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Controlling intracellular signal network dynamics with light

Optogenetic investigations by the Dehmelt group reveal mechanism for regulation of cell contraction dynamics

DECEMBER 02, 2020

Individual cells generate dynamic contractions, which are critical for cell shape changes and directed cell migration. This plays a central role in numerous processes, such as embryonic development or tumor progression. How cells regulate these contractions locally and spatially is therefore of great interest for biomedical research. In a current publication in the prestigious journal *Cell Reports*, an international research team led by Leif Dehmelt combined experimental and theoretical approaches to gain a better understanding of this process.

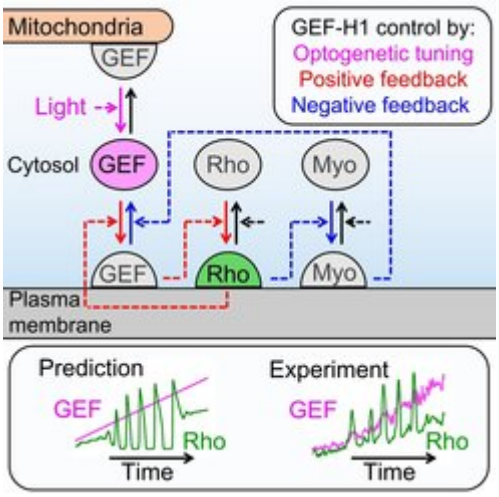
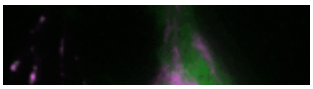
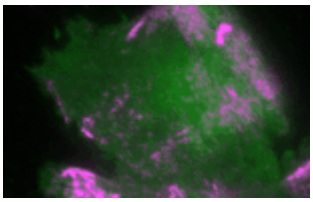


Figure 1: Top panels: Causal connections between GEF-H1 (GEF), Rho, and Myosin (Myo) in the cell contraction signal network. The effective, cytosolic concentration of GEF-H1 is tuned in living cells via light-controlled release from mitochondria-bound anchors. Bottom panels: Prediction and experimental confirmation of altered Rho activity dynamics (green lines) in response to gradually increasing GEF-H1 concentrations (magenta lines).





Video 1: Regular pulses of the cell contraction regulator Rho (green) and time-delayed pulses of the motor protein myosin (magenta), which generates contractile forces in cells.

In the new study, the Dehmelt group uses microscopy-based, light-switchable perturbations to specifically and acutely manipulate a signal network that controls cell contractions in individual, living cells. At the same time, the dynamic response of this signal network was measured to investigate the mechanism, how these perturbations are processed by cells. Based on these results, a theoretical model was derived which quantitatively describes the components and interactions of this signal network. A central aspect of this system are positive and negative feedback loops, which generate highly dynamic pulses of the cell contraction regulator Rho and the molecular motor myosin (Video 1). The theoretical model of the Dehmelt group made it possible to predict how the dynamics of this signal network would react to specific perturbations of these feedback loops. These predictions were confirmed by controlling a key signal network component with light in individual, living cells. Figure 1 illustrates causal connections in this signal network and how light was used to manipulate the concentration of one key component, the Rho activator GEF-H1, via “optogenetic tuning”. With this technique it was discovered that this signal network generates particularly intense pulses of the cell contraction regulator Rho at intermediate concentrations of GEF-H1. In contrast, the sensitivity of the signal network to process physiologically relevant mechanical and biochemical signals is maximal at low concentrations of this network component. These new theoretical and experimental findings form the basis for a better understanding of more complex processes in embryonic development and tumor progression.

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Original Publication

Kamps, D, Koch J, Juma VO, Campillo-Funollet E, Graessl M, Banerjee S, Mazel T, Chen X, Wu YW, Portet S, Madzvamuse A, Nalbant P, Dehmelt L. (2020). **Optogenetic Tuning Reveals Rho Amplification-Dependent Dynamics of a Cell Contraction Signal Network.** *Cell Reports*
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