

EMERGING RESEARCH FRONTS - 2009

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Gabriel Nuñez talks with *ScienceWatch.com* and answers a few questions about this month's Emerging Research Front Paper in the field of Microbiology.



Article: NODs: Intracellular proteins involved in inflammation and apoptosis

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SW: Why do you think your paper is highly cited, and does it describe a new discovery, methodology, or synthesis of knowledge?

This article represents one of the first reviews on NODs, currently called Nod-like receptors (NLRs), a new and fast-growing topic in the field of innate immunity. The high citation rate probably also reflects that fact that genetic variation in some NLR family members such as NOD2 is linked to a susceptibility to inflammatory disease.

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

The detection of invading microbes allows the rapid initiation of a defense response against the microbe, which is critical for the survival of living organisms, including humans. The sensing of harmful microbes is mediated by a class of proteins called innate immune receptors, which are rapidly activated upon the encounter with the invading microbe.

NLRs, a class of receptors that senses microbes inside cells, are activated by bacterial products and this leads to a defense response against the invading microbe. Certain individuals carry faulty forms of certain NLR genes and this increases their susceptibility to inflammatory disorders such as Crohn's disease.

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

Naohiro Inohara, a postdoctoral fellow in my laboratory, discovered NLR genes about 10 years ago, when we were looking for proteins with homology to the apoptosis regulator Apaf-1. At the beginning of the work, we thought that NOD1 and NOD2, the first NLR family members to be identified, were involved in the regulation of apoptosis. However, after much work we found that NOD1 and NOD2 activate NF- κ B, an activity that is typically associated with inflammation.

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Furthermore, NOD1 and NOD2, as well as other NLR family members, contain remarkable structural homology to proteins involved in recognition of invasive microorganisms and host defense in plants. Finally, we, and others, found that genetic variation in NOD2 was associated with susceptibility to Crohn's disease, a common inflammatory disorder of the bowel. Together, these observations suggested a link between NLRs and microbial recognition.

The next task was the identification of the microbial molecules recognized by NOD1, NOD2 and other NLR family members. This work was difficult, but after hard work, our laboratory and other laboratories, including that of [Dana Philpott](#), who is currently a member of the Faculty of Medicine at the University of Toronto—and who was then at the Institut Pasteur in Paris—were successful in the identification of the microbial activators of NOD1, NOD2, and other NLRs.

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

We need a better understanding of the NLR pathways and the link between genetic variation in NLR genes and disease.

SW: Do you foresee any social or political implications for your research?

Perhaps work in the field may lead to better treatment for inflammatory diseases or development of more effective vaccines against infectious agents. Actually, work by several laboratories in the NLR field has already led to a specific treatment for patients with autoinflammatory syndromes, which is highly effective.

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