

Abstract 4639: Unraveling the oncogenic network of USP37 and USP14 in gynecological cancers: Decrypting the molecular landscape of chemoresistance **FREE**

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Abstract

Background: Gynecological cancers (GC) involve female reproductive system malignancies, and acquired chemoresistance is a challenge in the treatment of GC. Protein deubiquitination, mediated by deubiquitinating enzymes (DUBs) like ubiquitin-specific proteases (USPs), holds therapeutic promise in cancer treatment. This study delves into the mechanistic understanding of DUBs, particularly in acquired chemoresistance in GC.

Methodology: We initially examined TCGA database to assess the impact of Ubiquitin Specific Proteases (USPs), specifically USP37 and USP14, on prognosis in Gynaecological Cancers (GCs). Subsequently, we evaluated their expression in various GC cell lines at both protein and RNA levels. Cell proliferation and metastasis assays were performed to analyze the effect of depleting these USPs on survival and metastasis in GC cells under replication stress. Proteomics analysis was conducted on cells with altered expression of USP37 and USP14 to identify interacting proteins regulating proliferation and metastasis. To investigate DUBs role in chemoresistance, we generated chemoresistant (CR) cell lines with cisplatin exposure, characterized their viability and proliferation, conducted cell cycle and apoptosis analyses, and performed proteomic profiling to explore the USP37 and USP14 specific interactome in chemoresistant cell lines.

Results: Examination of TCGA database revealed an association between elevated USP37 and USP14 expression and poor Overall Survival (OS) and Disease-free Survival (DFS) in

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resistant GC cell lines were successfully established, demonstrating prolonged survival and increased proliferative capacity after cisplatin treatment compared to chemosensitive (CS) cell lines. FACS analysis indicated altered cell cycle distribution and increased proliferation in CR cells. Comparative interactome analysis revealed altered protein sets associated with USP37 and USP14 in CR and CS GC cells.

Conclusion: This study provides evidence that supports the participation of USP37 and USP14 in the onset of gynecological cancers (GC). We present evidence of alterations in the oncogenic network linked to USP37 and USP14 in GC. Additionally, we elucidate the roles of these deubiquitinating enzymes (DUBs) in chemoresistant cell lines.

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