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Phosphoinositide 3-Kinases: From Retroviral Oncoproteins to Drug Targets

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PI3K signaling shows gain of function in numerous and diverse human cancers. The gene coding for the catalytic subunit p110 α of class IA PI3K frequently carries point mutations that map to one of three “hot spots” in the gene. p110 α proteins carrying one of these mutations show increased lipid kinase activity compared to wild type p110 α . The mutants also strongly stimulate Akt signaling and are oncogenic in cell culture and in the animal. The mutated p110 α proteins are ideal targets for small molecule inhibitors; they are cancer specific, they are enzymes, and they show gain of function.