TOUCHING BASE

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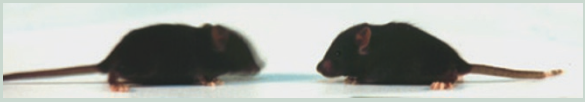
Mutant of the Month



Bruce Hamilton

The mutation responsible for the mouse *vibrator* phenotype was identified in 1997 by Bruce Hamilton, Eric Lander and colleagues (*Neuron* 18, 711–722; 1997). It is a retroposon insertion in an intron of the phosphatidylinositol transfer protein α gene (*Pitpn*). The insertion creates a hypomorphic *Pitpn* allele with reduced mRNA expression. Homozygous *vibrator* mice (at left in the slow–shutter speed photo above) have severe action tremor and progressive neurodegeneration in the brain and spinal cord, and they die by postnatal day 30 when the allele is carried in the BXD background. However, the phenotype is less severe when the *vibrator* allele is present on different strain backgrounds, such as CAST/Ei. Bruce Hamilton and colleagues used this suppression phenomenon to identify a modifier gene, *Nxf1*, that encodes an mRNA export factor (*Nat. Genet.* 35, 221–228; 2003; this paper contains supplementary videos of the *vibrator* phenotype). The CAST/Ei allele of *Nxf1* increases the level of correctly processed and exported *Pitpn* mRNA produced from the *vibrator* allele. Interestingly, the CAST/Ei allele of *Nxf1* also acts as a suppressor of other mouse retroviral insertion mutations, suggesting that it represents a general defensive strategy against mobile elements. ***EN***

Progress for newborn screening

In 2004, the American College of Medical Genetics issued recommendations calling for every baby born in the US to be screened for 29 disorders, the majority of which are inborn errors of metabolism (see *Nat. Genet.* **36**, 1127; 2004). At that time, more than 60% of newborns were screened for fewer than ten of those conditions. Since then, the March of Dimes and other interested groups have advocated for the adoption of these recommendations in every state. Now the March of Dimes has issued a Newborn Screening Report Card based on analyses of state-by-state newborn screening requirements. The report shows that the percentage of babies born in states that require at least 21 recommended screening tests has more than doubled since 2005, increasing from 38% to almost 90% of babies born in the US. The report also shows that 13 states and the District of Columbia require screening for all 29 conditions, and three more states are expected to join this group next year. The March of Dimes has set a goal of having all babies screened for at least 20 of the recommended disorders by 2008. The Newborn Screening Report Card can be found at the March of Dimes website (http://www.marchofdimes.com), and a list of screening tests provided by each state can be found at the National Newborn Screening and Genetics Resource Center website (http://genes-r-us.uthscsa.edu). *EN*

Genomics of Common Diseases

2007 is the year of the genome-wide association study (GWAS). With this pronouncement, Tim Aitman opened the joint Wellcome Trust/*Nature Genetics* meeting on the Genomics of Common Diseases, held 7–10 July 2007 at the Wellcome Trust Conference Center in Hinxton, UK. This meeting, held in celebration of the 15th anniversary of *Nature Genetics*, was organized jointly by Myles Axton, Tim Aitman, David Altshuler and Eddy Rubin, and included keynote addresses by Walter Bodmer, Francis Collins and Leena Peltonen. GWASs have yielded a rapid burst of publications in the past few months reporting novel genetic associations, as is evident from even a quick look at the pages of this journal (referred to by speakers as the "birthday journal"). After these GWAS talks, a commonly asked question was, "Where to, next?" For some, this meant moving past initial associations, using fine-mapping to pinpoint the gene and functional variants, as well as making the leap to functional studies to address questions of mechanism. For others, this meant tackling issues of individual risk prediction and translation to clinical medicine. For still others, the focus was on resequencing and analysis of rare variants, the subject of two additional sessions. The characterization of disease associations would not have been complete without a session on structural variation—also the subject of the July 2007 Supplement to *Nature Genetics* (http://www.nature.com/ng/journal/v39/n7s/index.html). Of course, the platforms used in these studies continue to improve, as highlighted in a session entitled the 'Edge of Technology'. In addition, in a session on statistical genetics and genetic epidemiology, speakers discussed how to make the most of power to detect associations. Finally, sessions on population genetics and natural selection and one on keeping pace with the ethical, legal and social implications of personal genetic information rounded out the meeting's timely take on the current state of the genomics of common diseases. *OB*

CNV map, phase 2

The Genome Structural Variation Consortium has announced plans to produce a second-generation, high-resolution map of human copy number variants (CNVs) using whole-genome oligonucleotide tiling arrays. Last year, the Consortium, led by Matthew Hurles, Nigel Carter, Chris Tyler-Smith, Stephen Scherer and Charles Lee, published a first-generation human CNV map based on a survey of the 270 HapMap samples using tiling resolution BAC arrays and 500K Affymetrix SNP arrays (*Nature* **444**, 444–454; 2006). The new set of tiling oligonucleotide arrays, designed in collaboration with NimbleGen, will achieve a roughly 100-fold increase in resolution, thus enabling more precise mapping of CNV breakpoints and the identification of smaller-sized variants that lay below the limits of resolution of previous genome-wide array-based surveys. These efforts will also complement ongoing sequencing-based studies aimed at defining the spectrum of normal human genetic variation, including common structural variants, as recently outlined by Evan Eichler and colleagues on behalf of the Human Genome Structural Variation Working Group (*Nature* **447**, 161–165; 2007). Collectively, these studies should yield a comprehensive catalog of common structural variants and provide an essential framework for evaluating the role of such variants in disease and normal phenotypic variation. *KV*

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