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REVIEW

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Ubiquitin-specific peptidase 37: an important cog in the oncogenic machinery of cancerous cells

Ravi Chauhan[1], Ajaz A. Bhat[2†], Tariq Masoodi[3†], Puneet Bagga[4], Ravinder Reddy[5], Ashna Gupta[1], Zahoor Ahmad Sheikh[6], Muzafar A. Macha[7], Mohammad Haris[2,5,8*] and Mayank Singh[1*]

Abstract

Protein ubiquitination is one of the most crucial posttranslational modifications responsible for regulating the stability and activity of proteins involved in homeostatic cellular function. Inconsistencies in the ubiquitination process may lead to tumorigenesis. Ubiquitin-specific peptidases are attractive therapeutic targets in different cancers and are being evaluated for clinical development. Ubiquitin-specific peptidase 37 (USP37) is one of the least studied members of the USP family. USP37 controls numerous aspects of oncogenesis, including stabilizing many different oncoproteins. Recent work highlights the role of USP37 in stimulating the epithelial-mesenchymal transition and metastasis in lung and breast cancer by stabilizing SNAI1 and stimulating the sonic hedgehog pathway, respectively. Several aspects of USP37 biology in cancer cells are yet unclear and are an active area of research. This review emphasizes the importance of USP37 in cancer and how identifying its molecular targets and signalling networks in various cancer types can help advance cancer therapeutics.

Keywords: Ubiquitin, Deubiquitylating enzymes, Ubiquitin-specific peptidase, Ubiquitin-specific peptidase 37, Oncogene, Epithelial–mesenchymal transition

Background

Cancer is characterized by the complex evolution of a healthy cell to a cancerous cell in which the gradual accumulation of mutations provides a survival advantage for growth and nutrition. Douglas Hanahan and Robert Weinberg first described the hallmarks of cancer in 2000 and later updated them in 2011 [1, 2]. These hallmarks of cancer comprise evading apoptosis, sustaining angiogenesis, being insensitive to antigrowth signals, developing limitless replicative potential, reprogramming energy metabolism, evading immune responses, acquiring genome instability, and promoting inflammation. They characterized the complexity of cancer and emphasized that treatment failure is related to unknown facets of cancer biology that drive the uncontrolled growth of cancerous cells. Because of advances in research methodologies and the emergence of new technologies, multiple factors controlling cancer cell evolution are being discovered, and posttranslational modifications of oncoproteins have emerged as an important factor for cancer cell evolution. These protein modifications include ubiquitinylation, Phosphorylation etc. which often occur in response to extracellular stimulus and reversal of these modifications also happens rapidly on the removal of stimulus. Ubiquitination refers to the covalent attachment of a 76 aa peptide to substrate proteins that control the half-life of proteins in a cell, coordinating the cellular localization

*Correspondence: mharis@sidra.org; mayank.osu@gmail.com
†Ajaz A. Bhat and Tariq Masoodi contributed equally to this work.
[1] Department of Medical Oncology (Lab), All India Institute of Medical Sciences, New Delhi, India
[2] Laboratory of Molecular and Metabolic Imaging, Cancer Research Department, Sidra Medicine, Doha, Qatar
Full list of author information is available at the end of the article