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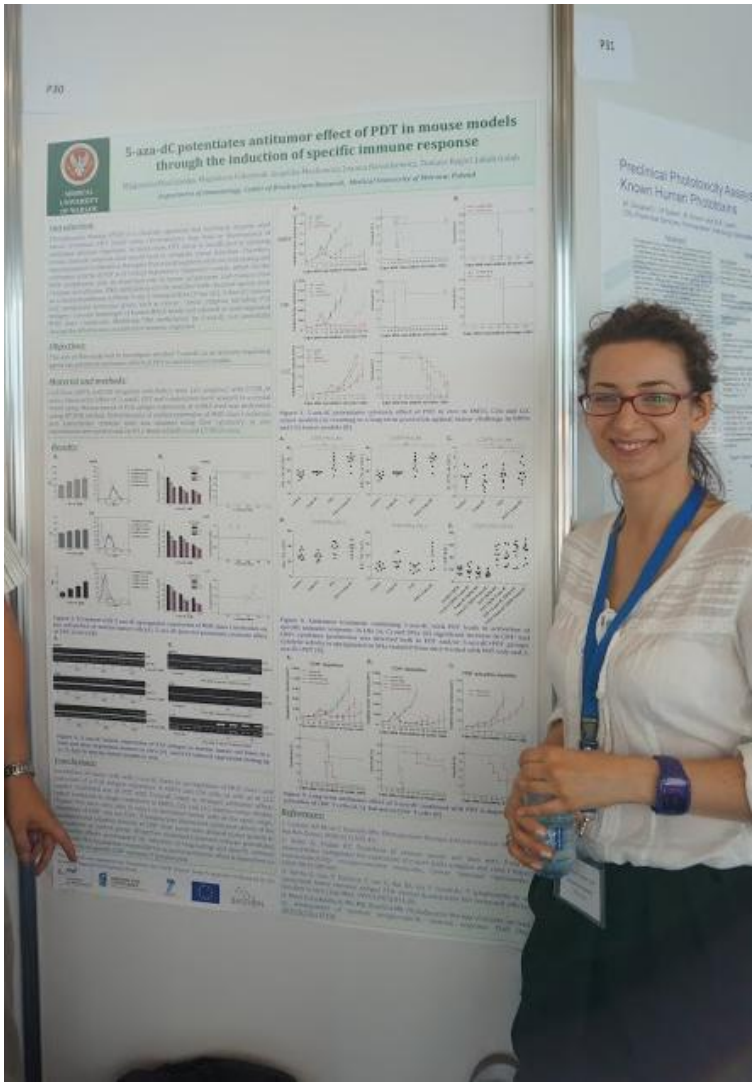
BASTION - FROM BASIC TO TRANSLATIONAL RESEARCH IN ONCOLOGY

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



Dr Wachowska during poster sesion 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: "5-aza-dC potentiates antitumor effect of PDT in mouse models through the induction of specific immune response."

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Photodynamic therapy (PDT) is a clinically approved and minimally invasive solid tumor treatment. It is a two step procedure involving administration and tumor accumulation of a photosensitizer followed by exposure to a visible light. Activated photosensitizer produces cytotoxic reactive oxygen species (mainly singlet oxygen) that result in cellular damage. PDT under some circumstances may lead to development of antitumor immune responses. In most cases PDT alone is insufficient in inducing robust immune response that would lead to complete tumor rejection. Therefore, development of combination therapies that would augment immune-stimulating and antitumor activity of PDT is of critical importance. Epigenetic mechanisms, which involve DNA methylation, act as regulators of gene expression. Aberrant silencing of numerous genes is one of the most frequent molecular changes observed in tumor cells. Epigenetic events play an important role in tumor progression and evasion from immune surveillance. DNA methylation can be modified with chemical agents such as a methyltransferase inhibitor 5-aza-2'-deoxycitidine (5-aza-dC). 5-Aza-dC induces and upregulates numerous genes, such as cancer – testis antigens, including P1A antigen - a mouse homologue of human MAGE family and silenced or downregulated MHC class I molecules. Modifying DNA methylation by 5-aza-dC can potentially change the effectiveness of antitumor immune responses. The aim of this study was to investigate whether 5-aza-dC as an immuneregulating agent can potentiate antitumor effects of PDT in murine tumor models. Incubation of tumor cells with 5-aza-dC led to up-regulation of MHC class I and induction of a P1A antigen expression in EMT6 and CT-26 cells, syngeneic with BALB/c mice, as well as in LLC cells syngeneic with C57BL/6 mice. Combined use of PDT with 5-aza-dC result in stronger antitumor effects when compared to single treatments in EMT6, CT-26 and LLC murine tumor models. Tumor free mice were able to reject re-inoculated tumor cells of the same origin. Depletion of CD8+, but not CD4+, T lymphocytes diminished antitumor effects of the treatment and adoptive transfer of CD8+ from curred mice delayed tumor growth in comparison to control group. Altogether, we observed that combined treatment induces potentiated antitumor effects accompanied by induction of long-lasting and specific immune response. The mechanism responsible for acquired antitumor effect is dependent on the activity of specific CD8+ cytotoxic T lymphocytes.