NEWS BRIEFS

Gene variant common among Asians presents evolutionary trade-off

An immune system variant common among Asians may have evolved in response to a rise in leprosy, but it increases the risk of certain autoimmune disorders in carriers. The mutation in a human leukocyte antigen (HLA) gene arose and spread rapidly in Southeast Asia about 50,000 years ago, but it took some molecular sleuthing to figure out why. The Stanford University–based research team showed that the variant encodes an antigen-presenting peptide that more efficiently binds to the organism that causes leprosy, a disease that arrived in Asia from Africa around the same time this variant became prevalent in the population. The *Cell Reports* article, published 16 May 2017, also reveals that the variant is less effective in binding HIV and influenza than HLA counterparts not containing this variation. Previous population studies had suggested that carriers are protected against developing the most severe forms of leprosy. Conversely, the variant predisposes carriers to autoimmune disorders such as myasthenia gravis and Graves disease, in addition to a rare type of head and neck cancer. "New HLA gene variants, or alleles, are thought to arise in human populations during episodes of Darwinian selection, but there is little direct evidence for the nature of this process," says senior study author Peter Parham of Stanford University School of Medicine. Population expansion, cultural changes, and migration over the past 100,000 years exposed humans to pathogens against which they had not evolved effective resistance. This study demonstrates that exposure to new pathogens can relatively rapidly lead to the rise of novel immune system variants that, while protective against the new threat, carry a trade-off in predisposition to other diseases. The HLA-B*46:01 allele is now carried by approximately 110 million individuals of Southeast Asian descent. *—Karyn Hede, News Editor*

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Rare skin disease caused by mutation in gene enhancer

Michele Ramsay

Mutations in a noncoding enhancer region of DNA have been identified as the cause of a rare skin disease found both in Norway and among Afrikaners descended from Dutch, German, and French settlers in South Africa. Keratolytic winter erythema (KWE), or "Oudtshoorn skin," in Afrikaners causes excessive shedding of skin in winter. A research team at the University of the Witwatersrand, Johannesburg, South Africa, in collaboration with peers in Europe, the United States, and Canada published the finding in the May 2017 issue of the *American Journal of Human Genetics*. Graduate student Thandiswa Ngcungcu identified a duplicated region in the noncoding region of chromosome 8 during a large-scale DNA screen. The region had been identified by linkage mapping prior to sequencing of the human genome. Conventional DNA analysis came up empty in a search for mutations in coding regions. Ngcungcu, senior author Michele Ramsey, and colleagues then investigated copy-number variants and identified a noncoding region that was duplicated in affected individuals. The evidence became much stronger when Torunn Fiskerstrand, of the University of Bergen, Norway, independently discovered a different overlapping DNA duplication in Norwegian families with KWE. Collaboration among the scientists revealed that a duplicate enhancer causes a nearby gene involved in skin turnover to produce more protein than normal and that this abnormal expression likely leads to peeling skin. The finding allows definitive diagnosis of KWE in patients and may help researchers understand similar skin disorders. It also provides a basis for research into potential treatment. *—Karyn Hede, News Editor*