Splice Modulation Synergizes Cell Cycle Inhibition.

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Public Summary:
While recognized as a therapeutic target, the spliceosome may offer a robust vector to improve established therapeutics against other protein targets. Here, we describe how modulating the spliceosome using small molecule splice modulators (SPLMs) can prime a cell for sensitivity to a target-specific drug. Using the cell cycle regulators aurora kinase and polo-like kinase as models, this study demonstrates how the combination of SPLM treatment in conjunction with kinase inhibition offers synergy for antitumor activity using reduced, sublethal levels of SPLM and kinase inhibitors. This concept of splice-modulated drug attenuation suggests a possible approach to enhance therapeutic agents that have shown limited applicability due to high toxicity or low efficacy.

Scientific Abstract:
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