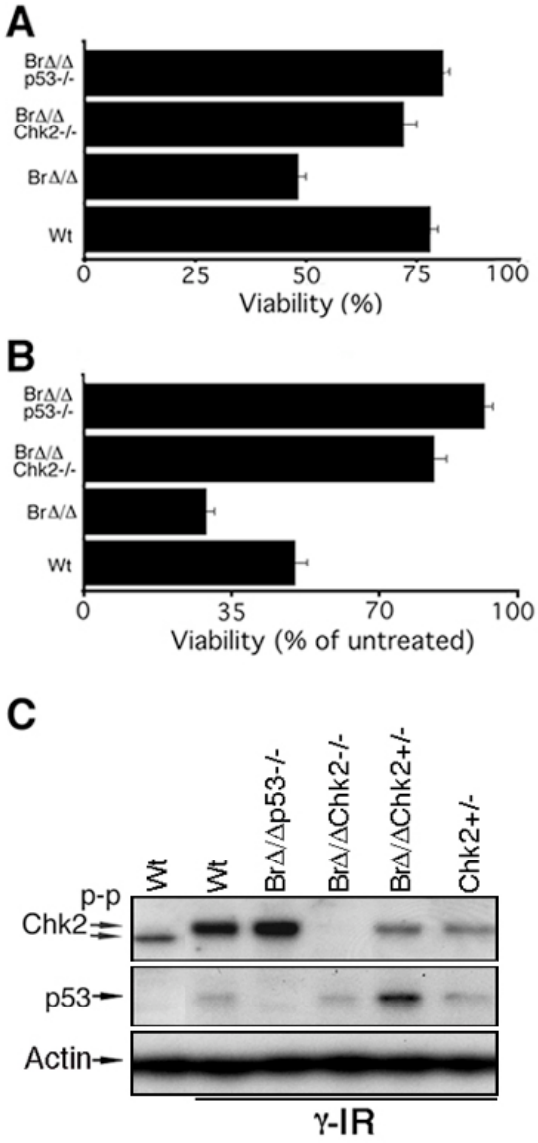
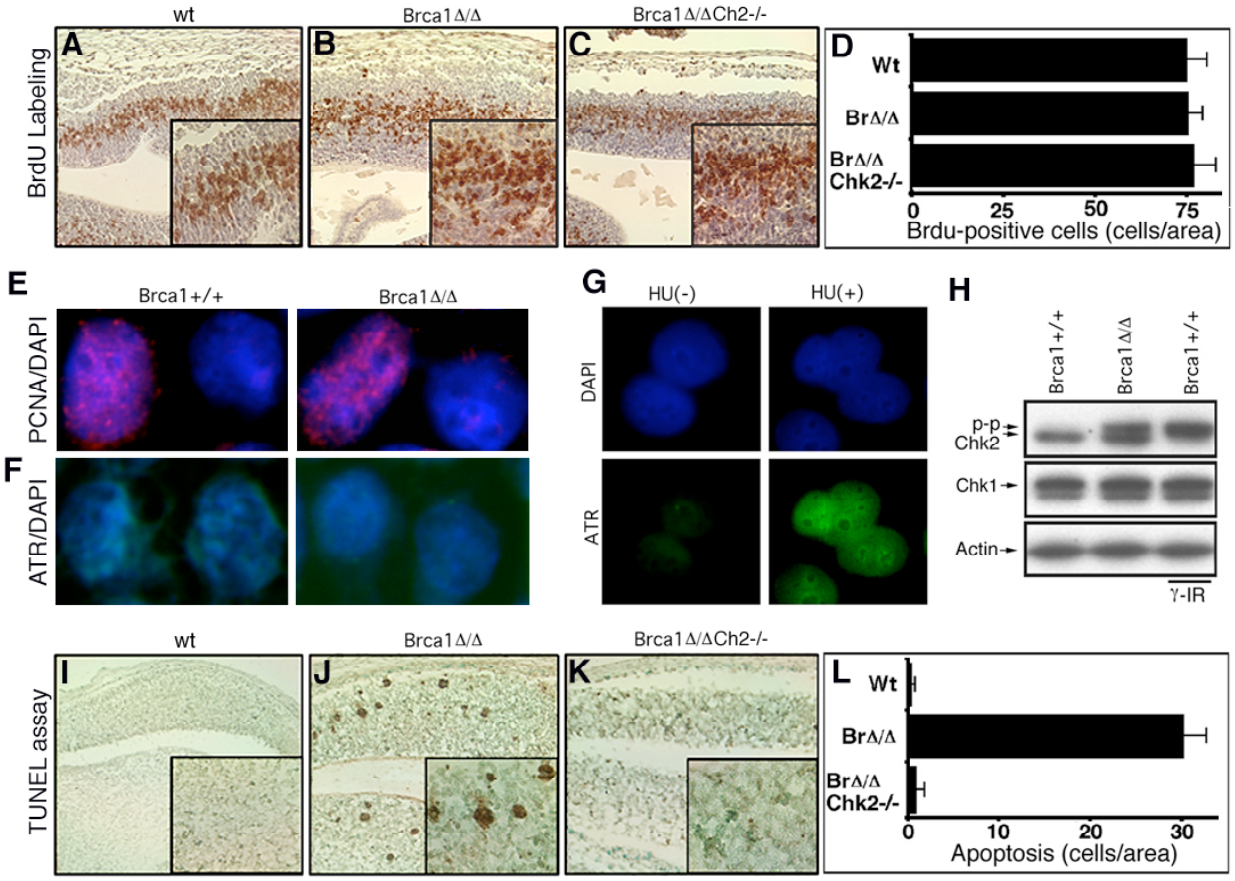
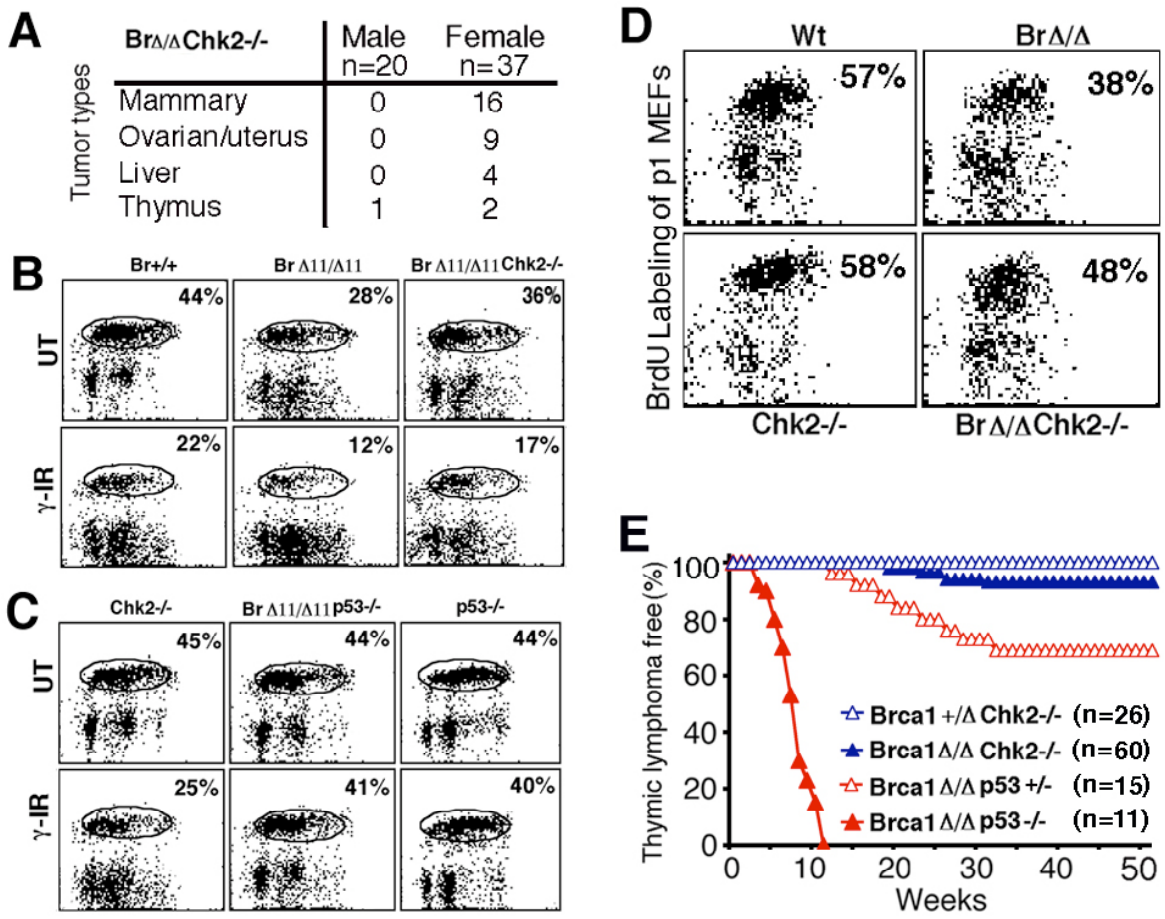
Supplement Figure 1-4



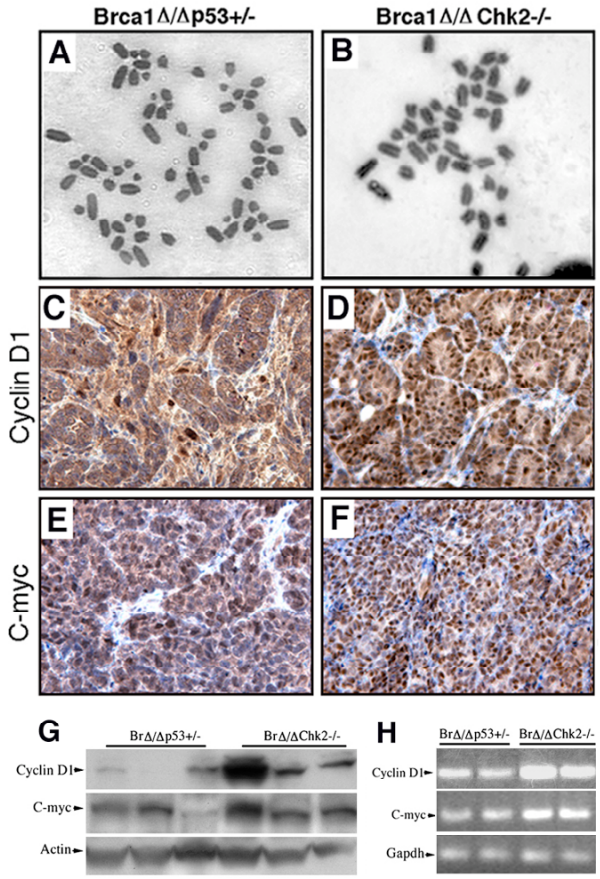
Supple. Figure 1 p53-dependent survival and apoptosis in thymocytes. (**A**) Viability of thymocytes from 3 month old wild type, *Brca1*$^{\Delta 11/\Delta 11}$, *Brca1*$^{\Delta 11/\Delta 11}$*Chk2*$^{-/-}$ and *Brca1*$^{\Delta 11/\Delta 11}$*p53*$^{-/-}$ male mice measured after they were cultured for 24 hr (n=4 of each). (**B**) Viability of thymocytes from 3 month old wild type, *Brca1*$^{\Delta 11/\Delta 11}$, *Brca1*$^{\Delta 11/\Delta 11}$*Chk2*$^{-/-}$ and *Brca1*$^{\Delta 11/\Delta 11}$*p53*$^{-/-}$ male mice 24 hrs after 2.5 Gy γ-irradiation (n=4). (**C**) Western blot analysis of thymocytes of Chk2 and p53 expression 4 hrs after 10 Gy γ-irradiation (n=3).



Supple. Figure 2 Brca1 mutant embryos showed normal DNA replication and increased apoptosis. (**A-D**) BrdU-labeling on brain tissues of wild type, *Brca1*$^{\Delta 11/\Delta 11}$ and *Brca1*$^{\Delta 11/\Delta 11}$ *Chk2*$^{-/-}$ E12.5 embryos (n=3) (**A-C**). No obvious differences were observed (**D**). **(E,F)** PCNA (**E,** red) and ATR (**F,** green) staining on brain tissues of wild type and *Brca1*$^{\Delta 11/\Delta 11}$ E12.5 embryos. No significant differences in PCNA foci were detected between wild type and*Brca1*$^{\Delta 11/\Delta 11}$ cells. ATR staining was negative in brain tissues. To provide a positive control for ATR antibody, we stained HCF-7 cell prior to and after they were treated with 2mM Hydroxyurea (HU) for 1 hour (**G**). Significant increased ATR levels were detected after HU treatment in these cells. (**H**) Western-blot analysis of MEF cells from wild type and *Brca1*$^{\Delta 11/\Delta 11}$ E14.5 embryos for Chk1 and Chk2 expression. (**I-L**) TUNEL assay of brain tissues from wild type, *Brca1*$^{\Delta 11/\Delta 11}$ and *Brca1*$^{\Delta 11/\Delta 11}$ *Chk2*$^{-/-}$ E12.5 embryos (n=4).



Supple. Figure 3 G1/S cell cycle checkpoint, cell proliferation and tumorigenesis in Brca1 mutant mice. (**A**) Tumor types of *Brca1*$^{\Delta 11/\Delta 11}$*Chk2*$^{-/-}$ mice. (**B,C**) Analysis of G1/S checkpoint of passage 1 MEF cells of wild type, *Brca1*$^{\Delta 11/\Delta 111}$, *Brca1*$^{\Delta 11/\Delta 11}$*Chk2*$^{-/-}$, *Chk2*$^{-/-}$, *Brca1*$^{\Delta 11/\Delta 11}$*p53*$^{-/-}$ and *p53*$^{-/-}$ upon 10 Gy γ-IR. % BrdU-positive cells were shown (n=3). (**D**) BrdU labeling of passage 1 MEF cells from wild type, *Brca1*$^{\Delta 11/\Delta 11}$, *Chk2*$^{-/-}$ and *Brca1*$^{\Delta 11/\Delta 11}$*Chk2*$^{-/-}$. (**E**) Profiles of Brca1 associated thymic lymphoma in *Brca1*$^{+/\Delta 11}$*Chk2*$^{-/-}$, *Brca1*$^{\Delta 11/\Delta 11}$*Chk2*$^{-/-}$, *Brca1*$^{\Delta 11/\Delta 11}$*p53*$^{+/-}$, and *Brca1*$^{\Delta 11/\Delta 11}$*p53*$^{-/-}$ mice. Number of animals for each genotype was indicated.



Supple. Figure 4 Cytogenetic analysis of tumors from *Brca1*$^{\Delta 11/\Delta 11}$*p53*$^{+/-}$ and *Brca1*$^{\Delta 11/\Delta 11}$*Chk2*$^{-/-}$ mice. (**A, B**) Chromosome spreads of *Brca1*$^{\Delta 11/\Delta 11}$*p53*$^{+/-}$ and *Brca1*$^{\Delta 11/\Delta 11}$*Chk2*$^{-/-}$ mice mammary tumors. Primary tumors of each genotype were cultured briefly (passage 2) before chromosome spreads were prepared. Most of the cells (94%) from *Brca1*$^{\Delta 11/\Delta 11}$*p53*$^{+/-}$ tumors (n=4) were aneuploid (from 17 spreads, 1 spread has 40 chromosomes, 8 have >100, 2 have 80-99, and 6 have 41-79 chromosomes), while much less aneuploid cells (7.1%) were found from *Brca1*$^{\Delta 11/\Delta 11}$*Chk2*$^{-/-}$ tumors (n=3) (from 28 spreads, 26 have 40 chromosomes and 2 have 40-50 chromosomes). (**C, D**) Cyclin D1 stained mammary tumors from *Brca1*$^{\Delta 11/\Delta 11}$*p53*$^{+/-}$ and *Brca1*$^{\Delta 11/\Delta 11}$*Chk2*$^{-/-}$ mice. (**E, F**) C-myc stained in mammary tumors from *Brca1*$^{\Delta 11/\Delta 11}$*p53*$^{+/-}$ and *Brca1*$^{\Delta 11/\Delta 11}$*Chk2*$^{-/-}$ mice. (**G**) Western-blot analysis of mammary tumor from *Brca1*$^{\Delta 11/\Delta 11}$*p53*$^{+/-}$ and *Brca1*$^{\Delta 11/\Delta 11}$*Chk2*$^{-/-}$ mice for cyclin D1 and C-myc expression. (**H**) RT-PCR analysis of mammary tumor from *Brca1*$^{\Delta 11/\Delta 11}$*p53*$^{+/-}$ and *Brca1*$^{\Delta 11/\Delta 11}$*Chk2*$^{-/-}$ mice for cyclin D1 and C-myc expression.