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Précis: ERCC2 is somatically mutated in patients with urothelial carcinoma who exhibit complete response to cisplatin, and may be a predictive biomarker of clinical benefit from neoadjuvant chemotherapy.

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Précis: High levels of activated NOTCH1 and expression of the target gene HES4 are correlated with a robust response to NOTCH pathway inhibition with gamma-secretase inhibitors in NOTCH1-mutant 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 NFB-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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