THE CRM APPLIED MATHEMATICAL PHYSICS (CAMP) SEMINARS

CENTRE DE RECERCA MATEMÀTICA

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Virus infection fate regulation: transcriptional dynamics reveals a critical role of the Xcl1-Xcr1 communication axis in chronic infection

Abstract:

The dynamic interplay between an expanding virus and the concomitantly activated host immune response during the primary infection phase is critical for establishing a chronic infection. However the key sensors and regulatory mechanisms that ultimately move the virus-host dynamics towards virus persistence and immune system exhaustion are still poorly understood. Our objective is the identification of key elements during the establishment of viral persistence using the Lymphocytic Choriomeningitis Virus (LCMV) mouse model system.

Our experiments revealed modules of highly connected genes (hub genes) that represent the main biological pathways involved in acute versus persistent infection outcomes. Module comparisons from both infection outcomes showed a positive correlation between module size and preservation, indicating that few genes are involved in outcome-specific pathways. A chronic infection-specific module suggested an important biological role for the chemokine Xcl1 and responsive $Xcr1^{+}$DC. Depletion of this cell population resulted in reduction of LCMV-specific CD8 T cells, increased virus loads and death. Virus-specific CD8 T cell exhaustion during persistent LCMV infection is followed by an increase of cross-presenting $Xcr1^{+}$DC in spleen that maintain a low level of cytotoxic effector cells and control virus loads to non-pathogenic levels. Immunotherapeutic strategies to boost $Xcr1^{+}$DC-dependent T cell responses may present a mean to better control virus loads in persistent virus infections.

Date:	**May 11, 2017**
Place:	**Room C1/028**
Time:	**12:00**