Steve Brown (St. Mary's Hospital) led a lively discussion of the future of mouse ESTs. Although the number of mouse ESTs is currently only 1% that of human ESTs, a large-scale mouse EST program could make important contributions to genome research. The mouse provides access to tissues and such developmental stages as the period between gastrulation and early organogenesis, for which human material is difficult to obtain. Obtaining 5 and 3 sequences from each cDNA and access to arrayed cDNA clones were generally seen as high priorities in any mouse EST program.

With regard to EST mapping strategies, YAC contigs and radiation hybrid panels for the mouse panels are still incompletely developed. Promising panels of mouse-hamster radiation hybrids are under development in Goodfellow's laboratory. More than 400 STSs derived from 3 untranslated sequences have been mapped genetically using single-strand confirmational polymorphism (SSCP) analysis (David Beier, BWH). The resolution theoretically obtainable by genetic mapping with the 1000-animal EUCIB backcrosses would approach that of YAC clones and the resulting map would be highly reliable, but automation of SSCP typing has not yet been implemented. For purposes such as identifying candidates for quantitative trait loci (QTLs) and positional-cloning projects, low-resolution genetic mapping of ESTs may suffice. ESTs may be a good source of the estimated 10,000 STSs needed to complete the physical map of the mouse genome, in addition to the 6200 microsatellites developed by the Whitehead-MIT Genome Center. To test the feasibility of using human EST primer pairs as a source of mouse markers, Phillip Avner (Institut Pasteur) and Charles Auffray (Center National de la Recherche Scientifique and G,n,thon) tested 2700 human primer pairs from the Gene Express program and found that 12% could amplify mouse genomic DNA. Screening mouse YAC libraries was successful with more than 80% of the human primers that amplified mouse genomic DNA.

A panel discussion of mouse mutagenesis was led by Rudi Balling (Institut fuer Genetik). The development of mutagenesis protocols using such mutagens as ethylnitrosourea (ENU) and chlorambucil (Lorraine Flaherty, Wadsworth Center) that produce in vivo mutation rates >1 per locus/1000 gametes means that generating mutant mice is now feasible with virtually any phenotype for which a reliable assay can be

developed. Development of innovative screening protocols is the key to obtaining mutants in novel pathways, as exemplified by the ENU-induced clock mutation with altered diurnal rhythm (David King, Northwestern University). Bill Dove (UWM) described the value of breeding mutagenized mice to "sensitized" partners, such as mutation carriers in the pathway of interest, to facilitate detection of desired mutants. Monica Justice and Rick Woychik (Oak Ridge National Laboratory) described a mutagenesis scheme in which the sensitized parent carries targeted deletions marked with coat color genes. Enthusiasm was expressed for the concept of collaborative mutagenesis projects, in which mutagenized mice would be generated at central facilities such as Jackson Laboratory, Harwell, or Munich and screened by visiting investigators bringing various expertise and assay systems.

MGD, the mouse genetic database maintained by the informatics group at Jackson Laboratory, now provides online access to the Chromosome Committee reports, genetic-marker information including primers and probes, the Mouse Locus List with descriptions of mouse mutants, the induced mutant list of available targeted and transgenic mutants, integrated searches of OMIM and MLC, and mammalian homolology data. MGD can be accessed via the Jackson Laboratory Home Page (http://www.jax.org) or a mirror site at the U.K. Human Genome Mapping Project Resource Center (http://mgd.hgmp.mrc.ac.uk). To inquire about the mouse community bulletin board, send the message help to listserver@informatics.jax.org.

Other topics included progress in QTL mapping, analysis of complex traits, and development of new technology. A collection of probes from each mouse chromosome, developed at the Institut Pasteur and used to generate "molecular karyotypes" for mapping mouse genes by FISH, will be available through Oncor in the near future (Avner).

The conference was organized by Miriam Meisler and Sally Camper of UMAA and sponsored by the International Mammalian Genome Society (IMGS), the National Center for Human Genome Research, and DOE. It was dedicated to the memory of Verne M. Chapman (1938 1995), founding member of IMGS and long-time conference coordinator.

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