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Abstract

Deciphering the Role of USP16 in Lung Cancer †

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Deubiquitylating enzymes are proteases that reverse the ubiquitination of proteins, an important process for maintaining normal homeostasis.

USP16 is a deubiquitylating enzyme that belongs to the family of ubiquitin-specific proteases (USPs) and is involved in cell cycle progression and chromatin remodeling.

To elucidate the role of USP16 in lung cancer progression, we first analyzed its expression in a cohort of biopsies obtained from patients with non-small cell lung cancer, NSCLC (N = 18). Real-time PCR analysis and Western blot analysis showed that USP16 is highly expressed in NSCLC tissues compared to normal tissues. To characterize the role of USP16, we used two lung cancer cell lines (NCI-H460 and A549), in which USP16 was knocked down by lentiviral RNA interference (shUSP16).

The knockdown of USP16 affects cancer cell behavior in terms of proliferation and drug sensitivity. The knockdown of USP16 reduces the proliferation of cancer cells (≈40%) compared to control cells, which is due to defects in mitotic cell phase. These effects could be attributed to the deubiquitinating effect on its substrates. Indeed, the silencing of USP16 decreased the protein stability of the transcription factor Myc and Polo like kinase-1 (PLK1). Conversely, we found that USP16 impaired the response of lung cancer cells to platinum-containing compounds. The reduction of USP16 expression impairs the cytotoxicity of cisplatin by approximately 50% compared to control cells. This could likely be due to the impaired recruitment of repair proteins in proximity of double-strand breaks (DSBs) in lung cancer cells. These results prompted us to perform further analysis to investigate the role of USP16 in DNA repair and drug sensitivity.

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