Development of chemical probes for capturing protein arginine kinases

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Protein kinases play a critical role in controlling numerous cellular regulation pathways and signal transduction.[1] Protein arginine phosphorylation, one of the relatively acid-labile N-phosphorylations, has been identified in numerous prokaryotic and eukaryotic proteins.[2] The only known protein Arg kinase is McsB in Gram-positive bacteria, which was characterized in 2009.[3] McsB is a heat-stress responsive kinase and phosphorylates Arg residues in aggregated cytosolic proteins so that phosphoarginine (pArg) acts as a protein degradation tag recognized by the ClpC/ClpP protease system. Recently, bacterial-PROTAC was developed using pArg and ClpC-binding cyclic peptide to induce the degradation of the target protein.[4]

In contrast, no eukaryotic or mycobacterial protein Arg kinase has been identified despite the abundance of pArg sites in those organisms, hindering further studies of Arg phosphorylation. Herein, we report our progress in developing mechanism-based chemical probes to label and capture the elusive Arg kinase.

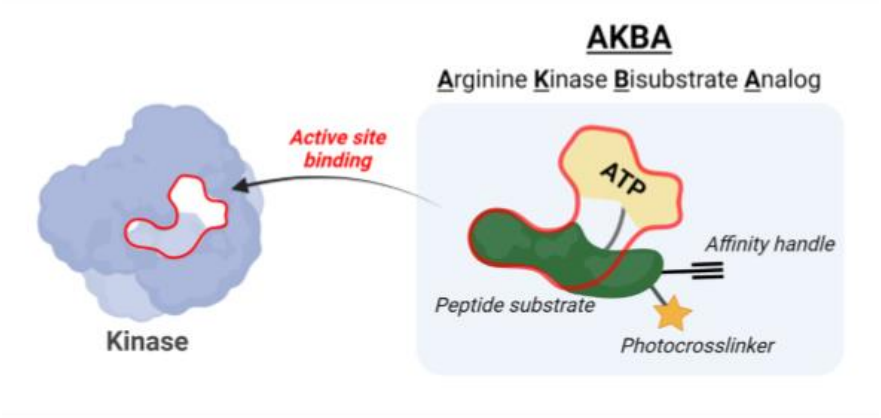

Figure 1. Schematic design of chemical probes for arginine kinases.

References

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