Specifying the role of the immune system's sentry guards

PUBLISHED

An immune response involves different immune cells interacting with one another to dispose of an invading organism or 'antigen'. Dendritic cells (DCs) capture viruses or bacteria, process them, then deliver information to other immune cells known as T follicular helper cells (Tfh), which in turn deliver information to B cells, the makers of antibodies.

Bioscientists Kumar Krishnaswamy and Johan Mattsson from our IMED Biotech Unit, have together with scientists at Yale University School of Medicine, been trying to define the rules that govern T cell mediated humoral immune responses. Since his publication in 2015 in *PNAS*, lead author Kumar Krishnaswamy, is now Senior Bioscientist in the IMED Biotech Unit at AstraZeneca. He commented, "In PNAS, we revealed a protein called DOCK8 was critical for migration of dendritic cells but questions remained which type of dendritic cells in the lung or lung-draining lymph nodes induce T follicular helper cells to inhaled antigens".

In their recent publication in *Science Immunology*, the scientists describe which subset of DCs are responsible for priming the Tfh cell response, and where within the lymph nodes this takes place.

DCs are the immune system's sentinels that regulate whether or not an antigen will be presented to activate a cell response. In the case of a Tfh response, appropriate control is essential to human health as activation promotes long-lived, antibody production by B cells. Yet it remained unclear how the cells are primed and where in the lymph nodes they are activated, until now.

Using model systems with DOCK8 knock-outs, the researchers identified a particular type of DC, known as a conventional type 2 DC (cDC2), uniquely triggers Tfh cell priming. As this immune response is key to generating an effective vaccine response, this insight could inform where in the body vaccines should be given in order to directly reach those dendritic cells. "What we believe is that when we're vaccinating into the muscle, we're probably not targeting the type 2 dendritic cells well," said co-corresponding author Stephanie Eisenbarth, Associate Professor of Laboratory Medicine at Yale University. "But if we deliver the same vaccine into the skin or the lung, the dendritic cells are right there, enabling a more potent vaccine response. Location is very important."

Indeed, the recent publication confirms the location where the Tfh cell response is triggered, "By performing multi-color confocal microscopy studies at AstraZeneca, we were able to accurately confirm the localisation of the type 2 DCs in the lymph node. This is a prime location at the T/B cell border for this stimulus to happen. Our next step is to understand why this is unique to one DC subset only", added Kumar.

Identifying the primary cell responsible for an effective antibody response enables researchers to peruse new targets around this pathway for diseases where dysregulated antibody responses drive immunopathologies, including asthma, COPD and autoimmunity.

Read more

We know that innovation doesn't happen in isolation, so we partner with others to access the best science and contribute complementary technologies, know-how and molecules.

Read more

Our IMED Biotech unit is committed to driving scientific advances in small molecules, oligonucleotides and other emerging technology platforms to push the boundaries of medical science.

Read more