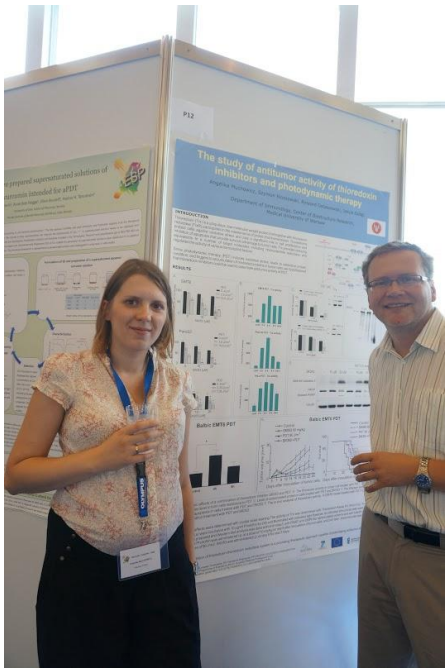
Report from active participation in 15th European Society for Photobiology Congress, Liège (Belgium), 3 - 6 September 2013 – Angelika Muchowicz



Dr. Muchowicz and Prof. Golab during her poster presentation at ESP, Liege, Belgium.

ESP Congress constitutes an important forum for dissemination of advanced knowledge and technological development in most photobiological fields of research, for scientific discussions and exchange of new ideas and for establishing new collaborations for your future research. It provides an exciting venue for scientific exchange and interaction with photobiologists.

Title of the poster: The study of antitumor activity of thioredoxin inhibitors and photodynamic therapy

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Thioredoxins are ubiquitous proteins which regulate the activity of a number of signaling pathways and transcription factors. Thioredoxins protect cells against oxidative stress and play a significant role in cell proliferation and inhibition of apoptosis that provide survival advantage to tumor cells. The thioredoxin capacity to reduce other proteins by cysteine thiol-disulfide exchange is essential for protein folding and cellular redox homeostasis. Since photodynamic therapy (PDT) induces oxidative stress, leads to extensive protein oxidation and elevates the amounts of misfolded proteins in tumor cells, we hypothesized that thioredoxin inhibitors could be used to potentiate antitumor activity of PDT.

Our results indicate that PDT induces transcriptional up-regulation of thioredoxin and thioredoxin reductase. Overexpression of thioredoxin protects tumor cells against PDT. Furthermore, it seems that thioredoxin participates in the elimination of carbonylated proteins in PDT-treated cells. Thus, we examined cytotoxic activity of the combination of PDT and thioredoxin inhibitors: PX-12 and SK053. PX-12 is an investigational compound evaluated in clinical trials, while SK053 is a novel and originally designed peptidomimetic compound that inhibits the activity of thioredoxin and thioredoxin reductase system. Our results show that both thioredoxin inhibitors effectively sensitize different tumor cell lines to cytotoxic activity of PDT. These compounds activate unfolded protein response and effectively induce apoptosis in tumor cell treated with PDT. Additionally, the antitumor activity of PDT was potentiated by thioredoxin inhibitors in vivo in EMT6 (murine breast carcinoma) and Panc02 (pancreatic carcinoma) tumor models. We conclude that inhibition of thioredoxin-thioredoxin reductase system is a promising therapeutic approach capable of potentiating antitumor effectiveness of PDT.