Protein Post Translational Modification Analysis Enabled by Supramolecular Receptors

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Protein modifications such as methylation play important roles in regulation of gene transcription, strongly impacting cellular development, and they also respond to different stimulations leading to the development of pathological conditions.[1] Comprehensive characterization of PTMs on proteins is typically carried out by LC-MS/MS. Still, it could be problematic in resolving PTMs causing little change in peptide hydrophobicity or charge. Also high throughput screening of PTM enzyme activity currently requires antibodies which are expensive, difficult to be obtained, and are often lack of specificity for PTM sites and modification levels. Synthetic receptors could provide diverse solutions for analysis of protein PTM, because their structures can be judiciously designed to provide selectivity against various modification situations and they are much cheaper and easier to be obtained than antibodies. They can be used to design sensors for specific recognition of methylated peptides; and can also act as the additives in the matrix of column separation for separation of the unmethylated and methylated peptides. Both directions have been explored by our group. A series of displacement sensors formed by various deep cavitands (see Figure 1)[2] were employed to form a sensor array for detection of methylated peptides in solution and enzyme mix.[3] The array was also applied for monitoring enzyme activity and screening for specific enzyme substrates.[4] In addition, several synthetic receptors including tetrasulfonatocalixarene (CX4), cavitand, and cucurbit[7]uril (CB7) were used to separate histone peptides with or without methylation using capillary electrophoresis (CE). Our work proves the great potential of synthetic receptors in enabling the study of protein methylation.

References:

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