Publications de l’équipe
Régulation spatio temporelle de la présentation des antigènes et migration cellulaire

Année de publication : 2017

Hélène D Moreau, Philippe Bousso, Ana-Maria Lennon-Duménil (2017 Mar 4)
**Microchannels for the Study of T Cell Immunological Synapses and Kinapses.**

**Résumé**

T Cells can form very stable (synapses) or very transient and migratory (kinapses) contacts with antigen-presenting cells. Here, we describe how microchannels can be used to conveniently study the distinct dynamics of T cells during antigen recognition. Microchannels provide a controlled confined environment that promotes T cell migration and recapitulates kinapse and synapse behaviors when coated with appropriate pMHC molecules. We also depict the advantages of this in vitro approach for addressing mechanistic issues and for analysis.

Année de publication : 2016

**The Heterogeneity of Ly6C(hi) Monocytes Controls Their Differentiation into iNOS(+) Macrophages or Monocyte-Derived Dendritic Cells.**
*Immunity* : 1205-1218 : DOI: 10.1016/j.immuni.2016.11.007

**Résumé**

Inflammation triggers the differentiation of Ly6C(hi) monocytes into microbicidal macrophages or monocyte-derived dendritic cells (moDCs). Yet, it is unclear whether environmental inflammatory cues control the polarization of monocytes toward each of these fates or whether specialized monocyte progenitor subsets exist before inflammation. Here, we have shown that naive monocytes are phenotypically heterogeneous and contain an NR4A1- and Flt3L-independent, CCR2-dependent, Flt3 (+)CD11c (-)MHCII (+)PU.1 (hi) subset. This subset acted as a precursor for FcγRIIIL (hi)PD-L2 (hi)CD209a (hi), GM-CSF-dependent moDCs but was distal from the DC lineage, as shown by fate-mapping experiments using Zbtb46. By contrast, Flt3 (-)CD11c (-)MHCII (lo)PU.1 (lo) monocytes differentiated into FcγRIIIL (hi)PD-L2 (lo)CD209a (lo)iNOS (hi) macrophages upon microbial stimulation. Importantly, Sfp1 haploinsufficiency genetically distinguished the precursor activities of monocytes toward moDCs or microbicidal macrophages. Indeed, Sfp1 (+/-) mice had reduced Flt3 (+)CD11c (-)MHCII (hi) monocytes and GM-CSF-dependent FcγRIIIL (hi)PD-L2 (hi)CD209a (hi) moDCs but generated iNOS (hi) macrophages more efficiently. Therefore, intercellular disparities of PU.1 expression within naive monocytes segregate progenitor activity for inflammatory iNOS (hi) macrophages or moDCs.
Paolo Pierobon, Ana-Maria Lennon-Duménil (2016 Dec 22)

**To use or not to use the force: How B lymphocytes extract surface-tethered antigens.**

*The Journal of cell biology*: [DOI : jcb.201612043](https://doi.org/jcb.201612043)

**Résumé**

Using an exquisite cell imaging approach based on DNA nanosensors, Spillane and Tolar (2016. J. Cell Biol. https://doi.org/10.1083/jcb.201607064) explore how the physical properties of antigen-presenting cell surfaces affect how B cells internalize surface-tethered antigens. Soft and flexible surfaces promote mechanical force-mediated antigen extraction, whereas stiff surfaces lead to enzyme-mediated antigen release before subsequent internalization.


**ESCRIT III repairs nuclear envelope ruptures during cell migration to limit DNA damage and cell death**

*Science (New York, N.Y.)*: [DOI : 10.1126/science.aad7611](https://doi.org/10.1126/science.aad7611)

**Résumé**

In eukaryotic cells, the nuclear envelope separates the genomic DNA from the cytoplasmic space and regulates protein trafficking between the two compartments. This barrier is only transiently dissolved during mitosis. Here we found that it also opened at high frequency in migrating mammalian cells during interphase, allowing nuclear proteins to leak out and cytoplasmic proteins to leak in. This transient opening was caused by nuclear deformation and was rapidly repaired in an ESCRT (endosomal sorting complexes required for transport)-dependent manner. DNA double strand breaks coincided with nuclear envelope opening events. As a consequence, survival of cells migrating through confining environments depended on efficient nuclear envelope and DNA repair machineries. Nuclear envelope opening in migrating leukocytes could potentially have important consequences for normal and pathological immune responses.