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Mechanisms of gene regulation by chromatin adaptor proteins in health and disease

Chromatin, the physiological form of our genome, is composed of DNA and histone proteins. Post-translational modifications of these components, along with their regulatory factors, are essential for maintaining cellular integrity, tissue health, and the overall functioning of organisms. Large-scale sequencing efforts have revealed that alterations in chromatin and epigenetic regulators are commonly associated with human diseases, including developmental disorders and cancers. While significant attention has been directed toward understanding chromatin-modifying enzymes and their dysregulation in disease, less is known about the role of chromatin adaptor/scaffold proteins, which assemble these enzymatic complexes. Our research focuses on this underexplored area, particularly the catalytic-independent activities and scaffolding functions of chromatin-modifying enzymes. By leveraging our expertise in cancer biology and chromatin biochemistry, we investigate how chromatin adaptors decode chemical signals and regulate gene expression in both healthy and diseased states. One such adaptor, TRIM28 (KAP-1), has been identified as a key regulator of heterochromatin formation and cellular differentiation. Our recent studies have uncovered TRIM28 as an essential epigenetic regulator in acute myeloid leukemia (AML). Inhibiting TRIM28, either biochemically or genetically, significantly reduces leukemia cell proliferation *in vivo*, accompanied by changes in gene expression, including the upregulation of neutrophil-associated transcriptional programs. These findings suggest that TRIM28 functions as a dual transcriptional regulator, modulating gene expression through its context-specific interactions with proteins and chromatin. The scaffolding function of TRIM28 underscores its potential as a novel therapeutic target in AML treatment, with further research poised to advance targeted leukemia therapies and broaden clinical intervention strategies.

Upcoming speakers

Tue, September 16 2025 – Pavel Tomancak, MPI-CBG

Tue, October 14 2025 – James Briscoe, Francis Crick Institute

Tue, November 18 2025 – Margherita Turco, Friedrich Miescher Institute

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