

Figure 1 *Inactivation of one copy of $p110\alpha$ or $p110\beta$ does not affect survival of $PTEN^{+/-}$ mice*

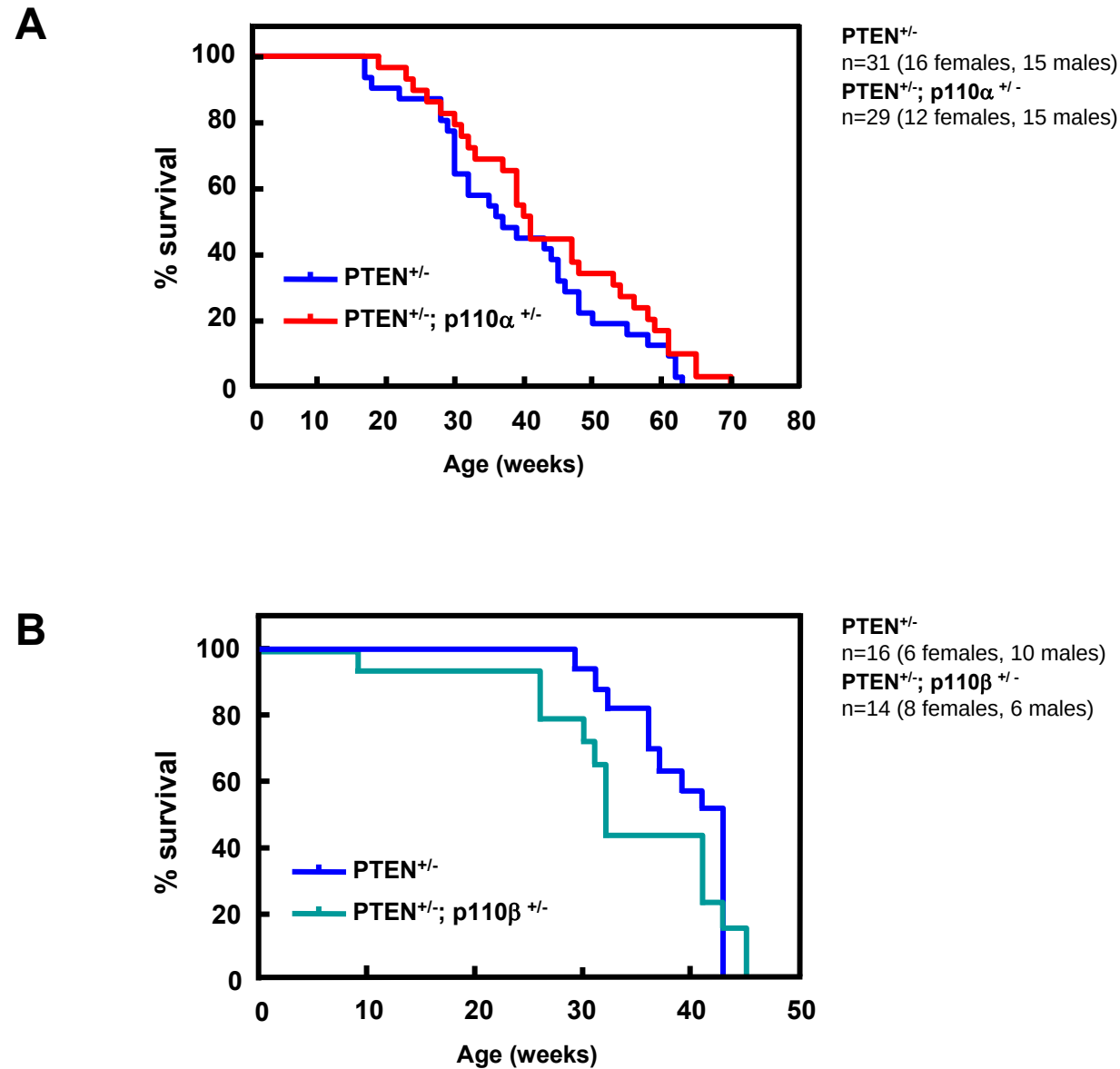


Figure 2

Tumour spectrum in $PTEN^{+/-};p110\alpha^{-/-}$ and $PTEN^{+/-};p110\beta^{-/-}$ mice

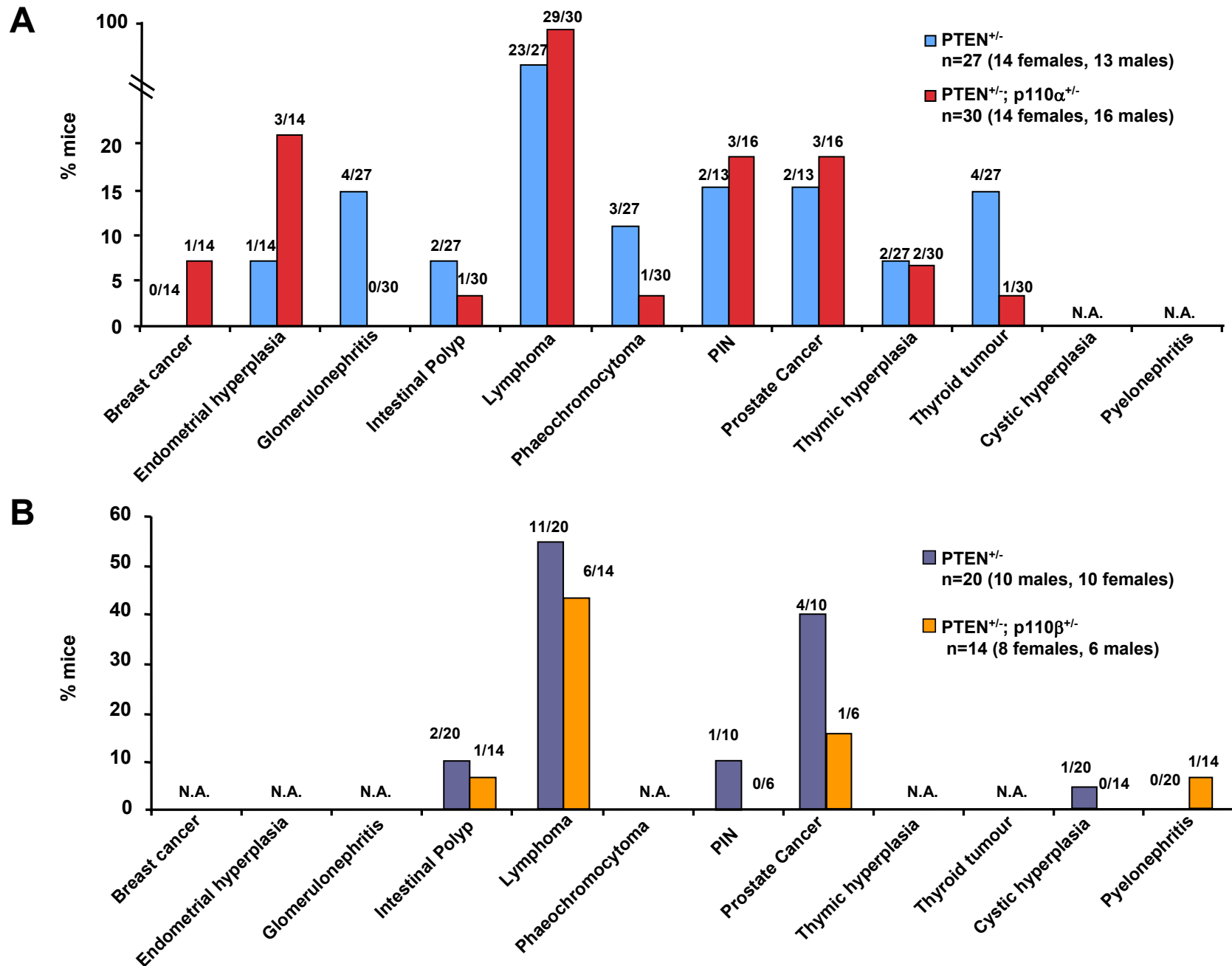
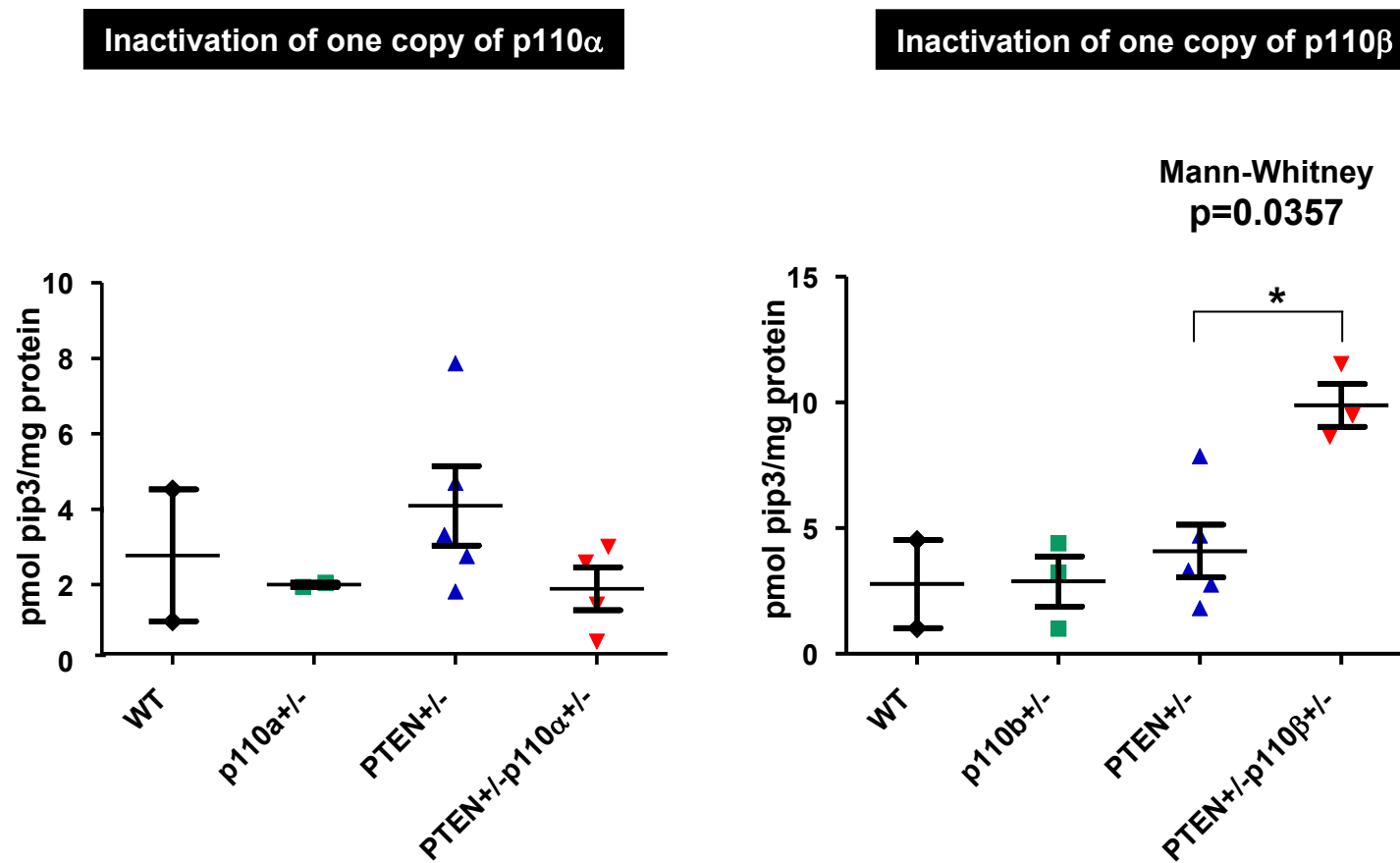


Figure 3 *PIP₃ levels in PTEN^{+/-};p110α^{+/-} and PTEN^{+/-};p110β^{+/-} prostates*



Lack of correlation between PIP_3 levels and PI3K-AKT signalling in $PTEN^{+/-};p110\alpha^{+/-}$ lymphomas

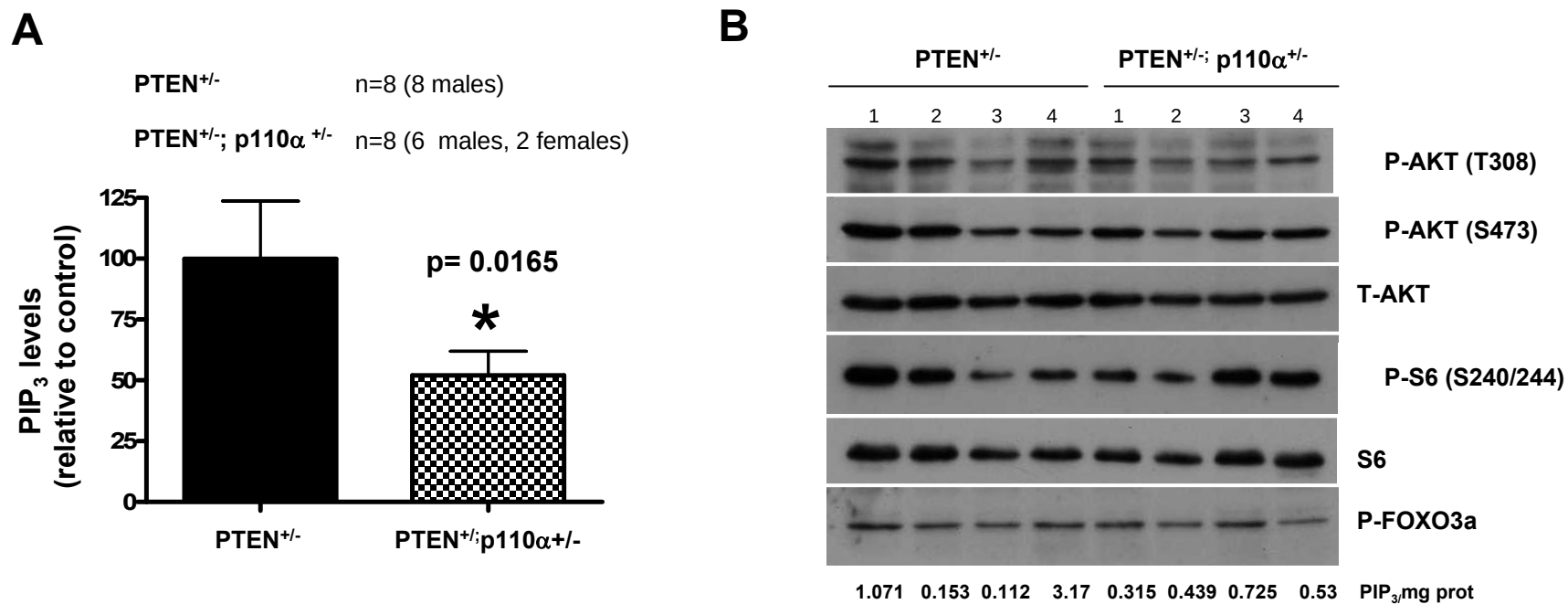


Figure 5 *Gene targeting strategy*

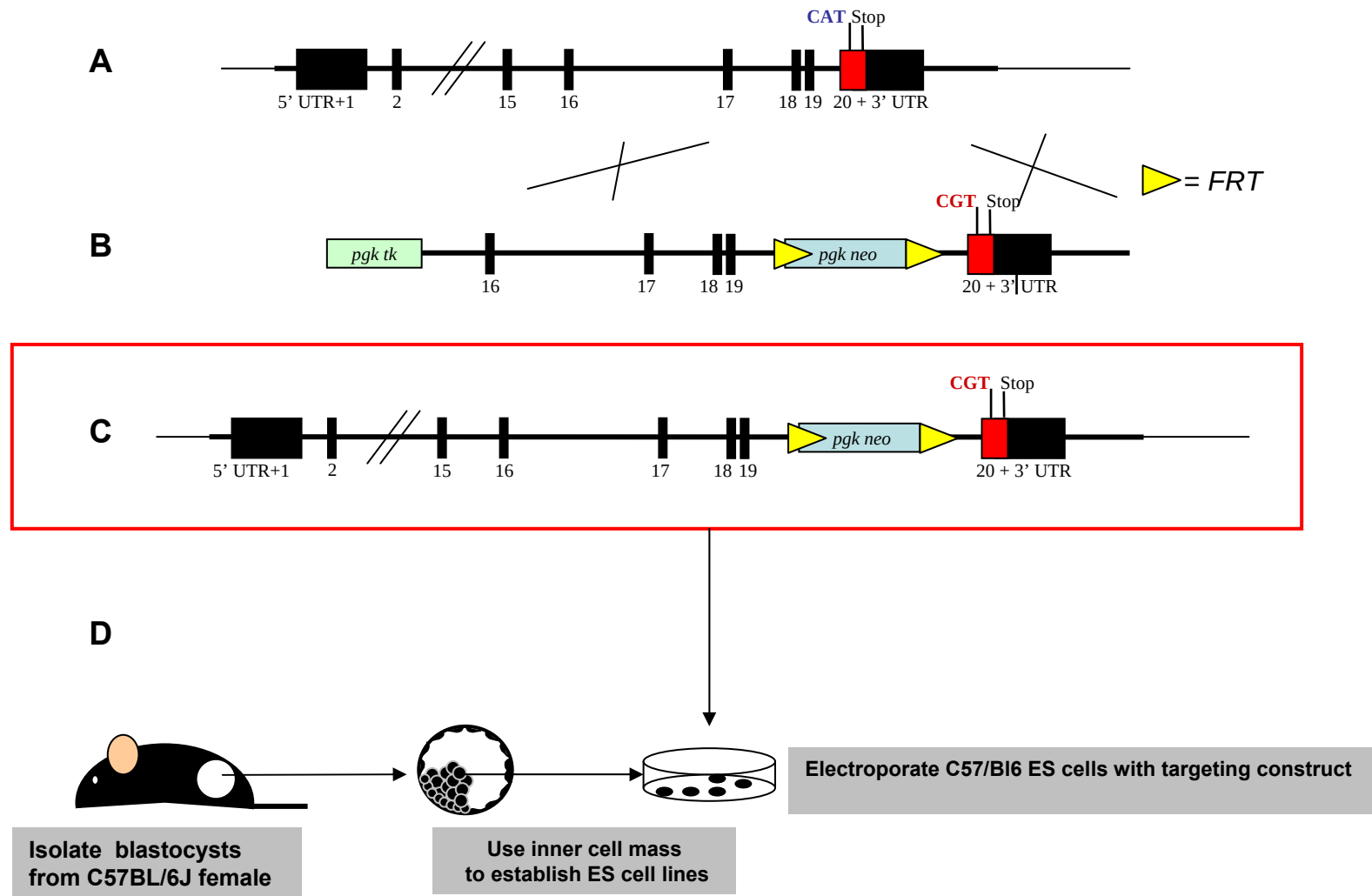
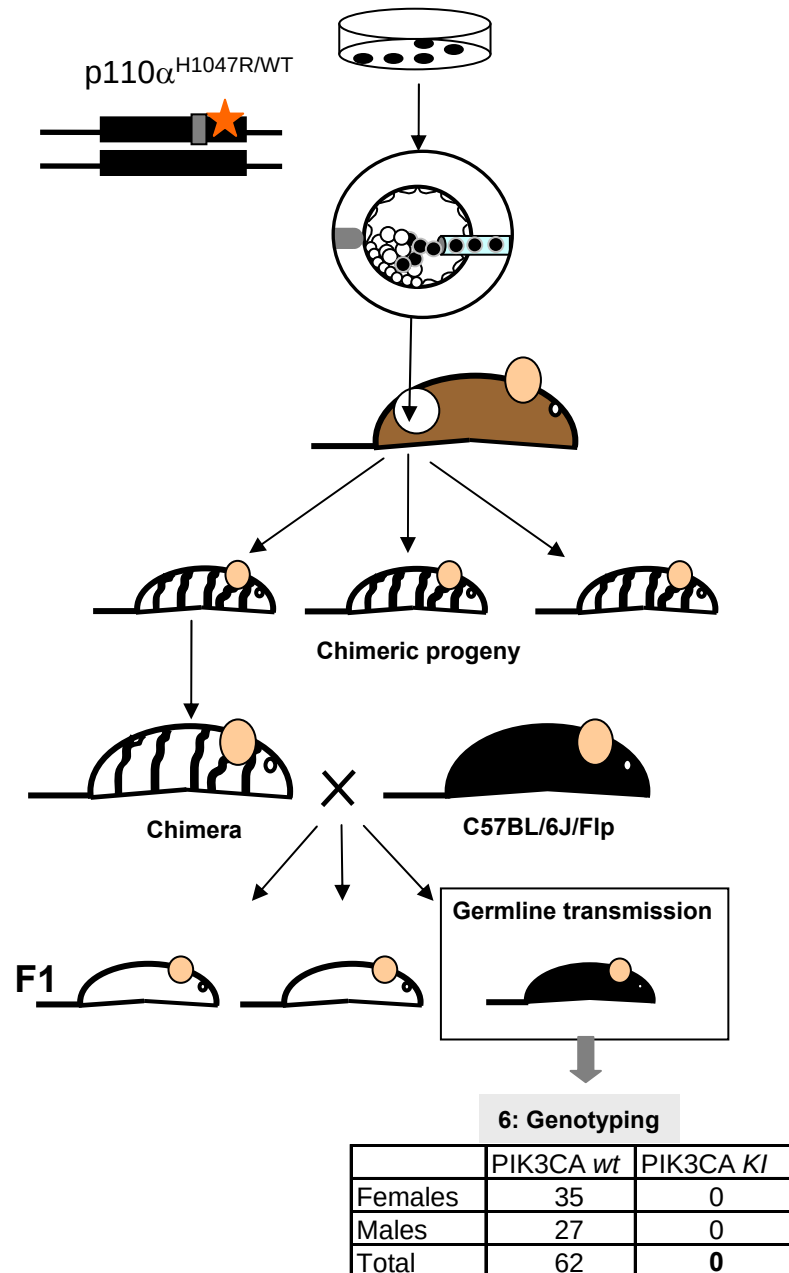


Figure 6 *Generation of p110 α H1047R mice*



1. - Electroporate C57/Bl6 ES cells with targeting construct
- Select for G418 neo resistance
- Characterise ES clones

2. Inject BALB/c ('white') blastocysts with targeted ES cells ('black')

- 3: Implant pseudo-pregnant mother with blastocysts

- 4: PCR to verify presence of p110 α H1047R mutation in tail tip (*not shown*)

- 5: Test cross of male chimera with C57BL/6J/Flp transgenic female, in order to:
(1) assess germline transmission
(2) remove selection cassette (by Flp-mediated recombination)

No viable pups carrying the p110 α ^{H1047R} allele can be obtained

Figure 7

Oncogenic p110 α H1047R is lethal in heterocigosity

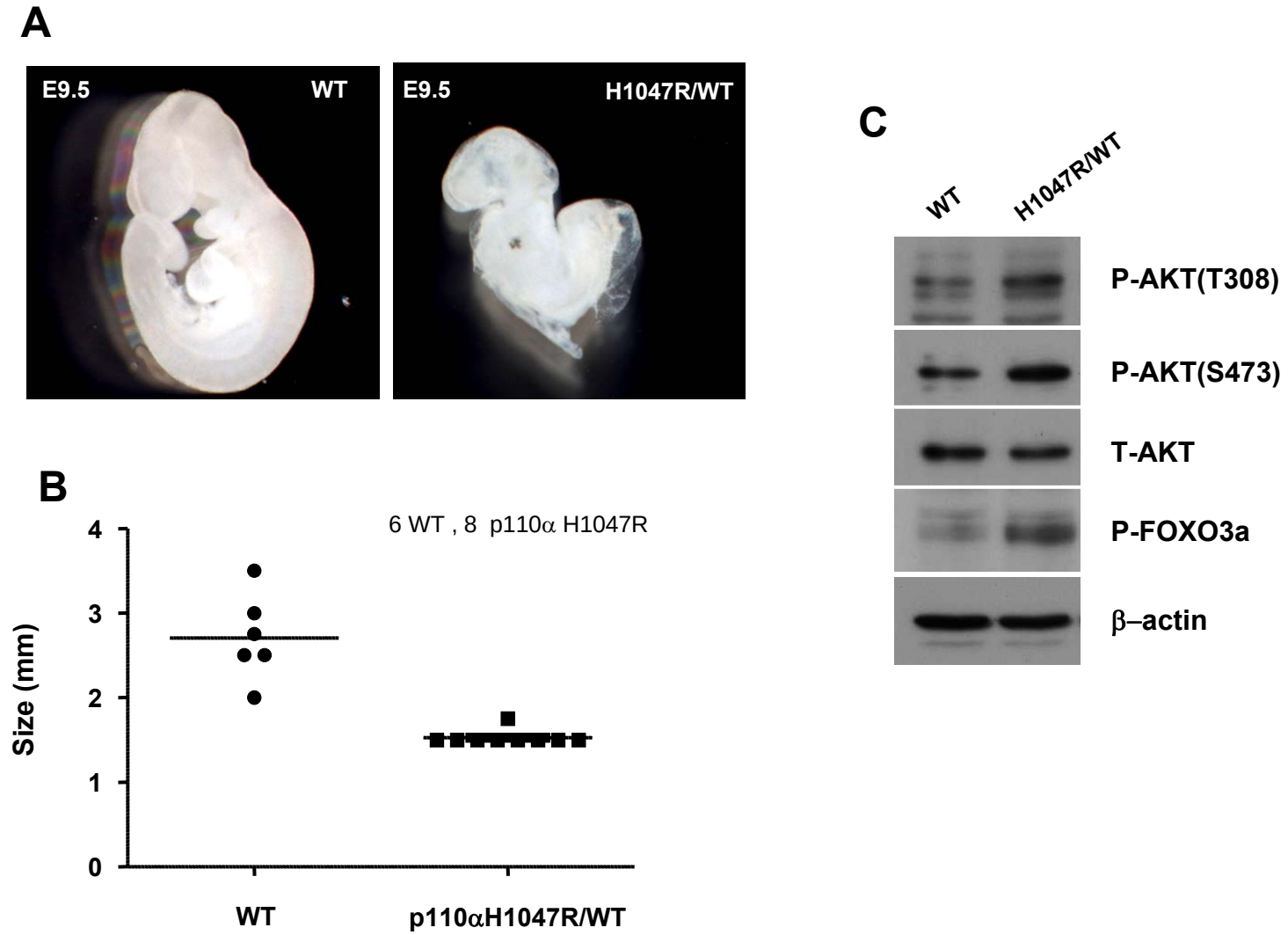
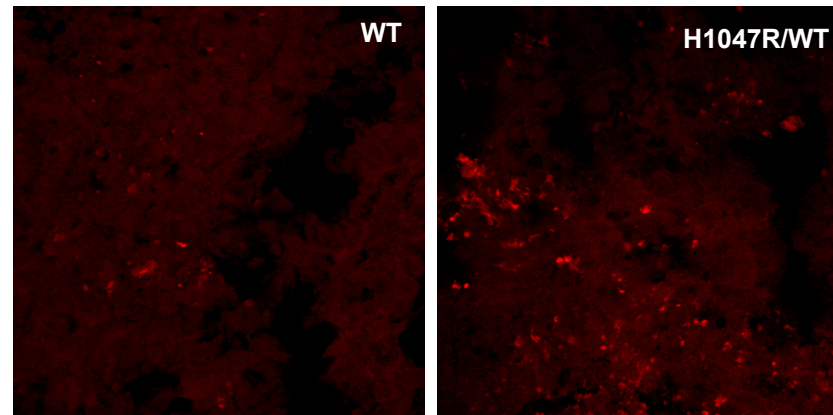


Figure 8

Increase apoptosis in E9.5 mutant embryos

A



B

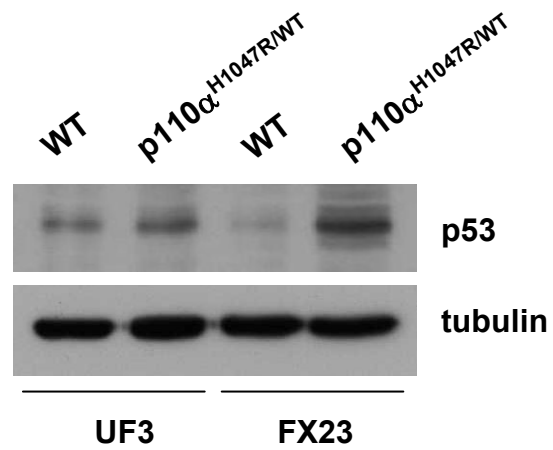


Figure 9

Hypomorphic allele:

the presence of the Neo-selection cassette dampens $p110\alpha^{H1047R}$ protein levels

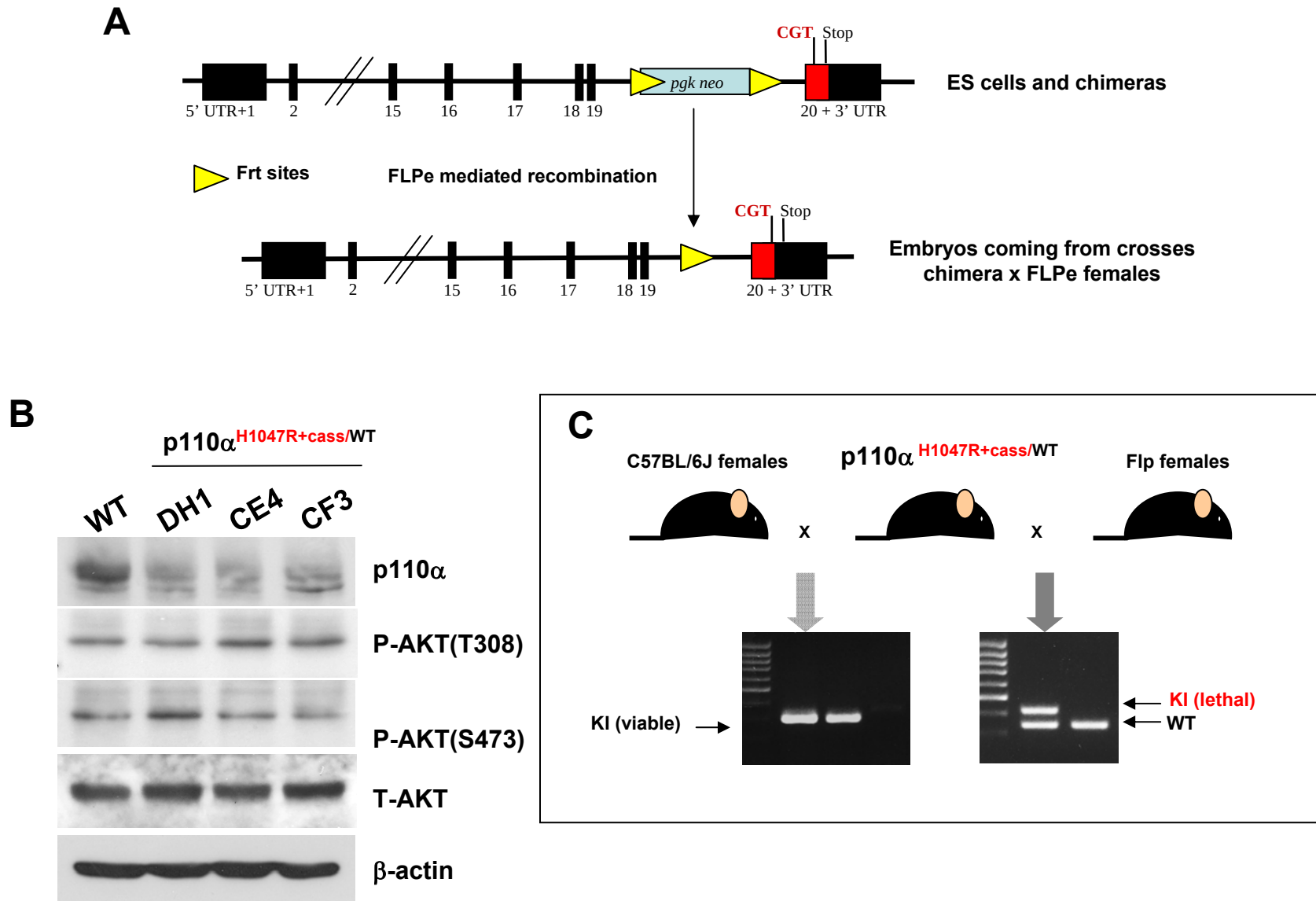


Figure 10

FLPeERT2-mediated recombination of the Neo-cassette in adult tissues upon tamoxifen treatment

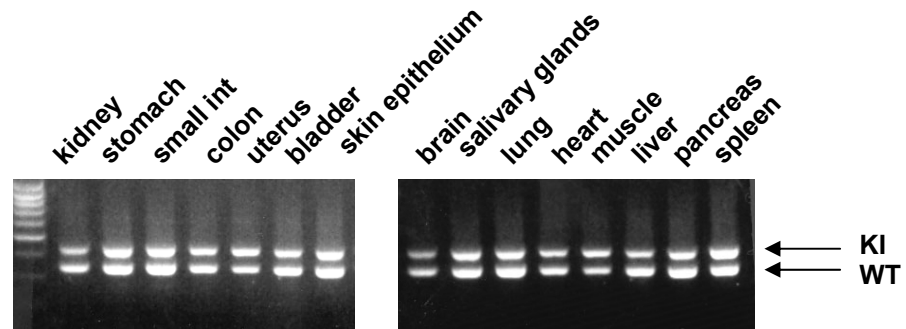
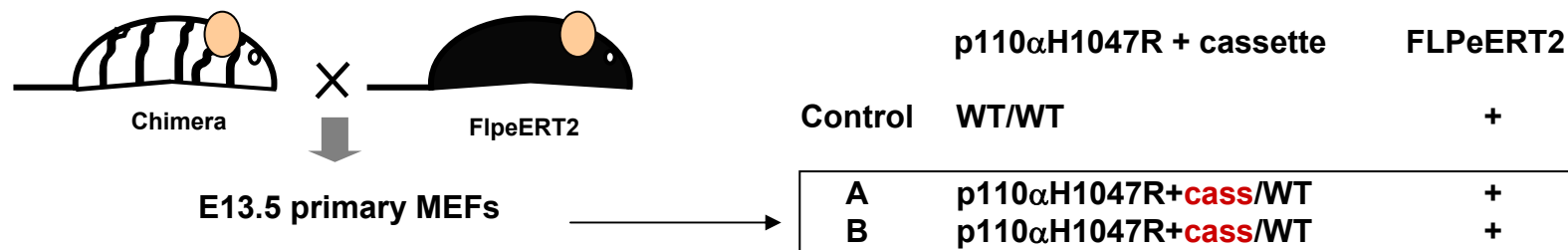


Figure 11 *Inducible p110 α H1047R MEFs*



- Treat MEFs with 1 μ M 4OHT

- PCR to check FLPe mediated recombination of the neo cassette:
only if the recombination occurred we can see the KI band in the oncop110 α PCR

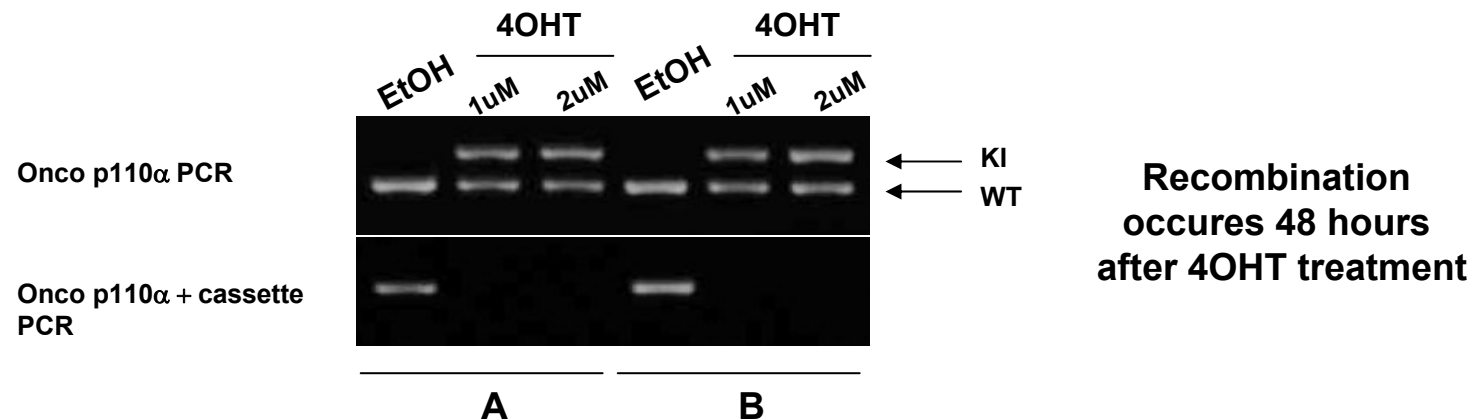


Figure 12 *Increase P-AKT in p110 α H1047R inducible MEFs*

