Chemical Biology Seminar

"Molecular recognition tools for chemistry in living systems"

Abstract: The introduction of unnatural functionality in biological systems coupled with detection using bioorthogonal chemical reactions revolutionized the field of chemical biology by enabling the investigation biological processes in live cells and simple organisms. However the translation to complex organisms has led to less than optimal results with high background noise due to cross reactivity with activated reagents. This work investigates the utilization of non-covalent chemistry and bioorthogonal host-guest pairs to obtain more efficient labeling of living systems. Complexation between a host and guest is diffusion-limited, hence can be efficient in dilute environments. The cucurbit[n]uril scaffold has been utilized to determine the minimum binding affinity required for efficient bioorthogonal complexation and investigate how guest size and charge affects the introduction of guests as unnatural metabolites. Carboranes, a cucurbit[7]uril guest class that can be removed "on demand" from the host cavity, were found compatible with metabolic glycoengineering and were successfully incorporated on the cell surface. The cucurbit[7]uril-carborane system serves as the first example of bioorthogonal complexation and answers fundamental questions required for the further development of bioorthogonal host-guest pairs.

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