Searching for phosphohistidine readers and acceptors with chemical tools

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Protein phosphorylation is one of the most studied post-translational modifications (PTMs), controlling cell signaling, gene expression, differentiation, and other biological phenomena. In vivo, phosphorylation is regulated through the action of kinases (writers), phosphatases (erasers), and readers or acceptors which recognize the phosphorylated amino acid residues. Due to the importance of protein phosphorylation in human diseases, many of these proteins are drug targets.[1]

Among the phosphorylations, phosphohistidine (pHis) is an underexplored PTM. Unlike the phosphoesters of Ser, Thr, and Tyr, the P-N bond in pHis is much less stable, making it difficult to investigate using transitional methods. With the development of antibodies and proteomics capable of detecting pHis, numerous pHis sites have been discovered in diverse organisms.[2] However, our understanding of the readers and acceptors for these pHis residues is still limited. Since these pHis-recognizing proteins play a crucial role in the biological functions of pHis, identifying novel pHis readers is essential.

Here, we report our progress in discovering the pHis readers and acceptors. Our data suggest novel candidates for pHis readers and acceptors and their potential functions in controlling central metabolism.

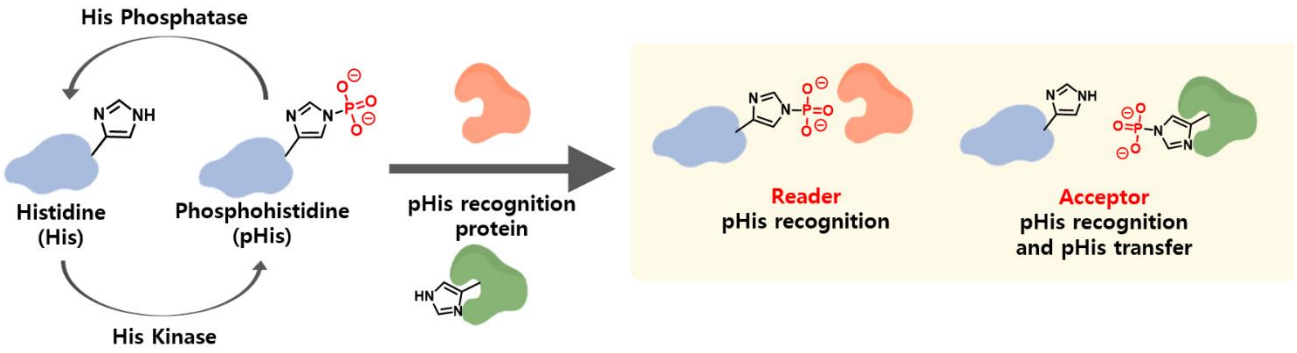

Figure 1. Readers and acceptors of phosphohistidine (pHis).

References

[1] Cohen, P.; Cross, D.; Jänne, P. A. *Nat. Rev. Drug Discov.* **2021**, *20*, 551-569.

[2] Ahn, S.; Jung, H.; Kee, J.-M. *ChemBioChem* **2021**, *22*, 319-325.