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Topic: SIGNALING AND EPIGENETICS IN CANCER

IGF1R signaling induces epithelial-mesenchymal plasticity via ITGAV in cutaneous squamous cell carcinoma

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Cutaneous squamous cell carcinoma (cSCC) is the second most prevalent human skin cancer. Early sCCs (WD- and MD-SCCs) show epithelial differentiation features and good prognosis, whereas advanced cSCCs (PD/S-SCCs) acquire mesenchymal traits associated with tumor relapse, therapy resistance, metastasis, and poor survival. Currently, the mechanisms involved in cSCC progression are unclear, and the established markers are suboptimal for accurately predicting the clinical course of the disease. Here, we observe that PD/S-SCCs are generated by the malignant advance of WD-SCCs, in a process in which epithelial cancer cells acquire plasticity to switch to the mesenchymal state. Characterization of preclinical models of cSCC shows that epithelial cancer cells expressing integrin ?V (ITGAV) promote the cSCC progression to a mesenchymal state. Consistently, ITGAV expression allows the identification of patients at risk of cSCC relapse above the currently employed clinical histopathological parameters. We also demonstrate that insulin-like growth factor-1 receptor (IGF1R) activation in epithelial cancer cells triggers epithelial-mesenchymal plasticity (EMP) and mesenchymal state acquisition through ITGAV. Collectively, our results demonstrate that ITAGV is a prognostic biomarker of relapse in cSCCs that would allow improved patient stratification. ITGAV also collaborates with IGF1R to induce EMP and cSCC progression, revealing a potential therapeutic strategy to block the generation of advanced mesenchymal cSCCs.