PIM–LKB1 crosstalk regulates AMPK phosphorylation and tumorigenic growth

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Video Byte

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Abstract

Oncogenic PIM kinases and the tumor suppressor LKB1 regulate cell growth and metabolism in different directions. LKB1 suppresses tumorigenesis largely by phosphorylating and activating the energy sensing kinase AMPK. Anti-oncogenic PIM inhibitors also increase AMPK phosphorylation. However, the exact mechanism by which PIM inhibition affects AMPK remains unclear. A recent study explored the potential PIM-LKB1 interaction related to AMPK phosphorylation in prostate (PC3) and breast (MCF7) cancer cells. Inhibition of activity (by DHPCC9 or AZD1208) or expression (by triple knockout, TKO) of all three PIM kinases increases AMPK phosphorylation. These effects are LKB1-dependent, suggesting that PIM kinases regulate AMPK via LKB1. Additional assays confirmed that PIM kinases phosphorylate LKB1 to inactivate it, identifying LKB1 as a novel PIM substrate. In a chick embryo xenograft model, LKB1 knockout increased tumorigenic growth of prostate cancer cells. Concurrent PIM knockout eliminated this effect, while PIM overexpression exacerbated it, indicating that PIM and LKB1 cooperate to regulate tumorigenesis. Although further research is needed to determine the downstream effects, the findings indicate crosstalk of PIM and LKB1 in the context of cancer and suggest that PIM inhibition is a rational strategy for restricting growth of LKB1-deficient tumors.