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CURIOSITY-DRIVEN RESEARCH: THE QTY CODE FOR PROTEIN DESIGN

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G protein-coupled receptors (GPCRs), including chemokine receptors, are a family of integral membrane proteins embedded in the lipid bilayer of cell membranes that transduce extracellular stimuli into cellular response. GPCRs are vital for diverse biological functions including vision, smell, taste, and ageing. They are involved in a wide range of diseases including cancer metastasis, autoimmune disease, asthma, addiction, immune system, neurological disorders, autism and more. GPCRs are among the most important targets of medicinal drugs. Tools that facilitate GPCR studies or GPCR-based technologies or therapies are thus critical to develop. We have devised a protein design tool called the QTY code, through which hydrophobic amino acids Leu, Ile, Val and Phe are replaced by Gln (Q), Thr (T) and Tyr (Y). Thus, the functional water-soluble equivalents of membrane proteins can be designed. In this talk, I will not only discuss the scientific basis of the QTY code, but also the application of the QTY code on the design of detergent-free chemokine receptors that retain ligand-binding activities, water-soluble chimeric chemokine receptors with tunable ligand affinity, water-soluble Fc-fusion cytokine receptors. This QTY code can be applied to diverse α -helical membrane proteins, and may aid in the development of other applications, including clinical therapies.

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