Development of multivalent affinity labeling probes for exploration of carbohydrate-binding proteins

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Identification of protein partners of carbohydrate ligands is important for understanding of their roles in diverse biological and pathological processes. However, characterization or modulation of carbohydrate-binding proteins remains a challenge due to their weak binding interaction when presented as monomeric ligands. To address this issue, various types of multivalent probes that mimic carbohydrate clusters on the cell surface and increase their affinity to proteins are synthesized.

Affinity labeling offers a powerful tool to explore cellular targets of bioactive molecules by covalently capturing transient protein-ligand interactions in the complex proteome. For successful target identification, the efficiency and selectivity must be optimized for each step of detection, capture and enrichment. Toward elucidation of carbohydrate-protein interactions, we have developed novel multivalent affinity labeling probes, which display multiple molecules of a carbohydrate ligand and a photoreactive group on gold-nanoparticles in high density.[1)] The introduction of gold-nanoparticles as the scaffoled for probes simplifies probe synthesis, improves the efficiency of labeling reactions, and enables the convenient separation and purification of the labeled proteins.

In this presentation, I will discuss a new approach to expanding the scope of gold-nanoparticles as probe scaffolds to facilitate more efficient exploration of low-affinity carbohydrate-binding proteins. Specifically, we are interested in the development of labeling reactions using electrophilic groups instead of photoreactive groups with low labeling efficiency.[2)] Electrophilic groups are not often used in the search for unknown binding proteins because of the difficulty in controlling selectivity. We found that by functionalizing the electrophilic groups on gold-nanoparticles, their inherent yet milder reactivity could be exploied to enable labeling and identification of binding proteins with higher efficiency than photoreactive groups.

References

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[2] Kamoshita, S. *et al. ChemBioChem*, **2022**, *23*, e202100388.

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