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Molecular & Experimental Surgery

Progenitor cells from gene-engineered human induced pluripotent stem cells as synthetic cancer alternatives

Background:

Recent studies revealed limitations in genetic stability and recapitulating accurate pathophysiological properties of patient-derived (PD) cancer models opposing challenges for reproducible and translational research. Recent studies revealed limitations in genetic stability and recapitulating accurate pathophysiological properties of patient-derived (PD) cancer models opposing challenges for reproducible and translational research. In an attempt to develop functional cancer test systems in alternative to PD models, we have genetically engineered a portfolio of isogenic human induced pluripotent stem cells with different pan-cancer relevant onco-protein signatures.

Results:

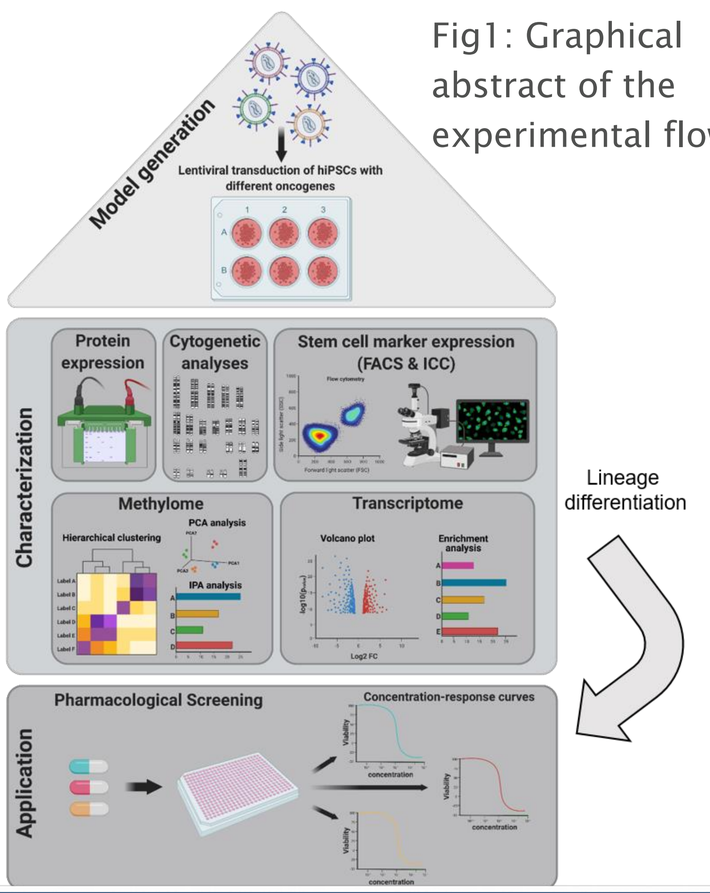

Fig1: Graphical abstract of the experimental flow

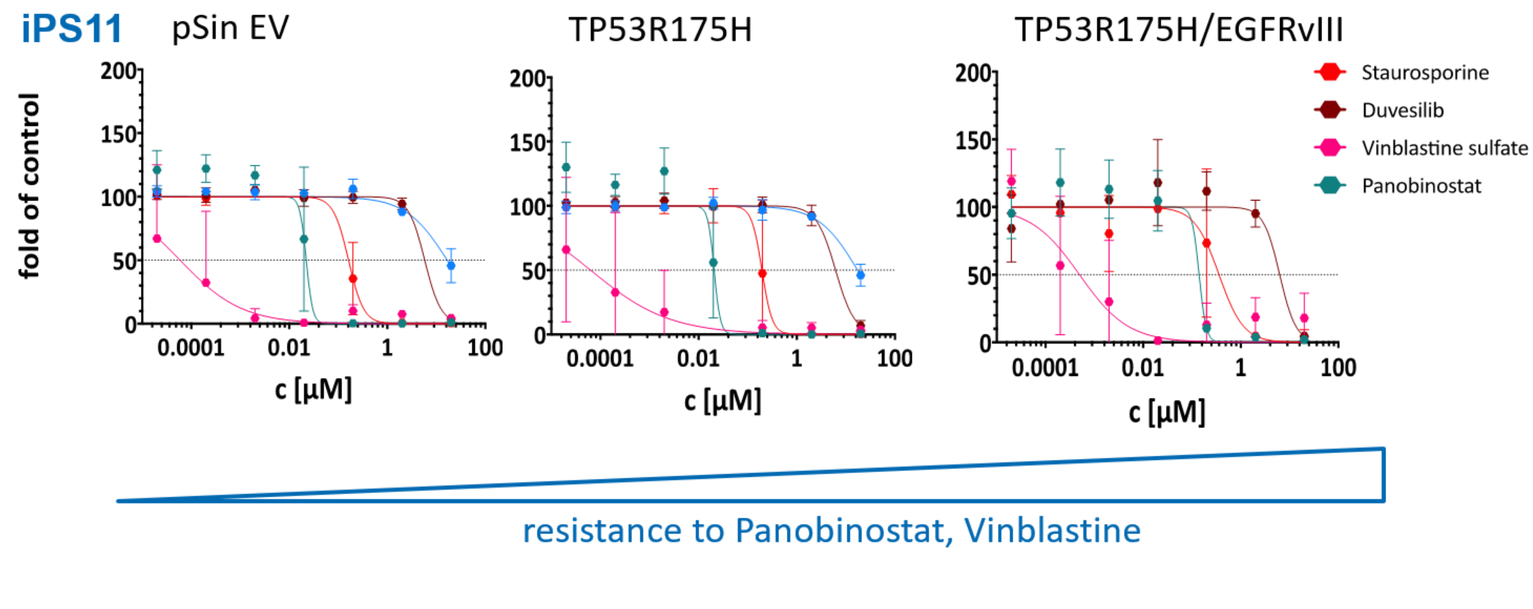

Fig4: Identification of altered resistance levels towards substance interventions in a highly biomarker-specific, isogenic controlled conditions

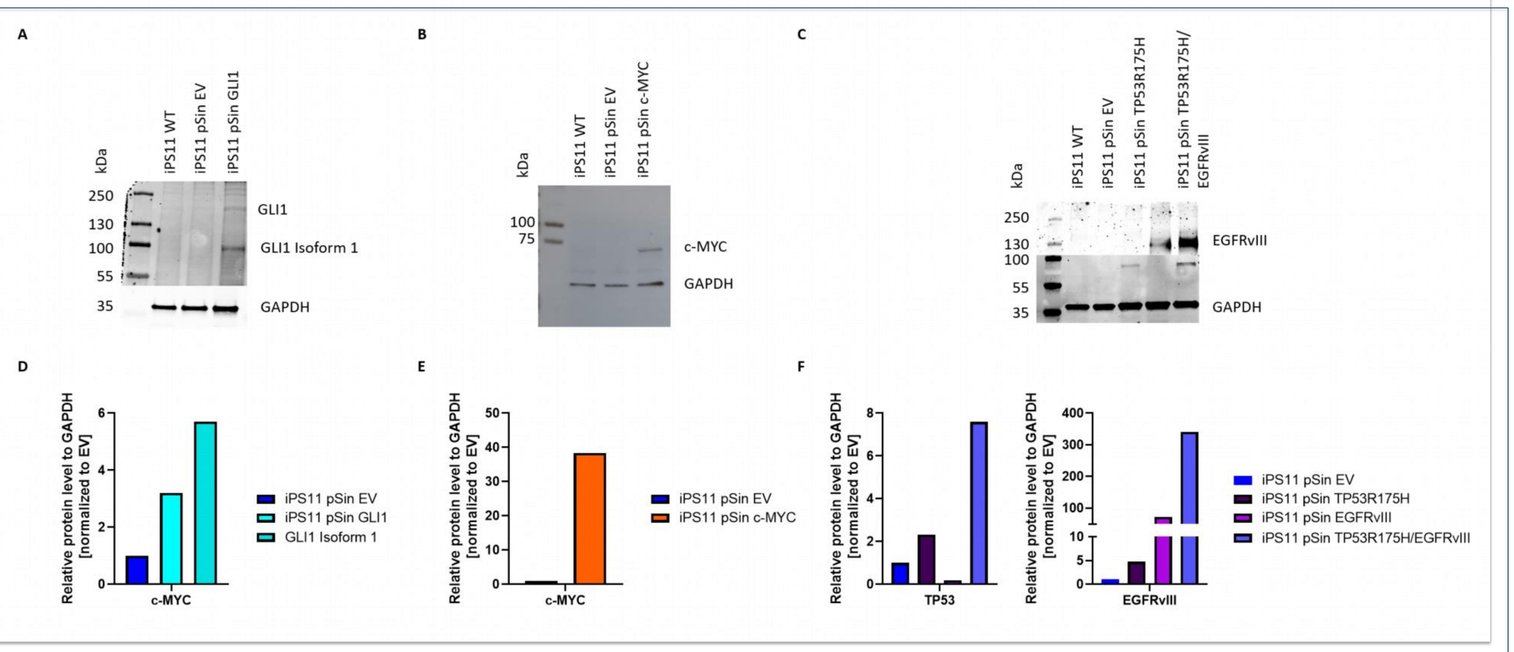

Fig2: Protein-level validation of stable oncogene activation in human induced pluripotent stem cells (hiPSC, commercial cell lines)

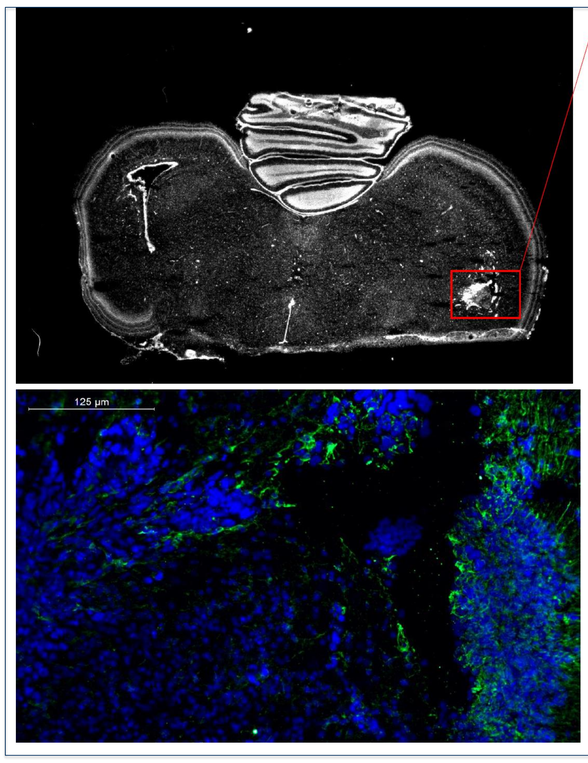

Fig5: *In vivo* tumor formation capacity assays (chicken embryo, green GFAP staining)

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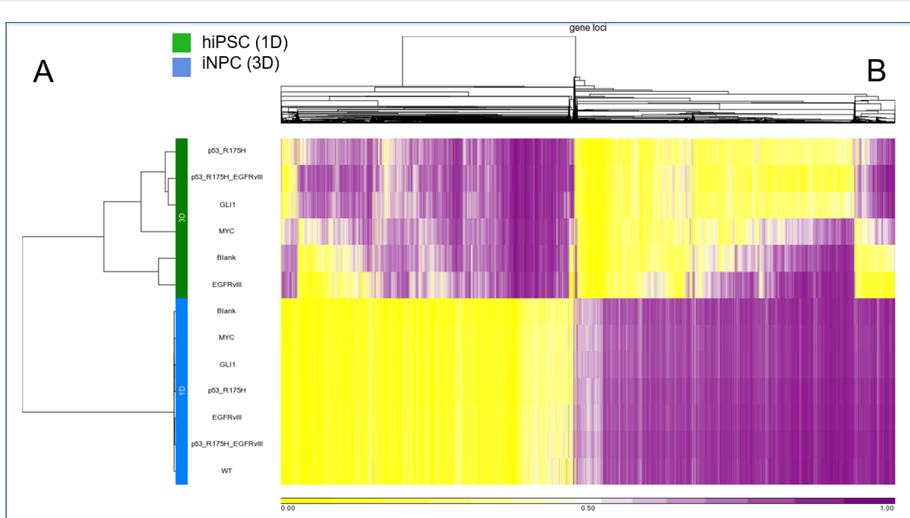

Fig3: Differentiation in tissue-specific progenitors (in this case neural differentiation) meanwhile maintaining stable oncogene expression

model	PAX6	OCT3/4	Nestin
NPC-EV	50.8	7.9	78.4
NPC-c-Myc	68.8	7.6	89.2
NPC-Gli1	26.5	74.2	97.4
NPC-TP53R175H	62	58.2	94.5
NPC-EGFRvIII	50.5	15.3	91.8
NPC-EGFRvIII/TP53R175H	47.3	33.8	88.1

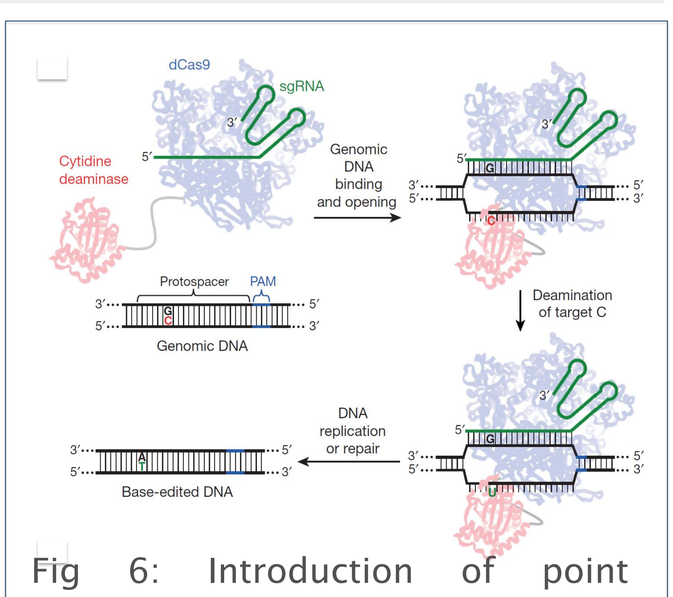

Fig 6: Introduction of point mutations via base-editing, *adjusted after Komor et al., 2016*

References:

[1] Uhlmann et al., 2022;
[2] Kahn et al., 2021;