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SIgN Immunology Seminar



Dr Aymeric Silvin

Department of Immunity and Cancer,
Institute Curie Research Centre

Selective resistance of CD141+ DCs and pDCs to HIV and Influenza infection

Host
Dr Florent Ginhoux
Singapore Immunology Network, A*Star

Date
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Time
11am – 12pm

Venue
SIgN Seminar Room
Immunos Building
Level 4
Biopolis

Dendritic cells (DCs) respond to viral particles to induce immune responses. DCs are developmentally organized in distinct subsets. How these human DC subsets are organized to induce immune response against viruses remains unclear. It has been shown that viruses can replicate in DCs, engaging cytosolic immune responses. In the case of human pathogen HIV, a cytosolic innate sensing mechanism was recently described in monocyte-derived DCs (MDDCs). Cytosolic innate sensing of HIV requires efficient replication of viruses in MDDCs. The pathogenic HIV-1 inefficiently infects DCs. HIV-1 infection and sensing can be rescued by adding the Vpx protein found in HIV-2, a virus with reduced pathogenicity. Whether this mechanism of infection-associated HIV sensing is restricted to MDDCs or conserved in other DC subsets was not known. Another pathogenic virus, Influenza, has been reported to induce strong innate immune response. It has been shown that influenza infection was restricted to CD11b+ DCs from lungs infected mice. To explore human functionalization of DC subsets during infection, we investigated three primary DC subsets found in blood, plasmacytoid DCs, CD1c+ DCs and CD141+ DCs. We find that HIV and influenza preferentially infect CD1c+ DCs over CD141+ DCs and pDCs. Replication in CD1c+ DCs was essential for efficient CD8+ T cell activation and cytosolic sensing, while CD141+ DCs and pDCs responded to exogenous virus through TLR recognition. We found that viral fusion was constitutively reduced in CD141+ and pDCs compared to CD1c+ DCs. These results suggested that the different DC subsets might selectively engage distinct innate sensing pathway according to viral infection. Selective resistance of CD141+ DC and susceptibility of CD1c+ DCs may thus represent a mechanism of regulated tolerance to viral infections to orchestrate and maximize antiviral responses.