

Scientists Discover a New Player in Innate Immune Response

All multicellular animals have an innate immune system: When bacteria, parasites or fungi invade the organism, small protein molecules are released that eliminate the attackers. Scientists of the German Cancer Research Center (Deutsches Krebsforschungszentrum, DKFZ) have now discovered a new molecule that plays an important role in triggering the innate immune response of the fruit fly *Drosophila*, mice and even humans. Their work has just been published in the journal *Nature Immunology*.

The cells of the innate immune system recognize hostile invaders with the aid of receptors on their surface: The moment these receptors recognize a foreign structure, they send a message, via a complicated signaling pathway, into the cell's interior. The cell then releases immunologically active proteins. The components of this signaling pathway have been conserved surprisingly well through evolution; the various signaling molecules are very similar from fly to man, both in structure and in function.

A group of scientists headed by Dr. Michael Boutros of the German Cancer Research Center (Deutsches Krebsforschungszentrum, DKFZ), collaborating with colleagues of the Centre National de la Recherche Scientifique (CNRS) in Strasbourg, made use of this fact: Using the Nobel prize-winning method of RNA interference (RNAi), they switched off individual molecules of the signaling pathway in *Drosophila* and have thus come across a new member: Akirin, meaning "making things clear" in Japanese. When they suppressed Akirin production in the immune cells of the flies, these were significantly more susceptible to bacterial infections. And when they knocked down the protein in all body cells, the fly larvae died in an early stage. Colleagues at Japan's Osaka University investigated the corresponding mouse Akirin: In mice, too, the protein fulfills the same function as in the fruit fly and in man.

"What is called the NF- κ B signaling pathway plays an important role in inflammations, and inflammations are highly relevant in cancer development," said Michael Boutros. "Therefore, the search is on for small molecules that can inhibit this signaling pathway." First inhibitors acting against other links in the signaling chain are already being tested in clinical trials. "The more links of this chain we know, the more possibilities we have to interfere with it," said Boutros explaining the aim of his work.

Akira Goto, Kazufumi Matsushita, Viola Gesellchen, Laure El Chamy, David Kutteneuler, Osamu Takeuchi, Jules A Hoffmann, Shizuo Akira, Michael Boutros & Jean-Marc Reichhart: Akirins are highly conserved nuclear proteins required for NF- κ B -dependent gene expression in *drosophila* and mice. *Nature Immunology* Volume 9 Number 1 January 2008

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The task of the Deutsches Krebsforschungszentrum in Heidelberg (German Cancer Research Center, DKFZ) is to systematically investigate the mechanisms of cancer development and to identify cancer risk factors. The results of this basic research are expected to lead to new approaches in the prevention, diagnosis and treatment of cancer. The Center is financed to 90 percent by the Federal Ministry of Education and Research and to 10 percent by the State of Baden-Württemberg. It is a member of the Helmholtz Association of National Research Centers (Helmholtz-Gemeinschaft Deutscher Forschungszentren e.V., HGF).

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