DPY30 loss leads to DNA re-replication and immunoediting in pancreatic ductal adenocarcinoma

1. DPY30 expression associates with poor prognosis

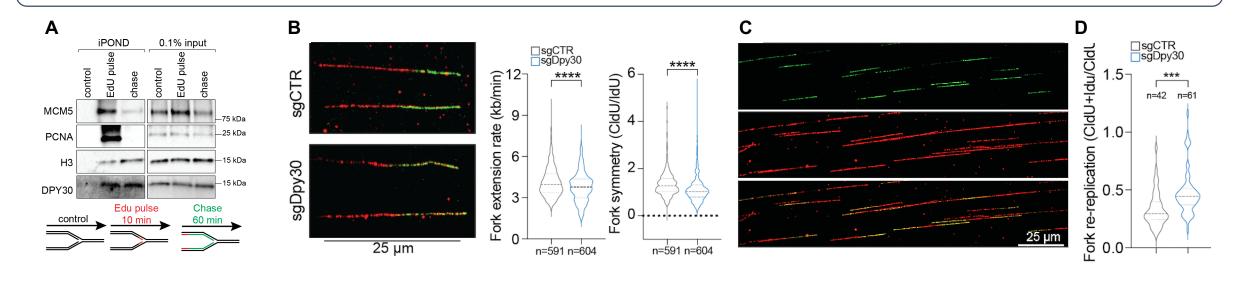
WDR5 RBBP5 ASH2L DPY30 WDR5 low WDR5 high Probability of Survival HR 1.378-0.723 HR 0.693-1.444 1000 1500 2000 1000 1500 2000 1000 1500 2000 1000 1500 2000 days days days days Ε **PDAC** metaplasia **PanIN** anaplastic PDAC normal

2. In mouse model of PDAC, DPY30 expression associates with tumor grade

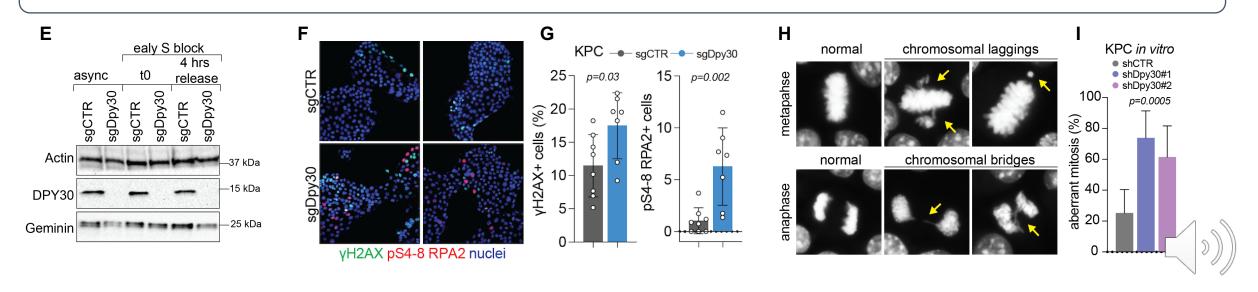


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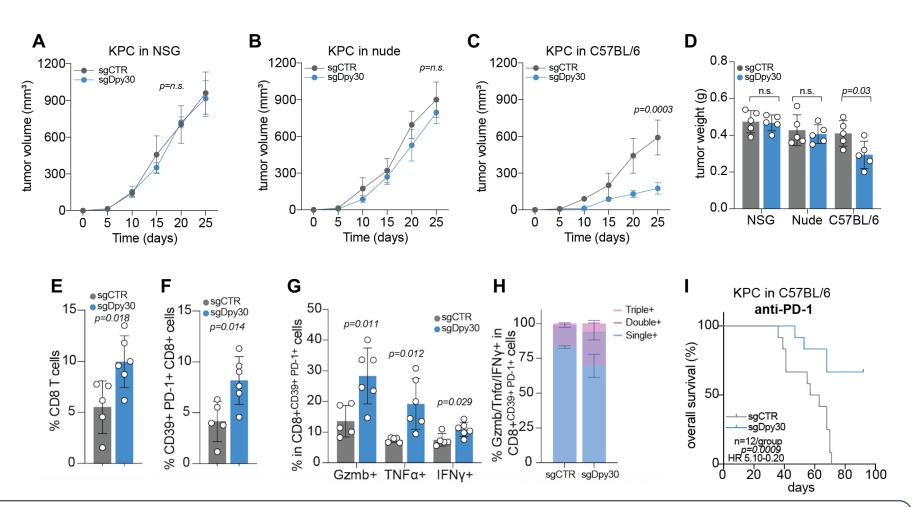
3. DPY30 loss favorites uncoordinated DNA replication



4. DPY30 loss induces DNA damage and chromosomal instability



5. DPY30 loss impairs tumor growth only in immune-competent mice



6. DPY30 knockout tumors display higher CD8+ T cell infiltration and respond better to anti-PD-1

Conclusions: our findings indicate that, in PDAC, DPY30 promotes genome stability, thus providing a rationale for targeting DPY30 or its effector proteins in combination with immune-checkpoint inhibitors.

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