PHYSICS OF CELLULAR INTERACTIONS

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We study how immune cells communicate with each other, both in natural and immunotherapy contexts: how do immune cells use molecular signaling pathways to process and respond to information, both precisely and unambiguously? Our approach is based on microscopy that pushes technical boundaries and on synthetic biology. Combining signaling pathway reconstitution with single-molecule biophysics, our work provides a unique mechanistic and quantitative perspective on cell signaling. We work closely with theoreticians to develop predictive models and with immunologists to apply physical insights to problems in immunology.

Highlights

- Signaling in synthetic cells. We developed methods for the in vitro reconstitution of signaling molecules in lipid vesicles, the groundwork for our goal to develop communicating synthetic cells [1-3].
- Engineering signaling pathways. We pioneered the application of a hybrid in vitro-in vivo approach, interfacing cell surface models with immune cells, to understand chimeric antigen receptors (CARs), funded by a Vidi grant and in collaboration with Majzner (Stanford, US) and Fernandes (U Oxford, UK).
- Technique development. My group developed a new approach (DNA-PAINT SPT) that allows us to follow single molecules for minutes rather than seconds [4,5].

Plans

The central aim will remain to understand how cell function – information exchange between cells – emerges from its molecular constituents. We will continue to push the boundaries of in vitro reconstitution to build communicating synthetic cells, and further expand our research on signaling pathways relevant to cancer therapies. Even once molecules are known to play a pivotal role in cell function, many open questions remain at the molecular level – a gap we can often address with our biophysics approach. Using model membrane systems and single-molecule microscopy, we ultimately aim to generate findings of therapeutic value.

Key research items

1. KA Ganzinger and P. Schwille, *More from l ess–bottom-up reconstitution of cell biology,* Cell Sci., 132, jcs227488 (2019)
2. L. Van de Cauter et al, *Optimized cDICE for efficient reconstitution of biological systems in giant unilamellar vesicles*, ACS Synth. Biol., 10, 1690 (2021)
3. L. Van de Cauter and K.A. Ganzinger, *Design plan, parts list and protocols for our cDICE setup (lipid vesicles fabrication),* https://github.com/Ganzinger-Lab/cDICE-plans
4. C. Niederauer, et al., *The K2: Open-source simultaneous triple-color TIRF microscope for live-cell and single-molecule imaging,* Non-research article in HardwareX, 2023 (https://doi.org/10.1016/j.ohx.2023.e00404). See also https://ganzingerlab.github.io/K2TIRF/K2TIRF/index.html
5. C. Niederauer et al., *Dual-color DNA-PAINT single-particle tracking enables extended studies of membrane protein interactions,* Nature Commun. 19;14(1):4345 (2023)

Longer visualization of single proteins (colored trajectories) in cell membranes (cell outline shown with dotted line) with DNA-PAINT-SPT technique. Scale bars 5 um.