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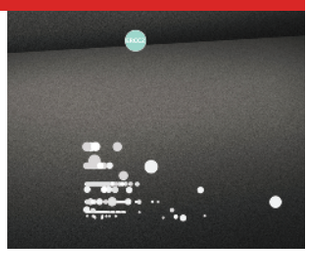
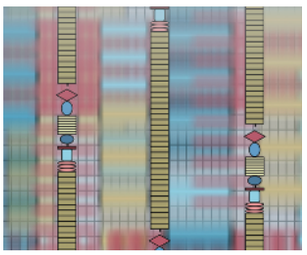
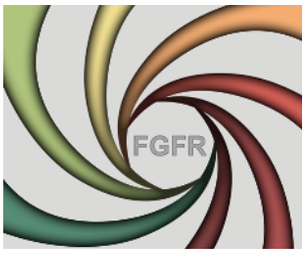

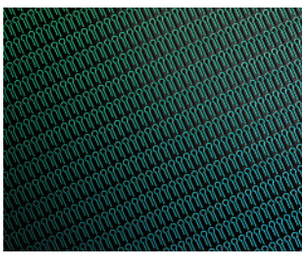

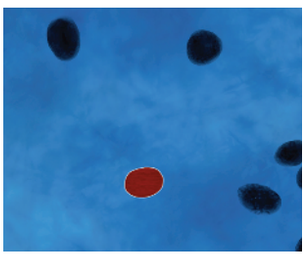
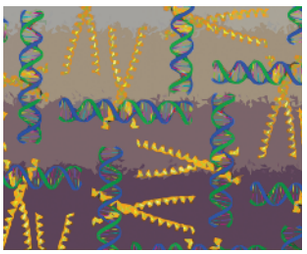

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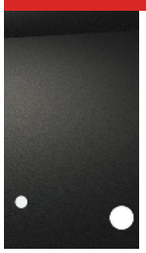
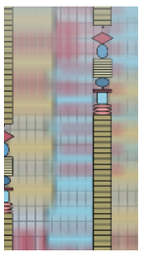
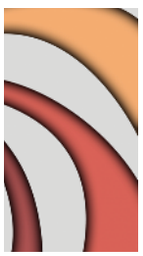
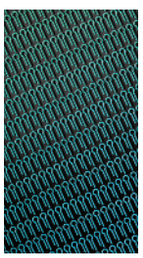

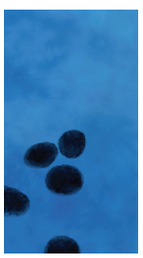
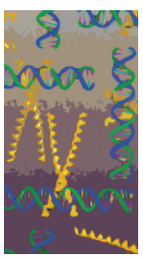

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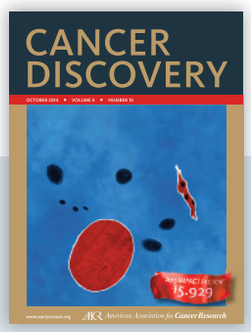

ON THE COVER Smith, Sanchez-Laorden, and colleagues found that macrophage-derived TNFα was required for *BRAF*^{V600E}-positive melanoma cell survival and protected these cells from MEK inhibitor (MEKi)–induced cell death via NFκB-dependent upregulation of microphthalmia-associated transcription factor (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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