TBP-associated Factor 12 Doppelgangers: Defining their Specificity and Differential Control of Stress Regulated Gene Expression

Krishnamurthy Natarajan, School of Life Sciences, Jawaharlal Nehru University, New Delhi

Abstract: How pathogens respond to stimuli under often adverse host environments is critical for their survival in vivo. In this context, chromatin and transcriptional control are major determinants in the cellular response to stress conditions. Transcriptional regulators comprise gene-specific DNA-binding activators and repressors, and coregulators such as chromatin modifying and remodelling complexes. TBP-associated factors (TAF) are critical for initiation of transcription by RNA polymerase II. Studies in metazoans have shown that paralogs of TBP and TAFs contribute to tissue- or cell-type specific transcription. The relative contribution of the TAF doppelgangers (paralogs) determines specification of cell-type gene expression. We reported that the genome of a unicellular eukaryote, the human fungal pathogen *Candida albicans*, surprisingly has evolved two paralogs of TAF12. The two TAF12 proteins have high homology only in their C-terminal histone-fold domain. We showed that the paralogous TAF12 specifically associate with the TFIID and the SAGA histone acetylase coactivator complexes. Whereas TAF12 is essential for cell growth, TAF12L is non-essential for growth in vitro, but is required for virulence of *C. albicans* in mouse model of infection. In this seminar, I will discuss how the specificity of their association with the multisubunit TFIID and SAGA complexes are achieved. Depletion of TAF12 or TAF12L does not lead to incorporation of the alternate TAF12 into the TFIID or SAGA complexes in vivo. Systematic mutational analysis showed that the TAF12L-bearing SAGA complex has modular organization, and revealed dual role of SAGA in transcriptional activation or repression under distinct cell growth conditions. Recent studies that have shed light on molecular mechanism of assembly of multisubunit complexes through co-translational assembly will finally be discussed.