Mechanism of chromatin remodeling revealed by the Snf2-nucleosome structure

Subject Code: C05

With the support from the National Natural Science Foundation of China, a collaborative study by the research teams led by Chen Zhucheng (**陈柱成**) and Li Xueming (**李雪明**) at the School of Life Sciences, Tsinghua University, recently reported their work, titled "Mechanism of chromatin remodeling revealed by the Snf2-nucleosome structure", in *Nature* (2017, 544: 440—445). The structure of chromatin remodeler bound to the nucleosome substrate has been pursued for a long time in the world, and yet only low resolution data are available. The paper reported the cryo-electron microscopy structure of chromatin Snf2 bound to the nucleosome, which illustrates the mechanism of chromatin remodeling.

Chromatin remodelers are RecA-like, ATP-dependent motor proteins that alter chromatin structure and nucleosome position to regulate accessibility of genomic DNA. While chromatin remodeling is a fundamental process and a part of the central dogma of life, how it happens is not entirely clear. In 2016, Chen's group reported the crystal structure of chromatin remodeler Snf2 in the resting state in the absence of the nucleosome. In the current work, they made a breakthrough, reporting the cryo-EM structure of Snf2 bound to the nucleosome at a resolution of 4.69 Å. The structure shows that the two core domains (core1 and core2) of Snf2 are realigned upon nucleosome binding, suggesting activation of the enzyme. The core domains contact each other through two induced Brace helices, which are crucial for coupling ATP hydrolysis to chromatin remodeling. Snf2 binds to the phosphate backbones of one DNA gyre of the nucleosome mainly through its helicase motifs within the major domain cleft formed by the catalytic domains, suggesting a conserved mechanism of substrate engagement across different remodelers. Snf2 contacts the second DNA gyre via a positively charged surface, providing a mechanism to anchor the motor at a fixed position of the nucleosome. Snf2 deforms the nucleosomal DNA at the site of binding, priming the substrate for the remodeling reaction. Together, these findings provide mechanistic insights into chromatin remodeling.

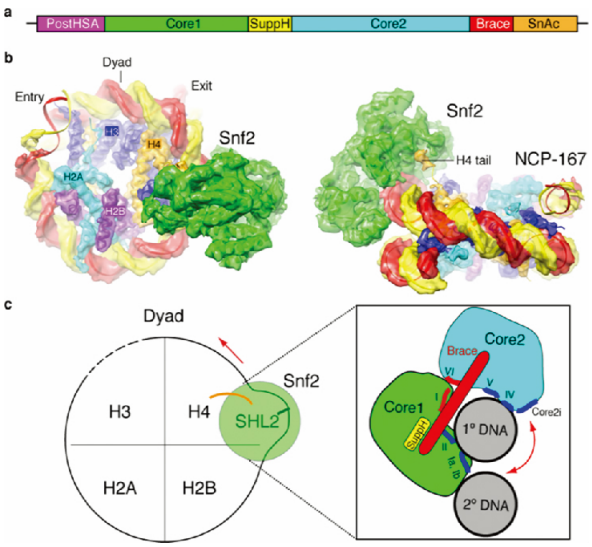

Figure Mechanism of chromatin remodeling mediated by Snf2. (a) Domain architecture of Snf2. (b) Cryo-EM density map superimposed with the structures of Snf2 and the nucleosome. (c) Model of nucleosome sliding by Snf2. Red arrows indicate Snf2 motions in an ATPase cycle and sliding of the DNA on the surface of the histone octamer core.