

Scientists uncover a genetic switch that turns immune responses on and off

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Scientists are keeping their eye on a new discovery published in the November 2011 print issue of the *FASEB Journal* that explains what causes some genes to go out of control. Scientists have identified a "cellular switch," called eye transformer, that controls the flow of information from chemical signals outside of the cell to genes in the cell nucleus. This study demonstrates that when eye transformer is turned off, the information pathway it controls (the "JAK/STAT pathway") hyper-activates. Because this pathway exists in humans and is involved in many conditions such as cancer, severe immune deficiencies, autoimmune diseases, and allergies, this discovery reveals a new and potentially important drug target for these conditions.

"We hope that our study will open new horizons for researchers studying mammalian JAK/STAT signaling which eventually leads to better understanding how mammalian JAK/STAT signaling is regulated," said Mika Rämetsä, Ph.D., co-author of the study from the Institute of Medical Technology at the University of Tampere in Finland. "We hope that this information can be then used in developing better treatments for diseases that are influenced by malfunctioning JAK/STAT signaling."

To make this discovery, Rämetsä and colleagues "silenced" all of the fruit fly [genes](#) one by one using RNAi-based screening methods in cultured *Drosophila* (fruit fly) cells and then analyzed which genes were important for JAK/STAT signaling. They identified five novel regulators, one of which was a negative regulator of eye transformer that proved to negatively regulate the JAK/STAT response during microbial

challenge. Further research showed that suppression of eye transformer expression in the eyes of fruit flies by in vivo RNAi causes hyper-activation of JAK/STAT signaling indicated by drastic eye overgrowth when JAK/STAT signaling was activated.

"We tend to treat immune diseases after the inflammation switch has been turned on," said Gerald Weissmann, M.D., Editor-in-Chief of the [FASEB Journal](#) and a past president of the American College of Rheumatology. "This study sheds new light on how we might to control diseases like rheumatoid arthritis or lupus by keeping our hands on the switch."

More information: Jenni Kallio, Henna Myllymäki, Juha Grönholm, Morag Armstrong, Leena-Maija Vanha-aho, Leena Mäkinen, Olli Silvennoinen, Susanna Valanne, and Mika Rämetsä. Eye transformer is a negative regulator of *Drosophila* JAK/STAT signaling. *FASEB J.* 2010 24: 4467-4479. [DOI: 10.1096/fj.10-162784](https://doi.org/10.1096/fj.10-162784)

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