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Research Article

NAT10, a nucleolar protein, localizes to the midbody and regulates cytokinesis and acetylation of microtubules

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ABSTRACT

The midbody is a structural organelle formed in late phase mitosis which is responsible for completion of cytokinesis. Although various kinds of proteins have been found to distribute or immigrate to this organelle, their functions have still not been completely worked out. In this study, we demonstrated that NAT10 (N-acetyltransferase 10, NAT10) is not only predominantly distributed in the nucleolus in interphase, but is also concentrated in the mitotic midbody during telophase. The domain in N-terminal residues 549–834 of NAT10 specifically mediated its subcellular localization. Treatment with genotoxic agents or irradiation increased concentration of NAT10 in both the nucleolus and midbody. Moreover, DNA damage induced increase of NAT10 in the midbody apparently accompanied by in situ elevation of the level of acetylated α-tubulin, suggesting that it plays a role in maintaining or enhancing stability of α-tubulin. The depletion of NAT10 induced defects in nucleolar assembly, cytokinesis and decreased acetylated α-tubulin, leading to G2/M cell cycle arrest or delay of mitotic exit. In addition, over-expression of NAT10 was found in a variety of soft tissue sarcomas, and correlated with tumor histological grading. These results indicate that NAT10 may play an important role in cell division through facilitating reformation of the nucleolus and midbody in the late phase of cell mitosis, and stabilization of microtubules.

Introduction

Cytokinesis is a fundamental phase of cell division and failure of this process causes abortive cytoplasmic abscission leading to formation of bi- or multi-nucleated cells or apoptotic cell death. The completion of cell mitosis is dependent on many components of the mitotic apparatus, and among these the midbody has attracted increasing attention [1]. The mammalian midbody is a dense structure containing microtubules derived from the mid-zone which are tightly bundled by the cytokinetic furrow, and the midbody has functions in cytokinesis and the completion of mitosis similar to the phragmoplast of plants [2]. Disruption of components in the midbody induces defective cleavage furrow formation or completion, or germline cytokinesis [3]. Proteomic analysis of the mammalian midbody shows that in addition to microtubules and associated regulatory proteins it also contains a variety of other proteins including ribosomal proteins, heat shock proteins, and proteins from various subcellular compartments such as mitochondria and the nucleus [3]. Previous studies have demonstrated that many centrosomal proteins immigrate to the midbody during the late phase of mitosis and take part in formation or functioning of the midbody, which gives rise to a new model of cell cytokinesis [4–6]. Thus, exploration of the dynamic traffic of proteins from other cellular organelles to the

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midbody should greatly facilitate understanding of midbody-associated mechanisms in cytokinesis.

NAT10 (or hALP, human N-acetyltransferase-like protein) is primarily identified as an activator for up-regulating telomerase activity through stimulation of transcription of hTERT together with histone acetyltransferase activity [7]. This gene also responds to DNA damage, in which the transcriptional activity of the NAT10 promoter may be specifically stimulated, and it thus also serves to