



**Figure S1.** Clonogenic survival and DNA damage response of 2BN hTERT XLF<sup>-/-</sup> and RPE-1 PAXX<sup>-/-</sup> cells as well as respective control cells. (A, B) Clonogenic survival assay of 2BN hTERT XLF<sup>-/-</sup> cells irradiated with X-ray photons, EP and SOBP protons (1–8 Gy). (C) RBE values calculated for 10% survival of the indicated cell lines. (D, E)  $\gamma$ H2A.X foci removal over time (4–24 h) normalized to initial foci number at 30 min in 2BN hTERT XLF<sup>-/-</sup> cells as well as respective control cells upon irradiation with 3 Gy of X-ray photons (D) and SOBP protons (E). (F, G) Clonogenic survival assay of RPE-1

PAXX<sup>-/-</sup> cells irradiated with X-ray photons, EP and SOBP protons (1–8 Gy). Data represent mean values  $\pm$  SD from 3 independent experiments. One-way ANOVA. **(H)** RBE values calculated for 10% survival of the indicated cell lines. **(I, J)**  $\gamma$ H2A.X foci removal over time (4–24 h) normalized to initial foci number at 30 min in RPE-1 PAXX<sup>-/-</sup> cells as well as respective control cells upon irradiation with 3 Gy of X-ray photons **(I)** and SOBP protons **(J)**. **(K, L)** Comparison of radiation source effects in tested cell lines as log2 values of  $\gamma$ H2A.X foci quantification. Data represent mean values  $\pm$  SD **(A,F)** or SEM **(B,D,E,G,I,J)** from 3 independent experiments. One-way ANOVA with Tukey's multiple comparisons post-test **(B,G)** or two-way ANOVA with Tukey's multiple comparisons post-test **(D,E,I,J)**; \* $p < 0.05$ ; \*\* $p < 0.01$ ; \*\*\* $p < 0.001$ .