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The Transcriptional Coregulatory Protein YAP1 Interacts with RNA Binding Protein NPM1

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RNA binding proteins (RBPs) regulate all aspects of RNA biogenesis from transcription, splicing, translation to degradation, and they have a critical role in cellular homeostasis and functional diversity. Recent studies have indicated that altered expressions of RBPs are associated with many human diseases ranging from neurologic disorders to cancer. The transcriptional coregulator yes-associated protein 1 (YAP1), a critical nuclear effector of the mammalian Hippo pathway, regulates cell fate, cell contact, metabolism, and developmental processes. This study aims to demonstrate a link between YAP1 and nucleophosmin1 (NPM1) protein. NPM1 is an RNA-binding protein that regulates many cellular activities, including ribosome biogenesis, RNA processing, chromatin remodeling, DNA repair, and genomic stability. Using proteomics approaches, we identified NPM1 from YAP1 protein complexes of androgen-responsive human cancer cells. Our proximity ligation assay demonstrated that YAP1 and NPM1 physically interacted with each other. The interaction between YAP1 and NPM1 occurred in cell nuclei and was regulated by androgen hormone signaling. In addition, our GST-pulldown assay demonstrated that NPM1 formed a protein complex with the proline-rich domain of YAP1. Furthermore, our enhanced RNA interactome capture (eRIC) assay showed that androgen also regulated the interaction of RBPs to polyA+ mRNA within the cell. Consistent with this observation, our eRIC assay combined with the mass spectrometry method enabled identifying distinct RBP patterns in human cancer cells that are genetically related but phenotypically different. These observations indicate that global alterations of RBPs under changing environmental conditions may have important roles in cellular physiology and disease biology.

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