TOUCHING BASE

QUESTIONS? THOUGHTS? IDEAS?
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Mutant of the Month

Courtesy of Joe Nadeau

This month we highlight the *disorganized* mouse. This very unusual spontaneous mutant was identified by Katherine Hummel at the Jackson Laboratory in 1958. The name is fitting for a strain with such remarkable characteristics—affected mice have a wide array of birth defects, but the phenotype is so variable that no two mice share the same pattern of anomalies. *disorganized* is an autosomal dominant trait with reduced penetrance; only 1%–15% of *disorganized* mice develop an anomaly, and most affected mice have only a single malformation. Malformations caused by the *disorganized* mutation, which can range from mild to severe, occur in derivatives of every germ layer and involve all organ systems. Among the malformations found in affected mice are neural tube defects, orofacial clefting, hamartomatous skin papillae, reduction or mirror-image duplication of limbs, microopthalmia and polydactyly. The identification of limb duplications and papillary hamartomas in humans has prompted hypotheses that there may be a human homolog of *disorganized*. In addition, Joe Nadeau, who mapped *disorganized* to mouse chromosome 14, points out that similarities between common human birth defects and the unusual phenotypes and inheritance pattern of *disorganized* suggest that its human homolog may contribute to spontaneous birth defects. ***EN***

The $64,000 question

As new genetic variants are confirmed as risk factors for common disease thanks to robust association studies, attention will turn to how this information will affect decisions made by individuals in regard to their health care. To begin to address this question, the National Human Genome Research Institute and the National Cancer Institute, in partnership with the Group Health Cooperative in Seattle and the Henry Ford Health System in Detroit, has announced the 'Multiplex Initiative'. This initiative will recruit 1,000 healthy individuals between the ages of 25 and 40 who will be genotyped for common variants that affect risk of type 2 diabetes, coronary heart disease, high cholesterol, hypertension, osteoporosis and lung, colon and skin cancer. The particular genes to be included, though not detailed in the initiative's press release, were selected by a team of scientific advisors. Initially, participants will be provided with information about these tests, and their responses will be evaluated to learn more about how individuals decide whether to be tested. Those who consent to the tests will receive the results in writing along with follow-up telephone calls by trained educators to help them evaluate the results. Additional follow-up interviews and newsletters will inform participants about new information pertaining to the variants for which they've been tested. According to lead investigator Colleen McBride, "the Multiplex Initiative will inform the field about how to communicate genetic risk to patient populations and will establish an infrastructure for additional research studies aiming to answer social and behavioral questions important for the genome era." At the very least, it will provide a first glimpse into what happens when the fruits of complex disease genetics become available to the broader public. *AP*

Touching Base written by Myles Axton, Emily Niemitz and Alan Packer.

Disease InfoSearch and GINA

Genetic Alliance recently launched a website portal called 'Disease InfoSearch' that brings together information on genetic diseases from various sources. This marks the entry of Genetic Alliance into the provision of consumer-oriented access to information. For each genetic disease of interest, the portal provides basic descriptions of the disease and links to relevant websites, such as the National Library of Medicine's Genetics Home Reference, the University of Washington's GeneTests.org, ClinicalTrials.gov, MedlinePlus and PubMed. The purpose of this resource is to "make it significantly easier for patients and others to find the information they need about genetic disorders," says Sharon Terry, president and CEO of Genetic Alliance. Genetic Alliance (http://www.geneticalliance.org), a coalition of genetic disease–oriented advocacy organizations, is well known for representing the voice of individuals and families with genetic diseases in policy-making forums. It recently met with success when the Genetic Nondiscrimination Act (GINA) was passed in the US House of Representatives by a vote of 420–3. Congratulations! *EN*

Developmental genetics honored

March of Dimes

Anne McLaren (center left) and Janet Rossant (center right) shared the March of Dimes Prize in Developmental Biology in recognition of their individual pioneering work in mammalian reproductive biology. Their medals were awarded during a dinner on May 7th at the Pediatric Academic Societies' Annual Meeting in Toronto by March of Dimes president Jennifer Howse (left) and trustee Elizabeth Roosevelt Johnston (right), a great-granddaughter of the charity's founder, Franklin D. Roosevelt. In her prize lecture, Rossant emphasized the importance of tackling the simplest developmental decisions taken by the embryo (which also happen to be the most fundamental). In isolating stem cell lines for all three of the mouse embryo's earliest cell lineages, Rossant and her colleagues have been able to identify transcription factors committing the cells to each lineage. McLaren gave a comprehensive overview of the many ways that the environment can stably influence gene expression in development, putting in context the roles of epigenetics and imprinting. This pioneer of *in vitro* fertilization (IVF) later made a public plea relevant to the charity's campaign to reduce the incidence of premature birth: she requested that human embryos be implanted one at a time after IVF. *MA*