T cell activation mechanics

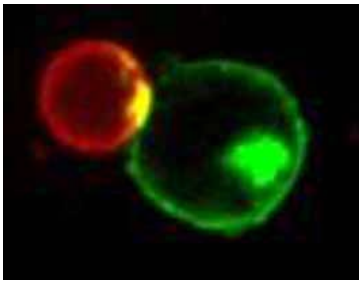
CNRS - UMR168, Institut Curie / INSERM – U932, Institut Curie / LCMD – UMR 7612, ESPCI / Paris - France

Colloidal tools development

We have developed various strategies of surface chemistry and physicochemistry to engineer artificial colloidal systems enabling well-defined engagement of relevant T cell activation receptors in a 2D and collective configuration. Both solid and liquid particles have been developed exhibiting TCR and/or integrin ligands at the cell surface providing different models of artificial antigen presenting cells (APC).

On the left, the two pictures show liquid colloids under the form of a biocompatible emulsion grafted with specific complementary receptors and ligands, one of these is fluorescently labelled enabling to observe molecular concentration in the interdroplet specific contact. The picture on the right shows micro-patterned systems resulting from different colloids assembling. Colloids represented here have a diameter of about 5 µm.

T cell interaction and activation



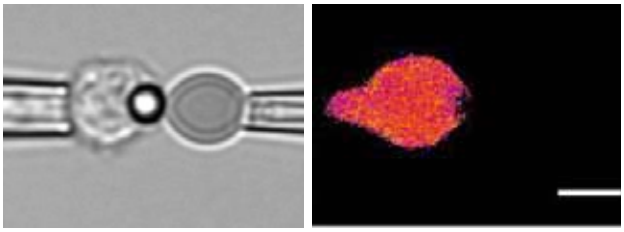
Specific contact between a Jurkat T cell expressing a ζCD3-GFP-labeled receptor (green) and an emulsion droplet which exhibits TCR-CD3 ligands (red) on its fluid surface.

See also : Carpentier et al., 2009, PLoS ONE; Henry, N., and Hivroz, C., 2009, *HFSP* Journal; Fattaccioli et al., 2009, *Soft Matter*; Husson et al., 2011, *PLoS ONE*.

We have explored into details the interactions of the artificial model systems with the T cells using the Jurkat cell line. The microscope image just above shows the specific and dynamical molecular contact formed between a droplet grafted with specific ligands and a T cell. We have found that the formation of a stable contact between the artificial APC and the T cell was a key limiting step that could be achieved with a small number of activating ligands supplemented with adhesion molecules.

T cell mechanical responses

To examine the mechanical cues involved in T cell activation we have implemented a biomembrane force probe (BFP) setup and combined the use of well-defined colloids as artificial antigen presenting cells with real time monitoring of Ca^{2+} intracellular waves, which reported T cell activation triggering. We have then been able to show that upon bi-dimensional engagement of its surface receptors, the T cell developed a timed sequence of pushing and pulling forces against its target. Tuning the BFP mechanical properties, we could show that the loading rate during the pulling phase increased with the target stiffness. This indicated that a mechanosensing mechanism is implemented in the early steps of the T cell activation. The challenge is now to analyze in depth the molecular levers of such a process.



A BFP experiment is shown here with a T cell held in the left pipette and the artificial APC held in the right one coupled to a red blood cell which serves as a force sensor. Intracellular Ca^{2+} is monitored in fluorescence (left image) to attest T cell activation. Bar is 5 µm.

CONTACT :
Nelly.henry@curie.fr
Claire.hivroz@curie.fr
Jerome.bibette@espci.fr