Rosetta Briegel Barton Lecture

We Are Pleased to Announce a Seminar
Presented By

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Friday, April 14, 2023
4:15 pm
NWC 1313

1+1 > 2: Combination of experimental structural biology and AI-predicted protein fold to understand biological functions

The application of AlphaFold in structural function analysis has greatly accelerated biological studies in all aspects. In this context, we provide a few examples of how AI has facilitated our research as case studies to inspire wider usage. For instance, a bacterial group II intron-like reverse transcriptase (G2L4 RT) functions in double-strand break repair (DSBR) via microhomology-mediated end joining (MMEJ). Experimental and AI-predicted structures have revealed an activation mechanism that transitions the protein from a self-inhibitory to an activated state. Our findings provide insight into molecular mechanisms by which non-LTR-retroelement RTs could function in DSBR in a wide range of organisms, identify structural features of G2L4 RT that evolved to optimize this activity and provide a structural basis for engineering group II intron-like and related RTs for genome editing and other biotechnological applications.

In eukaryotes, RNA polymerase II undergoes dynamic post-translational modification during transcription, generating a sophisticated landscape for the spatiotemporal recruitment to transcriptional regulators for mRNA products. The chemical diversity generated by such a combinatorial approach provides various binding motifs to transcriptional regulators, allowing for high-specificity recruitment. Using an extensive collection of kinases and phosphatases confirmed by ultraviolet photodissociation mass spectrometry, we could in vitro reconstruct the PTM landscape of RNA polymerase II at the different stages of transcription. To delineate the protein interactomes recruited to Pol II-mediated transcription, we identified specific protein interactomes by the different phosphorylation patterns. In particular, we found a new aspect of CTD-recruitees as a driving force for the phase transition.

Refreshments will be served.