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BASTION – FROM BASIC TO TRANSLATIONAL RESEARCH IN ONCOLOGY

Report on the stay of Dr. Rut Klinger at the Department of Immunology, Medical University of Warsaw, Warsaw, Poland within the 7PR21/BASTION/WP1 (Twinning, T1.10)

Between the 9th of December 2014 and 4thJanuary 2015 Dr. Rut Klinger was visiting the laboratory of Prof. Jakub Golab (under direct supervision of Dr. Radoslaw Zagozdzon) at Department of Immunology, Medical University of Warsaw. The stay at Medical University of Warsaw was carried out within the confines of BASTION twinning programme.The overall scientific goal of Dr. Klinger's stay was to generate a hydrogen peroxide reporter system utilizing a HyPer3-based fluorescent marker.

Reactive oxygen species are products of incomplete molecular oxygen reduction. Among others, the superoxide anion radical $O2^{*-}$and hydrogen peroxide $H_2O_2$are the most investigated in biology as they are produced by a wide range of enzymes and have a number of well-known biological effects including playing roles in malignancies such as various cancer types. High-performance sensors for reactive oxygen species are instrumental to monitor dynamic events in cells and organisms. Recently, HyPer3, a genetically encoded fluorescent indicator for intracellular H_2O_2 exhibiting improved performance (as compared to previously established systems) has been described.

Dr. Zagozdzon has been working for several recent years on oxidative stress-related mechanisms in cancer. He has focused specifically onperoxiredoxin (PRDX) protein family and has recently published his work onPRDX1 in breast cancer in collaboration with Dr. Klinger's home research group (O'Leary *et al*., 2014). PRDX1 is a multifunctional protein, acting as a H_2O_2 scavenger, molecular chaperone and immune modulator. Its differential expression has been described in many tumours and in this published work the role of PRDX1 in breast cancer has been described as an independent predictor of improved outcomes in ER-positive breast cancer.

During her stay in laboratory at Warsaw Medical University, Dr. Klinger was working on generation of HyPer-3 expressing constructs with single (GFP) and double (GFP and RFP) fluorescence indicators that could subsequently be used for Dr. Zagozdzon's research in the area described above. Created vectors would be applied to establish stable lentiviral-based genetically modified cell models and would be used to efficiently monitor cellular H_2O_2 levels. Dr. Klingerhas been cloning HyPer-3 gene insert in lentiviral systems used previously in Dr. Zagozdzon's lab. It allowed her to exchange information between the lab regarding the molecular cloning protocols. At the same time generation of these lentiviral constructs would

allow genetic modification of multiple cell models that could progress the course of research of both teams.

Dr. Klinger has also participated and added her expertise to help establishing other stable genetically modified cancer cell models related to Dr. Zagozdzon's research in the area (see the image below).