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Active CREB1 Promotes a Malignant TGFB2 Autocrine Loop in Glioblastoma .......... 1230
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Précis: TGFB activates CREB1- and SMAD3-dependent TGFB2 transcription and hyperactivation of TGFB signaling in human glioblastoma cell lines and tumors.
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Smith, Sanchez-Laorden, and colleagues found that macrophage-derived TNFα was required for BRAFV600E-positive melanoma cell survival and protected these cells from MEK inhibitor (MEKi)-induced cell death via NFκB-dependent upregulation of microphthalmia-associated transcription factor (MITF). MEK/BRAF inhibitor treatment increased tumor-associated macrophage recruitment and TNFα and MITF expression in BRAF-mutant melanomas. Intriguingly, dual treatment with IκB kinase inhibitors (IKKi) and MEKi suppressed both macrophage-derived TNFα expression and MITF expression in melanoma cells and resulted in enhanced inhibition of tumor growth in mice. These findings highlight the role of the immune microenvironment in MAPK inhibitor resistance and suggest that IKKi therapy may improve the efficacy of MAPK pathway inhibitors by preventing TNFα-mediated resistance. For details, please see the article by Smith, Sanchez-Laorden, and colleagues on page 1214.

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