KEYNOTE: VIRUSES, VACCINES AND DENDRITIC CELLS: A QUESTION OF LIFE, THE UNIVERSE AND EVERYTHING?

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Dendritic cells (DC) play a critical role in immune defence development by mediating the interaction of various components within the innate and adaptive immune compartments. Of particular importance is the interaction between conventional DC (cDC) and plasmacytoid DC (pDC). During the last decade, the increase in our knowledge on the critical roles of DC has elaborated our understanding of how viruses evade and modulate immune defence processes, as well as promoted research and development of vaccines for targeting DC.

The efficacy of immune defence development is open to manipulation by viral pathogens, particularly when infecting DC. Classical swine fever virus (CSFV) and porcine circovirus type 2 (PCV2) offer insights into the diversity of virus-induced manipulation of immune responsiveness. CSFV infects and replicates in both cDC macrophages where it antagonises the type I interferon (IFN) induction pathway, by Npro-mediated proteasomal degradation of interferon production is induced and itsαregulatory factor (IRF)3. In pDC IFN overproduction during acute disease results in immunopathological consequences. As for PCV2, its main mode of immunomodulation appears to rely more on the viral nucleic acid, which has immunoregulatory characteristics by preventing "danger" recognition by cells of the innate defences. In addition, PCV2 may also divert immune responsiveness against another virus or vaccine into a more regulatory pathway, seen as a promotion of IL-10 production following immune stimulation by another antigen.

As can be seen from these examples, an important element in virus interaction with the immune system is the manner by which the DC respond to pathogen-associated molecular patterns. While viruses have mechanisms to interfere with this "danger" recognition, such processes of detection have permitted the development of vaccines targeting DC. Recent efforts in the latter field have focussed on synthetic vaccine carriers, often based on biodegradable polysaccharide particles or gel-like meshes. The surface of these particles can be decorated with ligands for DC receptors. Examples of the ligands tested to date include mannose for the C-type lectin mannose receptor and lipopeptides for the toll-like receptors TLR2/1 and TLR2/6. Others approaches have employed antibodies specific for structures including integrins, Siglecs, galectins, and other C-type lectins such as DC-SIGN and DEC205. There is also interesting comparison to be made with vector vaccines employing virus-like particles, whereby natural viral ligands for cell receptors such as heparan sulphate glycosaminoglycan structures and integrins may prove applicable.

In conclusion, the DC family represents a critical immune defence element open to modulation by virus infection, but also central for targeted, and therefore efficacious vaccine delivery. The characteristics of the immune modulation depend on how the virus or targeted vaccine interacts with the DC subsets, and the outcome offers either pathological problems for the host or efficient protection form the pathogen.