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Précis: A DNA damage–induced alternative splicing pathway that includes induction of the β isoform of TP53 as a mediator of damage-induced cellular senescence.

Correction

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Using acute myeloid leukemia (AML) patient-derived xenografts, Farge and colleagues investigated the molecular mechanisms underlying resistance to the chemotherapeutic cytarabine (AraC) in vivo. Previous reports suggested that a refractory quiescent leukemic stem cell (LSC) population underlies AraC resistance, but AraC treatment unexpectedly reduced the number of LSCs as well as mature AML cells, indicating that AraC resistance is not mediated by LSCs. Instead, AraC induced chemoresistance by selecting for a preexisting population of resistant cells that exhibited enhanced oxidative phosphorylation (OXPHOS). AraC-resistant cells showed elevated mitochondrial respiration, and blocking OXPHOS increased AraC sensitivity. Together, these findings demonstrate that high OXPHOS activity is associated with chemoresistance in AML and suggest the possibility that therapeutic targeting of mitochondrial metabolism may enhance chemosensitivity. For details, please see the article by Farge and colleagues on page 716.