

INVITED LECTURE T7

Mechanisms of ATP-dependent chromatin remodeling revealed by single-molecule manipulation studies

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Chromatin structures are established and remodeled mainly by a large family of highly conserved and specialized ATP-dependent chromatin remodeling complexes (remodelers) in cooperation with histone-modifying enzymes. The core of these remodelers is a DNA translocase, a molecular motor capable of actively moving along DNA. It remains unclear how the energy of ATP hydrolysis is converted to the mechanical work for DNA translocation and in turn to nucleosome remodeling by remodelers, and how the remodeling process is regulated by different protein subunits of remodelers, nucleosome substrates, and histone modifications. Using high-resolution optical tweezers, we studied the nucleosome remodeling process by SWI/SNF and RSC, two prototypes of remodelers containing 11 and 15 subunits, respectively. We found that both remodelers can forcefully translocate along DNA and produce DNA loops of a broad range of sizes in a nucleosome-dependent manner. Interestingly, when anchored to DNA, the isolated translocase subunit of RSC alone can efficiently translocate along the DNA to produce DNA loops even on bare DNA. Our single-molecule experiments revealed a powerful and versatile DNA translocase engine for remodelers, which may be crucial for their role of disrupting DNA-histone interactions in a regulatory fashion.