USP7

Ubiquitin-specific-processing protease 7, also known as ubiquitin carboxyl-terminal hydrolase 7 or herpesvirus-associated ubiquitin-specific protease, is an enzyme that in humans is encoded by the USP7 gene

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Dysregulation of these processes mediated by USP7 may contribute to many diseases, such as cancers. Moreover, USP7 with aberrant expression levels and abnormal activity are found in cancers. Therefore, given the association between USP7 and cancers, targeting USP7 could be considered as an attractive and potential therapeutic approach in cancer treatment. This review describes the functions of USP7 and the regulatory mechanisms of its expression and activity, aiming to emphasize the necessity of research on USP7, and provide a better understanding of USP7-related biological processes and cancer [1)]

Li et al. investigated the mechanism of ubiquitin-specific processing protease 7 (USP7) on the immune escape of glioma cells via the regulation of programmed cell death ligand-1 (PD-L1).

USP7 and PD-L1 expressions in glioma and normal brain tissues were detected using quantitative reverse transcriptase polymerase chain reaction and Western blot. The glioma cells U-251 MG were transfected with si-USP7 and pcDNA3.1-PD-L1 or treated with anti-PD-L1, after which the cell viability, colony-forming ability, and apoptosis rate were evaluated using cell counting kit-8, colony formation, and TdT-mediated dUTP nick-end labeling assays. Then, CD8+ T cells were purified, extracted, then co-cultured with U-251 MG cells. CD8+ T cell proliferation and the concentrations of interferon (IFN-γ), tumor necrosis factor (TNF)-α, transforming growth factor (TGF)-β, interleukin (IL)-1β, and IL-10 were verified using carboxyfluorescein succinimidyl amino ester proliferation assay and enzyme-linked immunosorbent assay. Afterward, the interaction between USP7 and PD-L1 and the ubiquitination level of PD-L1 were also assessed.

USP7 was highly-expressed and PD-L1 mRNA levels did not change, while PD-L1 protein levels were up-regulated in the glioma cells. Silencing USP7 in U-251 MG cells limited the growth of the glioma cells, promoted glioma cell apoptosis, and facilitated the proliferation of CD8+ T cells, thus inhibiting immune escape. USP7 stabilized PD-L1 expression through deubiquitination. PD-L1 overexpression reversed the inhibitory effect of silencing USP7 on the immune escape of glioma cells.

USP7 stabilized PD-L1 through deubiquitination and accelerated the immune escape of glioma cells [2)].

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Zhou L, Ouyang T, Li M, Hong T, Mhs A, Meng W, Zhang N. Ubiquitin-Specific Peptidase 7: A Novel Deubiquitinase That Regulates Protein Homeostasis and Cancers. Front Oncol. 2021 Nov 19;11:784672. doi: 10.3389/fonc.2021.784672. PMID: 34869041; PMCID: PMC8640129.
2)
Li B, Wang B. USP7 Enables Immune Escape of Glioma Cells by Regulating PD-L1 Expression. Immunol Invest. 2022 Jul 19:1-17. doi: 10.1080/08820139.2022.2083972. Epub ahead of print. PMID: 35852892.