Redesigning protein function via unnatural amino acids: *de novo* organelles & enzyme design

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The molecular structuring of space can be facilitated by the creation of functional enclosed space,[1] e.g. to confine reactions and to build chemical potentials, and the formation of structural skeletons presenting molecular functions, both facilitating interactions, reactions & signaling processes. The combination of the synthetic power of chemical biology with the rational combination of modular elements within the cell in synthetic biology allows us to access complex chemical systems *in vivo* with high precision.

Here we iterate on the use and functionalization of proteins as architectural building blocks (tectons) to realize a new concept to form *de novo* organelles and steps towards their functional programming.[2] The latter is currently realized via the genetically encoded site-specific introduction of bioorthogonal chemical functionalities via unnatural amino acids. They are introduced by expanding the genetic code via the redesign of the translational network. First examples for site-specific *in vivo* functionalization of such *de novo* organelles are demonstrated. In order to justify the complex meaning of the term "organelle" we are currently expanding the functionality of our *de novo* organelles via redesigned enzymes. In the frame of the talk a novel strategy will be presented used to chemically alter enzyme functionalization.[3] In this context we introduce carbohydrate and lipid building blocks allowing to create a modular combinatorial glycolipid library as tool-box also allowing to use these building blocks to site-selectively modify proteins.

The combination of our synthetic chemical tool-box of reactions, reagents, methods and molecules with the design of a protein-based toolbox of biogenic tectons as cellular building blocks allows to introduce new chemical structures, functions and synthetic possibilities within the living cell which did not previously exist in nature.[4]

Literature

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