

Poster Presentation

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CTD Code: a Combinatorial Code for Eukaryotic Transcription

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In eukaryotes, the C-terminal domain of RNA polymerase II (CTD) orchestrates the temporal and spatial control of transcription and is involved in the epigenetic regulation of gene expression. Errors in CTD regulation can result in cell death, cancer and severe developmental defects. The CTD executes its function as transcription modulator through various post-translational modifications on its heptad repeat sequences. Recently, novel modifications on new regulatory sites of CTD have been identified, setting the stage for the possibility of combinatorial mechanisms for transcription regulation. We focused on two well-characterized modification of CTD, namely serine phosphorylation and prolyl isomerization, and discuss the interplay between the enzymes regulating these modification states. Our results established that the selectivity of prolyl isomerization state of CTD on phosphatases can lead to differentiated outcome for the CTD phosphorylation state and therefore, transcription. To further investigate the prolyl selectivity, we developed chemical compounds that can be used to probe such subtle structural variation in the CTD binding proteins. These compounds closely mimic the cis or trans proline state and can be effectively recognized by CTD phosphatases. The application of such chemical probes can help us understand the molecular mechanism of the interplay between phosphorylation and prolyl isomerization state and how that affect the conformational status of CTD in transcription temporally and spatially.

Keywords: transcription, post-translational modification, cis-trans prolyl isomerization