

Figure W1. Genetic instability in p21^{-/-}p53^{+/-} MSCs. (A) G-banded karyotypes representative of the indicated MSCs. (B) Percentages of metaphases containing the indicated number of chromosomes. At least 50 metaphases of each MSC type were counted. (C) Cell cycle analysis of the indicated MSCs. 2N DNA content peak according to the G₁ population of wild-type MSCs and corresponding to 4N and 8N DNA content peaks are pointed.

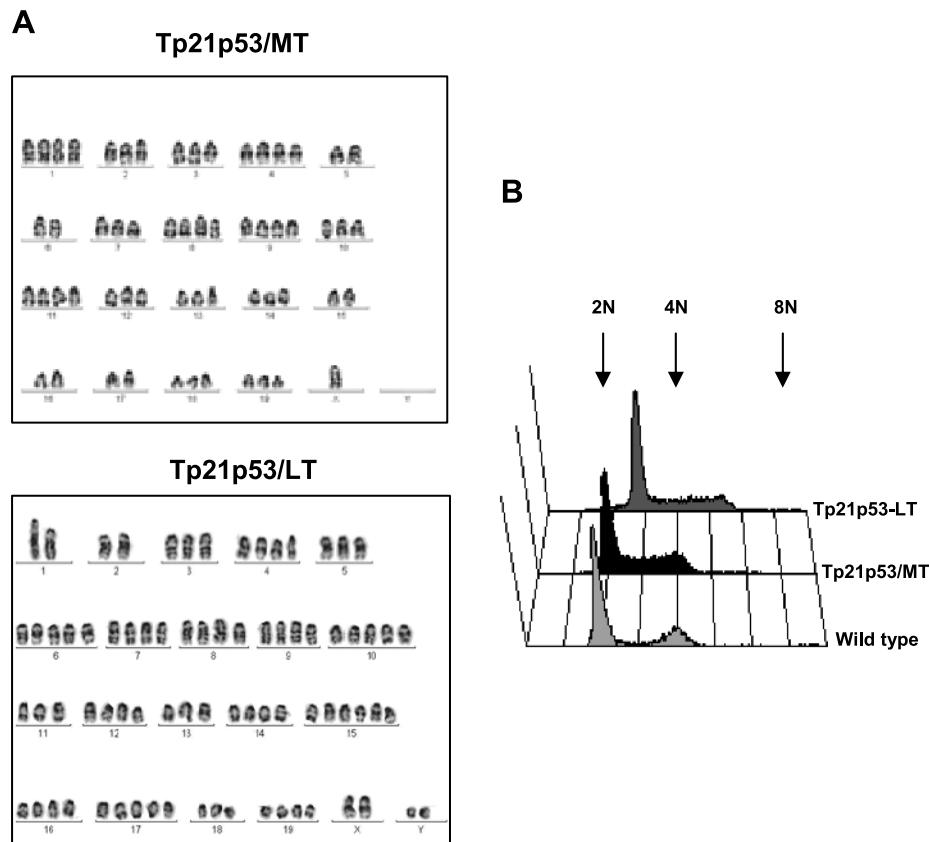


Figure W2. Genetic instability in Tp21p53 tumor cells. (A) G-banded karyotypes representative of the indicated tumor cell lines. (B) Cell cycle analysis. 2N DNA content peak according to the G_1 population of wild-type MSCs and corresponding to 4N and 8N DNA content peaks are pointed.

Summary of transforming events in p21^{-/-}p53^{+/-} MSCs cultures

| | | <i>in vitro</i> culture periods | | |
|---|---|--|---|---|
| | | Short term (0-15 pass.) | Medium term (16-35 pass.) | Long term (36-60 pass.) |
| Wild type | - senescence | | No progression of cultures after senescence | |
| p21^{-/-}p53^{+/+} | - senescence - apoptosis | | No progression of cultures after senescence/apoptosis | |
| p21^{-/-}p53^{+/-} | - increased chromosome instability - increased levels of c-myc | - senescence bypass - immortalization - reduction of p53 and p16 levels - <i>in vivo</i> tumorigenicity | | - reduction of Sca-1 expression - complete loss of p53 and p16 - loss of serum dep. induced senescence - increased <i>in vivo</i> tumorigenicity |

Figure W3. Summary of transforming events in p21^{-/-}p53^{+/-} MSCs cultures.