Overcoming anti-melanoma drug resistance with reverse transcriptase inhibitors (RTIs)

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Abstract

Combination therapy with BRAF and MEK inhibitors have become the standard of care for patients with metastatic melanoma harboring BRAF mutations. But one persistent problem is the emergence of drug resistance. A new study reports that one way to overcome this obstacle could be the incorporation of reverse transcriptase inhibitors, or RTIs. RTIs target genetic elements called retrotransposons, which are activated by tumor formation and have been frequently used in treating HIV. Combining the RTI SPV122 with BRAF and MEK inhibitors was shown to have a favorable effect against BRAF-mutant melanoma, inhibiting cell growth, inducing cell death through apoptosis, and delaying the emergence of drug resistance. Further experiments revealed the RTI mechanisms giving rise to these effects, including DNA double-strand breaks, mitochondrial membrane depolarization and increased levels of reactive oxygen species. The results offer new insights into the anti-cancer mechanisms of RTIs and could lead to new, powerful therapies against melanoma.