

PhD Opportunity in Single-Molecule Insights into BiTE-Mediated T Cell Activation

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Second Supervisor: Prof. Vijay Chudasama (Chemistry Department, UCL)

Research Areas: Biophysics, Chemistry, Immunology, Optics

Start Date: September 2025, at the beginning of the 2025-2026 academic year.

Why is this research important? Bispecific T cell engagers (BiTEs) represent a groundbreaking class of immunotherapies that harness the power of the immune system to target and destroy cancer cells. By linking T cells to cancer cells, BiTEs facilitate precise, targeted killing of malignant cells, offering an exciting alternative to traditional cancer treatments. Despite their promise, BiTEs currently face several challenges, such as suboptimal therapeutic efficacy and the risk of off-target effects that could harm healthy tissues.

What you will be doing? This PhD project focuses on optimizing the design and spatial arrangement of BiTEs to improve their therapeutic performance and minimize side effects. The study will combine state-of-the-art chemistry with advanced super-resolution fluorescence imaging techniques to dissect BiTE interactions with T cells and cancer cells, driving the development of next-generation cancer immunotherapies. Key objectives include:

- Synthesizing and characterizing different BiTE constructs
- Investigating the impact of BiTE structural variations on T cell activation and cytotoxicity.
- Assessing BiTE-induced T cell signaling and immune synapse formation through advanced 2D and 3D imaging techniques.

Techniques and methodologies:

- **Organic synthesis and bioconjugation** to construct BiTEs
- **Super-resolution imaging (DNA-PAINT)** to quantify the distribution of proteins in the presence of BiTEs.
- **Lattice light sheet microscopy** for whole-cell 3D imaging to study cell-cell interactions in real-time.

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, organic chemistry and a collaborative mindset. While training will be provided, a strong interest in single-molecule fluorescence microscopy, bioconjugation and immunological research is essential. This studentship offers a unique opportunity to develop expertise in advanced optics and bioconjugation chemistry.

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.