Conformational elasticity of TALE-DNA complex

With the support by the National Natural Science Foundation of China and the Ministry of Science and Technology of China, new progress on the structure and dynamics of TALE (transcription activator-like effector) was reported by a research team led by Prof. Lei Hongxing at Beijing Institute of Genomics, Chinese Academy of Sciences, which was published in *Adv Protein Chem Str* (2014, 94: 347—364).

Sequence-programmable TALE proteins have emerged as a highly efficient tool for genome engineering. However, recently revealed crystal structures depict a transition between an open unbound solenoid and the more compact DNA-bound solenoid formed by the 34 amino acid repeats. How TALEs switch its conformation between these two forms without substantial energetic compensation, and how the repeat-variable di-residues (RVDs) discriminate between the cognate base and other bases still remain unclear.

In order to achieve a better understanding of the energetics, Prof. Lei and his research team conducted computational analyses on these two aspects of TALE-DNA interaction mechanism. High elasticity was observed in the molecular dynamics simulations of DNA-free TALE structure that started from the bound conformation, where it sampled a wide range of conformations including the experimentally determined apo and bound conformations. This elastic feature was also observed in the simulations starting from the apo form, which suggests low free energy barrier between the two conformations and small compensation required upon binding. To analyze the binding specificity, the researchers also performed free energy calculations of various combinations of RVDs and bases using Poisson-Boltzmann surface area (PBSA) and other approaches. The PBSA calculations indicated that the native RVD-base structures had lower binding free energy than mismatched structures for most of the RVDs examined. These theoretical analyses might have provided some new insights into the dynamics and energetics of TALE-DNA binding mechanism.

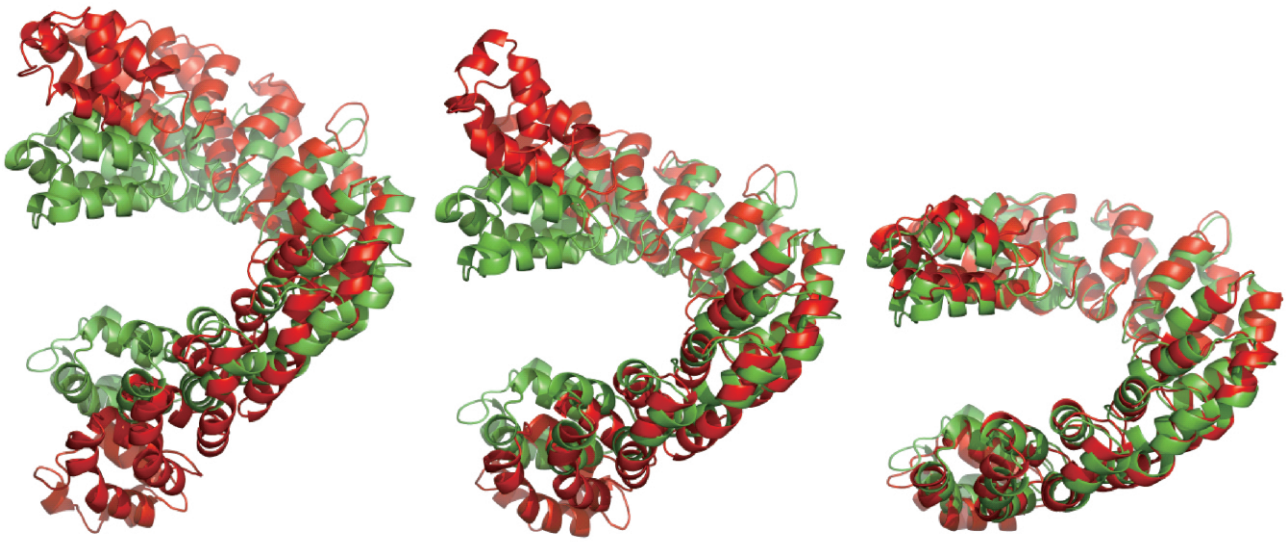

Figure Three representative snapshots from the MD simulation trajectory. **Left**, 68.25 ns, highly extended; **middle**, 73.95 ns, close to the apo form; and **right**, 130.29 ns, close to the bound form. The structures from the simulation are shown in red, the reference bound structure is shown in green.