Supplementary Information

X-ray Radio-Enhancement by $Ti_3C_2T_x$ MXenes in Soft Tissue Sarcoma

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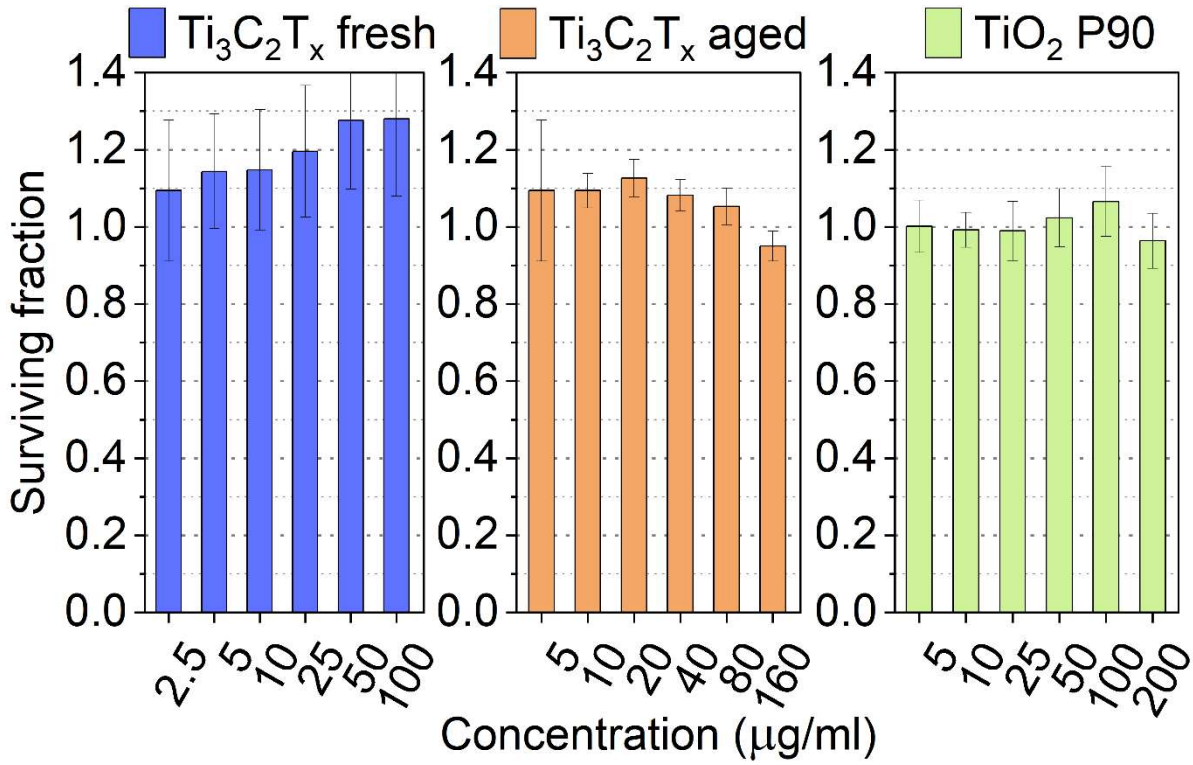
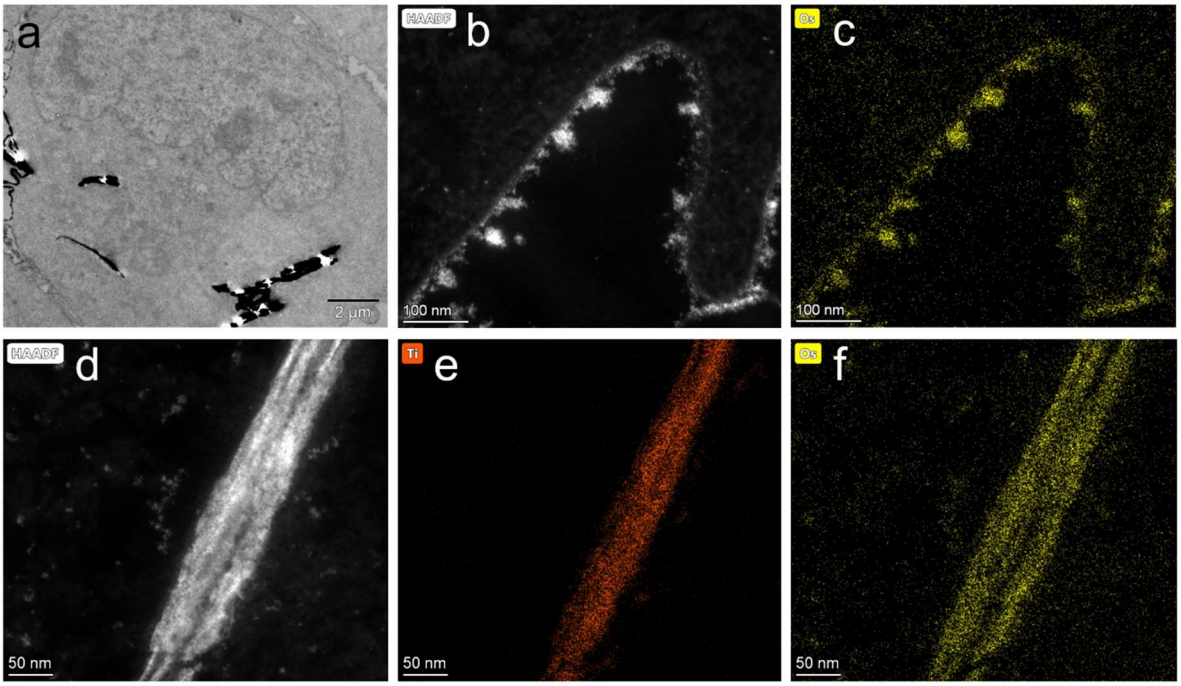
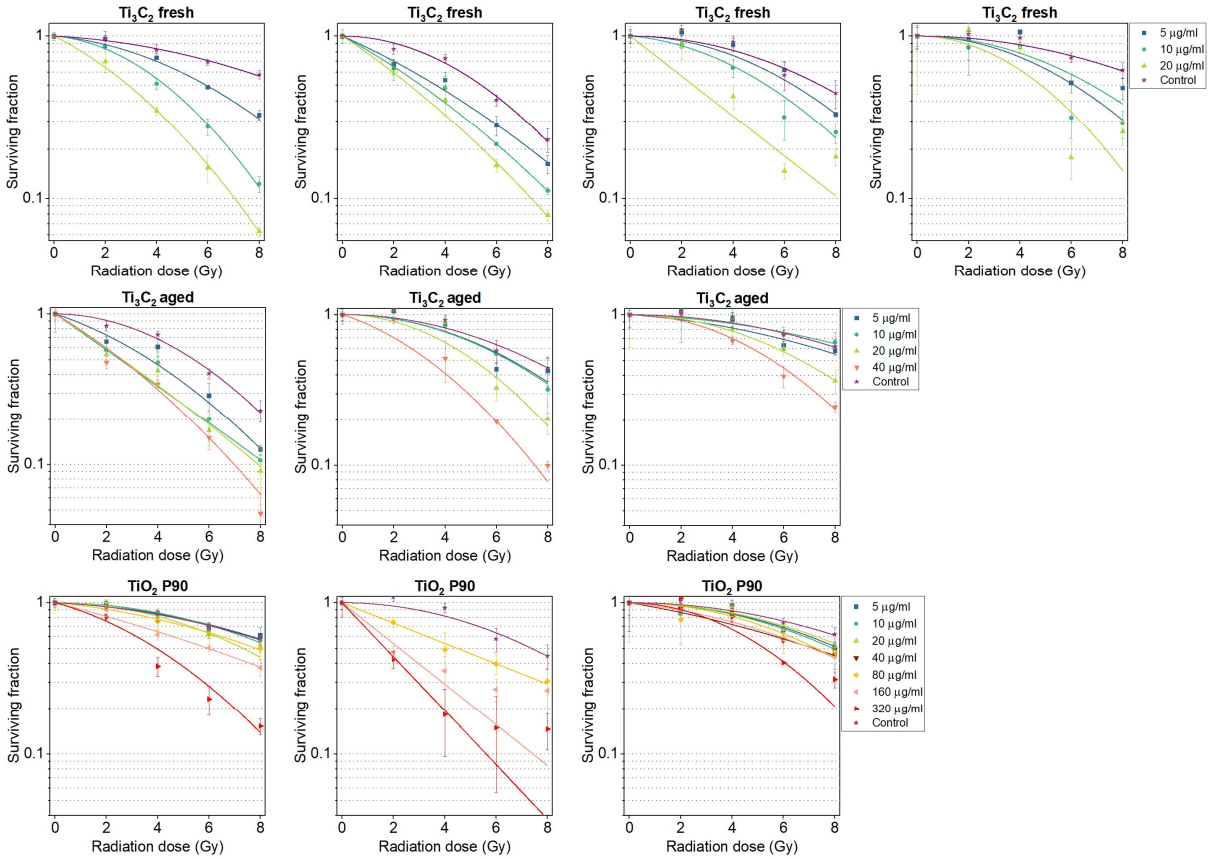


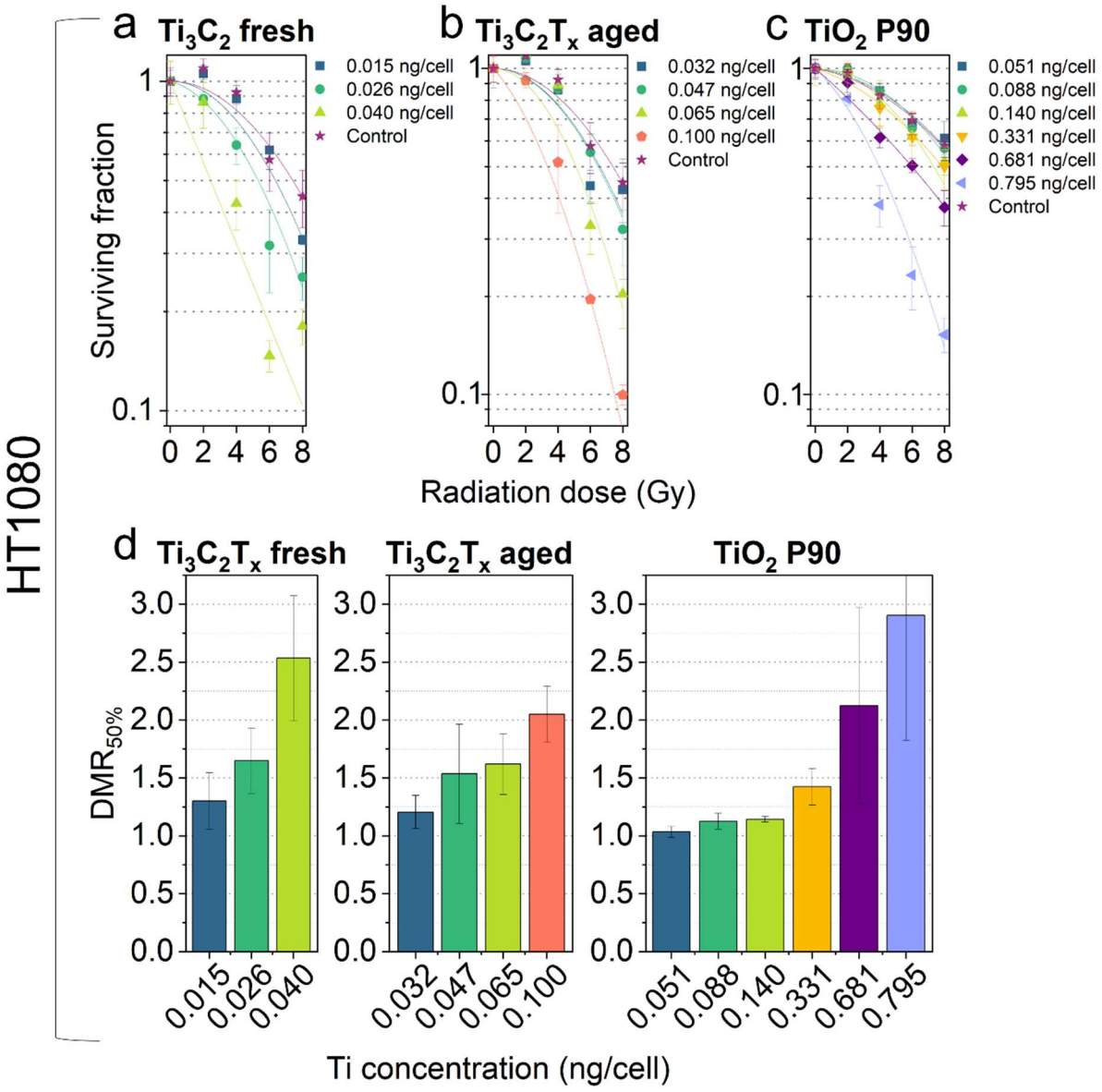
***Supplementary Figure S1**: Surviving fractions of healthy NHDF cells incubated during 24h with fresh MXenes, aged MXenes or TiO_2 P90 nanoparticles, at different concentrations. Cell viability was measured directly afterwards. None of the nanoparticle concentrations tested here impaired the viability of NHDF cells significantly, suggesting that healthy cells cope very well with the presence of these nanoparticles at concentrations yielding significant radio-enhancement effects.*



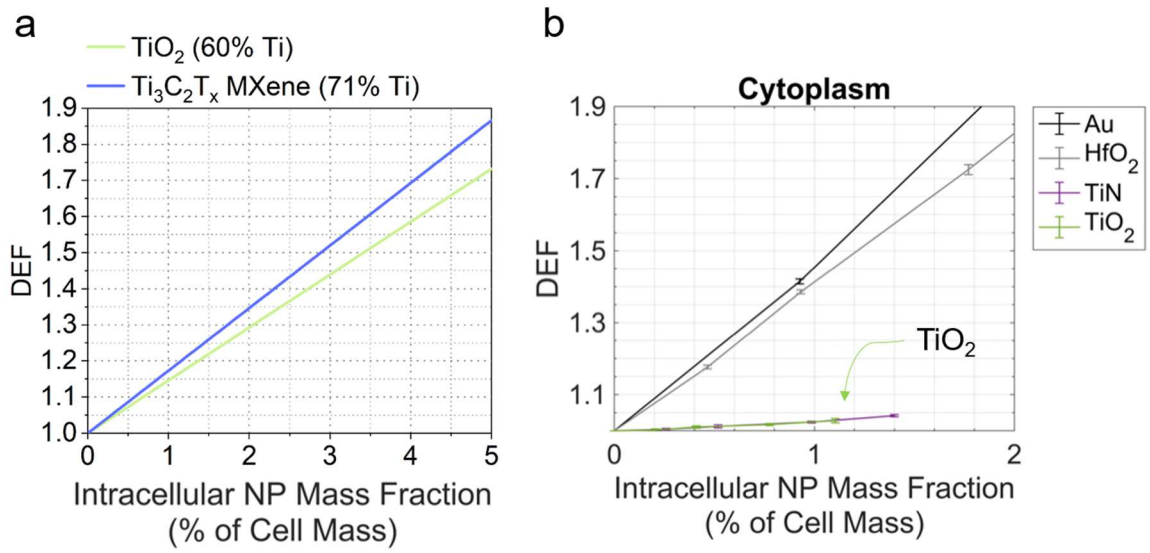
Supplementary Figure S2*: Osmium deposits observed in TEM samples stained with osmium tetroxide as part of the standard TEM sample embedding protocol. a) TEM imaging shows osmium accumulating along the outer cell membrane and around MXenes, as confirmed by STEM EDXS: b) HAADF and c) EDX map of osmium. d) Dark field image of a MXene sheet and corresponding EDXS maps for e) Ti and f) Os indicate osmium deposition on and around the MXenes. Due to the osmium accumulation, osmium-free sample preparation protocols were used for TEM data acquisition.*



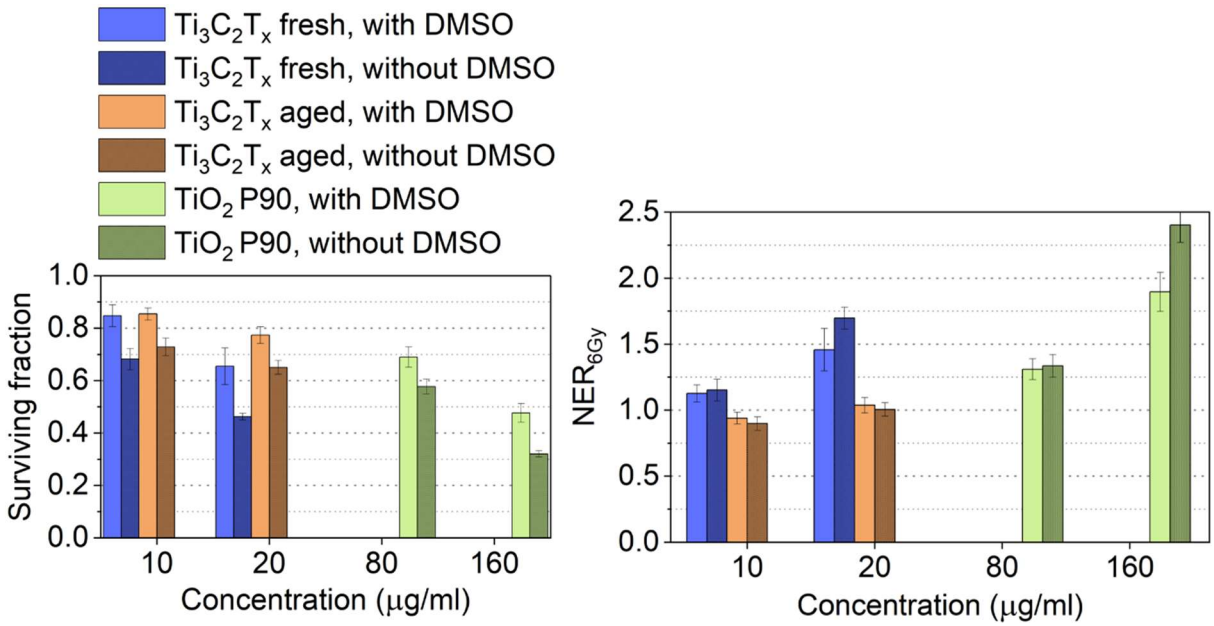
***Supplementary Figure S3**: Surviving fractions of human sarcoma cells incubated with fresh $Ti_3C_2T_x$ MXenes, aged $Ti_3C_2T_x$ MXenes and TiO_2 P90, which were used to compute the $DMR_{50\%}$. Some marked differences in the viabilities may stem from slowed cell regrowth after suffering from nanoparticle incubation at very high concentrations and irradiation.*



Supplementary Figure S4: *Surviving fractions of human soft tissue sarcoma cells irradiated at different x-ray doses, relative to untreated, non-irradiated control, treated with fresh (a) $Ti_3C_2T_x$ MXenes, (b) aged $Ti_3C_2T_x$ MXenes and (c) TiO_2 (P90), expressed as function of Titanium mass per cell. (d) Dose-modifying ratio (DMR) at 50% cell survival for aforementioned particle types and different concentrations in HT1080, expressed as function of Titanium mass per cell.*



Supplementary Figure S5: *(a) Macroscopic dose enhancement factors (DEFs) for TiO_2 and $Ti_3C_2T_x$ MXenes, computed with the corresponding energy mass absorption coefficients and an energy beam spectrum simulated to represent the experimental setup used for irradiation experiments in this study. (b) Physical DEFs in the cytoplasm for 50-nm-sized Ti-based and high-Z nanoparticles simulated using Monte Carlo simulations. Figure in b adapted from Gerken et al. Nature Communications, 2022.*



Supplementary Figure S6*: Surviving fractions of HT1080 cells exposed to fresh MXenes, aged MXenes or TiO_2 P90 nanoparticles at selected concentrations during 24h, and irradiated at 6 Gy in the presence or absence of DMSO 0.66 M. The cell viability measured 5 days after irradiation was higher for cells irradiated with DMSO than without DMSO throughout all nanoparticle concentrations, as well as for the control cells, which can be explained by the fact that X-rays cause hydrolysis and thereby create $OH^{\cdot}$ radicals. NER (nanoparticle radiation enhancement ratio) at 6 Gy irradiation for the same conditions showed that only fresh MXenes at 20 µg/ml and TiO_2 P90 nanoparticles at 160 µg/ml lead to a higher radio-enhancement without DMSO than with DMSO, indicating that the nanoparticles in these two conditions yielded a measurable increase of $OH^{\cdot}$ radical production.*