Talk

Chemical neomorphs: Reprogramming biological circuits with small molecules

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Host: Gaia Novarino

Chemical modulation of protein function enables us to understand biological mechanisms and represents the foundation for most medicines. For decades, efforts in small-molecule discovery focused on ligands that block the biochemical activity of their target proteins. However only around 20% of all human proteins feature biochemically active ligand binding sites that can be addressed with small-molecule inhibitors. The resulting shortage in chemical tools hampered our ability to functionally interrogate many biological processes and precipitated in a lack of treatment options for a plethora of diseases.To close this gap and to chemically access the entirety of the human proteome, our group is thus exploring the new paradigm of “chemical neomorphs”. Chemical neomorphs are small molecules that can reprogram biological circuits beyond evolutionary constraints by endowing target proteins with new functions. Mechanistically, they function by installing novel protein-protein interactions, don’t require additional genetic manipulations and thus also harbor tremendous translational and therapeutic potential.In my seminar, I will discuss our research on chemical neomorphs that can reprogram E3 ubiquitin ligases to induce the degradation of a variety of disease-causing target proteins that are traditionally considered to be “undruggable”. In particular, I will share how we connect functional genomics and other multi-omics approaches with synthetic chemistry to identify and mechanistically characterize such small-molecule degraders. Moreover, I will discuss how the concept of chemical neomorphs can be expanded beyond the scope of chemically induced targeted protein degradation, for instance by developing pharmacologic strategies to rewire transcriptional circuits.

Tuesday, October 10, 2023 10:00am - 11:00am
Mondi 2, Central Building

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