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BASTION – FROM BASIC TO TRANSLATIONAL RESEARCH IN ONCOLOGY

Report on the visit of Aleksandra Dudek-Perić to the Medical University of Warsaw, within the 7PR21/BASTION/WP1 (Twinning, T1.1)

I. Visitor: Aleksandra Dudek,

II. Host: prof. Jakub Golab, Medical University of Warsaw, Poland

Dates: 09.10.2014 – 20.11.2014

Aleksandra Dudek is a 4th year PhD student at the Cell Death Research and Therapy Laboratory, KU Leuven, Belgium. Between October 9th and November 20th, 2014, she visited the Department of Immunology, Center for Biostructure Research, Medical University of Warsaw, Poland. This visit was coordinated under the twinning agreement between the Medical University of Warsaw and the KU Leuven in WP1 (Task 1.1) and was a follow up on the experiments during previous stay (17.06.2013 – 05.07.2013).

During her PhD, Aleksandra studies key molecular and immunological parameters underlying the process of immunogenic cell death (ICD) elicited by various chemotherapeutics, using metastatic melanoma as cellular/ *in vivo* model. ICD is a concept exploiting the double targeting of tumour, whereby the ICD-inducing treatment combines a direct induction of cancer cell death with the simultaneous stimulation of anticancer immune response triggered by the dying cancer cells. At the molecular level, currently, ICD is characterised by the 'emission' of damage-associated molecular patterns (DAMPs) during various phases of the apoptotic cell death process. Once exposed on the cell surface, these endogenous molecules (i.e., DAMPs) are able to evoke anticancer immune response. A widely used method to

investigate the stimulation of anticancer immune response by the dying cancer cells is the mice prophylactic vaccination model. Initially (1st step) syngeneic mice are vaccinated with the treated cancer cells, followed by (2nd step) a challenge with the live version of the same tumour cells. If the treated cancer cells (the vaccine) are able to incite a long lasting protective anticancer immune response, this will prevent the establishment and growth of the same tumour upon re-challenging. During the previous visit few different anticancer therapies were tested. Out of them, one showed an interesting result: neither similar to the effect of the ICD-inducer (Hypercin-based photodynamic therapy), nor to the tolerogenic cell death-inducer (Brefeldin A). This valuable result was considered worth further investigation.

The main question that was addressed during this visit was if the partial, but still significant protective antitumour immunity induced by the specifically treated cancer cells is due to the stimulation of adaptive immune response and immune system related effects. Because of that we carried out the sophisticated experiment where immunocompetent mice were depleted of CD4+ or CD8+ T cells (antibody-based depletion) and only then were vaccinated with treated cancer cells and injected with live, not treated cancer cells.

While performing the experiment Aleksandra further improved her mice handling skills and learned valuable techniques like intraperitoneal injection and collection of blood from submandibular vein from mice.

The collaboration between the Cell Death and Therapy Laboratory and the Department of Immunology, supported by BASTION will be summed up with a research article that is currently under revision.