Alterations in the expression and subcellular localization of the SWI/SNF chromatin remodeling complexes subunits and their potential clinical significance in clear cell renal cell carcinoma

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The SWI/SNF chromatin remodeling complexes (CRCs) play a critical role in gene expression control by modifying the nucleosome structure of chromatin, thereby enabling access to genomic DNA for processes such as transcription and DNA repair. The functional diversity and specificity of SWI/SNF CRCs arise from the complex assembly of multiple subunits, post-translational modifications of certain subunits, and interactions with various proteins. Up to 25% of cancers are linked to mutations in genes encoding SWI/SNF subunits, even minor alterations in the levels of individual SWI/SNF subunits can impact the overall complex activity. In 40% of clear cell renal cell carcinoma (ccRCC) cases, mutations in the PBRM1 gene, which encodes the BAF180 SWI/SNF subunit, have been identified. Additionally, ccRCC is characterized by a multitude of epigenetic alterations. The investigation utilized ccRCC cell lines along with a non-cancer control. The expression levels of genes encoding SWI/SNF subunits and their subcellular distribution were evaluated through qPCR, cell fractionation, and Western blot analyses. Epigenetic alterations were investigated using ChIP-qPCR, treatment of cells with DNA methyltransferase inhibitors and bioinformatic analysis. IHC staining of clinical samples was conducted to determine the abundance of the proteins. Changes in the gene expression patterns of SWI/SNF CRCs subunits were noted, with an increase in BAF60A and BAF60B levels observed in the metastatic cell line. Additionally, certain SWI/SNF subunits, typically localized in the nucleus, were found in the cytoplasm. The presence of the BAF60B subunit in the cytoplasm appears to be associated with tumor recurrence. The upregulation of SWI/SNF subunits in metastasis may become a target for new therapy. The increased cytoplasmic abundance of BAF60B linked to cancer recurrence may be viewed as a potential novel biomarker.

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