Combinatorially screened peptide as targeted covalent binder

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Finding targeted covalent binders (also known as covalent drugs) is one of the cutting-edge disciplines such as biomedical sciences / chemical biology / pharmaceuticals fields. As shown in the figure below, we present here a novel concept for finding a peptide covalent binder from fluoroprobe-modified peptide library [1] on T7 bacteriophage constructed *via* the 10BASE α -T [2], followed by a structure alteration into a reactive warhead [3]. Site- and position-specific conjugation toward the target protein and target selectivity were confirmed. This is the first demonstration for finding peptide-type targeted covalent binder by a combinatorial screening, instead of a rational designing. We believe the discovery technology would be generally applied to the discovery of novel covalent drugs for clinically-important proteins (e.g., cancer-related cell-surface proteins).

Figure 1

References

- [1] Taki et al., Anal. Chem. 2016, 88, 1096; Uematsu et al., AIP Conf. Proc. 2017, 1807, 020028.
- [2] Fukunaga et al., Chem. Commun. 2014, 50, 3921; inside cover article.
- [3] Uematsu and Tabuchi et al., Bioconj. Chem. 2018, in press.