TOUCHING BASE

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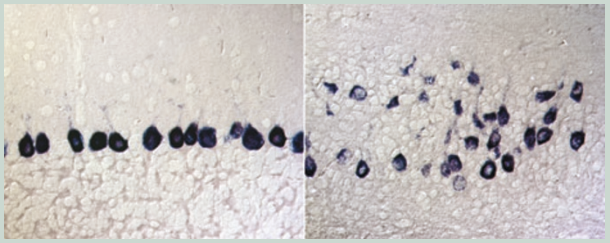
Mutant of the Month



Eric Raponi

This month's mutant, *staggerer*, was first reported in 1962 after it was discovered at the Jackson Laboratory. It was recognized as a spontaneous mouse mutant with phenotypes characteristic of cerebellar lesions such as ataxic gait and hypotonia. The cerebellum of homozygotes is smaller than in the wild-type, with fewer granule and Purkinje cells and disorganized architecture (shown in right panel above). Thirty-four years later, the mutation underlying *staggerer* was reported: a 6.4-kb deletion that removes an exon of the retinoic acid–related orphan receptor alpha (*RORα*) gene and causes a frameshift and premature stop codon. RORα is a transcription factor whose target genes are thought to have many roles in the developing cerebellum, such as protecting Purkinje cells from oxidative stress and regulating proliferation signals. In addition, RORα has been implicated in the development and regulation of cell types outside of the nervous system, as atherosclerosis, immunodeficiency and musculoskeletal phenotypes have been recognized in *staggerer* mice. RORα was long thought to be constitutively active, as it had no known physiological ligand, but recent structural studies have raised the possibility that RORα may be regulated by cholesterol. ***EN***

Funding large-scale sequencing centers

The National Human Genome Research Institute (NHGRI) recently announced the renewal of funding for three large-scale sequencing centers: the centers at the Broad Institute of MIT and Harvard, Washington University School of Medicine and Baylor College of Medicine. According to the press release issued by the NHGRI, almost half of the sequencing centers' capacity will be used for medical sequencing, and a significant portion will be dedicated to the Cancer Genome Atlas pilot project. It is expected that the combined sequence output from the centers will be approximately 12 billion base pairs per month with current technologies. The centers will also be expected to focus on the testing and use of new sequencing technologies. Two sequencing centers previously funded by the NHGRI did not receive renewed funding; they are at Agencourt Bioscience and the Institute for Genomic Research of the J. Craig Venter Science Foundation Joint Technology Center. *EN*

Touching Base written by Emily Niemitz and Alan Packer.

Mystery, Alaska

According to a report in *The New York Times*, the National Geographic Society's Genographic Project has run into the same sort of trouble that plagued its predecessor, the Human Genome Diversity Project. The Genographic Project is a multimillion dollar effort to collect blood samples from a worldwide panel of indigenous populations and gain a better understanding of the patterns of human migration by following particular Y chromosome and mitochondrial markers. Despite the efforts of project scientists to assuage the concerns of local tribal leaders that the research being carried out might be of little benefit to them (or cause some harm), the project has been on hold for several months because of difficulties in collecting samples from tribes that remain skeptical. The greatest reluctance seems to be among Alaskan natives. Only a small number of samples have been obtained from this group, and a review board in the town of South Naknek has asked that samples be stored in a specimen bank until their concerns have been addressed. These concerns seem to be twofold: first, that deeply held beliefs about the place of some of these tribes in human history may be overturned, and second, that societal benefits that flow to these tribes based on the current understanding of their ethnicity will be taken away should this history prove mistaken. While it is clear that there is enthusiasm for the project among some native Alaskans, researchers are nonetheless being asked to revise the consent form to elaborate on potential risks to the participants. *AP*

"I don't think humans at their core are ostriches. Everyone has an interest in where they came from, and indigenous people have more of an interest in their ancestry because it is so important to them."

—Spencer Wells, director of the Genographic Project, as quoted in *The New York Times*

iHOP stacks 'em high

A short correspondence published in the July 2004 issue of *Nature Genetics* seems to have attracted a fair bit of attention. Entitled 'A gene network for navigating the literature', the correspondence by Robert Hoffmann and Alfonso Valencia described a new database called iHOP (Information Hyperlinked over Proteins) that uses genes and proteins as hyperlinks to convert the abstracts in the published literature into a navigable network of information. Hoffmann is now a postdoctoral fellow at the Sloan-Kettering Institute (SKI) in New York, and, according to a recent SKI press release, iHOP is accessed by up to 200,000 different users per month, making it one of the most used resources in biomedical research. The SKI release also notes that iHOP has now been upgraded to include summary information on more than 80,000 genes and proteins, with information from 2,000 new publications included every day. It goes on to say that "Rather than providing long lists of entire abstracts upon keyword searches, iHOP selectively retrieves information that is specific to genes and proteins and summarizes their interactions and functions. The system adds value by filtering and ranking extracted sentences according to significance, impact factor, date of publication, and syntax." iHOP can be found at http://www.ihop-net.org. *AP*