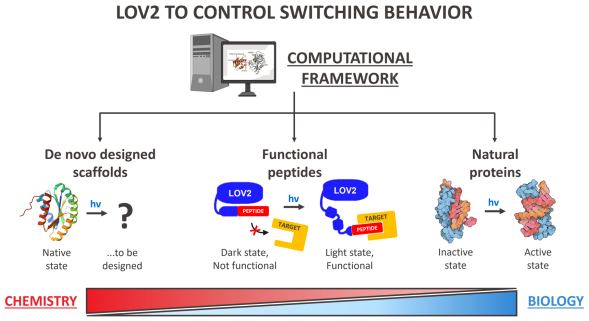
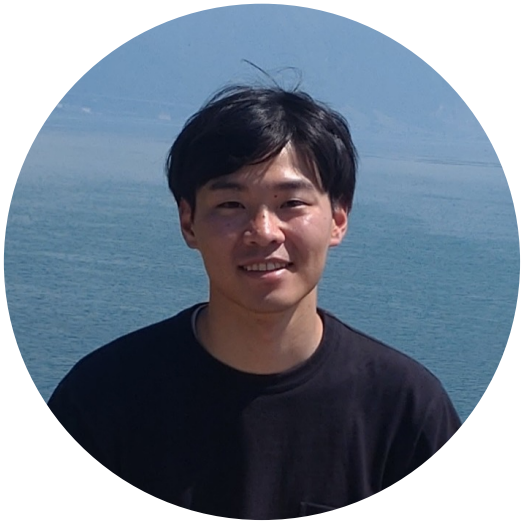
Lorenzo Scutteri
LPCE

De Novo Design Light-Responsive Protein Switches

Designing proteins that can dynamically and reversibly switch between different states remains challenging. To address this, we developed a computational framework for engineering light-mediated switchable properties in target molecules. We leveraged the LOV2 optogenetic domain to control the conformational dynamics of de novo designed scaffolds, creating light-responsive protein switches. We anticipate that functionalizing these switches will lead to impactful biological applications.





Yuji Kamei
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Development of peptide binders for oncogenic transcription factor AML1-ETOle

Protein–protein interactions (PPIs) involving transcription factors play a critical role in mediating gene expression, and their dysregulation drives numerous diseases, including cancer. Consequently, the chemical modulation of PPIs is of interest to medicinal chemists. However, targeting PPIs with small molecules remains challenging, as PPIs often lack well-defined binding pockets, hampering small-molecule drug discovery.

Peptidic inhibitors are gaining attention as a new modality to address these undruggable PPIs. Due to the inherent challenges in rational peptide design, large peptide libraries are typically required for screening.

Here, we leverage an automated pipeline for de novo peptide binder design based on machine learning and chemical modifications to discover highly affinitive and specific binders. Using this approach, we successfully identified a de novo peptide binder for AML1-ETO, an oncogenic transcription factor previously considered undruggable.