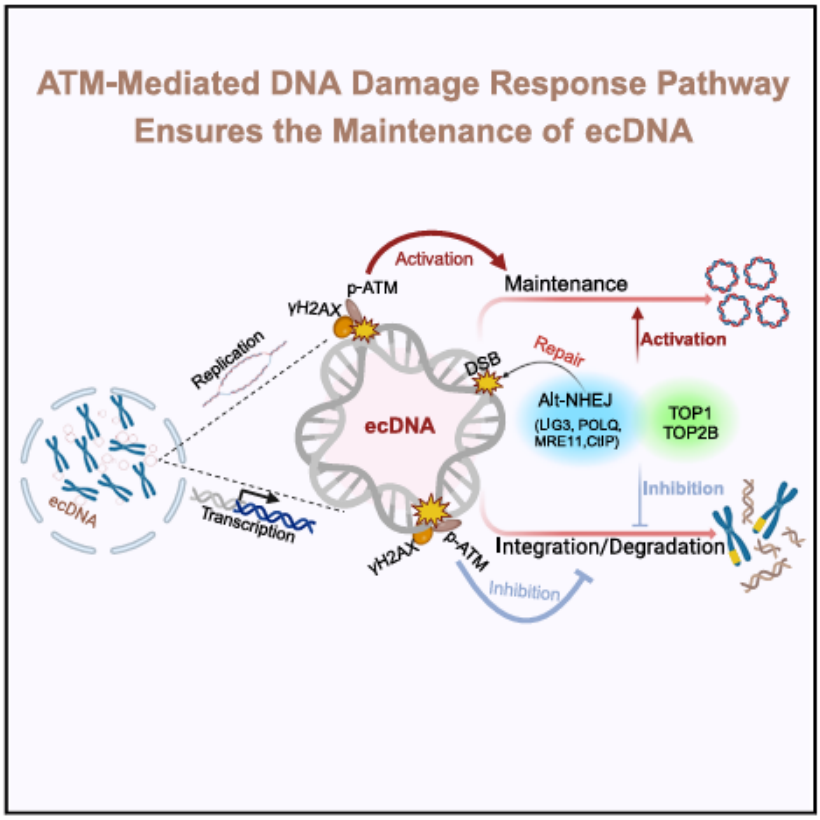
Article

Cell

Extrachromosomal DNA replication and maintenance couple with DNA damage pathway in tumors

Graphical abstract



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In brief

This study demonstrates that extrachromosomal DNA (ecDNA) replication induces DNA double-strand breaks and activates the DNA damage response (DDR). The DDR pathways, such as alt-NHEJ, are critical for ecDNA maintenance in tumor cells. Mechanistic insights into ecDNA replication and maintenance unveil a therapeutic approach for treating tumors harboring ecDNA.

Highlights

- ecDNA replication-dependent activation of ATM and DDR ensures ecDNA maintenance
- TOP1 and TOP2B are critical regulators of ecDNA-induced DDR
- Alt-NHEJ pathway promotes ecDNA maintenance
- ATM-mediated DDR is a promising therapeutic target for treating ecDNA+ tumors

Kang et al., 2025, Cell *188*, 1–17
June 26, 2025
https://doi.org/10.1016/j.cell.2025.04.012

CellPress