Engineering Biomaterial Properties Using SpyTag-SpyCatcher Chemistry: From Protein Topology to the Network of Spies

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The spontaneous formation of an isopeptide bond between a peptide tag (SpyTag) and its protein partner (SpyCatcher) is a genetically encodable, highly specific and efficient chemistry for protein/peptide conjugation that is compatible with cell environment.[1] We have successfully applied the SpyTag-SpyCatcher chemistry to engineer the biomaterial properties. Strategic placement of the sequences encoding SpyTag and SpyCatcher within protein-coding genes programs the post-translational modification of the expressed proteins *in situ*, and enables whole-protein or domain-selective cyclization of proteins, affording circular proteins and tadpole-like proteins. In vitro topology diversification may also be achieved by reacting purified telechelic proteins containing different number of reactive units (either SpyTag or SpyCatcher), leading to a variety of unconventional protein topologies, such as 3-arm, 4-arm star proteins and H-shaped proteins.[2] Furthermore, by reacting telechelic proteins containing 3 or more reactive units, an all-protein-based hydrogel is formed in minutes, providing a robust platform for the incorporation of bioactive units into the hydrogel for use as artificial extracellular matrix. The hydrogel is thus named "the network of spies". In light of its high fidelity, simplicity, and robustness, the SpyTag-SpyCatcher chemistry offers an invaluable way to do "bio-orthogonal" chemistry in the biological reactivity space and opens up numerous possibilities for engineering biomaterial properties through protein topological variation and network formation.

Keywords： Protein, Topology, Hydrogel, SpyCatcher, SpyTag

References

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