transcription elongation factor TEFM and of an anti-termination complex consisting of TEFM bound to the transcribing polymerase. These structures illustrate how TEFM interacts with both the nucleic acid and the polymerase in the elongation complex to facilitate processive transcription and drive gene expression over primer formation for DNA replication. Together, these results elucidate the mechanistic basis of transcription initiation and processive elongation in human mitochondria and provide the framework for studying the regulation of mitochondrial gene transcription.

Keywords: Mitochondria, Transcription, RNA

MS11-O2

Structural and functional insight into human O-GlcNAcase

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O-GlcNAc hydrolase, OGA, removes O-linked N-acetylglucosamine (O-GlcNAc) from myriad nucleocytoplasmic proteins. O-GlcNAcylatation plays a vital role in a range of cellular processes including, for example, transcriptional regulation and the stress response (reviewed in Ref [1,2]). Dysregulation of O-GlcNAcylation has been implicated in diseases including cancer[3], and neurodegenerative diseases.[4,5] Notably, therapeutic agents targeting the O-GlcNAc modification have entered phase I clinical trials against neurodegenerative disorders, stimulating interest in the molecular and chemical basis of *O*-GlcNAcylation and its manipulation with small molecules.[6] We aimed to shed light on the multi-domain architecture of OGA and the structural basis of activity. Through co-expression and assembly of OGA fragments we determined the 3-D structure of human OGA, revealing an unusual helix exchanged dimer that lays a structural foundation for an improved understanding of substrate recognition and regulation of OGA.[7] Structures of OGA in complex with a series of different inhibitors define a precise blueprint for the design of lead structures having potential clinical value.

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