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Hedgehog Signaling In Prostate Regeneration, Neoplasia and Metastasis

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Abstract:

Metastatic cancers adopt certain properties of normal cells in developing or regenerating organs, such as the ability to proliferate and alter tissue organization. We find here that activity of the Hedgehog (Hh) signalling pathway, which has essential roles in developmental patterning, is required for regeneration of prostate epithelium, and that continuous pathway activation transforms prostate progenitor cells and renders them tumorigenic. Elevated pathway activity furthermore distinguishes metastatic from localized prostate cancer, and pathway manipulation can modulate invasiveness and metastasis. Pathway activity is triggered in response to endogenous expression of Hh ligands, and is dependent upon the expression of Smoothened, an essential Hh response component that is not expressed in benign prostate epithelial cells. Monitoring and manipulating Hh pathway activity may thus offer significant improvements in diagnosis and treatment of prostate cancers with metastatic potential.