MedicalXpress

Scientists discover new routes for immune cells to tackle infections of the gut

September 4 2013

An international collaboration between scientists in Trinity College Dublin (TCD) and the Icahn School of Medicine at Mount Sinai (MSSM) New York has led to novel discoveries involving new routes of cellular traffic to the gastrointestinal (GI) tract. The discovery may have a potential impact on the design of new vaccines against infections such as HIV and E. Coli.

The study led by Dr. Saurabh Mehandru (MSSM) and Dr. Ed Lavelle (TCD), recently published in the leading peer reviewed medical journal *The Journal of Experimental Medicine*, shows for the first time, direct evidence of cellular movement between the lung and GI tract.

The movement of immune cells to the GI tract is critical for the body's defence against infectious agents; therefore, studying the mechanisms by which immune cells are directed to the GI tract is the key to developing novel vaccines against mucosal infections such as HIV. This could broaden the potential vaccination routes available to tackle such infections. Traditionally, vaccines are administered via injection but opening up needle-free, particularly mucosal routes, is valuable because it can enhance patient compliance and facilitate the induction of stronger immune responses at the site of infection.

The human immune system has a type of cell called the dendritic cell (DC), which is responsible for inducing immune responses during infections. These cells orchestrate the movement of lymphocytes to various compartments in the body, a key event in the immune response.

Current theories suggested that only intestinal dendritic cells had the capacity to endow lymphocytes with the capacity to travel to the small and large intestine to fight infection. However, the research teams have shown for the first time that dendritic cells in the lung can strongly promote homing of lymphocytes to the intestine.

The Dublin and New York research groups targeted dendritic cells in the lung via a nasally administered immunisation which resulted in a successful immune response being activated against a highly infectious strain of Salmonella. The results also showed that as a result of using this pathway the immunisation was significantly more potent at triggering the immune response to Salmonella than an orally administered vaccine which would have selectively targeted dendritic cells in the gut.

Dr. Ed Lavelle, Associate Professor in Immunology in the School of Biochemistry and Immunology, Trinity College Dublin said "These are very exciting findings which may provide opportunities to develop novel vaccine strategies for gastrointestinal infections. While oral vaccination can be effective the option of vaccination in the respiratory tract could be invaluable in cases where the oral route is not optimal."

Lead author of the paper, Dr. Darren Ruane, a recently graduated Ph.D. student from Trinity College Dublin and currently at MSSM who conducted the research between MSSM, TCD and The Rockefeller University New York said "This study reveals that pathways of cellular recruitment to the gut are much more diverse than previously appreciated. There appears to be considerable, DC-mediated traffic of lymphocytes between distinct mucosal compartments thereby confirming the classical theory of a common mucosal immunological system. This theory predicts that the immune system at the various mucosal surfaces including the lung, digestive and reproductive tracts are connected, offering the potential to vaccinate at one site yet induce immunity at other mucosal sites. This mucosal cross talk has the potential to open up

the possibilities for developing new types of vaccines for infections affecting the gut."

Commenting on the significance of the findings, Dr. Mehandru, Assistant Professor of Gastroenterology at the Icahn School of Medicine at Mount Sinai, New York said "This initial, proof of concept study shows that dendritic cells resident in the lung direct cellular traffic to the intestines. Further studies need to be done to better understand the physiological relevance of this pathway and to manipulate it in the design of enteric vaccines." This work is a major collaboration between three centres including the Icahn School of Medicine at Mount Sinai New York, The Rockefeller University New York and Trinity College Dublin.

More information: jem.rupress.org/content/210/9/1871.abstract

Provided by Trinity College Dublin