Molecular Switches for Regulation of Growth Factor Activity

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The possibility to trap small signaling molecules in cages and to subsequently uncage them in a controlled manner at the site of interest allows for the spatiotemporal manipulation of signaling processes. Caging has successfully been applied to a vast array of small signaling molecules, leading to a revolutionized understanding of the biological processes controlled by these molecules. As many cellular processes rely on proteins rather than on small signaling molecules, the ability to cage proteins in a similar manner is highly desirable. Techniques potentially applicable to the caging of proteins have been reported; however, these are complicated and must be tailored for each specific protein of interest. A method enabling the caging of arbitrary proteins is thus much needed. Here, we demonstrate a general procedure utilizing a pharmacological-based cage to trap one or several proteins of choice equipped with an immunoglobulin (IgG) Fc-tag. In addition, to further address the high demand of time-resolved control of protein-governed processes, a “protein switch” enabling the protein activity to be switched on and off by the addition of small molecules was developed. The potential of the caging technique and the protein switch to manipulate growth factor-controlled signaling pathways was demonstrated by stimulating time-resolved migration of mesenchymal progenitor cell and human umbilical vein endothelial cells, respectively. The concepts presented here are believed to be valuable for fundamental and applied research ranging from elucidating signaling pathways to the targeted differentiation of cells in tissue engineering.