2020 年度陈嘉庚科学奖专辑

陈嘉庚科学奖——生命科学奖

施一公

结构生物学家, 中国科学院院士, 现任西湖大学校长, 中国科学技术协会第九届全国委员会副主席, 清华大学生命科学与医学研究院院长。主要学术领域包括: 运用生化和生物物理的手段研究细胞凋亡的分子机制、重要膜蛋白以及细胞内生物大分子机器的结构与功能; 尤其是解析了真核信使 RNA 剪接体关键复合物结构, 揭示了活性部位及分子层面机理。

获奖项目名称

剪接体的结构与分子机理研究

获奖项目介绍

报道了世界首个完整剪接体近原子分辨率三维结构, 揭示了剪接体组分的组装原则及催化活性中心的分子结构。解析了酵母剪接体工作过程中全部 8 个基本关键状态及人源剪接体 7 个状态的高分辨率三维结构, 完整地覆盖整个剪接通路中关键的催化步骤。从组装到被激活, 从发生两步转酯反应到剪接体的解聚, 提供了迄今为止最为清晰的剪接体不同工作状态下的结构信息, 将我们对 RNA 剪接的分子机理的理解推向原子层面, 为理解高等生物的 RNA 剪接过程提供了重要基础, 推动了整个 RNA 剪接领域的发展。同时, 为进一步探索与剪接异常相关疾病的致病机理和药物开发提供分子基础。

Structural and mechanistic investigations of the spliceosome

Yigong Shi^{1,2,3,4}

¹Beijing Advanced Innovation Center for Structural Biology & Frontier Research Center for Biological Structure, School of Life Sciences, Tsinghua University, Beijing 100084, China;

²Key Laboratory of Structural Biology of Zhejiang Province, School of Life Sciences, Westlake University, Hangzhou 310024, China;

³Institute of Biology, Westlake Institute for Advanced Study, Hangzhou 310024, China;

⁴Tsinghua University-Peking University Joint Center for Life Sciences, School of Life Sciences, Tsinghua University, Beijing 100084, China

Shi's group has been focusing on the structural and mechanistic elucidation of pre-mRNA splicing in the past decades. After the success of crystal structural elucidation of subcomplexes within spliceosome, they took a direct assault on the intact spliceosome and made the breakthrough in the summer of 2015. They determined the structure of intron lariat spliceosome ILS complex from *S. pombe* at an average resolution of 3.6 Å, which is the first atomic structure of the intact spliceosome, revealing the organization of the spliceosomal components and the conformation of the splicing active site for the first time in the world. Since then, Dr. Shi's group has reported the high-resolution structures of the spliceosome in all eight major fully-assembled functional states, as well as the structure of the largest pre-assembled subcomplex U4/U6.U5 tri-snRNP from *S. cerevisiae*. The ten structures give rise to a complete structural view for spliceosome activation, catalysis and disassembly. His group also captured 7 key intermediates of human spliceosome, providing structural basis of the evolution of the spliceosome machinery from lower to higher eukaryotes. Taken together, these accomplishments represent a major contribution in this field, which conceptionally advance our understanding to the molecular mechanism of pre-mRNA splicing and provide unprecedented insights into the research on pathogenesis of related diseases and drug discovery.

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