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seminar

Wednesday, 2nd February, 9.30am, Online

Host: Prof. Aitziber L. Cortajarena

Mapping and using the extracellular matrix to reveal its role as a cell regulator

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Organ function depends on an intact three-dimensional architecture. Structural stability is ensured by the extracellular matrix (ECM), a biomaterial made of proteins and glycans that shapes all tissues while regulating cell behavior. During disease, remodeled ECM compels cells to behave abnormally, disrupting homeostasis and promoting disease progression, oftentimes leading to organ failure and patient death. Understanding ECM structure during health and disease is a fundamental biological challenge. Here, we demonstrate methods to map ECM architecture and then use it as a cell culture substrate to reveal its role as a regulator. First, we generate 3D maps of the ECM during health and disease, revealing major structural abnormalities previously unseen by existing methodologies. Using Machine Learning (ML), we identify disease-specific patterns of structural remodeling, including the altered spatial relationship between ECM proteins. Second, we design an ECM-based perfusion bioreactor to model metastatic cancer, showing that lung ECM coerces cells into mimicking *in vivo* tumor signaling, while allowing them to refashion normal ECM into a cancer-like niche. In summary, our ECM mapping and ML analysis can guide the design of future diagnostic tools and explain the detrimental effects of disease. Similarly, we reveal new roles of ECM in metastatic progression, using a novel, ECM-based disease model.

References:

1. Mayorca-Guiliani et al. ISDoT: in situ decellularization of tissues for high-resolution imaging and proteomic analysis of native extracellular matrix. **Nature Medicine**. 2017; 23:890-898. doi: 10.1038/nm.4352.
2. Mayorca-Guiliani AE et al. Decellularization and antibody staining of mouse tissues to map native extracellular matrix structures in 3D. **Nature Protocols.** 2019; 14:3395-3425. doi: 10.1038/s41596-019-0225-8.
3. Rafaeva M et al. Modeling Metastatic Colonization in a Decellularized Organ scaffold-based Perfusion Bioreactor. **Advanced Healthcare Materials**. 2021 3:e2100684. doi: 10.1002/adhm.202100684.

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