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In Vitro and In Vivo Supramolecular Biomembrane Engineering and Membrane Fusion Using a Lipidated Coiled-coil Motif

Alexander Kros
Dept. Supramolecular & Biomaterials Chemistry, Leiden Institute of Chemistry
Leiden University, PO Box 9502, 2300RA
Leiden the Netherlands
a.kros@chem.leidenuniv.nl

Extended Abstract

For many years, nature has been a source of inspiration for supramolecular chemistry. Here, scientists design relatively simple molecules which assemble into functional materials with well-defined properties, typically following the bottom up approach. Recent progress has resulted in molecular systems which are responsive to multiple stimuli and are therefore highly controlled, emulating nature ever more closely. A relatively new branch of development is the application of supramolecular constructs in an in vitro and in vivo environment, to directly study and influence biological processes in live cells.

In this contribution we have designed a simple and generic tool for the efficient formation of coiled coils at the surfaces of cells and zebrafish embryos. A pair of complementary coiled-coil-forming peptides, denoted "E" and "K", were synthesized and conjugated to a cholesterol anchor. The resulting lipidated peptides inserted spontaneously into CHO cell membranes *in vitro* and in the skin of zebrafish embryos *in vivo*. Addition of the acetylated complementary peptide resulted in efficient coiled coil formation at the surface of cells and zebrafish embryos. As the coiled coil unit acts as a molecular velcro, this supramolecular tool enables the modification of biomembranes with a wide range of molecular constructs.

As a case study, the docking of liposomes to cell membranes and zebrafish skin was investigated. Liposomes bearing the complementary peptide efficiently docked at these biological interfaces through coiled coil formation. Importantly, this is the first time that *in vivo* membrane modification has been achieved. We envisage that this tool will aid the study of membrane processes by modulating the chemistry of these bio-interfaces. Furthermore, applications in the area of pharmacology and drug delivery such as high-throughput screening of drugs are expected.