

Humans and chimps share genetic strategy in battle against pathogens

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A genome-wide analysis searching for evidence of long-lived balancing selection—where the evolutionary process acts not to select the single best adaptation but to maintain genetic variation in a population—has uncovered at least six regions of the genome where humans and chimpanzees share the same combination of genetic variants.

The finding, to be published Feb. 14 in the journal *Science*, suggests that in these regions, <u>human genetic variation</u> dates back to a <u>common</u> <u>ancestor</u> with chimpanzees millions of years ago, before the species split. It also highlights the importance of the dynamic co-evolution of human hosts and their pathogens in maintaining genetic variation.

Balancing selection allows evolution to keep all hereditary options open. The classic human example is the persistence of two versions of the hemoglobin gene: a normal version and hemoglobin S., a mutation that distorts the shape and function of <u>red blood cells</u>. Those who inherit two normal hemoglobin genes are at high risk for malaria, a <u>parasitic disease</u> that infects more than 200 million people each year. Those who inherit one normal gene and one <u>hemoglobin</u> S. gene are partially protected from malaria—a potentially life-saving benefit. Those with two copies of the gene suffer from sickle-cell anemia, a serious and lifelong <u>circulatory disease</u>.

"When we looked for <u>genetic clues</u> pointing to other, more ancient, examples of balancing selection, we found strong evidence for at least six such regions and weaker evidence for another 119—many more than



we expected," said study author Molly Przeworski, PhD, professor of <u>human genetics</u> and of ecology and evolution at the University of Chicago.

"We don't yet know what their functions are," she said. None of the six regions codes for a protein. There are clues that they are involved in host-pathogen interactions, "but which pathogens, what immune processes," she said, "we don't know."

The researchers used genetic data from 10 chimpanzees from Western Africa and 59 humans from sub-Saharan Africa who were part of the 1,000 Genomes Project.

The scientists looked for cases in which genetic variations that arose in the ancestor of humans and chimpanzees have been maintained through both lines. The fact that variation in these regions of the genome has persisted for so long argues that they "must have been functionally important over evolutionary time," said Ellen Leffler, a graduate student in Przeworski's laboratory and first author of the study.

The researchers, from the University of Chicago and Oxford University, designed the study to be very conservative. "We wanted to find the cases we believed the most, rather than the most cases," Przeworski said.

Computers sorted snippets of the <u>genetic data</u> from humans and chimps into clusters depending on how similar the subjects were to each other. For almost every snippet, they found a cluster of humans and a separate cluster of chimpanzees, as expected. But there were a few segments of the genomes in which each cluster included both chimpanzees and humans; in those regions, some humans were more closely related to some chimpanzees than to other humans.

"Instances in which natural selection maintains genetic variation in a



population over millions of years are thought to be extremely rare," the authors wrote. The oldest and best known example of balanced polymorphism shared between humans and chimpanzees is the major histocompatibility complex (MHC), a group of genes that help the immune system distinguish between the body and potential invaders, such as bacteria or viruses.

Last year, a team led by Przeworski found that humans and gibbons shared <u>genetic variation</u> related to the ABO blood-group system from a common ancestor.

The six new examples of balanced selection described in this study appear to play a role, like the MHC, in fending off infectious disease. This requires a variety of evolutionary tools, including balancing selection. When a population moves to a new environment—for example the exodus out of Africa to northern Europe—they face many one-time adjustments, such as adapting to less intense sunlight and decreased ultraviolet radiation. Over many generations, their offspring manage to decrease melanin production—a static adaptation for a static environment.

Fighting off pathogens is more dynamic, a constant arms race. Balancing selection may have enabled humans and chimps to retain multiple lines of defense that can be called on when a pathogen evolves new weapons.

"Our results imply that dynamic co-evolution of human hosts and their pathogens has played an important role in shaping human variation," Przeworski said. "This highlights the importance of a different kind of selection pressure in <u>human</u> evolution."

Provided by University of Chicago Medical Center



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