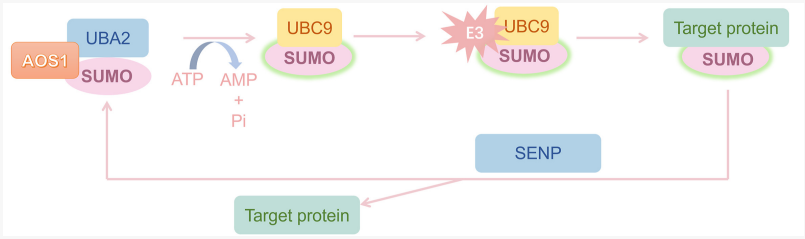
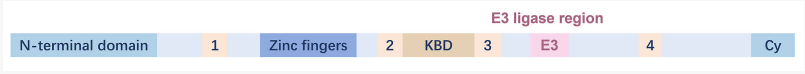
RANBP2: A Key Player in Solid Malignancies and Potential Therapeutic Target

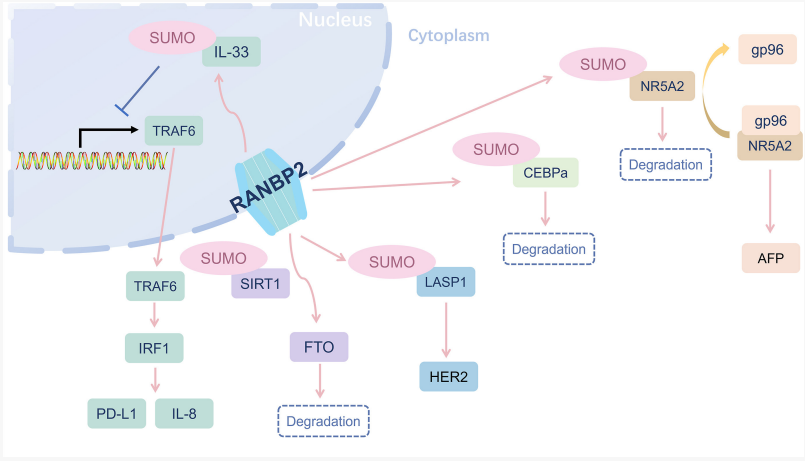
SHANNON, CLARE, IRELAND, May 12, 2025 /EINPresswire.com/ --
The nuclear pore complex protein RANBP2 has emerged as a critical factor in the development and progression of various solid malignancies. As a SUMO E3 ligase, RANBP2 plays a pivotal role in post-translational modification, specifically SUMOylation, which is essential for regulating the cell cycle. Recent insights have highlighted the multifaceted involvement of RANBP2 in tumorigenesis, suggesting its potential as a therapeutic target for cancer treatment.



The schematic model of the SUMOylation process.



The functional domains of RANBP2 (RAN binding protein 2) protein.



The molecular mechanism of RANBP2 in the development of hepatocellular carcinoma.

SUMOylation is a crucial process that influences oncogenes and other cell cycle regulators, making it highly relevant in cancer biology. Among the SUMO E3 ligases, RANBP2, located within the nuclear pore complex (NPC), has drawn particular attention due to its involvement in both nucleocytoplasmic transport and mitosis regulation. Its interaction with other cellular components and the modulation of protein SUMOylation have linked RANBP2 to numerous malignancies, including hepatocellular carcinoma (HCC), cholangiocarcinoma, gastric cancer, breast cancer, cervical cancer, and prostate cancer.

In HCC, RANBP2 influences the expression of HER2 through SUMOylation of LASP1, promoting cancer cell proliferation. Moreover, its interaction with NR5A2 modulates alpha-fetoprotein (AFP) levels, while its role in the SUMOylation of IL-33 impacts immune evasion. In cholangiocarcinoma, RANBP2-mediated SUMOylation of p27kip1 promotes tumor cell

proliferation by facilitating its nuclear translocation.

In gastric cancer, RANBP2 interacts with DAXX, promoting the nuclear localization of this protein, which correlates with poor prognosis. Meanwhile, in breast cancer, the SUMOylation of β-arrestin 2 by RANBP2 disrupts the MDM2-p53 signaling axis, thereby enhancing p53 activity and suppressing tumor growth. Additionally, in cervical cancer, RANBP2 enhances TCF4 activation through SUMOylation, facilitating the Wnt/β-catenin signaling pathway that drives tumor progression. In prostate cancer, RANBP2's regulation of p53 SUMOylation modulates androgen receptor-mediated pathways, affecting cancer proliferation.

Emerging research also associates RANBP2 with other solid tumors, including glioblastoma, oral cancer, colorectal cancer, and lung cancer. In glioblastoma, RANBP2's role in SUMOylation appears linked to DNA repair and chromatin organization, while in colorectal cancer, its depletion disrupts mitotic spindle stability, promoting apoptosis. In lung cancer, RANBP2's interaction with DNA Topoisomerase II hints at its involvement in maintaining genetic integrity during cell division.

Given its extensive involvement in multiple cancers, targeting RANBP2 could open new avenues for therapeutic intervention. However, the complexity of its interactions with various cellular mechanisms calls for further research to validate its role as a clinical target.

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