RNA-bound PGC-1α controls gene expression in liquid-like nuclear condensates

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Plasticity of cells, tissues, and organs is controlled by the coordinated transcription of biological programs. However, the mechanisms orchestrating such context-specific transcriptional networks mediated by the dynamic interplay of transcription factors and coregulators are poorly understood. The peroxisome proliferator-activated receptor γ coactivator 1α (PGC-1α) is a prototypical master regulator of adaptive transcription in various cell types. We now uncovered a central function of the C-terminal domain of PGC-1α to bind RNAs and assemble multiprotein complexes including proteins that control gene transcription and RNA processing. These interactions are important for PGC-1α recruitment to chromatin in transcriptionally active liquid-like nuclear condensates. Notably, such a compartmentalization of active transcription mediated by liquid-liquid phase separation was observed in mouse and human skeletal muscle, revealing a mechanism by which PGC-1α regulates complex transcriptional networks. These findings provide a broad conceptual framework for context-dependent transcriptional control of phenotypic adaptations in metabolically active tissues.
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