

## **Evolution in action: Our antibodies take 'evolutionary leaps' to fight microbes**

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With cold and flu season in full swing, the fact that viruses and bacteria rapidly evolve is apparent with every sneeze, sniffle, and cough. A new report in the January 2009 issue of *The FASEB Journal*, explains for the first time how humans keep up with microbes by rearranging the genes that make antibodies to foreign invaders. This research fills a significant gap in our understanding of how the immune system helps us survive.

"We've known for a long time that our antibody-forming system adapts itself to every microbe we encounter," said Gerald Weissmann, M.D., Editor-in-Chief of *The FASEB Journal*, "but what we didn't understand fully is exactly how this happens. Now that we know, we can begin to find ways to manipulate this process so illnesses can be prevented or made significantly less dangerous."

When the body encounters a foreign invader, like a virus or bacterium, it immediately begins to find a way to neutralize it by means of cellular or antibody-mediated defenses. Part of the process involves tailoring the genes that code for antibodies to specific viruses or bacteria. Researchers have known that this involves two types of genetic manipulation. One type changes a single gene at a time, and the other type changes multiple genes at the same time. In the report, scientists from Wayne State University in Detroit describe how multiple genes can be modified simultaneously to make the "evolutionary leap" necessary to stave off infection.

The basic setup of the experiment treated DNA responsible for making



antibody molecules with an enzyme, called activation-induced deaminase, while the DNA was being copied by RNA polymerase. Like a scanner, RNA polymerase moves across the DNA to copy it. When this scanning process moved smoothly, there were either single mutations or no mutations. When the researchers made the RNA polymerase stall along the DNA (under certain conditions), it caused several mutations at once (cluster mutations) in the DNA, adapting our antibodies for a rapid and effective response to a new microbial invader.

"As the planet warms, infectious diseases may be one the biggest threats to human survival," Weissmann added. "Nowadays, mosquitoes, parasites and viruses cause diseases in the United States that were once isolated to warmer parts of the world. They evolve, and - a la Darwin - so does our immune system each time we meet a new microbial invader."

Article details: Chandrika Canugovi, Mala Samaranayake, and Ashok S. Bhagwat. Transcriptional pausing and stalling causes multiple clustered mutations by human activation-induced deaminase. FASEB J. 2009 23: 34-44. www.fasebj.org/cgi/content/abstract/23/1/34

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