

Chronic TGF- β exposure drives stabilized EMT, tumor stemness, and cancer drug resistance with vulnerability to bitopic mTOR inhibition

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Revisiting TGF- β and EMT

During cancer progression, cells gain the ability to move, invade, and adapt. Cells may gain these abilities through a process called "EMT" (epithelial-to-mesenchymal transition) that allows them to acquire properties of cancer stem-like cells (CSCs). Signaling by the growth factor TGF- β majorly contributes to EMT (see also the Review by Derynck and Budi), and EMT is generally accepted to be reversible as largely assessed in cell culture. To better mimic the patient context, Katsuno *et al.* examined EMT and tumor progression in cells that were exposed to TGF- β for far longer than traditional studies (weeks rather than days) and found that long-term exposure caused a stable transition that was not reversed by TGF- β withdrawal but in which major CSC-associated traits were reversed by a new-generation inhibitor of the kinase mTOR. The findings, extended to metastatic breast cancer models in mice, not only identify a potential therapy for aggressive carcinomas but also reveal the need to use more physiologically relevant models to better understand tumor biology.

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