MECHANICS AND MECHANOTRANSDUCTION OF EFFEROCYTOSIS

LABORATORY : Institut Lumière Matière

TEAM(S) : BIOPHYSIQUE

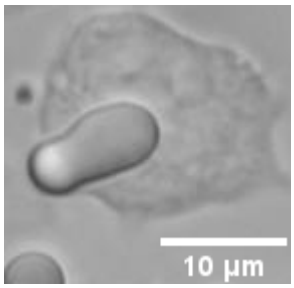
CONTACT(S) : MONTEL Lorraine

CONTACT(S) DETAILS: lorraine.montel[at]univ-lyon1.fr / Tel. 0472431218 Tel. 0472446201

KEYWORD(S) : Phagocytosis / cell mechanics / emulsions

SCIENTIFIC CONTEXT :

During cell death, immune cells internalize and degrade the dying cells to protect the surrounding tissue from the toxicity of the corpses. This process, called efferocytosis, is essential for wound healing and inflammation resolution. Deficient efferocytosis has been linked to inflammatory and auto-immune disease such as Lupus and atherosclerosis[1].
During efferocytosis, the engulfing cell (phagocyte) identifies a dying cell through the lipids it presents on its surface, and internalizes it bit by bit in small portions. The phagocyte applies forces on the dying cell to nibble at it, and deforms itself to engulf the bites. Yet, the mechanics of this process are not known[2], as it necessitates the use of soft and divisible objects, very different from the solid beads usually used to study other forms of internalization.



Live microscopy image of a macrophage internalizing a functionalized droplet.

During ANR project Dropdead, we aim to create biomimetic oil droplets, recapitulating the physical and chemical properties of dying cells: surface lipids, deformability, divisibility[3], [4]. The first step will be to characterize the mechanical properties of the dying cells we mean to mimick. The tunable droplets will be used to understand the role of mechanics and mechanotransduction during efferocytosis. Through observation of the cell-droplet interaction before, during and after internalization for droplets with different mechanical properties, we will evaluate the role of mechanotransduction during efferocytosis, and identify the actors of the process.

MISSIONS :

As part of the project, the PhD student will:

- Build a magnetic tweezers set-up to measure dying cell rheology

- Fabricate micro-emulsion droplets with different surface tension and viscosity and characterize them

- Functionnalize emulsion with different ligands recognized by macrophage receptors.

- Observe the internalization of functionalized droplets in microscopy and measure the influence of physical parameters

- Identify the relevant molecular actors of the process (cytoskeleton, signaling proteins) that participate in mechanotransduction during efferocytosis

- Participate in the identification of the molecular signaling pathways leading to changes in genetic expression and in inflammatory profile of the macrophages.

OUTLOOKS :

An interdisciplinary project between physics, chemistry and cell biology.

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