

Why Not to Look Under the Lamppost?

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The long-term goal of the Systems Biology Group is to understand how transcription regulators and epigenetic modifications regulate gene expression programs controlling key cell fate decisions during cellular development, differentiation, and pathogenesis. To this end, we use integrative interdisciplinary approaches—merging systems biology, functional genomics, and biochemistry—to reconstruct and characterize developmentally- and environmentally-responsive gene networks in embryonic stem (ESCs). Research within the group is largely data-driven, through computational analyses of published and in-house-generated high-throughput genomic and proteomic datasets, with the goal of generating testable hypotheses. The laboratory component provides the means to not only test some of the hypotheses that come out of computational analyses but also to perform traditional biochemical experiments to gain mechanistic insights. Over the years, we have not only shed light on many genes and pathways with previously unknown roles in ESC biology but also help connect the dots on gene networks controlling the pluripotent state. Our ongoing studies on signaling networks will build on these findings and contribute to the comprehensive understanding of how signaling cascades instruct epigenetic and/or transcriptional programs controlling cell fate decisions. Collectively, our studies will provide a foundation for defining the mechanism and scope of developmentally- and environmentally-responsive gene networks for a better understanding of how ESCs can be used as effective model systems for regenerative medicine, disease modeling, and toxicity/drug testing.