Mapping the molecular interactome of the human ATAC complex: uncovering its role in transcriptional regulation

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Abstract

In eukaryotes, DNA is packaged into chromatin, a dynamic structure that regulates transcription, replication, and DNA repair. Chromatin accessibility is finely modulated by coactivator complexes like SAGA (Spt-Ada-Gcn5 acetyltransferase) and ATAC (Ada-Two-A Containing), which promote transcription initiation through histone acetylation. Although they share a catalytic module, ATAC is metazoan-specific, structurally uncharacterized, and contains a unique core module, suggesting distinct regulatory roles compared to SAGA. ATAC is crucial for the expression of housekeeping genes (e.g., ribosomal protein genes), acetylates non-histone targets, and binds RNAs, suggesting a broader role in transcription regulation. However, how ATAC integrates these molecular interactions to coordinate transcription remains unknown. This project aims to bridge this gap by mapping the molecular interactome of the ATAC-specific core subunits: YEATS2, ZZZ3, ATAC2, and MBIP. To capture both stable and transient interactions within the nuclear environment, we are employing a proximity labelling strategy coupled with mass spectrometry. This approach enables the identification of proximal proteins in their endogenous environment, providing a comprehensive view of the ATAC interactome and its regulatory partners. By characterizing these subunit-specific networks, we aim to uncover how ATAC coordinates multiple molecular interactions to regulate gene expression, chromatin recruitment, and cellular homeostasis.

Keywords: Transcriptional regulation, ATAC complex, Proximity labelling, Chromatin

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