Targeting AMPK to overcome resistance to anti-colorectal cancer drugs

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Video Byte

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Abstract

Antibody treatments such as cetuximab are powerful against colorectal cancer, but colorectal cancer cells are known to develop resistance to these drugs in large part due to overactivation or mutation of the gene KRAS. To understand how KRAS might give rise to cetuximab resistance, researchers treated two types of lab-grown cells with the antibody, normal cancer cells and cancer cells containing a mutated KRAS gene. They then monitored the effects on AMPK, an enzyme that is toxic to various cancer cells. KRAS mutation impaired this AMPK-based defense, enabling mutant cancer cells to outlive normal cancer. Exposing cells with drugs known to activate AMPK, such as metformin, recovered the anti-cancer defense, overcoming the cetuximab resistance induced by a mutated KRAS gene. That same mechanism was observed in colorectal tumors grafted onto mice. The results indicate that targeting AMPK could be a powerful therapeutic strategy, possibly boosting anti-cancer defenses in patients with colorectal cancer.