New vaccine hope in fight against pneumonia and meningitis

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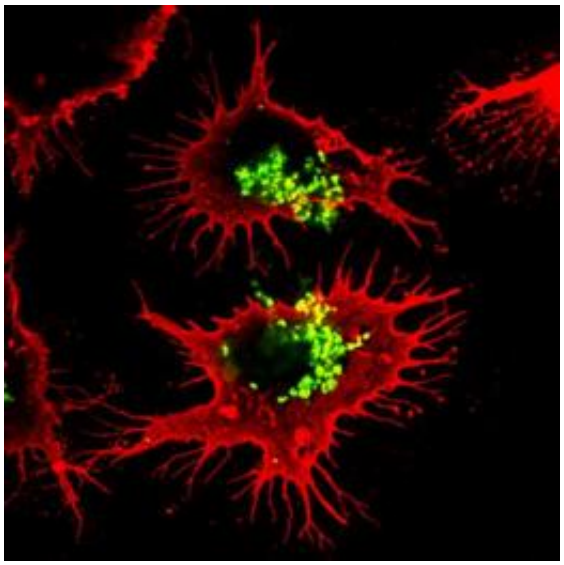

This is a dendritic cell infected with *Streptococcus pneumoniae*. Credit: Courtesy of Edel McNeela and Jim Harris

A new breakthrough in the fight against pneumonia, meningitis and septicaemia has been announced today by scientists in Dublin and Leicester.

The discovery will lead to a dramatic shift in our understanding of how the body's immune system responds to infection caused by *Streptococcus pneumoniae* and pave the way for more effective vaccines.

The collaborative research, jointly led by Dr Ed Lavelle from Trinity College Dublin and Dr Aras Kadioglu from the University of Leicester, with Dr Edel McNeela of TCD as its lead author, has been published in the international peer-reviewed journal *PLoS* Pathogens.

The research was carried out by the teams from Dublin and Leicester with other collaborators from Trinity College Dublin, the U.S and Switzerland over four years and supported by Science Foundation Ireland, Enterprise Ireland, the Medical Research Council (MRC) and the Meningitis Research Foundation.

The two teams say they have shown for the first time that the bacterial toxin pneumolysin triggers an immune response by activating a recently discovered group of proteins, called the NLRP3 inflammasome. Once activated, the inflammasome provides protection against infection caused by this pathogen.

The Leicester and Dublin research groups demonstrated that this mechanism operates independently of other previously described immune response proteins - contrary to a dogma in the field.

Importantly, this paper is the first to demonstrate that the NLRP3 inflammasome is essential in the immune response against infection by the pathogen and that the bacterial toxin pneumolysin is the key driver of this process. The researchers state that this new knowledge of how the toxin interacts with the immune system will mean that new vaccines can be developed and targeted more effectively.

Describing the results as exciting, the researchers say it will potentially have a significant impact in the development of vaccines against pneumococcal disease.

Dr Lavelle, who is Lecturer in Immunology in the School of Biochemistry and Immunology, Trinity College Dublin, said: "This is a very exciting finding and supports the development of inflammasome activating vaccines to prevent pneumococcal diseases including pneumonia and septicaemia. If a protein based vaccine could be produced that can protect against all strains of the pneumococcus, this would be of tremendous value and our discovery that NLRP3 is needed for protection will point us in the right direction in terms of how to

develop such vaccines."

Dr. Aras Kadioglu, Reader in Respiratory Infection in the Department of Infection, Immunity & Inflammation at the University of Leicester said: "This is a major breakthrough in our understanding of the immune response to Streptococcus pneumoniae; a human pathogen of global significance, responsible for over one million infant deaths annually and the major cause of illness and death in the elderly from infections of the respiratory tract. In order to develop improved pneumococcal vaccines for both the very young and the elderly, it is essential to understand how this bacterium interacts with the host immune system. The discoveries described in our paper represent a huge stride towards this objective. That is why these are exciting new findings, discovered in the course of a unique collaboration between scientists at the University of Leicester and Trinity College Dublin."

More information: McNeela EA, Burke Á, Neill DR, Baxter C, Fernandes VE, et al. (2010) Pneumolysin Activates the NLRP3 Inflammasome and Promotes Proinflammatory Cytokines Independently of TLR4. *PLoS Pathog* 6(11): e1001191. doi:10.1371/journal.ppat.1001191

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