Report on the visit of Magdalena Winiarska in the Institute of Tumor Immunology, Cancer Research Center of Marseille, University of Mediterranean, Marseille, France within 7PR21/BASTION/WP1 (Twinning)

Visitor: Magdalena Winiarska, PhD

Host: Daniel Olive MD, PhD, Laboratoire d'Immunologie des Tumeurs et Centre INSERM de Recherche en Cancerologie de Marseille, IBiSA Cancer Immunomonitoring platform, Institut Paoli Calmettes, Marseille, FRANCE

From August 21st until October 16th, 2013 I was visiting the Laboratoire d'Immunologie des Tumeurs, INSERM, Marseille, France. The main goal of my visit was to get familiar with a vast series of methods used to study NK cell functions. I employed flow cytometry techniques used to determine the efficacy of natural cytotoxicity as well as ADCC (antibody-dependent cell-mediated cytotoxicity) mechanisms. Furthermore, I performed experiments with intracellular cytokine staining.

The aim of my project was to evaluate the influence of various kinase inhibitors (SRC inhibitors and BCR inhibitors – ibrutinib, R406, CAL-101, MK-2206) on the activity of NK cells and ADCC process. Experiments were performed on freshly isolated NK cells from 3 donors in 3 variants (Fig.1) and included evaluation of:

A. Target and effector cells co-incubated for 4h of assay

B. Target cells pre-incubated for 24h with inhibitors, assay performed for 4h without inhibitors

C. NK cells pre-incubated 24h with inhibitors, assay performed for 4h without inhibitors

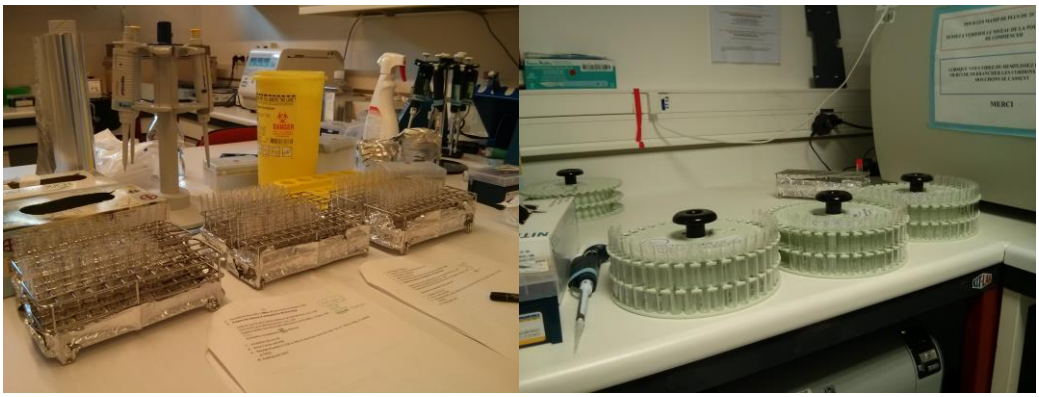

Fig.1 Experiments performed with NK cells from 3 donors incubated with 6 different inhibitors in 3 variants.

In a co-incubation model, where both target Raji cells and effector NK cells were co-cultured for 4h in presence of BCR inhibitors I observed severely impaired rituximab-induced degranulation of NK cells as well as impaired production of cytokines.

The results of experiments performed during my stay in the Laboratoire d'Immunologie des Tumeurs are included into two manuscripts:

1. B-cell receptor pathway inhibitors affect CD20 levels and impair antitumor activity of anti CD20 monoclonal antibodies. Kamil Bojarczuk, Marta Siernicka, Michal Dwojak, Malgorzata Bobrowicz, Beata Pyrzynska, Pawel Gaj, Marta Karp, Krzysztof Giannopoulos, Dimitar G Efremov, Cyril Fauriat, Jakub Golab and Magdalena Winiarska
2. SRC family kinases are involved in the regulation of CD20. Magdalena Winiarska, Kamil Bojarczuk, Beata Pyrzynska, Jacek Bil, Marta Siernicka, Nina Miazek, Piotr Zapala, Michal Dwojak, Malgorzata Bobrowicz, Agnieszka Zagozdzon, Magdalena Krol, Aleksandra Syta, Paulina Podszywalow-Bartnicka, Anna Dabrowska-Iwanicka, Przemyslaw Juszczynski, Dimitar Efremov, Mikolaj Slabicki, Thorsten Zenz, Aude Le Roy, Daniel Olive, Jakub Golab

Moreover, during my stay we managed to discuss topics for future collaboration (Fig.2).

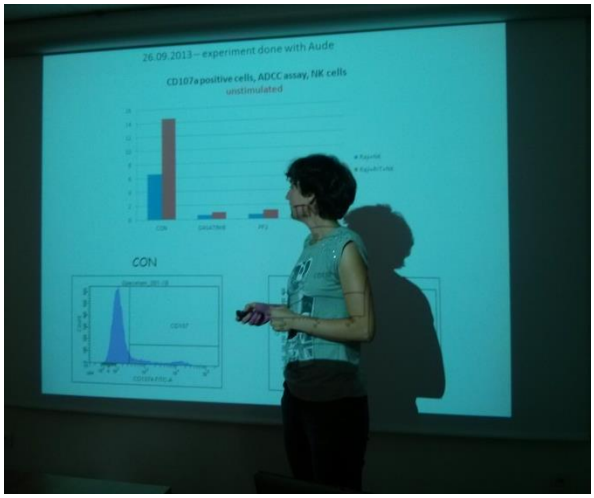

Fig.2 Seminar given by Magdalena Winiarska at Laboratoire d'Immunologie des Tumeurs, INSERM.