

Experimental oncothermia in nude mice xenograft tumor models

Dr. Gabor Andocs¹, Dr. Nora Meggyeshazi², Dr. Peter Galfi¹, Dr. Lajos Balogh³, Dr. Laszlo Fonyad², Dr. Linda Muller⁴, Dr. Oliver Szasz⁶, Prof. Dr. Andras Szasz^{5,6}

(1) Department of Pharmacology and Toxicology, Faculty of Veterinary Science, St Istvan University, Budapest, Hungary

(2) 1st Department of Pathology and Experimental Cancer Research, Semmelweis University, Budapest, Hungary

(3) National Research Institute for Radiobiology and Radiohygiene, Budapest, Hungary

(4) Department and Clinic of Reproduction, Faculty of Veterinary Science, St Istvan University, Budapest, Hungary

(5) Biotechnics Department, St. Istvan University, Hungary (Szasz.Andras@gek.szie.hu)

(6) Oncotherm Group, Germany

Experimental oncothermia in nude mice xenograft tumor models

Dr. Gabor Andocs¹, Dr. Nora Meggyeshazi², Dr. Peter Galfi¹, P. Dr. Lajos Balogh³, Dr. Laszlo Fonyad², Dr. Linda Muller⁴, Dr. Oliver Szasz⁶, Prof. Dr. Andras Szasz^{5,6}

(1) Department of Pharmacology and Toxicology, Faculty of Veterinary Science, St Istvan University, Budapest, Hungary,

(2) 1st Department of Pathology and Experimental Cancer Research, Semmelweis University, Budapest, Hungary,

(3) National Research Institute for Radiobiology and Radiohygiene, Budapest, Hungary,

(4) Department and Clinic of Reproduction, Faculty of Veterinary Science, St Istvan University, Budapest, Hungary,

(5) Biotechnics Department, St. Istvan University, Hungary (Szasz.Andras@gek.szie.hu)

(6) Oncotherm Group, Germany

Background: Oncothermia method (OTM) uses well controlled modulated radiofrequency (RF) current-flow through the target tumor. It is an emerging technique for oncology [1]. OTM is based on solid scientific roots [2], and its experimental support connects the in-silico, in-vitro and in-vivo experiments in a synergic harmony with the permanent development of its clinical success [3]. Oncothermia has not simple a benefit from the rising temperature, but due to its non-equilibrium conditions it has a strong non-temperature dependent cell killing behavior, which is at least three times higher than the temperature induced conventional hyperthermia (HT) actions, [4]. Our present article summarizes the in-vivo experimental proofs of OTM mechanisms, pointing the direction of further development.

Method: The in vivo studies were performed using a BalbC/nu/nu mice xenografted with HT29 human colorectal carcinoma cell line. Numerous experiments were performed with highly specialized experimental setup (EHY110, Oncotherm, Germany) studying the various effects of OTM alone and compared to HT. Control better the anyway huge biovariability of the mice, the tumor was inoculated into the animals to two distant localizations (left and right femoral region) using this pair for treatment-control comparison. Regularly the right side tumor was treated with single shot OTM by 30min, and the effects were studied histomorphologically (HM) and immunohistochemically (IHCH) by various antibodies with digital microscopy system (MiraxWiev, 3D Histech).

Results: Both HM and IHCH experiments showed drastic and selective tumor-destruction by single shot OTM treatments. Compare to HT the quantity of destroyed area was larger. Definite dynamic (time-delay) processes were observed in OTM samples, suggesting to study the apoptotic initialization of the method. According to the IHCH analysis of OTM treated samples immediate activation of p53 and special relocation of β -catenin from the cell-membrane to the nuclei was detected after 24 h. Indications of reestablished gap-junction connections (connexin) was also measured in this time period.

Conclusion: Tumor-distortion effect of OTM is mainly time-delayed, the treatment probable activates mechanisms to disintegrate the tumor and destroy the malignant cells. Further experimental support and repeating controls are desired.

References:

- [1] Szasz A (2007) Hyperthermia, a modality in the wings. *J Cancer Res Ther* 3:56-66
- [2] Andocs G, Szasz O, Szasz A (2009) Oncothermia treatment of cancer: from the laboratory to clinic. *Electromagn. Biol. Med.* 28(2):148-165
- [3] Szasz A, Szasz N, Szasz O (2010) Oncothermia: Principles and Practices. Springer Verlag (<http://www.springer.com/biomed/cancer/book/978-90-481-9497-1?changeHeader>) Heidelberg, Dordrecht
- [4] Andocs G, Renner H, Balogh L, Fonyad L, Jakab C, Szasz A (2009) Strong synergy of heat and modulated electromagnetic field in tumor cell killing. *Strahlenther. Onkol.* Feb; 185(2):120-126.