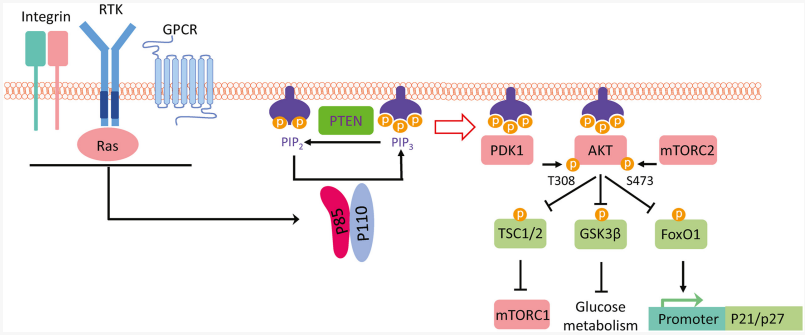
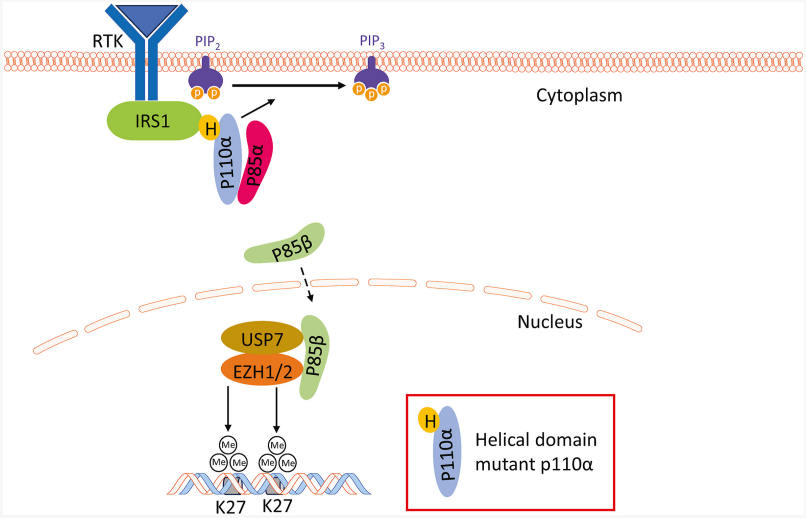
New Advances in Targeted Therapies for PIK3CA-Mutated Cancers

SHANNON, CLARE, IRELAND, February 25, 2025 /EINPresswire.com/ --
A newly published review in Genes & Diseases explores the oncogenic activation of PIK3CA in cancer and highlights emerging targeted therapies designed to improve treatment efficacy while reducing side effects. The research provides a comprehensive analysis of PIK3CA mutations, their role in tumor development, and novel therapeutic approaches currently in development.



PI3K signaling pathways. Upon activation by RTK, GPCR, Integrin, and Ras, p110 loses inhibition by p85 and converts PIP2 to PIP3.



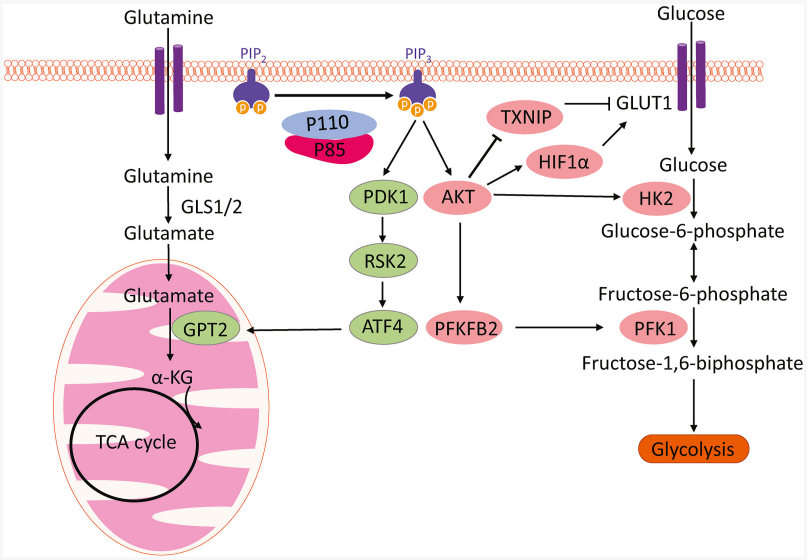
PIK3CA helical domain mutation rewires cell signaling.

The PIK3CA gene, which encodes the p110α subunit of phosphoinositide 3-kinase (PI3K), is among the most frequently mutated oncogenes in cancer. These mutations drive tumor progression, metabolic reprogramming, and resistance to existing treatments, making them a prime target for precision oncology. While current FDA-approved PI3Kα inhibitors, such as alpelisib, have demonstrated success in treating hormone receptor-positive (HR+) and HER2-negative (HER2-) breast cancer, their clinical effectiveness is often restricted by dose-limiting side effects, including hyperglycemia.

The review highlights next-generation therapies that specifically target PIK3CA mutations with improved selectivity and reduced toxicity. Several promising inhibitors, including RLY-2608, STX-478, and LOXO-783, have demonstrated potential in preclinical and clinical trials. These therapies aim to overcome the limitations of existing treatments by selectively inhibiting mutant PI3Kα without affecting normal PI3K activity, reducing adverse effects and enhancing patient

outcomes.

In addition to drug development, the study explores how PIK3CA mutations alter tumor metabolism, enhance immune evasion, and reshape the tumor microenvironment. These insights are paving the way for combination therapies that integrate PI3K inhibitors with immunotherapy and metabolic drugs to improve response rates and durability of treatment.



PIK3CA mutations reprogram cancer metabolism.

With continued advancements in precision oncology, PIK3CA-mutated cancers are now at the forefront of innovative treatment strategies. The development of mutant-selective therapies marks a significant step toward more effective and personalized cancer care.

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Reference
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