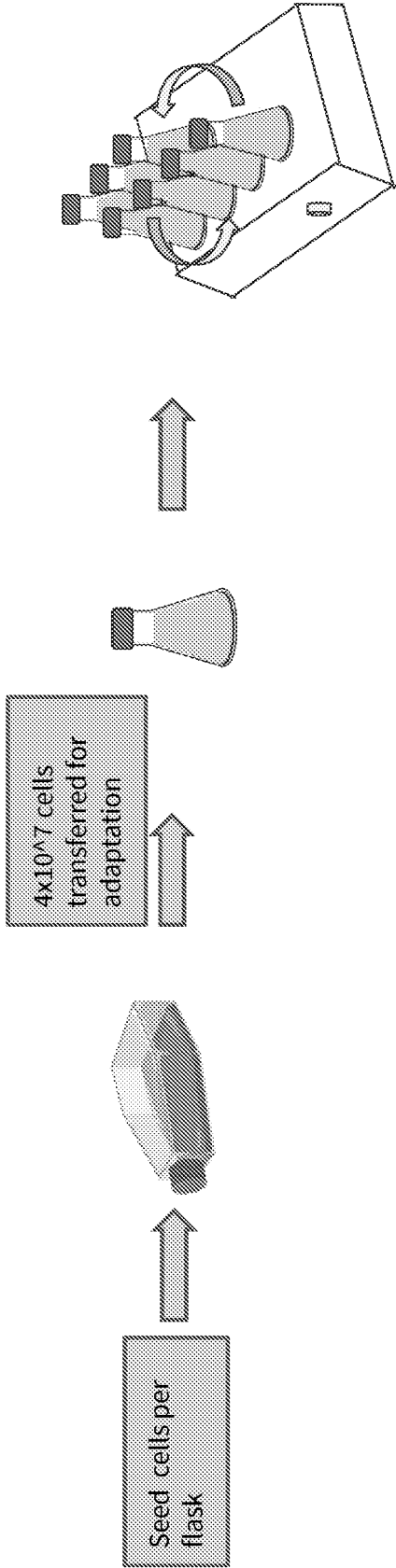


FIG. 1
Adaptation workflow and media



Seed culture and Pooling of CL from same genetic edit

Start Adaptation
Shake Flask
Suspension media

Continue Adaptation
Over 6-8 weeks with weekly trypsinization and sampling.

FIG. 2

Parent (Gen 2)	Gen 3 Edits	Targeting
CL115 Fibroblast -TERT-overexpression, -p53 KO	CASP3-KO	Apoptosis (mitochondrial apoptosis p'way)
	CASP8-KO	Apoptosis (mitochondrial apoptosis p'way)
	PTEN-KO	Suspension (causes apoptosis from cell detachment)
	CDH1-KO (cadherin-1)	Proliferation/suspension (cell-cell adhesion), may help with clumping in suspension

FIG. 3

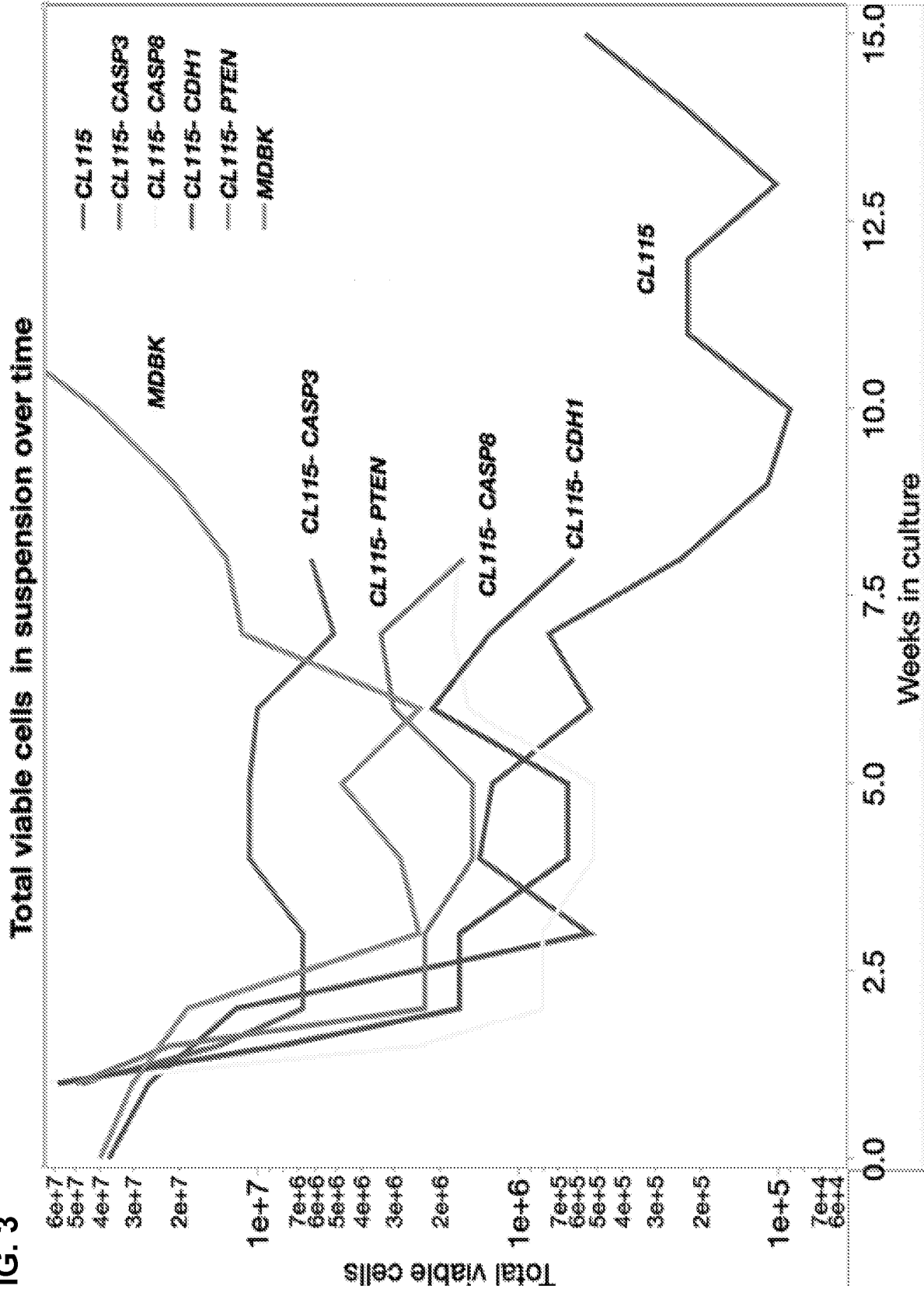


FIG. 4

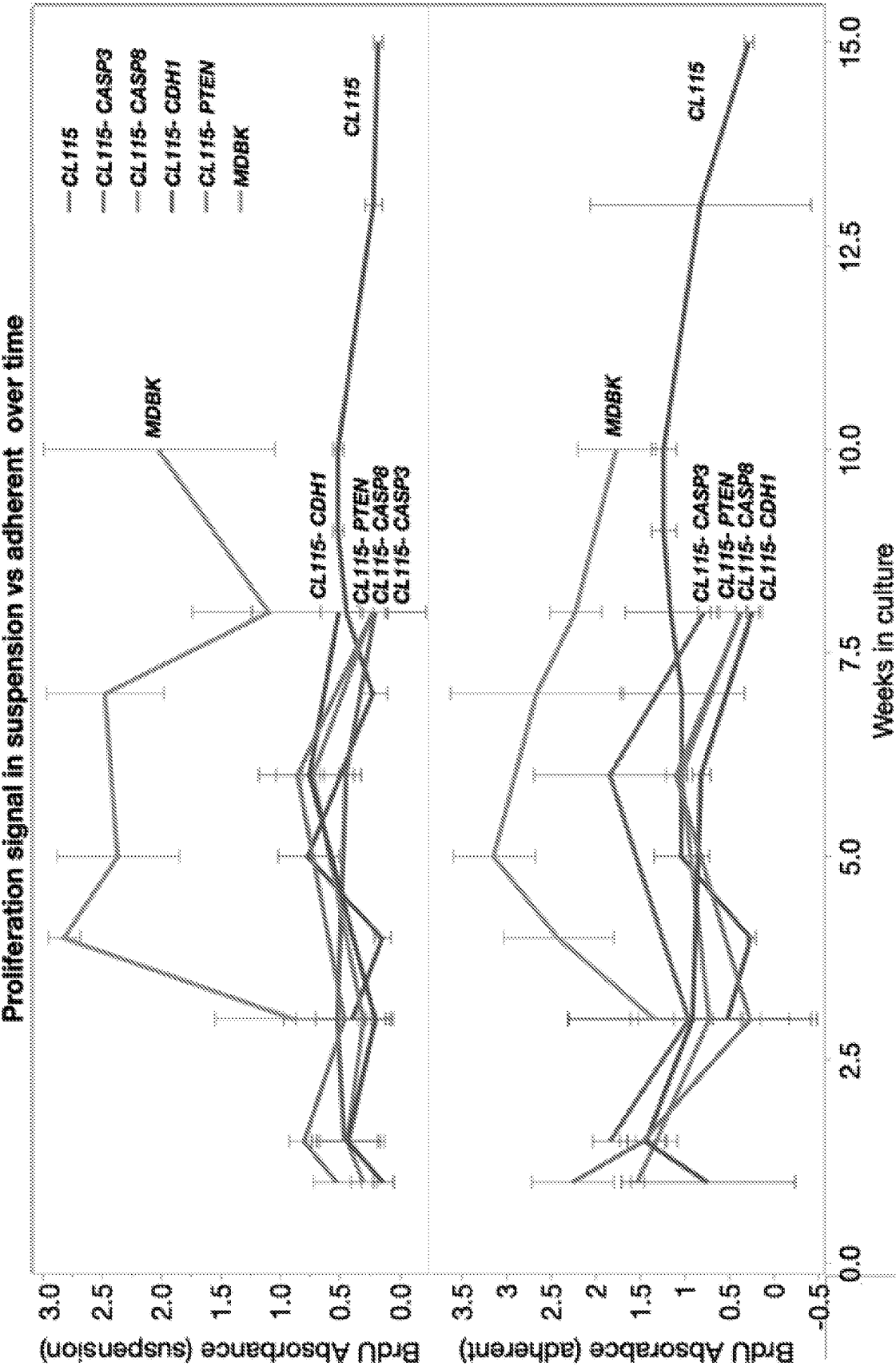
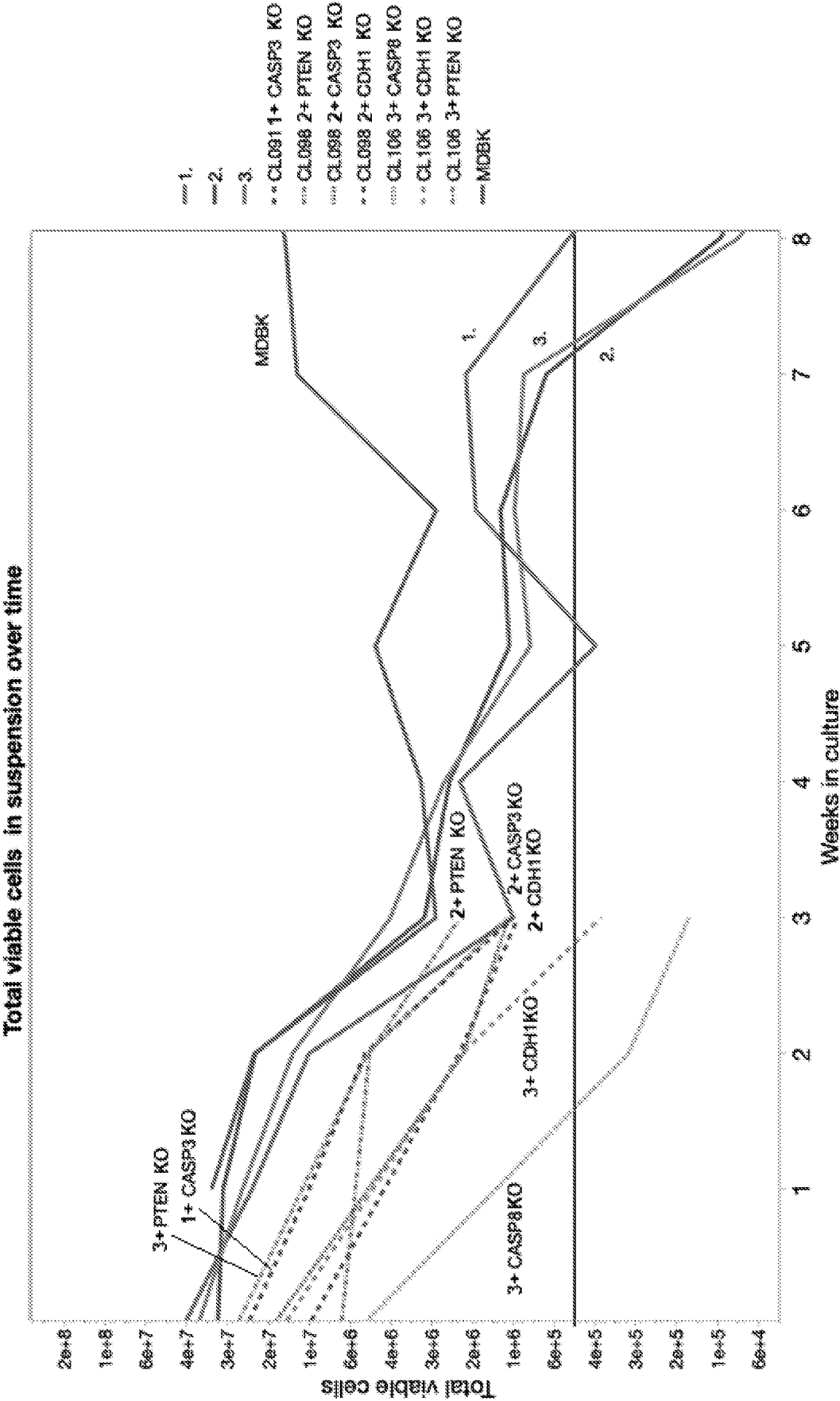


FIG. 5

Parent (Gen2)	Gen 3 Edits	Gen 4 Edits
CL050 myoblast -TERT-over-expression -p53-KO	Gene#1 KO (CL091, 093, 094)	1. CASP3* 2. CDH1 3. CASP8 4. PTEN
	Gene#2 KO (CL098, 099,113)	1. CASP3* 2. CDH1* 3. CASP8 4. PTEN*
	Gene#3 KO (CL 100, 101, 102)	1. CASP8 2. CASP3 3. CDH1
	Gene#4 (CL 103, 104, 105, 106, 107)	1. CASP3 2. CDH1* 3. CASP8* 4. PTEN*

*Confirmed for suspension culture

FIG. 6 Gen 4 (CLO50 derived) cell lines Results



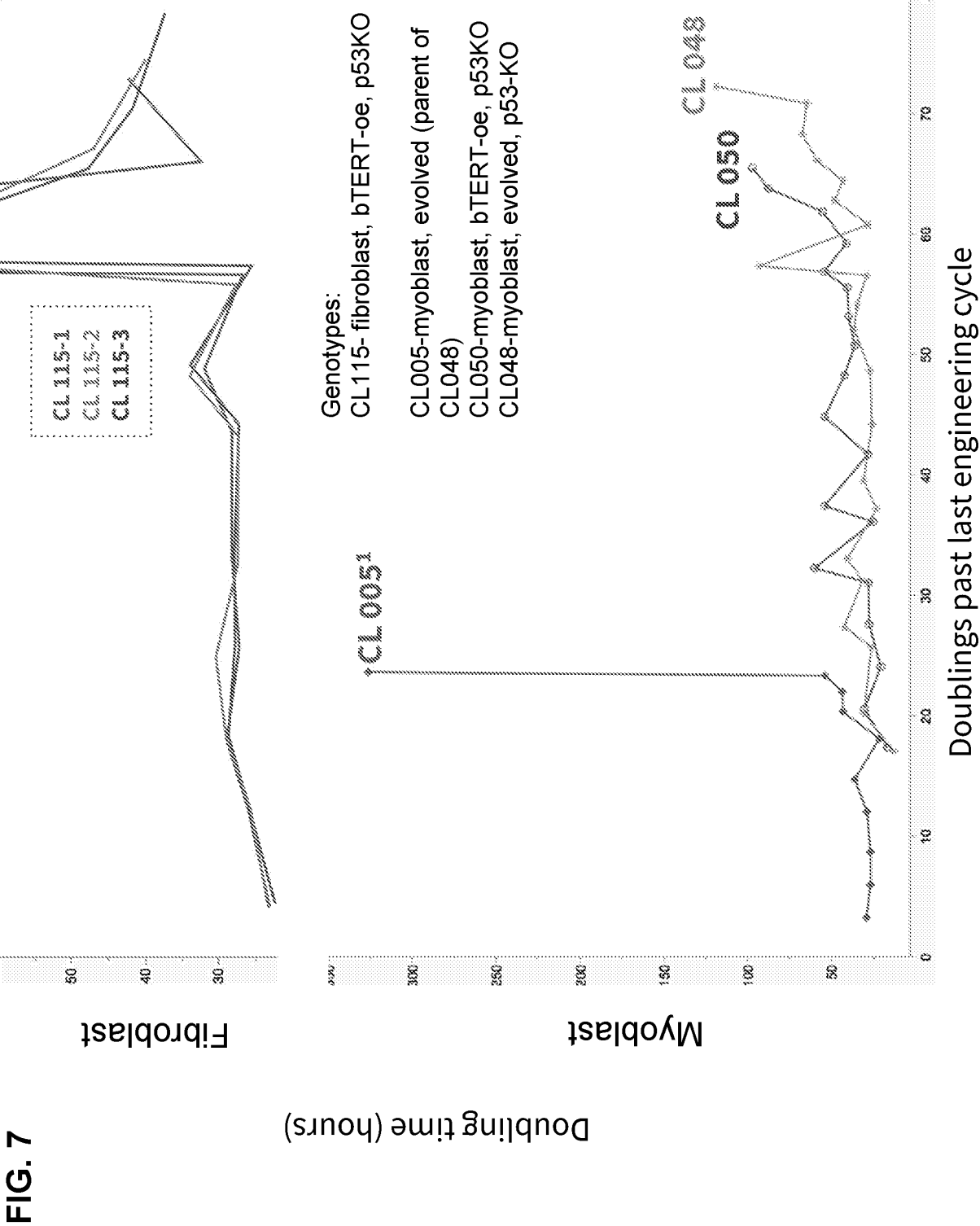
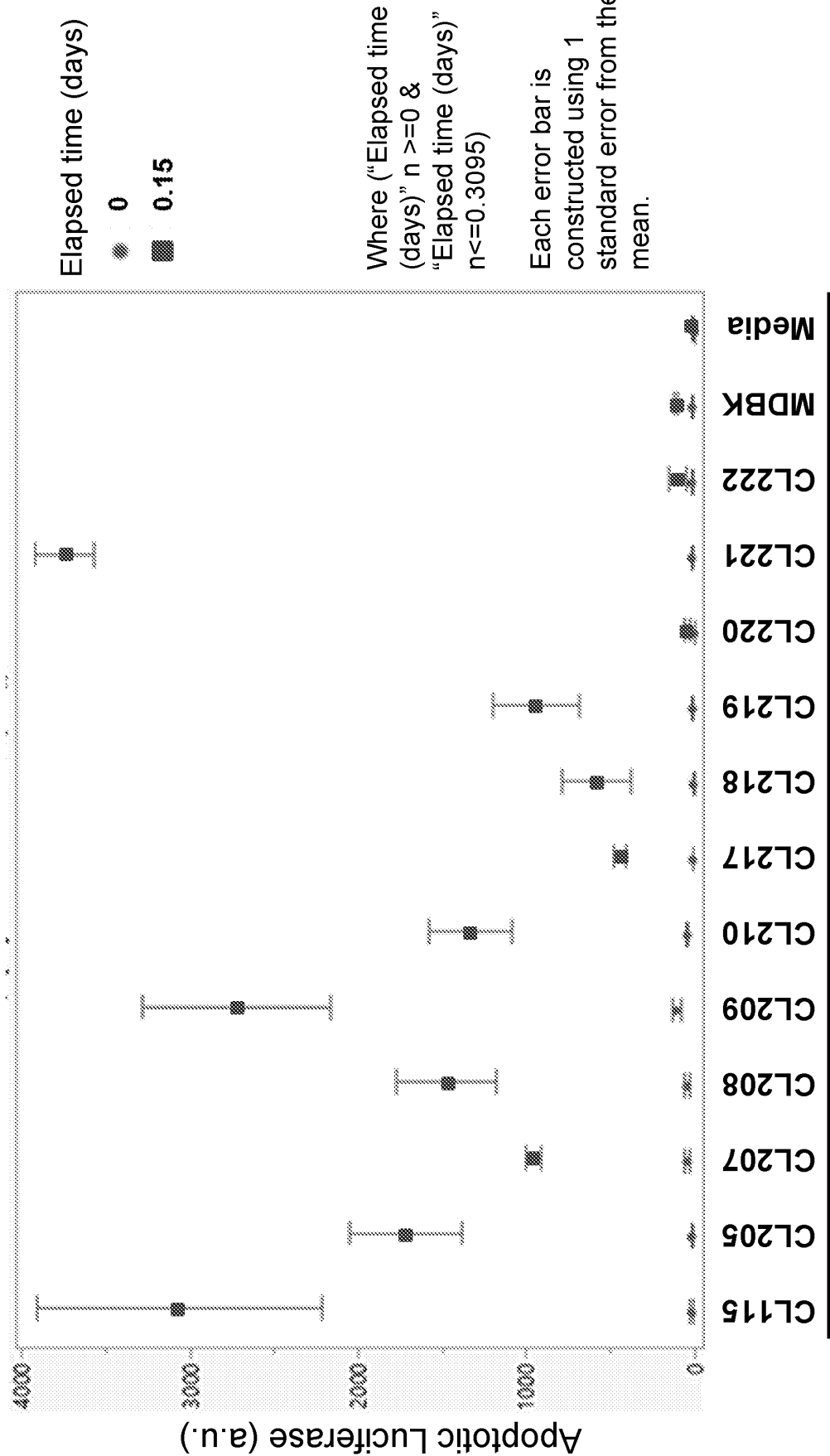


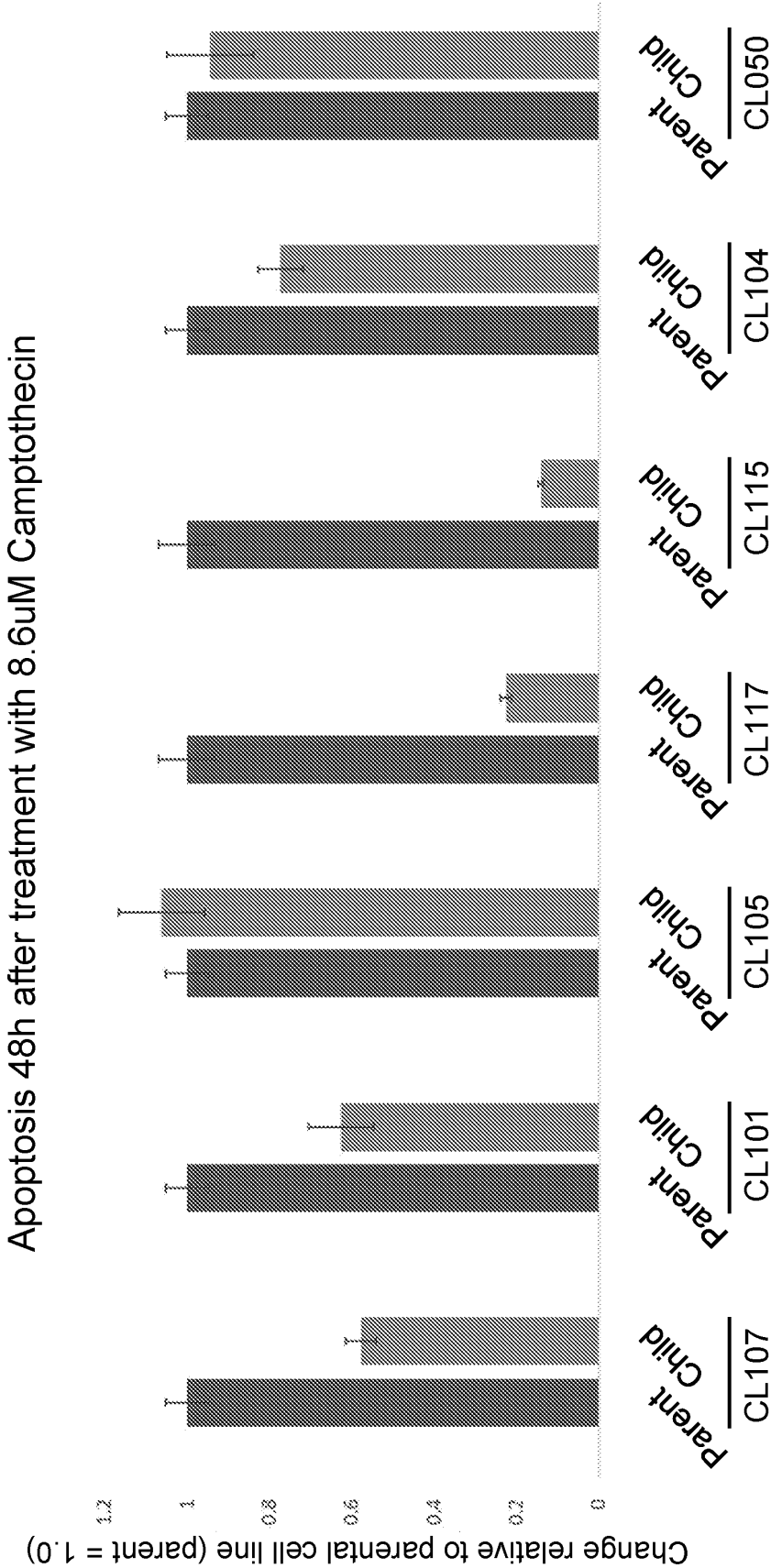
FIG. 8A



Where ("Elapsed time (days)" n >=0 & "Elapsed time (days)" n <=0.3095)

Each error bar is constructed using 1 standard error from the mean.

FIG. 8B



CL115, CL117 (fibroblast, TERT-oe, p53-KO)
CL050 (myoblast, TERT-oe, p53-KO); CL050 is the parent of CL101-CL107
Data are normalized to the parent for each cell line.

FIG. 9A

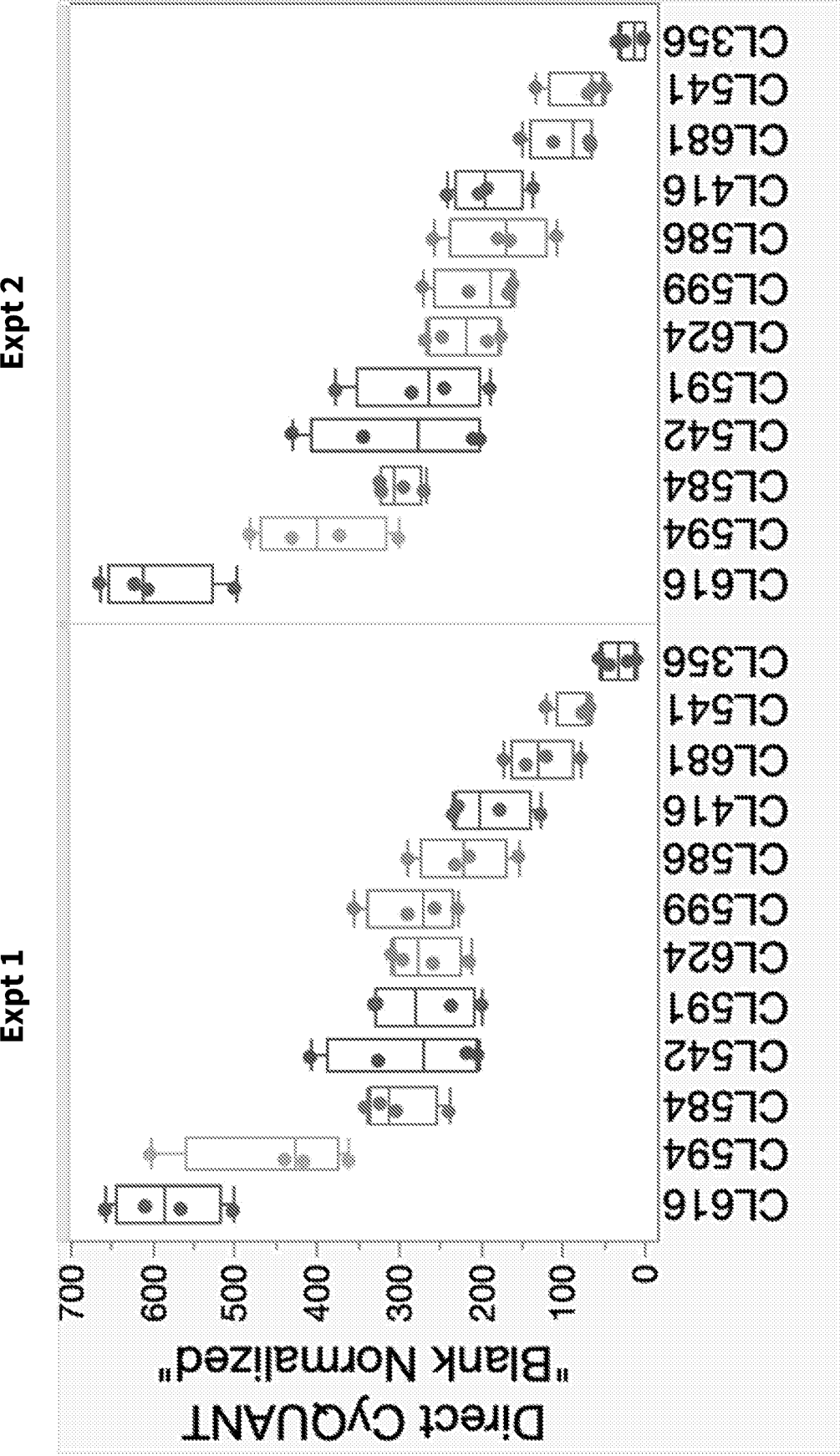
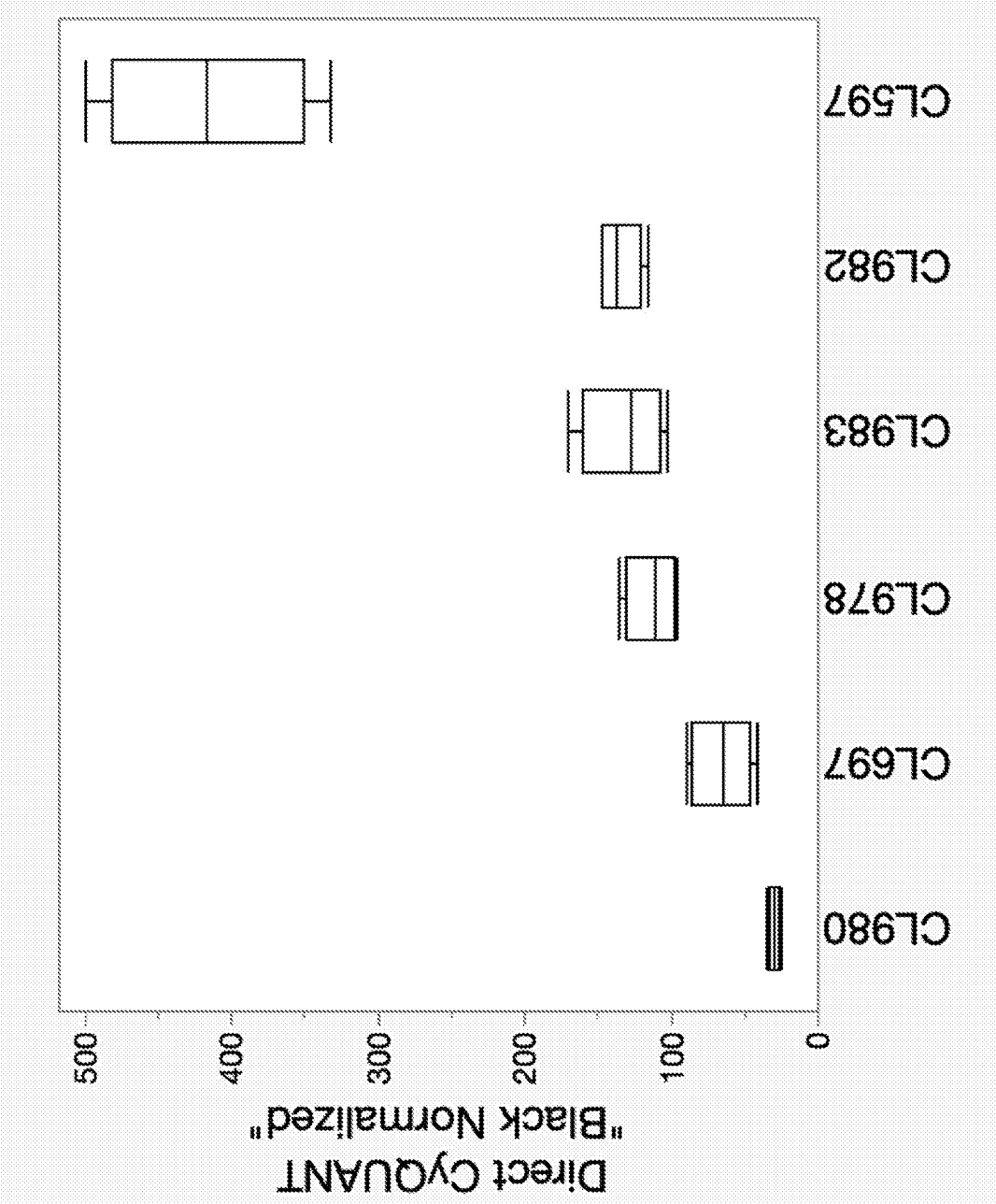


FIG. 9B



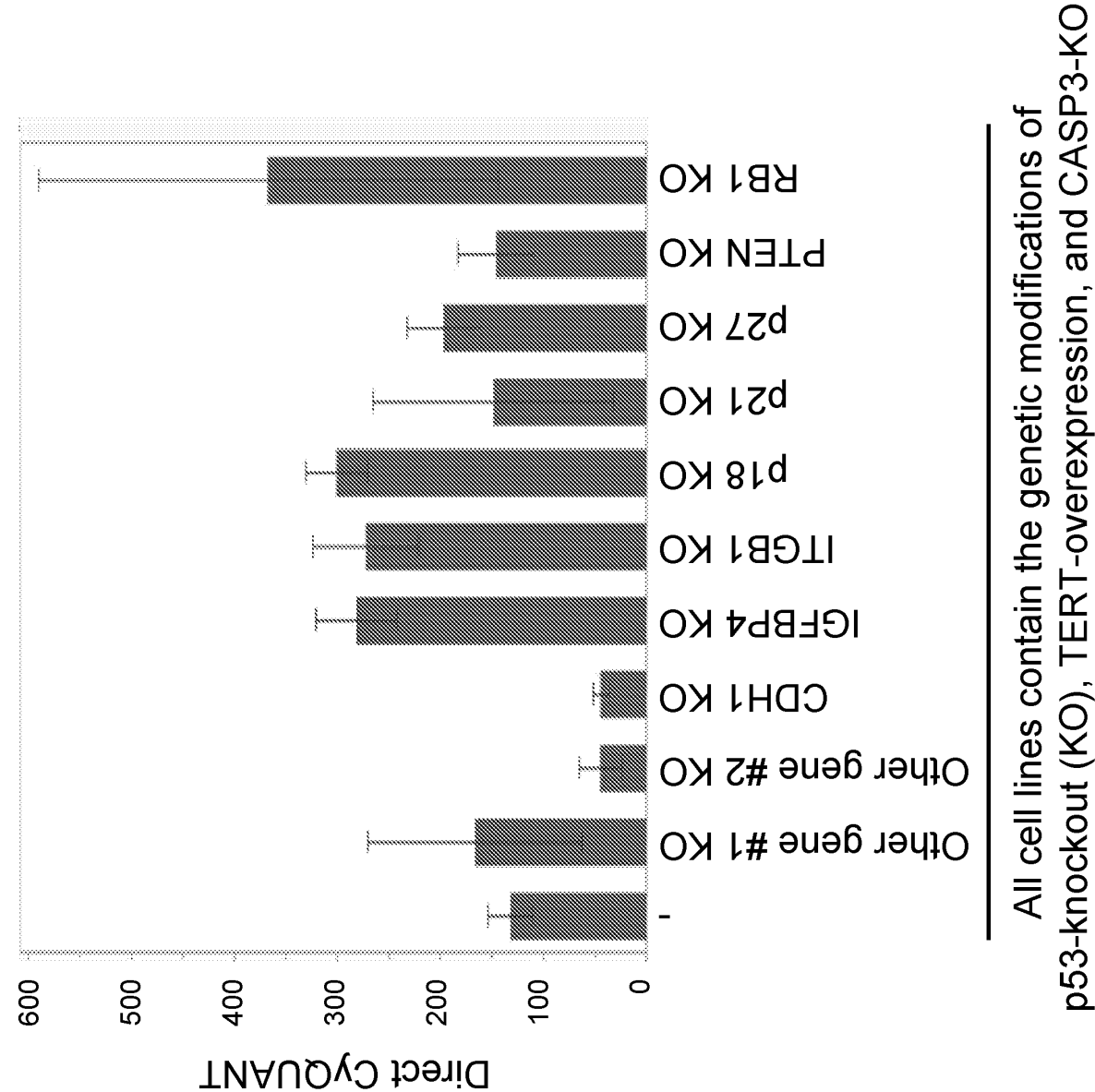
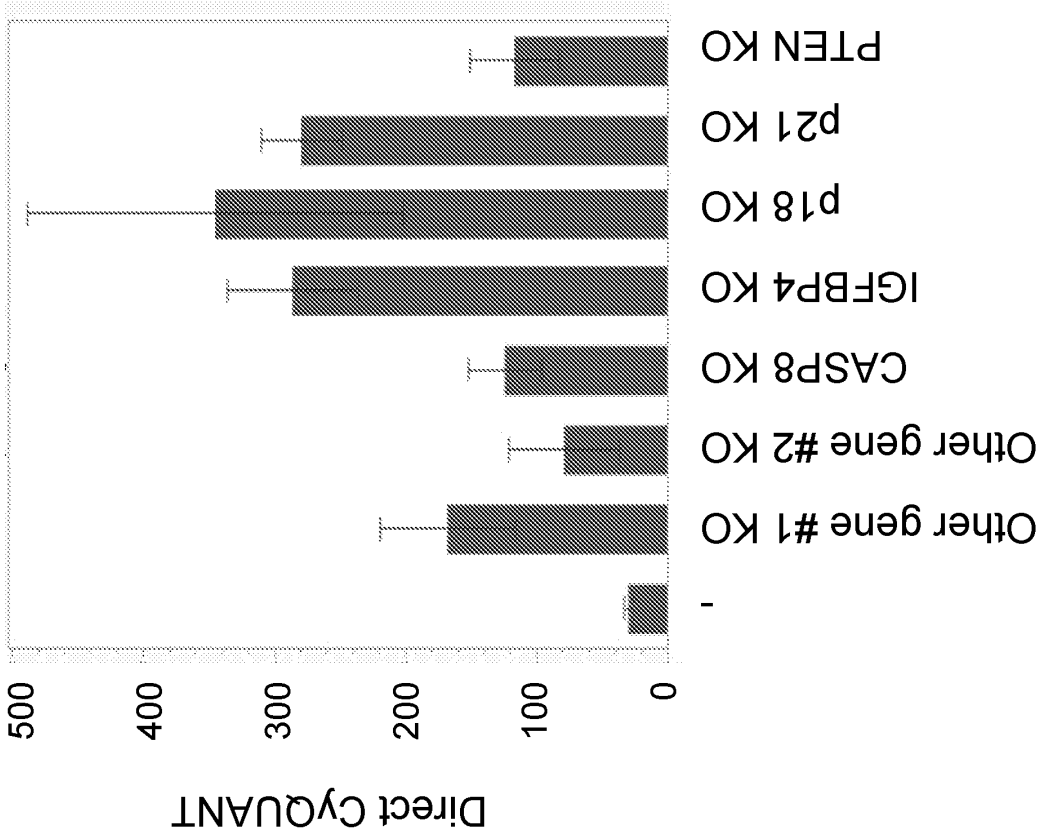
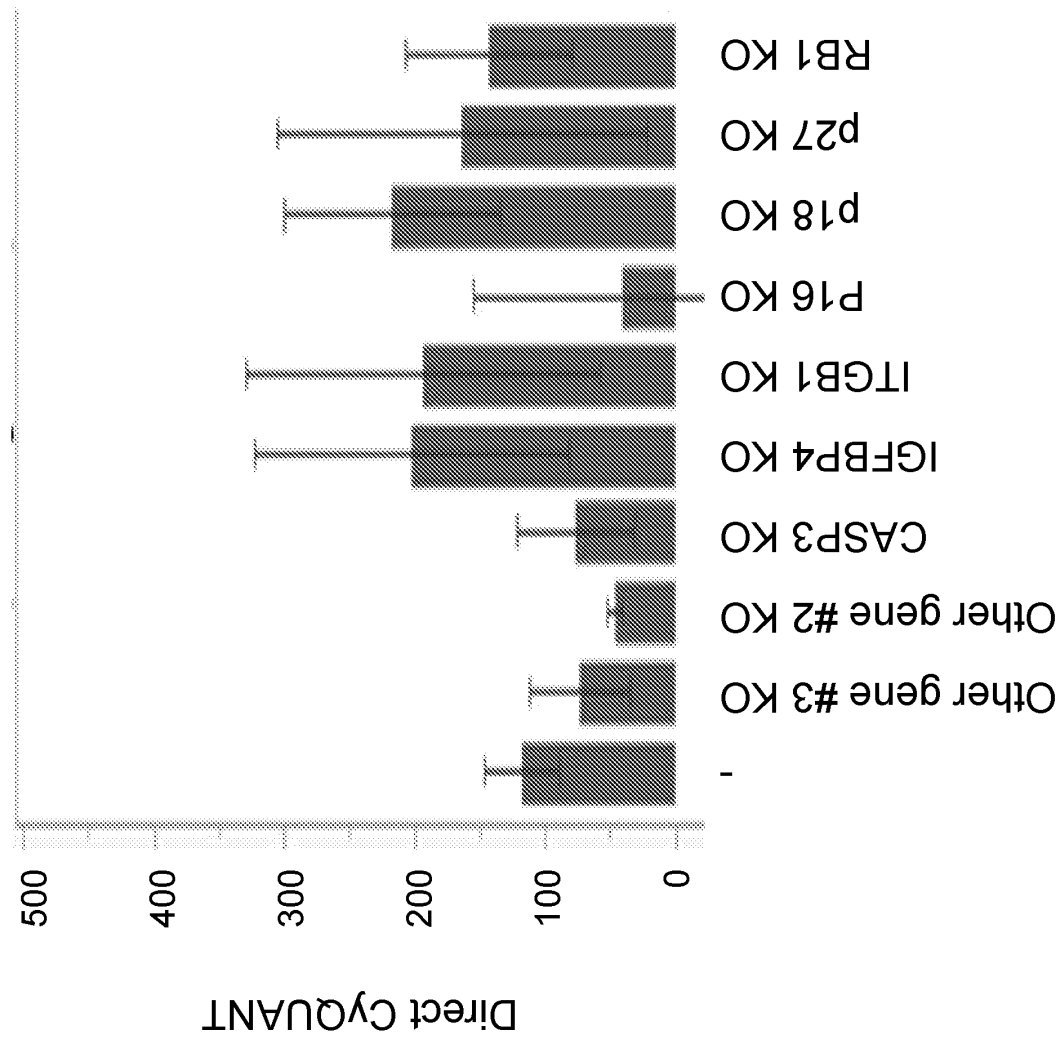


FIG. 9D



All cell lines contain the genetic modifications of p53-knockout (KO), TERT-overexpression, and CDH1-KO

FIG. 9E



All cell lines contain the genetic modifications of p53-knockout (KO), TERT-overexpression, and CASP8-KO

FIG. 10

