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18P Decoding the interplay of deubiquitinating enzymes (DUBs) in metastasis and chemoresistance of gynaecological cancers

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Background

Gynaecological cancers (GC) encompass malignancies affecting the female reproductive system, and dealing with acquired chemoresistance poses a significant challenge in their treatment. The study focuses on the therapeutic potential of deubiquitinating enzymes (DUBs), specifically ubiquitin-specific proteases (USPs), in addressing acquired chemoresistance and metastasis in GC.

Methods

The study utilized the TCGA database to assess the impact of (USPs), specifically USP37 and USP14, on the prognosis of GCs. Expression analysis at RNA and protein levels was conducted in various GC cell lines. Proliferation and metastasis assays were performed to evaluate the effect of depleting USP37 and USP14 on survival and metastasis in GC cells under replication stress. A 3D in-vitro culture platform was developed to study the impact of USP37 downregulation on cellular proliferation and

Results

Analysis of the TCGA database revealed elevated USP37 and USP14 expression associated with poor Overall Survival (OS) and Disease-free Survival (DFS) in GC. Increased expression of USP37 and USP14 was observed in GC cell lines, and their inhibition reduced proliferation and hindered metastasis. The 3D culture system proved effective in mimicking in-vivo conditions. Target exploration of USP37 revealed associations with EMT markers. Proteomics analysis identified proteins associated with replication, DNA damage, cell cycle, and metastasis. Cisplatin-resistant GC cell lines displayed altered cell cycle distribution and increased proliferation. Comparative interactome analysis revealed altered protein sets associated with USP37 and USP14 in CR and CS GC cells.

Conclusions

The research presents evidence that supports the participation of DUBs in GC, emphasizing changes in the oncogenic network. It underscores the sensitivity of the 3D culture system in assessing the oncogenic potential of DUBs, and elucidates the roles of these DUBs in chemoresistant cell lines.

Legal entity responsible for the study

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Disclosure

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