Programmed cell death induced by modulated electro-hyperthermia

Background: Modulated electro-hyperthermia (mEHT) is a non-invasive technique for targeted tumor treatment. The mEHT generated capacitive coupled modulated radiofrequency selectively accumulates in the tumor tissue without major effect in the surrounding normal tissues.

Method: HT29 human colorectal carcinoma cell line xenografted to both femoral region of Balb/C mice was treated when reaching ~1.5 cm by using a single shot mEHT treatment (Lubbe HW, Oncothermia Ltd., Paly, Hungary) for 30 minutes. Sampling was made after 0, 1, 4, 8, 14, 24, 48, 72, 120, 198, 216 h in 3 mice each group by keeping 5 untreated animals. Histomorphological, immunohistochemical and TUNEL assay results were tested in digital slides and analyzed semi-quantitatively. An apoptosis protein array was used to screen 35 apoptosis related proteins, results were evaluated using the ImageJ software.

Results: mEHT caused programmed cell death related destruction from the tumor centre. TRAILR2 was up-regulated 8h post treatment. Cleaved caspase-3 positive cells appeared only at the tumor periphery between 4-14h. AIF nuclear translocalization at 14h and cytochrome c release from the mitochondria at 8-14h and massive TUNEL positivity at 24-48h indicated DNA fragmentation.

Conclusion: In HT20 colorectal cancer xenograft mEHT (modulated electro-hyperthermia) caused programmed cell death. DNA fragmentation followed rather a caspase independent and AIF dependent subroutines with cytochrome c release.

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