FAST MOVING FRONTS - 2010

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Kate Fitzgerald talks with *ScienceWatch.com* and answers a few questions about this month's Fast Moving Fronts paper in the field of Immunology. The author has also sent along an image of her work.

Article: AIM2 recognizes cytosolic dsDNA and forms a caspase-1-activating inflammasome with ASC
Authors: Hornung, V;Ablasser, A;Charrel-Dennis, M;Bauernfeind, F; Horvath, G;Caffrey, DR;Latz, E;**Fitzgerald, KA**
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SW: Why do you think your paper is highly cited?

Innate immunity—immunity that occurs naturally as a result of a person's genetic constitution or physiology and does not arise from a previous infection or vaccination—is a fast-paced, exciting field. Over the last 10 years or so several classes of germline encoded innate immune receptors have been identified. There are probably not that many receptors remaining to be defined. We are starting to get a handle on the full compendium of pattern recognition receptors (PRRs).

Aim2 (absent in melanoma 2) is one of the last of these to be identified. Inflammasomes are known to be important in sensing microbial as well as endogenous danger signals. The discovery of NLR family, pyrin domain containing 3 (NLRP3) as a mediator of DNA virus-induced inflammation by Jürg Tschopp and colleagues in the Department of Biochemistry at the Université de Lausanne in Epalinges, Switzerland, was an exciting finding. Since then NLRP3 was also shown to detect influenza.

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IM2 inflammasome.

SW: Does it describe a new discovery, methodology, or synthesis

of knowledge?

Yes, the paper describes a new function for a previously studied protein. Aim2 is known to be induced in cells infected with viruses. Why Aim2 is elevated in this setting was unclear. Our study indicates that Aim2 is induced in cells during infection so it can detect DNA from pathogens to turn on IL-1, an inflammatory cytokine important in ultimately clearing the infection.

SW: Would you summarize the significance of your paper in layman's terms?

We identified a receptor which is present in the cytoplasm of cells, a strategic location to detect microbes which can replicate and spread through this compartment. Having Aim2 present at this site means there is a surveillance mechanism in place to sense infection and mount rapid defenses to eliminate the invading pathogen.

SW: How did you become involved in this research and were any particular problems encountered along the way?

We became interested in Aim2 as a potential mediator of DNA-induced inflammation when we looked for proteins in the genome which contained a pyrin domain (PYD), a domain which mediates protein-protein interactions with other components of inflammasomes.

SW: Where do you see your research leading in the future?

We hope to define what role Aim2 plays, not only in host defense to microbial infection (bacterial, viral, or parasitic), but additionally we would like to determine if Aim2 contributes to autoimmune diseases, such as lupus.

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