TOUCHING BASE

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Mutant of the Month

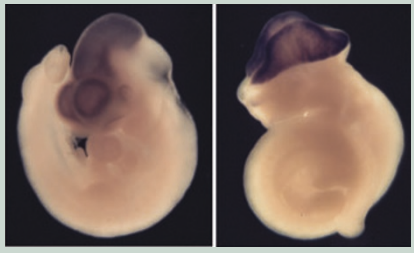

Image courtesy of Jonathan Eggenschwiler

This month's mutant, *open brain* (*opb*), was first described by Klaus Schughart and colleagues (*Development* 120, 3119–3130; 1994) as a recessive mouse mutant characterized by severe exencephaly (shown at right), expansion of ventral fates at the expense of dorsal fates in the developing spinal cord, defects of the axial skeleton and preaxial digit duplications. A few years later, Kathryn Anderson and colleagues identified a second *opb* allele in an *N*-ethyl-*N*-nitrosourea (ENU) screen for embryonic lethal mutations and subsequently showed that both *opb* alleles carry nonsense mutations in *Rab23*, encoding a small GTP-binding protein implicated in vesicle trafficking (*Nature* 412, 194–198; 2001). Genetic and molecular studies strongly implicate Rab23 as a negative regulator of the vertebrate Hedgehog (Hh) signaling pathway, consistent with the range of defects seen in *opb* embryos. Recent evidence suggests that Rab23 functions downstream of Smoothened, the key membrane-bound positive effector of Hh signaling, and upstream of the Gli family of transcription factors, probably by regulating the subcellular localization of key intermediate components of the Hh pathway. ***KV***

Annual Nobel haiku

In technical bout
RNA interference
Wins by a knock-down

Standing variation trumps RNAi

In December 2004, we ran a piece highlighting plans of a California-based company to develop and market a line of hypoallergenic cats. In their original proposal, the company, Allerca, said they would use RNA interference (RNAi) technology to reduce or eliminate expression of Fel d1, the most common protein allergen found in cat saliva and skin. It now seems that, in the course of developing their technology, the company fortuitously discovered several cats carrying naturally occurring variants encoding altered protein isoforms of Fel d1. The company subsequently bred these animals to produce kittens homozygous for these variant alleles, and exposed volunteer cat allergy sufferers to the selectively bred animals. The result? Volunteers showed no reaction to the hypoallergenic cats but reverted to their classic allergic symptoms when exposed to traditional, allergen-ridden breeds. The hypoallergenic animals are now being housed at a secret location to increase the size of the breeding pool and help meet demand for the prized pets. And as we join the scientific community in honoring the laudable achievements of our most recent Nobel laureates, we quietly note that the good old-fashioned coupling of standing variation with selective breeding remains nothing to sneeze at. *KV*

Touching Base written by Orli Bahcall and Kyle Vogan.

"Many thought that the unbelievable feat in 2001 of deciphering the human genome was the end of the story. Not so! We now firmly believe that it was only the beginning. The true challenge now appears to be in deciphering individual variations within the human genome. It is there that the true importance of genomics resides. Only by unearthing the blueprint details of each and every individual will we be able to fully fathom health and disease, mental and bodily faculties, and the true secrets of human biology."

—Doron Lancet, professor at the Weizmann Institute of Science and member of the Archon X PRIZE for Genomics Scientific Advisory Board

Archon X PRIZE for Genomics

The Archon X PRIZE for Genomics, a new genome sequencing award announced on October 4th, 2006 by the X PRIZE Foundation, will award a $10 million cash prize to the first team that creates a technology able to sequence 100 human genomes in 10 days. The contest rules further stipulate the sequencing of an additional 100 genomes from a preselected list of celebrities. The current guidelines require a high degree of accuracy, with no more than one error per 10,000 bases sequenced, accurate coverage of at least 98% of genome and recurring costs under $10,000 per genome. The Foundation's guidelines state that the aims are to "develop radically new technology that will dramatically reduce the time and cost of sequencing genomes." By opening the door to affordable sequencing of individual genomes, this will "accelerate a new era of predictive and personalized medicine". Several teams have already formally entered the competition, including VisiGen Biotechnologies, Inc. and 454 Life Sciences. Teams may also involve collaborative efforts between companies, such as the team led by Steven Benner, which includes the Foundation for Applied Molecular Evolution, Westheimer Institute for Science and Technology and Firebird Biomolecular Sciences LLC. This is the second prize announced by the Foundation. The Ansari X PRIZE for Private Spaceflight, with the goal of developing the first privately funded reusable spaceship, was announced in 1996 and awarded on October 4th, 2004 to Mojave Aerospace Ventures for completing two space flights in 6 days. We hope that this second prize will prove as successful as the first and that the unique combination of competition and collaboration will bring us a step closer to individualized genomics and further the possibilities for genomic research. *OB*