THE PROGRAM FOR EXPERIMENTAL & THEORETICAL MODELING (PETM)

Miri Adler, PhD

The Broad Institute of MIT and Harvard, Cambridge, MA, USA

Principles of Cell Circuits for Tissue Repair and Fibrosis

Tissue processes involve integration of multiple signals as well as communication between several cell types by means of diverse secreted factors and cell contact signals. In order to help make sense of this complexity, theoretical models coupled with experiments can play an important role. In my research, I developed a mathematical modeling approach to uncover principles of the social behavior of cells during tissue repair and fibrosis. Tissue repair is a protective response after injury, but repetitive or prolonged injury can lead to fibrosis, a pathological state of excessive scarring. To pinpoint the dynamic mechanisms underlying fibrosis, it is important to understand the principles of the cell circuits that carry out tissue repair. Using a mathematical framework for the myofibroblast-macrophage circuit in wound-healing, we find that fibrosis results from multi-stability between three outcomes, which we term 'hot fibrosis' characterized by many macrophages, 'cold fibrosis' lacking macrophages, and normal wound-healing. This framework clarifies several unexplained phenomena including the paradoxical effect of macrophage depletion, the limited time-window in which removing inflammation leads to healing, and why scar maturation takes months. We define key parameters that control the transition from healing to fibrosis, which may serve as potential targets for therapeutic reduction of fibrosis.

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3:00 p.m. (Central Time)

Zoom: https://luc.zoom.us/j/87036830337

PETM CO-DIRECTORS: HAREL DAHARI & SUSAN L. UPRICHARD

LOYOLA MEDICINE
Loyola University Chicago Stritch School of Medicine