Induced Proximity for Biology and Medicine

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Proximity, or the physical closeness of molecules, is one of the fundamental principles that governs diverse cellular processes. In recent years, chemical inducers of proximity (CIPs) or chemical inducers of dimerization (CIDs) were developed to mimic biologically regulated recruitment and understand the role of proximity in biological mechanisms. CIPs or CIDs technology employs bifunctional small molecules to bring two proteins in close proximity and subsequently enables precise temporal control of various cellular processes, such as cell signaling cascades, protein-protein interactions, cellular cargo transport, and genome editing. In this abstract, we present some representative conceptual advancements of CIPs and CIDs in recent years and showcase their valuable applications. The first part is chemo-optogenetics which was developed by combining CIP concept and optogenetics. Chemo-optogenetic tools can be considered as a “Chemistry” version of optogenetics, exhibiting unique features and advantages[1-3]. The second part is small molecule-nanobody conjugate induced proximity, or SNACIP[4], which was an integrated technology by combining three recent advancements from different fields, namely, i) CIP, ii) chemical nanobody engineering, and iii) cyclic arginine-rich peptide-based non-endocytic delivery system. SNACIP allows modulation of unligandable targets and endogenous intrinsically disordered proteins (IDPs), which represent challenging targets for traditional CIP/CID tools. The third part is the design of bifunctional biotin/fluorescein amplicon dimerizers that allow ultrasensitive detection of SARS-CoV-2 nucleic acid via recombinase polymerase amplification (RPA). This represents the first RPA detection method against SARS-CoV-2 worldwide[5]. These examples showcase the important roles and great potentials of induced proximity technologies for biology and medicine applications.

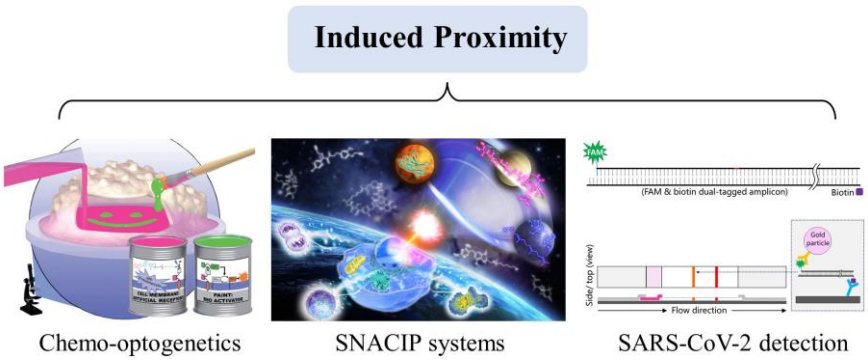

Figure 1. Induced proximity for biology and medicine

References

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