TOUCHING BASE

QUESTIONS? THOUGHTS? IDEAS?
e-mail us at ngfeedback@natureny.com

Mutant of the Month

Gail Martin

For our readers who fancy long-haired breeds, we present the classical mouse mutant angora as our May MoM. The original angora mutation, described in 1963 by Margaret Dickie, arose spontaneously in a litter of BALB/cJ mice at The Jackson Laboratory. The molecular defect responsible for this long-haired phenotype remained a mystery until the early 90's, when Gail Martin and colleagues used gene targeting to generate a null allele of *Fgf5* and discovered that these mice presented an exact phenocopy of the original angora mutation. They went on to show that the *Fgf5* null allele failed to complement the angora mutation and that angora mice carry a deletion spanning the *Fgf5* translational start site. Fgf5, a member of the fibroblast growth factor family of secreted ligands, is expressed in the outer root sheath of the hair follicle and is required for timely progression from the anagen (follicle generation and hair production) to catagen (follicle regression) stage of the hair cycle. In the absence of Fgf5, the transition to catagen is delayed, resulting in extended growth of the hair shaft and abnormally long fibers. The JAX website describes the appearance of angora mice as shaggy. We prefer lush and flowing, and we suspect the mice would agree. ***KV***

Necessary improvements

In the United States, most testing for mutations in *BRCA1* and *BRCA2* to identify genetic susceptibility to breast and ovarian cancer is performed by Myriad Genetics, which holds patent rights on the tests. Mutation screening includes sequencing of exons and flanking regulatory regions in *BRCA1* and *BRCA2* and testing for specific recurrent rearrangements in *BRCA1*. Since rare rearrangements or copy number changes are not detected with this approach, the interpretation of negative test results in high-risk women (those who have severe family histories of breast or ovarian cancer) is problematic. Mary Claire King and colleagues have now published a study that determines whether high-risk women who have received negative test results do in fact carry an undetected mutation (*JAMA* **295**; 1379–1388; 2006). The authors detected rearrangements in *BRCA1* or *BRCA2* in 35 of 300 (12%) high-risk women who previously received negative results from commercial tests, supporting the case for global screening for rearrangements in families with negative test results. By quantifying how often Myriad Genetics' tests yield false negative results, this study puts pressure on the company to improve the sensitivity of their tests and to provide more comprehensive testing to women at high risk. *EN*

Electropherogram and loathing

Life is too short to read bad sequence in good papers, so I propose a solution. It is rare for editors to endorse any product, but we are prepared to make an exception for software that makes the lives of our authors and readers easier. Most sequence traces submitted to us as figures are inadequate for the purposes of illustration. The electropherogram usually has insufficient pixels to meet the requirements of our Guide to Authors and often the baseline will be omitted. The relative size of the lettering must be greater than 4-point type when reduced and placed in the context of the figure. We prefer nice bright colors too. We will publish, in Touching Base, the names and links to any manufacturer whose software produces sequence traces that meet the exacting standards of our Production Editors. Freeware and available community software also qualify. Readers should also feel free to condemn inadequate software in our blog, Free Association. The prize for us will be that we will never have to return a figure to an author or to hold up publication of a paper because of its sequence data. *MA*

"You can tell a world-class scientist from the run-of-the-mill investigator by the speed with which he recognizes that he is heading into a blind alley. Blind alleys and garden paths leading nowhere are the principal hazards in research."

—Lewis Thomas, *Late Night Thoughts on Listening to Mahler's Ninth Symphony*, 1983

A jump-start for stem cell research

It was a big boost for stem cell researchers when the California Institute for Regerative Medicine recently announced that the first grant funding will flow from the state's stem cell agency, to the tune of $12.1 million. Up until now the agency had not been able to deliver the $3 billion of voter-approved funding because it has been mired in lawsuits brought by opponents of the research. But the agency, thought to be the largest funder of stem cell research in the world, has outmaneuvered its detractors by selling bond anticipation notes to private investors. Bypassing the ongoing litigation, the Institute used the money raised from these notes to immediately fund stem cell grants. The funds are being used to support training grants for predoctoral, postdoctoral and clinical researchers at 16 California research institutions. *EN*

Touching Base written by Myles Axton, Emily Niemitz and Kyle Vogan.