Supramolecular Chemical Biology

Applying synthetic concepts of self-assembly and molecular recognition to biology

Supramolecular chemistry has primarily found its inspiration in biological molecules, such as proteins and lipids, and their interactions. Currently the supramolecular assembly of designed compounds can be controlled to great extent. This provides the opportunity to combine these synthetic supramolecular elements with biomolecules for the study of biological phenomena. Supramolecular elements can for example be ideal platforms for the recognition and modulation of proteins and cells. This lecture will focus on two concepts in this respect.

Synthetic host-guest systems can be applied for the controlled and reversible dimerization of proteins. Host-guest elements can for example be appended to proteins to induce or stabilize weak protein heterodimerization. Other supramolecular host molecules can be used to recognize specific protein elements and applied as supramolecular inducers of protein homodimerization. As an example, caspase homodimerization is a key step in the activation of their enzymatic activity. Control over this protein homodimerization allows investigating the molecular processes underlying the activation mechanism. We have generated a so-called supramolecular inducer of dimerization that can act as an allosteric modulator of caspase-9 dimerization and allows highly efficient and reversible activation of caspase activity.

Self-assembling supramolecular architectures provide attractive scaffold for the organized display of biological ligands. Their dynamic nature allows for simple non-covalent synthesis of multivalent structures and for the introduction of multiple different functionalities. As an example, columnar supramolecular polymers can be decorated with biological ligands such as sugars and peptides for the recognition of cells or for the assembly of proteins along the supramolecular framework.

Luc Brunsveld
Professor of Chemical Biology
Department of Biomedical Engineering
Technische Universiteit Eindhoven