large, multi-generation families, and 31 from smaller families — to search for a genetic cause of celiac disease. From their analysis, the team zeroed in on IL21R, which had also been implicated in a genome-wide association study of the disease. However, Sanger confirmation studies showed that four unaffected family members had the SNP and four affected people did not. "I want to highlight the difficulties in finding potential mutation," Mistry said.

— *Ciara Curtin*

Genetics: Researchers Uncover Unexpected Genetic Relatedness Within HapMap 3 Populations

Members of Noah Rosenberg's lab at the University of Michigan were working on principal components analysis, genotype imputation, and other projects using the publicly available HapMap Phase 3 data set and were surprised to produce unusual experimental results — and consequently, abnormal plots — indicative of a statistical sensitivity to the presence of unreported close relatives in the cohort. Trevor Pemberton, a postdoc in the Rosenberg lab, decided to take a closer look at the data. Using allele-sharing and RELPAIR analyses, Pemberton and his colleagues were able to empirically ascertain familial relationships.

TREVOR PEMBERTON

Pemberton says that the aim of his team's study, published in the *American Journal of Human Genetics* in September, "was just to make the HapMap resource more useful for individuals that need to have a data set with clearly defined relatedness in it. … It started off being a 'We need this,' and then it became a 'This is something that will be useful to a lot more people,' so we reported it."

In a nutshell, Pemberton says that RELPAIR — which was developed by researchers at Michigan in 1997 — examines tracks of genomic sequence that are shared between individuals and based on the length and frequency of these shared tracks assigns a probabilistic relationship to the pair — whether they are likely parent and offspring, full siblings, or otherwise closely related.

Pemberton *et al*. confirmed the 358 relative pairs reported in notes that accompanied the release of the HapMap 3 data set and also identified 25 previously unreported parent-offspring pairs, 33 unexpected full sibling pairs, 118 unreported second-degree relative pairs, and five surprising parent-parent-offspring trios.

Using the same methodologies with which researchers constructed the HGDP-CEPH Human Genome Diversity Cell Line Panel, Pemberton and his colleagues assembled two subsets of individuals — dubbed HAP1161 and HAP1117 — that contain no known pairs of individuals with a first-degree relationship and no

>SHORT READS

Raindance Technologies has appointed Richard Lussier as vice president of worldwide sales and Ingrid Choupin as managing director of European sales and marketing. Lussier was previously vice president of worldwide sales and service at Cell Biosciences, and Choupin was most recently the associate director of global sales and strategy development at Affymetrix.

With a $9.6 million contract from the US Department of Health and Human Services' Biomedical Advanced Research and Development Authority, Northrop Grumman is developing a PCR-based diagnostic system to detect whether a person has been exposed to a biological threat.

The Evaluation of Genomic Applications in Practice and Prevention Working Group, an independent organization at the Centers for Disease Control and Prevention, found that there is no health benefit to be gained by using any of the eight genetic tests marketed to monitor cardiovascular disease risk, which analyze 58 variants and 29 genes.

Researchers from Emory University's Winship Cancer Institute and the Medical College of Georgia received a five-year, $7.6 million award from NASA to study the possible link between space radiation and lung cancer.

known pairs of individuals with a relationship closer than that of first cousins, respectively. Pemberton is now using these subsets in his investigations of genome-wide homozygosity across human populations worldwide.

He says that he and his collaborators hope that "the study we've reported on HapMap 3 is going to be the definitive study of relatedness in this project." Should the HapMap researchers release genetic data gleaned from additional populations in the future, Pemberton intends to "revisit this project and repeat what we've done," he says.

— *Tracy Vence*

Cancer: Wash U Investigators Infer Putative Metastasis Suppressor in Uveal Melanomas

Uveal melanoma, though rare in general, is the most common form of eye cancer — and a highly aggressive one at that. About half of all uveal melanomas that arise metastasize, at which point they're identified as class 2 tumors. Because approximately 90 percent of class 2 tumors — for which there is no treatment and the average patient's life expectancy is less than a year — are associated with monosomy at chromosome 3, the Washington University in St. Louis School of Medicine's Anne Bowcock and her colleagues sought to sequence candidate genes specific to class 2 uveal melanomas there.

However, Bowcock says that her group and others were unable to detect what they had hypothesized was a metastasis suppressor gene using that approach. "Then we decided to do a pilot experiment [involving] two class 2 melanomas and … do whole-exome sequencing on them," she says. Upon their initial analysis, one gene stood out, "and that was BAP1, which had a nonsense mutation in one tumor," which rendered a premature stop codon, Bowcock says. "This was exciting because no other gene had that characteristic," she adds. The other class 2 tumor exome had an 11-base pair deletion in exon 11 that "put the BAP transcript out of the frame, which would lead to premature termination and predicted nonsense-mediated decay," she says.

ANNE BOWCOCK

Next, the team interrogated all BAP1 exons in 29 additional class 2 and 25 class 1 samples via Sanger re-sequencing. Overall, they found that 84 percent of the class 2 tumors they surveyed showed mutations in BAP1, which led the team suggest that the gene is the "putative metastasis suppressor" they had been searching for, she says.

In subsequent *in vitro* analyses, Bowcock *et al.* found that BAP1-knockdown cell lines showed class 2 tumor characteristics, "both in terms of rounding up and looking more stem cell-like, and in terms of the genes that they [started] to express," she says.

Bowcock says her group's findings could have clinical implications. "It may be possible, in the long term, to assay for circulating cells with BAP1 mutations" in order to predict metastasis, she says, adding that researchers must first come to fully understand the BAP1-protein's functions.

— *Tracy Vence*

ASHG: Researchers Report on Users' Understanding of Direct-to-Consumer Genetic Test Results

One of the concerns with direct-to-consumer genetic testing is that no one knows whether people will understand their disease risks or how they will react to what they find out. Two recent studies found that early adopters of DTC genetic testing have a moderately good understanding of their risks and that some were even motivated to change their behaviors, as researchers reported at the American Society of Human Genetics meeting in Washington, DC, last month.

"Our research only scratches the surface of what the concerns are," noted David Kaufman from the Genetics and Public Policy Center at Johns Hopkins University.

Kaufman's team, which conducted an NHGRI-funded survey of 1,048 people who had purchased a DTC test from 23andMe, DecodeMe, or Navigenics, reported that nearly everyone indicated that the risk reports they received from the companies were