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Professor Yifan Cheng

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Dr. Yifan Cheng is currently an Investigator of Howard Hughes Medical Institute (HHMI) and a Professor at the Department of Biochemistry and Biophysics, University of California San Francisco (UCSF). He received his Ph.D. in 1991 from the Institute of Physics, Chinese Academy of Sciences. From 1991 to 1996, he continued his research in solid state physics and electron microscopy as a postdoctoral fellow at University of Oslo (NTNF Fellow) and Max-Planck-Institute of Metal Research (Alexander von Humboldt Fellow). In 1996, he changed his research direction to structural biology and received further training in cryo-electron microscopy (cryo-EM) from Professors Kenneth Taylor (Florida State University) and Yoshinori Fujiyoshi (Kyoto University). In 1999, he joined the laboratory of Thomas Walz to setup a cryo-EM operation at Harvard Medical School. He joined the faculty of UCSF in 2006 and has stayed there ever since. He has been an HHMI Investigator since 2015. He is the recipient of the Christian B. Anfinsen Award (The Protein Society, 2018), and elected members of the American Academy of Arts and Science (2019) and National Academy of Sciences (2020).

His laboratory uses cryo-EM to study structures of biological macromolecules, particularly integral membrane proteins and dynamic complexes. In addition, the development of cryo-EM methodology for structural biology is also a long-lasting interest of his laboratory. Previous works of his laboratory include developments of algorithms to correct electron beam-induced image motion and determination of the first atomic structure of TRPV1 by single particle cryo-EM. His current works focus on elucidating how conformational dynamics drives protein functions.

Dynamic allostery drives integrin avb8 mediate L-TGF-b activation

While single particle cryo-EM and AI-based protein structure prediction have made high-resolution structure determination more accessible, capturing protein dynamics – especially when they are integral to function – remains a major challenge. Using avb8-mediated activation of latent TGF-β1 (L-TGF-b1) as an example, I will illustrate the critical role of conformational dynamics in protein function. TGF-b, an essential regulator of development and immune homeostasis, is expressed as a latent complex (L-TGF-b1) that is non-covalently bound to its prodomain and presented on immune cell surfaces by covalent association with GARP. Binding of integrin avb8 activates L-TGF-b1/GARP complex. While it is traditionally thought that release of mature TGF-b1 is required for signaling, our previous work demonstrated that avb8-mediated autocrine signaling can occur without TGF-b1 release from its latent complex. We now show that avb8 binding induces a dynamic allosteric shift, redistributing the flexibility within L-TGF-b1 to transiently expose the active cytokine for receptor interaction – without its physical release. This highlights the importance of conformational dynamics in protein function and the need to study protein motions to uncover mechanisms missed by static structural approaches.