

Barrier to Transformation: Stasis

Telomere Dysfunction

Malignancy

Medium Pre-stasis (normal)

Post-stasis

Immortal (non-malignant)

Immortal (with AIG)

A

MM
(low serum
moderate
stress)

48,240..(~50 RM)

15-30 PD

184

benzo(a)pyrene (3/3)

Extended Life (p16^{-s}/p16^{-m})

184Ce

c-myc

(1/1)

184Be

c-myc

unknown errors

(1/1)

184Aa

c-myc

unknown errors

(5/5)

ZNF217

insertional mutagenesis at p53 locus

(3/3)

GSE22

(2/2)

GSE22

(2/2)

hTERT

(1/1)

184F-GSE22 (p16[±])

(1/2)

Immortal (non-malignant)

184CeMY1

184B5,184BE1

184BeMY1

184A1,184AA4

184AaMY1-5

184AaZN1-3

184FGS1

184FTERT

erbB2
K-ras
H-ras
raf-1
v-src
I-R
e1F4E

184B5ME(erbB2)

184A1-RF(raf-1)

184AA2,184AA3

184AaGS1-2

B

MCDB170
(no serum
high stress)

48,240..(~20 RM/P)

5-20 PD

184

hTERT

Post-Selection (p16^{-s})

ZNF217

(4/9)

c-myc

(4/5)

GSE22

(1/4)

c-myc

(1/10)

GSE22

(0/2)

184BTERT

48RTERT

161TERT

184ZN4-7

184ZNM1-4

184ZNGS1

184SMY1

neu

(2/2)

184ZNM2,3-N

no CGH changes

C

M85/87[±]
BSA or
oxytocin
(low serum
low stress)

48,90P,250MK...(~20 RM)

30-60 PD

184

240L

c-myc

(3/3)

p16shRNA

(3/3)

c-myc

(3/3)

hTERT

(2/2)

184F-p16sh,184D-p16sh
240L-p16sh

(1/2)

(1/1)

184FMY2

184DMY3

240LMY1

184Fp16s1

240Lp16s1

184Fp16sMY

184Dp16sMY

240Lp16sMY

184DTERT

no CGH changes

■ = complete growth arrest ■ = clonal escape from barrier "c-myc (5/5)" = perturbation or gene/genetic element overexpressed (#events/#expts)

p16^{-m};p16^{-s} = p16 mutated; p16 silenced; RM = reduction mammoplasty, P = non-tumor mastectomy, MK = milk, PD = population doublings