

P029 Inducible protein dimerisation for signal transduction
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Most cellular processes are triggered by a dynamic interaction of signaling proteins. To monitor and control these interactions in a spatial and temporal way, chemical inducers of protein dimerisation have been invented. These so called “dimerizers” are cell-permeable, organic molecules with two different motifs that recognize with high affinity a specific protein domain. The systems described are based on Rapamycin which induces a tight binding of FKBP12 to mammalian Target of Rapamycin (mTOR). Although elegant and fast, this method cannot be used to study proteins that are involved in growth and metabolism, because of its inhibitory effect on endogenous mTOR. Derivates of Rapamycin (Rapalogues) that have been designed to overcome this problem are still inhibiting mTOR.

Addressing this problem, we designed a new dimerisation system which is based on novel protein tags that have no endogenous counterparts. We obtained additional control of the dimerisation in time and space by introducing a photo-activatable protective group. With this system we were able to dimerise two different proteins, either recombinant or in cells, in cytoplasmic compartments and at the plasma membrane. Our photo-activatable system has the premises for a new tool to tamper different signaling events with the power of the Rapamycin system but without interfering with endogenous proteins.