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seminar

Wednesday, 15th February, 11.30am

Seminar Room

Host: Prof. Aitziber L. Cortajarena

Reconstitution biology – what we gain by rebuilding cellular processes from bottom-up

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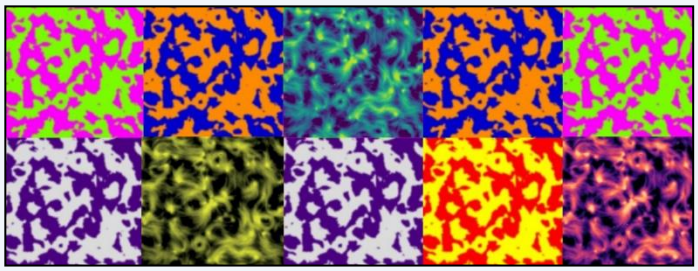
Cellular self-organization is a complex but fascinating process. In this seminar, I offer you become bioengineers that want to rebuild a living cell, or a given cellular function, from the bottom-up. In particular, I will guide you through the reconstitution of the dynamic processes that are difficult to investigate directly in live cells, such as: i. bacterial cytokinesis, ii. bacterial cell wall synthesis, and iii. recognition of microbial glycans by immune cells. My goal is not only to demonstrate the power of the reconstitution approach for fundamental cell biology but also to highlight how it can be used as a translational platform.



Bacterial cytokinesis relies on two mechanically active assemblies dynamically coupled across the cellular membrane: FtsZ cytoskeleton and cell wall, or peptidoglycan. The breakthrough in vivo studies revealed that treadmilling FtsZ filaments could actively move transmembrane cell wall synthases during cell division. However, the underlying molecular mechanisms behind such directional transport were difficult to resolve in a tiny bacterial cell. I reconstituted the intracellular part of the bacterial division machinery from purified components on biomimetic lipid membranes. Quantitative real-time microscopy confirmed that four membrane proteins could co-migrate with the treadmilling FtsZ cytoskeleton forming chiral rotating rings. In this manner, treadmilling FtsZ filaments create a moving zone of signaling activity at the division site to transmit the spatial information on when and where to activate cell division [1,2].

To investigate the mechanics of cell wall synthesis, I reconstituted a bifunctional transmembrane peptidoglycan synthase PBP1b in a polymer-supported lipid membrane. The assay allowed to track of the lateral diffusion of a single enzyme and monitor its peptidoglycan polymerization activity in real time. Since peptidoglycan is an essential component of the bacterial cell envelope and a direct target of the widely used β-lactams and glycopeptides, our assay can be further developed for high throughput screening of novel antibiotics[3].

Glycans of microbial cell walls not just act as mechanical exoskeletons but represent an important interface in host-pathogen communication. Still, we lack a detailed biophysical investigation of the mechanisms of their recognition by immune cells. Defined reconstitution of beta-glucans enabled us to investigate their recognition mechanism by C-type lectin receptors. The information gained in this project inspires the design of biomimetic ligands for controlled immune response activation.

1. Baranova N, Radler P, Hernández-Rocamora VM, et al. Nat Microbiol. 2020;5(3):407-417. doi:10.1038/s41564-019-0657-5
2. Radler P*, Baranova N*, Caldas P, et al. Nat Commun 2022 131. 2022;13(1):1-15. doi:10.1038/s41467-022-30301-y
3. Hernández-Rocamora VM*, Baranova N*, Peters K, Breukink E, Loose M, Vollmer W. Elife. 2021;10:1-79. doi:10.7554/ELIFE.61525