PhD Opportunity in Single-Molecule Insights into CAR-T Cell Synapse Dynamics

Primary Supervisor: Dr. Sabrina Simoncelli (LCN and Chemistry Department, UCL)
Secondary Supervisor: Dr. Alice Giustacchini (Infection, Immunity & Inflammation Dept, UCL)
Research Areas: Biophysics, Immunology, Optics
Start Date: September 2025, at the beginning of the 2025-2026 academic year.

Why is this research important? Chimeric Antigen Receptor (CAR) T-cell therapy has revolutionized cancer treatment, particularly for hematologic malignancies such as leukemia and lymphoma. However, patient responses remain highly variable, and many experience relapse. Understanding the molecular mechanisms that govern CAR-T cell activation, membrane trafficking, and spatial organization is critical to improving therapy efficacy.

What you will be doing? This PhD project aims to uncover the fundamental principles governing CAR activation and signaling dynamics at the immunological synapse. The study will focus on how antigen density, receptor-ligand binding affinity, and bispecific CAR interactions influence CAR-T cell activation and function. Key objectives include:

- Investigating the clustering dynamics of CARs and actin remodeling upon activation.
- Assessing the impact of ligand density and binding affinity on CAR-T cell synapse.
- Determining if dual CAR-T cells work synergistically or independently to enhance signal transduction and cytotoxic function.

Techniques and methodologies:

- **Whole-cell single-molecule tracking** to visualize CARs movement and clustering with single-protein precision over extended timescales.
- **Deep-learning-based trajectory analysis** to infer diffusion models and investigate CAR-T cell behavior in the immunological synapse.

Who are we looking for? We seek a highly motivated scientist with an MSc in Chemistry, Physics, Life Sciences, or a related discipline. Ideal candidates should have experience in interdisciplinary research and a collaborative mindset. While training will be provided, a strong interest in single-molecule fluorescence microscopy and immunological research is essential. This studentship offers a unique opportunity to develop expertise in advanced optics and immunology.

Funding and Eligibility: This four-year **PhD studentship** co-funded by the Royal Society and the LCN will cover UK Home Tuition Fees, a stipend of no less than standard UKRI rate per year (e.g., £21,237 for the 2024-2025 academic year), and allowance to support **training and conference attendance**. Due to funding restrictions, **applicants not eligible for UK home fee status will only be considered in exceptional circumstances.**

How to Apply: Applications will close at 5 pm on 5th March 2025. For informal enquiries, please email Dr. Sabrina Simoncelli at **s.simoncelli@ucl.ac.uk**. For applications, use the portal **https://www.london-nano.com/form/lcn-phd.** You will be asked for:

- A CV;
- A transcript of your undergraduate studies;
- The names of two referees familiar with your academic work.

For shortlisted candidates, the selection process will include an academic interview at UCL.