**SEMINAR – INVITED SPEAKER**

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## Nanoscale Ligand Organisation and Substrate Mechanics as Design Parameters for Immune Cell Activation

Cytotoxic lymphocytes — natural killer (NK) and T cells — read the physical structure of the surfaces they engage, not only its chemical identity. Using colloidal lithography and orthogonal, multifunctional surface chemistries, we fabricate substrates that independently control the nanoscale spacing of activating ligands, their clustering, and substrate topography, at resolutions of 20–500 nm. Anchoring ligands to nanowires and nanoparticle arrays rather than continuous films, we showed that NK and T cell activation depends critically on the spatial organisation of ligands, not merely their surface density: minimal receptor clustering at defined nanoscale distances is sufficient to trigger activation, while identical ligand densities distributed randomly are not (Advanced Materials 2019; Science Advances 2021; Nano Letters 2025). Extending this platform to CAR T cells, combining microtopography with substrate elasticity markedly improved activation and expansion efficiency (Advanced Materials 2025). Building on this platform, I establishing a collaboration with Marie-Christine Durrieu of the CBMN to decompose substrate viscoelasticity itself, separating loss tangent from characteristic relaxation time, using the PEG-DA hydrogel and dendrigraft chemistries developed by Marie-Christine Durrieu's team. This collaboration will establish how nanoscale ligand organisation, topography and viscoelastic kinetics jointly govern T-cell and NK-cell fate for CAR T/NK manufacturing, and extend the same nanopatterning platform to a parallel axis already underway within CBMN: human mesenchymal stem cell osteogenic commitment.

**Host:** Marie-Christine Durrieu, marie-christine.durrieu@inserm.fr

**September 17, 2026 | 1:15 PM**

**IECB Amphitheatre**