Scientists describe new protein's role in immune response to pathogens

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The human immune system is a double-edged sword. While it is finely adapted to fighting potentially deadly viruses, such as the H1N1 influenza, the mechanisms it uses to fight pathogens can have negative effects such as inflammatory disorders or autoimmune diseases.

A new finding by UNC scientists provides a window into how the immune system initially reacts to a virus invader, as well as how a subgroup of proteins plays a role in returning the immune system to a normal surveillance function. Their pre-clinical findings were published in the June 24, 2011 online edition of *Immunity*.

Coy Allen, PhD, first author of the paper and a postdoctoral fellow at UNC Lineberger Comprehensive Cancer Center, explains, "We knew that proteins called NLRs control the immune system's initial response to an invading pathogen, such as influenza. However, we did not realize that a sub-group of these proteins actually functions to bring an overactive immune response back under control after the pathogen threat has been resolved. Our study showed that a newly identified NLR protein called NLRX1 is capable of shutting down an overreaction by the immune system during an influenza infection."

Allen says, "We worked with influenza because the flu virus is an ongoing global health concern that results in a significant number of deaths each year. In 2009-2010, a new influenza virus emerged and rapidly spread throughout the world, ultimately resulting in the first global influenza pandemic in over 40 years. As part of our studies, we partnered with the Centers for Disease Control and Prevention and found that NLRX1 also functions in controlling the immune response following 2009 H1N1 influenza virus infection.

In most cases, individuals who die from influenza virus infection suffer from a hyperactive immune response to influenza. Thus, NLRX1 is one of the mechanisms that dampen this hyperactive immune response.

Allen is a postdoctoral fellow in the laboratory of Jenny Ting, PhD. Ting, UNC Alumni Distinguished Professor of Microbiology and Immunology and director of the Inflammation center at UNC, is a pioneer in the understanding of the NLR family of proteins. She is co-leader of UNC Lineberger's immunology program and senior author of the Immunity paper.

Allen explains, "These findings are also relevant to cancer. Several viruses are implicated in cancer, including adenovirus, Hepatitis C Virus, Epstein-Barr virus and Kaposi's sarcoma-associated herpesvirus. It is likely that NLRX1 may also mediate elements of the host immune response following onco-virus exposure

Allen says that the next steps are to examine other NLR proteins to determine if they too can act as an anti-inflammatory and to further describe how the NLRX1 protein shuts down the immune response at the appropriate time.

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