

## Abstract 5574: Exploring the therapeutic potential of USP14 in cervical cancer: mechanisms of oncogenesis and metabolic regulation **FREE**

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### Abstract

Cervical cancer is the most common cancer among women worldwide, predominantly caused by human papillomavirus (HPV) subtypes, particularly HPV 16 and 18. Although it is largely preventable through vaccination and early detection, cervical cancer remains a significant health issue, particularly in low- and middle-income countries, mainly due to acquired chemoresistance. This study explores the therapeutic potential of deubiquitinating enzymes (DUBs), with a focus on ubiquitin-specific proteases (USPs), in combating oncogenesis in cervical cancer. Using the TCGA database, we assessed the prognostic relevance of USP14, revealing that elevated levels of this enzyme correlate with poorer overall and disease-free survival among cervical cancer patients. In-silico analysis of publicly available gene expression datasets also indicates a significant upregulation of USP14 in cervical cancer tumor tissues compared to their paired normal tissues. USP14 expression was analyzed at both the RNA and protein levels across various cervical cancer cell lines, followed by assays for proliferation, metastasis, and invasion to assess the impact of USP14 depletion. Elevated USP14 expression was observed in the cervical cancer cell lines, and inhibiting USP14 resulted in significant reductions in cell proliferation, metastasis, and invasion. A novel USP14 inhibitor, IU-1, produced similar results. Proteomic analysis indicated that the lactate transporter MCT-4, a crucial metabolic regulator, was dysregulated following USP14 alteration. Immunoprecipitation studies confirmed stable interactions between USP14 and MCT-4. Cycloheximide and Deubiquitination assays further demonstrated that USP14 modulates MCT-4 stability via deubiquitination at specific sites.

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USP14 and MCT-4 and their correlation with patient prognosis. Collectively, our findings highlight the vital role of USP14 in the oncogenic and metabolic processes of cervical cancer, suggesting their potential as therapeutic targets. This research enhances the understanding of the molecular mechanisms driving cervical cancer progression and underscores the need for targeted therapeutic strategies.

Citation Format:

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