Description of a light inducible system to study the ERK signaling network topology at the single cell level

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Receptor tyrosine kinases enable to convert extracellular growth factor INPUTs into specific cellular OUTPUTs through the activation of dynamic signaling networks. While we have a good idea about the network components, we still miss crucial information about how these components are wired in a coherent signaling network. Due to the complexity of the system, we need to combine live ERK activity measurements with network perturbations to understand how the different molecular players involved in the ERK network affect its response. To do this, we have couple the FGF/MAPK pathway to an optogenetic FGF receptor and an ERK activity reporter. This allows us to activate the pathway with light INPUTs in a highly automated and reproducible way and to measure dynamic ERK signaling OUTPUTs in hundreds of single cells with high temporal resolution. Using this system, we will study the effect of drug and siRNA perturbations on ERK activity to identify the different molecular players involved in the regulation of the MAPK network.

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