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Mini-Symposium on Chemical and Synthetic Biology for Molecular Materials and Biomedicine

Abstracts

Synthetic biology based on modularity for protein design and mammalian cell regulation:

Modular protein design enables the creation of novel protein folds and the regulation of biological processes in mammalian cells. We have used coiled-coil dimeric modules to construct protein assemblies unknown in nature, such as polyhedral scaffolds. Recent advances include the determination of the structures of CCPO-based trigon and tetrahedron, along with chemically regulated assembly and preorganization strategies like protein cyclization. Modular coiled-coil interactions also enable the formation of **liquid-liquid protein condensates** from single or multiple polypeptide chains. In mammalian cells, coiled-coil dimers combined with **split proteases** allow rapid control of cellular processes, including protein secretion and membrane localization. The **INSRTR system** introduces a coiled-coil peptide into target proteins, disrupting function upon heterodimer formation. This approach enables **ON/OFF protein switches, small-molecule regulation, and logic functions** with fast cellular responses. INSRTR has been demonstrated in **ten different proteins**, including enzymes, signaling mediators, transcriptional regulators, fluorescent proteins, and antibodies. It has also been integrated into **chimeric antigen receptors on T cells**, highlighting its therapeutic potential. Overall, designable coiled-coil dimers offer powerful tools for protein engineering, synthetic biology, and **biomedicine**, enabling precise control of biological systems.

References: Ljubetič et al. Nat. Biotechnol. (2017); Lebar T, et al. Nat Chem Biol. (2018); Fink et al. Nat Chem Biol. (2019); Lebar et al. Nat. Chem. Biol. (2020); Praznik et al., Nat.Commun. (2023); Rihtar et al., Nat.Chem.Biol. (2023); Ramšak et al., Nat.Commun. (2023); Plaper et al., Cell Discovery (2024); Snoj et al., Chem.Sci. (2024); Satler et al., JACS (2024); Vidmar et al., Ang.Chem. (2025).

Enhancing RNA Delivery and Cell Specificity:

Lipid nanoparticles (LNPs) have unlocked the potential of RNA therapeutics and vaccines. Production and large-scale manufacturing methods for RNA-LNPs have been established and rapidly accelerate. Despite this, basic research on LNPs is still required, due to their high assembly complexity and fairly new development, including research on lipid organization, transfection optimization and in vivo behavior. Understanding

fundamental aspects of LNPs i.e., how lipid composition and physicochemical properties affect their biodistribution, cell recognition and transfection, could propel their clinical development and facilitate overcoming current challenges. A major challenge remains to target extrahepatic tissue and to enhance endosomal escape to increase the therapeutic effect of RNA-therapeutics. Herein, we review recent developments in the field of LNP technology and summarize main findings focusing on nano-bio interactions.