

B



# Figure S1

Days







Α













В





- DMSO 0.01%  $\star$
- **MEKi**
- CDK4i
- MEKi+CDK4i
- S6K1i ▼
- MEK+S6K1i •
- CDK4i+S6K1i 0
- MEKi+CDK4i+S6K1i

B

Α

WM1366<sup>E545K</sup> 1/ (% CFSE retaining cells) b 99 08 00 0-20 100 0 0 00 2º Time (h)

- DMSO 0.01%  $\star$
- MEKi
- CDK4i
- MEKi+CDK4i
- S6K1i
- MEK+S6K1i ٠
- CDK4i+S6K1i 0
- MEKi+CDK4i+S6K1i





С SB2 PIK3CA-WT 40 -Caspase 3/7 (FU) 30 20 10-0 **MEK162** + + + -+ \_ LEE011 + + + PF-4708671 + +

D



















С



#### SB2-E545K

## TUNEL

Vehicle

# MEKi+CDKi

S6Ki







DAPI



#### SB2-GFP

### TUNEL



DAPI

