

# The Biological and Biomedical Joint Seminar Series

(Hosted by the departments of Molecular & Cellular Biology, Chemistry & Biochemistry, Cellular & Molecular Medicine, and Plant Sciences)

## *“A synthetic circuit architecture for mutant stem cell suppression”*

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Chemistry 218 @ 11AM

Hosted By: Ingmar Riedel-Kruse (MCB)



Stem-cell differentiation is a crucial multicellular trait. However, it is inherently susceptible to mutant stem cells that fail to differentiate. These mutants can outcompete normal stem cells by excessive self-renewal, driving certain cancers. It remains unclear what mechanisms can suppress such mutations. I will talk about my recent work in demonstrating a solution to this problem by engineering a synthetic differentiation circuit in *Escherichia coli* that selects against these mutants. The circuit provides tunable production of stem, progenitor, and differentiated cells, and resists mutations by coupling differentiation to production of an essential enzyme — disadvantaging non-differentiating mutants. The circuit selected for positive differentiation rate and maintained this rate in long-term evolution. Surprisingly, the rate remained constant across vast changes in growth conditions. We found that transit-amplifying cells underlie this environmental robustness, suggesting similar roles for such cells in mammals. Our results provide insight into stability of natural differentiation and demonstrate a powerful method for engineering consistent cell-type ratios in multicellular consortia.

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