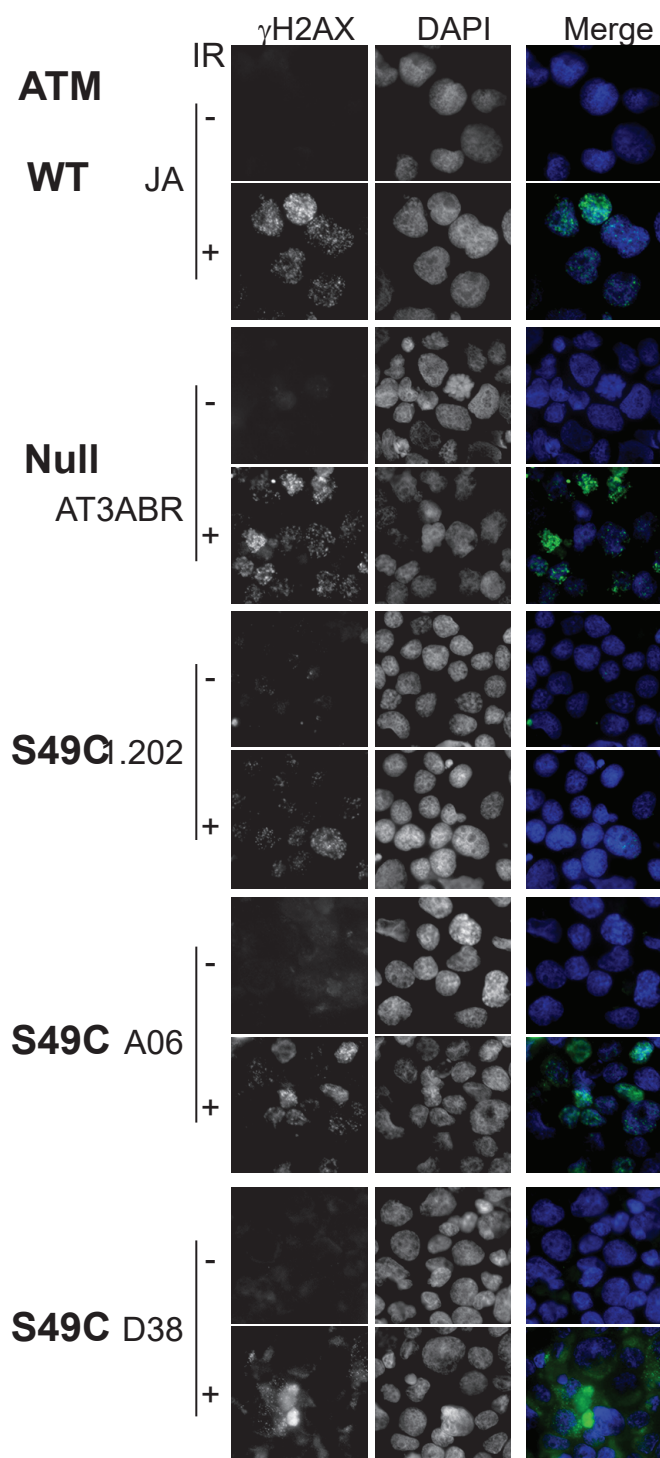
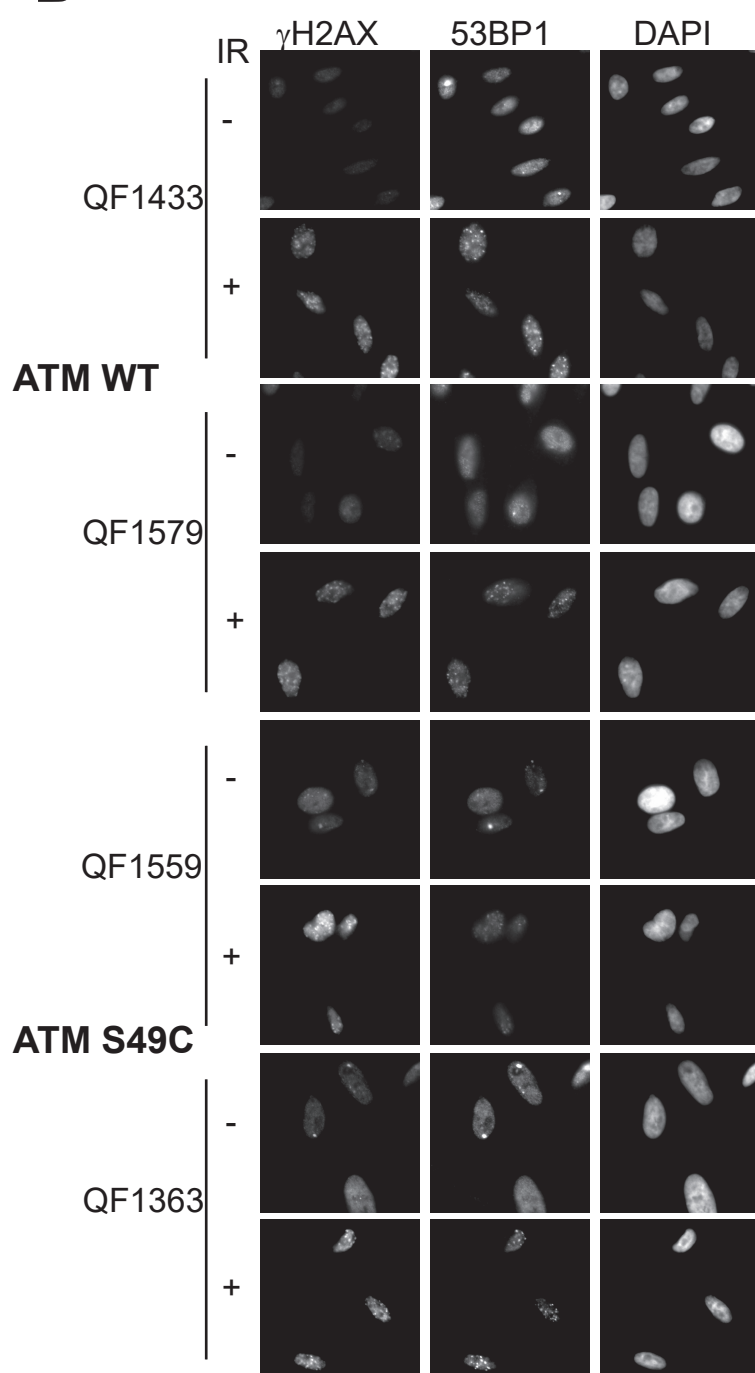
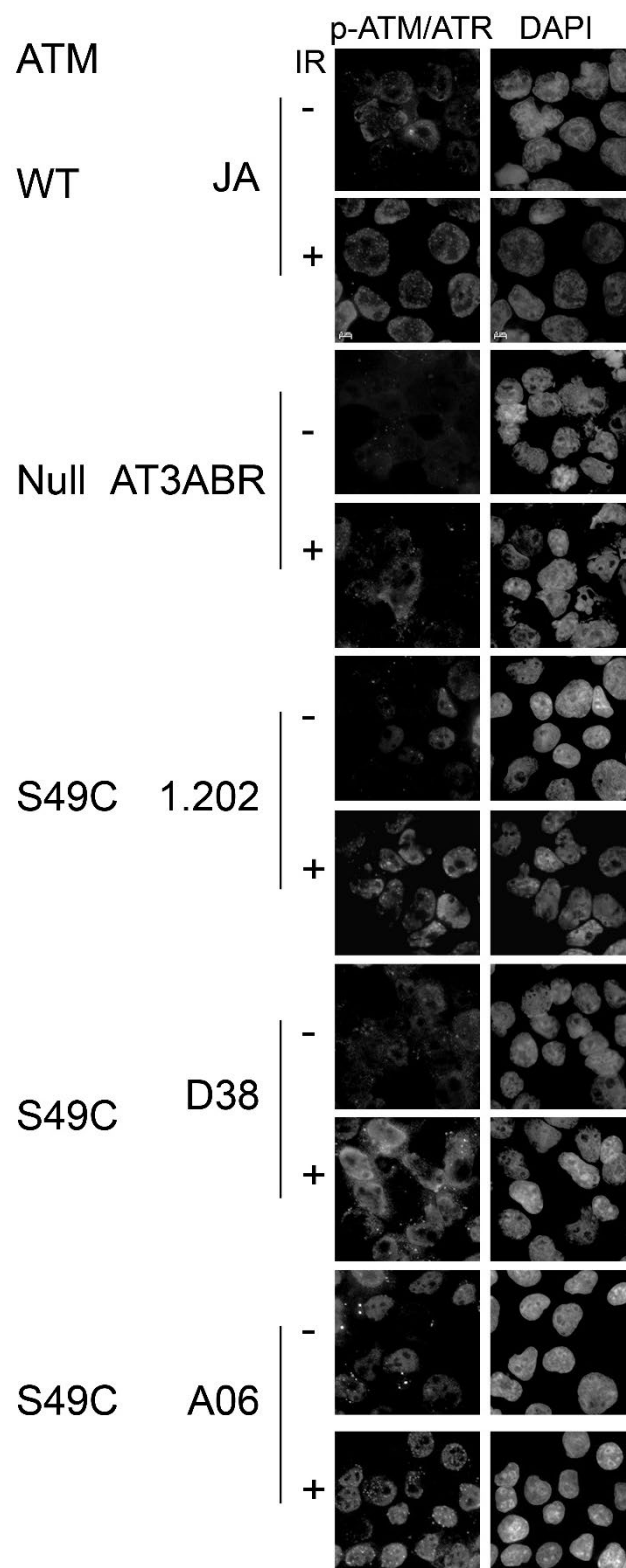


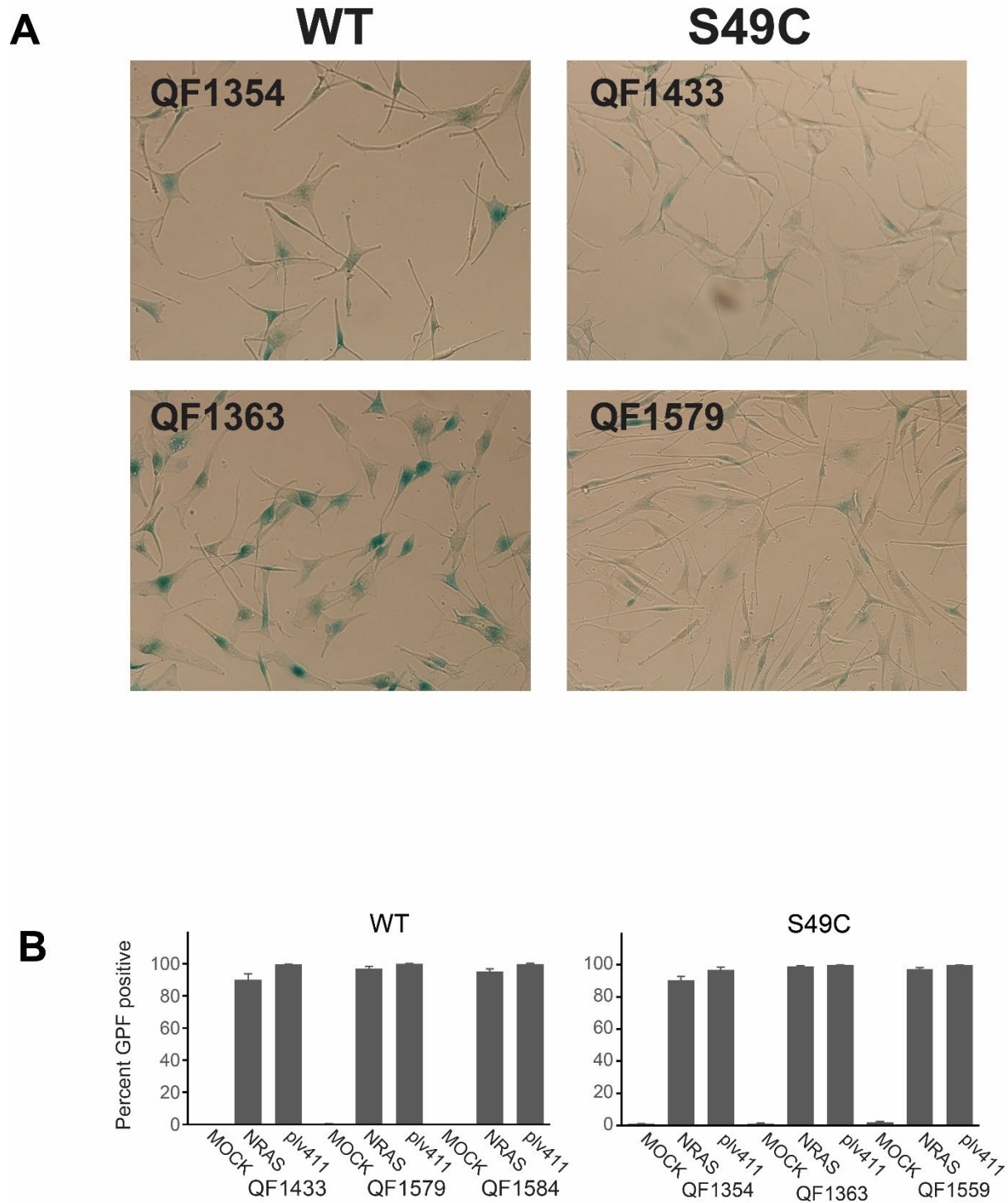
**Supplementary Figure S1:** The indicated LCLs were irradiated with 6 Gy IR then harvested at the indicated times. Whole cell lysates were immunoblotted for pp53, total p53 and  $\alpha$ -tubulin ( $\alpha$ -Tub) as a loading control.

**A****B**

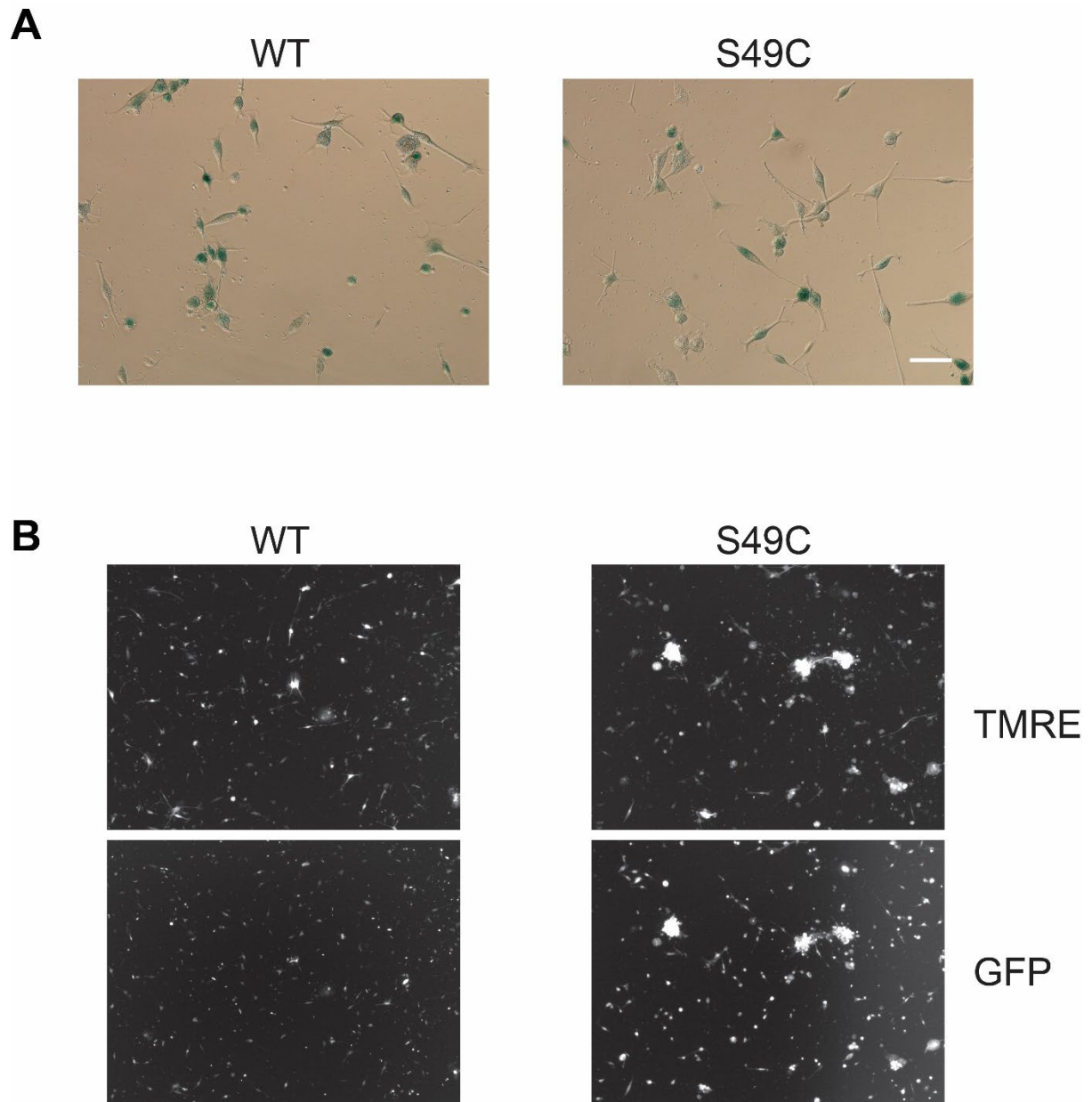
**Supplementary Figure S2:** Immunofluorescence staining of LCL (A) and melanoblast (B) cell lines. Cells were fixed 2 h with or without irradiation (6 Gy), and probed for  $\gamma$ H2AX and 53BP1. DAPI stained the DNA.



**Supplementary Figure S3:** Immunofluorescence staining of LCL lines. Cells were fixed 2 h with or without irradiation (6 Gy), and probed with the pATM/ATR substrate antibody, and DAPI for the DNA.



**Supplementary Figure 4:** A) Images of the indicated melanoblast lines 2 weeks after transduction with empty vector and stained for SA- $\beta$ -Gal. B) High content image analysis of melanoblasts transduced with either empty vector (pLV411), NRAS Q61K or mock transduced for 2 weeks. The percentage of GFP expressing cells are shown. This is the average and SD counting 100 - 3400 cells per well of 6 wells.



**Supplementary Figure S5:** A) Images of the indicated melanoblast lines 2 weeks after transduction with empty vector and stained for SA- $\beta$ -Gal. B) Fluorescence imaging of the same cells as in Figure 5D but for GFP to identify the transduced cells and TMRE fluorescence for mitochondrial viability.

Supplementary Table S1: ATM Genotype of LCLs

<b>LCL</b>	<b>ATM</b>	<b>Mutation</b>	<b>State</b>	<b>Protein</b>
JA	WT		hom	WT
AT3ABR	ATM null	A8266T	het/-	K2756X
Col 1.201*	WT		hom	WT
Col 1.202*	Variant	C146G	het	S49C
A06	Variant	C146G	het	S49C
D38	Variant	C146G	het	S49C

\* These LCL lines were derived from unaffected relatives of the proband of the melanoma and astrocytoma affected family [15] and genotyped as described in the Materials and Methods.

Supplementary Table S2: ATM Genotype of melanoblast lines used.

<b>QF #</b>	<b>MC1R</b>	<b>S49C</b>
1433	WT	S/S
1579	WT	S/S
1584	WT	S/S
1363	D84E +/-	S/C
1354	R163Q +/-	S/C
1559	WT	S/C