The spatio-temporal regulation of Src activity by optogenetics drives cell adhesion behavior

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Both in health and disease cells sense and integrate a multitude of instructional signals from their microenvironment through a diverse set of transmembrane receptors, such as integrins, growth factor receptors, and adhesion junctions. This information is then collected at the intracellular signaling nodes to later disperse down signaling cascades to alter cell fate. However, how one signaling node can understand multiple stimuli and diffuse the appropriate information remains poorly understood. Further, recent data suggest that signal integration in space and time is critical for proper signal transduction[1] [2]. In that respect, the proto-oncogene and a pleiotropic tyrosine kinase, c-Src, is one such node known to drive many cellular processes, such as migration, invasion, degradation, and cell division.

Here, we developed an optogenetic tool to investigate whether the spatiotemporal control of Src activity can be used to directly modify its downstream signaling. To achieve this, we designed a cytosolic form of Src fused to the light sensitive Cry2. Cry2 dual characteristic of homo-oligmerisation or hetero-dimerisation with a membrane anchored CIBN via blue light stimulation enabled us to position Src with micron-scale precision in space and minute-scale resolution in time. We characterized two spatio-temporal patterns of Src inside adhesion by its molecular mobility and aggregation state. We observed that the specific molecular flow of Src toward an adhesion sites is essential for the transmission of information. Such strategy allows, for the first time, to distinctly and precisely control differential cellular adhesive and cell-division behaviors in an epithelial cell type.

The development of these optogenetic tool shows great promise for the purpose of integrating space and time dimensions in cellular signaling, perturbing and manipulating cellular signaling networks to drive specific cellular behaviors.

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