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Identification of copper-binding nuclear proteins in mouse brain: its involvement in retinoic acid receptor signaling

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Abstract:
Copper is an essential micronutrient with numerous cellular functions. Previous studies have demonstrated that copper deficiency in P19 embryonal carcinoma cells by using a copper depletor, bathocuproinedisulfonic acid, suppresses the retinoic acid-induced neuronal differentiation and the retinoic acid receptor-mediated transactivation. In this study, we used an immobilized metal affinity chromatography (IMAC) technique to identify novel copper-binding nuclear proteins in mouse brain. Two copper-binding proteins, polypyrimidine tract-binding protein-associated splicing factor (PSF) and NonO/p54^{nrb} (NonO), were identified by IMAC loaded with copper ion and mass spectrometry. In transient transfection experiments, both PSF and NonO overexpression in Neuro-2a cells resulted in significantly increased expression of a luciferase reporter gene in response to retinoic acid. Our results suggest that the possible copper binding proteins, PSF and NonO, may act as a coactivator of retinoic acid receptor-dependent transcription.

Key words: immobilized metal affinity chromatography

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