Capacities/Research Potential
FP7-REGPOT-2012-2013-1

Project No. 316254

BASTION

"From Basic to Translational Research in Oncology"

Deliverable D1.2

Report on the secondments between twinning partners along with the analysis of added value for potential increase of research capacity / quality of MUW

Project start date:	1.09.2012
Project duration:	42 M
Due date of deliverable:	31.08.2015
Actual submission date:	31.08.2015
Dissemination level:	PUBLIC

Table of content

page

All reports are available on BASTION Webpage: http://bastion.wum.edu.pl/en/raporty/

Introduction

Deliverable D1.2 corresponds to the Task 1 (subtasks T1.1-T.1.11) in WP1, that was delivered in time.

Transferring and implementing the best research standards, new research methods and techniques from the EU institutions collaborating with the Medical University of Warsaw in 2014-2015 was executed via:

a) 12 incoming visits of the foreign Partners' representatives to the MUW (18 months in total)

b) 40 outgoing visits of the MUW staff to the foreign laboratories (43 months in total).

The reports on research activities and photographic documentation of the visits are available on the BASTION project webpage:

http://bastion.wum.edu.pl/en/raporty-z-projektow-twinningowych/

For all twinning and networking tasks within WP1 the following goals were achieved in months 19 – 36 of the Project:

Task 1.1.

MUW: Task leader - Prof. Jakub Golab

Foreign Partners: KUL Belgium (Prof. Patrizia Agostinis), additional partner: University College Dublin, Ireland (Prof. William Gallagher)

Subject: Induction of systemic antitumor immunity by the combination of photodynamic therapy (PDT) and endoplasmic reticulum stress-inducing compounds

	PLANNED	**CARRIED OUT**
OUTGOING VISITS	1 young researcher 3 months (2014)	yes, in 100%; change of the young researcher to an experienced researcher approved by the BASTION project EU Officer;
	1 experienced researcher 2 months (2015)	yes, in 100%
INCOMING VISITS	1 young researcher 1 week (2014)	yes, in 100%
	1 experienced researcher 1 month (2014)	yes, in 100%, change of the experienced researcher to a young researcher approved by the BASTION project EU Officer

Details of the executed outgoing visits:

Visit	Name and family name of visiting researcher	Date of the visit	Place of the visit
1	Dr. Pawel Gaj	17.09.-17.11.2014.	University of Ferrara, Italy; this change in the twinning schedule has been approved by the BASTION project EU Officer
2	Slawomir Gruca	04.11.-20.12.2014.	Bioinformatics Laboratory, University of Leeds, UK; this change in the twinning schedule has been approved by the BASTION project EU Officer
3	Dr. Pawel Gaj	02.02.-04.04.2015.	University of Ferrara, Italy; this change in the twinning schedule has been approved by the BASTION project EU Officer

Ad. visit 1:

Dr. Pawel Gaj during his two month stay in Italy was working in the field of bioinformatics carrying out studies focused on contribution of different kinds of molecular determinants to differential survival rates in cancer patients. He paid a special attention to the interplay between genetic molecules of different types and those exhibiting different functions on the regulation of transcriptome of the human cells. During the first month of his stay in Italy he developed his own scientific approaches, whereas during the second month Dr. Gaj has been working on a very promising collaborative project focusing on the genomic data of patients diagnosed with the acute myeloid leukemia. This part of the research will be continued in the future at the Medical University of Warsaw and/or in collaboration with other institutions giving it a great chance to sustain the international collaboration between the institutional and personal partners participating in the Twining Programme. During his stay at the Laboratory of Professor Stefano Volinia Dr. Gaj had an opportunity to use various cutting-edge bioinformatics tools to run analysis of the next-generation sequencing (NGS) data carrying out statistical analyses on various different levels i.e. starting from using low level data processing procedures and then further progressing with higher level statistical algorithms used for the NGS data normalization, differential gene expression between classes of samples selected in unsupervised analyses. Finally, Dr. Gaj investigated the influence of differential expression of genes on survival rates characterizing identified groups of cancer patients. As a validation measure for the differential gene expression the results obtained for the transcriptomics part of Dr. Gaj's study he performed a Geneset Enrichment Analysis (GSEA) for the terms included in the Gene Ontology (GO) data base. Dr. Gaj also contributed to the assembly and installation of a high performance workstation used to carry out complex and computationally intensive calculations which are nowadays an essential element of the modern approaches in bioinformatics. The server presently available under the

deepseq.unife.it web address will be very useful for the planned scientific collaboration in the future.

Ad. visit 2:

During his stay at the University of Leeds, Mr. Slawomir Gruca participated in the discussions over bioinformatics and biostatistics topics with Prof. David R. Westhead lab members, participated in the group journal club and university bio-med seminars; one regarding a large health informatics system, provided an opportunity to discuss digital pathology matters with Mr Owen Johnson. The e-pathology area has been one of Mr. Gruca's interests - he has been involved in setting up Digital Imaging Facility at Medical University of Warsaw. Visiting University of Leeds enabled him to get a feel of and discuss solutions for presentation of digital histopathology slides, developed and evaluated in the Virtual Pathology laboratory of Dr. Roy Ruddle, in the University of Leeds. Professor Westhead's laboratory has got well established collaborations with the scientists and clinicians located at the St James's University Hospital in Leeds. Dr. Jan Taylor, who participated in the bioinformatics journal club, gave Mr. Gruca a tour of the leukaemia diagnostic facility at the hospital; discussing the implementation of high throughput technologies (NGS) for diagnosis and disease management - a practical application of recent scientific advances in clinical oncology - was a valuable experience. Secondly, Mr. Gruca teamed up with the cancer biostatistics group of professor Tim Bishop. He participated in seminar meetings and talked over the analysis of the data the group has gathered over the years (genome sequencing, mRNA expression, histopathology) researching melanoma. The established collaboration will involve analysis of WGS data. Within the BASTION project, Mr. Slawomir Gruca designed and supervised installation of a computing cluster at Medical University of Warsaw. Coincidently, during the stay in Leeds, the bioinformatics group was in the process of formulating the requirements for the purchase of a computing system for bio-med purposes. Mr. Gruca joined the work and shared the knowledge gained earlier when designing MUW's cluster. He also visited the University of Leeds high performance computing facility and discussed HPC topics with Mr Mark Dixon. Overall, the visit was a diverse and gainful experience, accompanied with initiating two scientific collaborations in the area of oncology.

Ad. visit 3:

Dr. Pawel Gaj revisited the research group of Professor Stefano Volinia at the University of Ferrara, Italy between February 2nd and April 4th, 2015. During his two month stay in Italy Dr. Gaj was working in the field of bioinformatics continuing a research initiated during his first stay at the University of Ferrara. The project Dr. Gaj was working on in Italy was a collaborative project focusing on the transcriptomic and genomic data of patients diagnosed with the acute myeloid leukemia. During his second stay in Italy Dr. Gaj strongly advanced the project shaping the whole structure of the statistical data processing and running vast majority of the bioinformatics analyses. Having gathered the majority of the results he has also drafted manuscript of a scientific paper. Apart from the strictly biostatistics-oriented work Dr. Gaj has also contributed to the assembly and installation of a small scale data

storage which is going to be used to exchange data and perform bioinformatics analyses in the prospective collaboration with Professor Stefano Volinia research group.

Details of the executed incoming visits:

Visit	Name and family name of visiting researcher	Date of the visit	Place of the visit
1	Aleksandra Dudek, Cell Death Research and Therapy Laboratory, KU Leuven	10.09.-20.11.2014.	Department of Immunology, MUW

Ad. visit 1:

Ms. Aleksandra Dudek (now Mrs. Dudek-Perić, PhD) at the time of the secondment was a 4th year PhD student at the Cell Death Research and Therapy (CDRT) Laboratory, KU Leuven, Belgium. During her PhD, Ms Dudek studied 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. During her visit to the Medical University of Warsaw she followed up on the experiments from her previous stay at MUW (17.06.2013 – 05.07.2013). The main question that was addressed during this visit was if the partial, but still significant protective antitumor 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 she 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 has been be summed up with a research article accepted to the *Cancer Research* journal. Moreover, in March 2015 Aleksandra has successfully defended her Ph.D. thesis that also included some of the results obtained during her stay at Medical University of Warsaw.

Task 1.2.

MUW: Task leader – Dr.. Magdalena Winiarska

Foreign Partner: Universite de la Mediterranee, Marseille, France (Prof. Daniel Olive)

Subject: Application of anti-CD20 monoclonal antibody-mediated immunotherapy in cancer treatment.

	PLANNED	CARRIED OUT
OUTGOING VISITS	1 experienced researcher 2 months (2014)	yes, in 100%
INCOMING VISITS	1 young researcher 1 month (2014)	yes, in 100%; change of the young researcher to an experienced researcher approved by the BASTION project EU Officer
	1 young researcher 1 month (2015)	yes, in 100%; four weeks of in-coming visit of a young researcher has been changed to a visit of an experienced researcher and ceded to allow extended the visit of Dr. Jeff Palatini (Task 1.6) to the Medical University of Warsaw; the change has been approved by the BASTION project EU Officer

The collaboration between the lab of Prof. Daniel Olive and the group of Dr. Winiarska within BASTION project has been very successful. Lab of Prof. Daniel Olive provided an expertise in multiparameter flow cytometry and studies of NK cell biology. Three researchers were trained during twinning visits. Group of Dr. Winiarska provided its expertise in molecular biology and genetic modifications of blood cells. During BASTION project it turned out that one visit of Dr. Cyril Fauriat was sufficient to transfer knowledge and necessary experience to the lab of Prof. Daniel Olive. Since all goals planned for this cooperation have been achieved Dr. Winiarska and Prof. Olive decided to limit twinning visits to 4 visits of Polish researchers in Cancer Research Center of Marseille (CRCM), University of Mediterranean, INSERM, Institut Paoli Calmettes, Marseille, and 1 visit of French researcher to the Department of Immunology, Medical University of Warsaw.

Details of the executed outgoing visits:

Visit	Name and family name of visiting researcher	Date of the visit	Place of the visit
1	Dr. Magdalena Winiarska	18.06.-13.07.2014.	Institute of Tumor Immunology, Cancer Research Center of Marseille, University of Mediterranean, Marseille
2	Malgorzata Bobrowicz	26.01.-06.02.2015.	University of Cologne
3	Marta Siernicka	09.05.-10.07.2015.	Karolinska Institutet
4	Malgorzata Bobrowicz	20.06.-12.08.2015.	University of Cologne
5	Dr. Beata Pyrzynska	25.06.-24.07.2015.	Institute of Tumor Immunology, Cancer Research Center of Marseille, University of Mediterranean, Marseille

Ad. visit 1:

The main goal of Dr. Winiarska's visit to the Laboratoire d'Immunologie des Tumeurs, INSERM, Marseille, France was to continue the collaboration on studies of NK cell functions. During her 4-week stay she got familiar with flow cytometry techniques used to determine the activation state of NK cells. Moreover, Dr. Winiarska performed experiments with a vast series of antibodies recognizing both activating and inhibitory receptors of NK cells. The aim

of her project was to evaluate how redox state influences activation state of NK cells, their natural cytotoxicity and the activity of NK cells in ADCC process. Experiments were performed on freshly isolated NK cells from 3 donors in 3 variants and the obtained results were included into the manuscript accepted to the *Immunology* journal. Among the measurable effects of the twinning between Dr. Winiarska and Prof. Olive groups is original publication in journal MAbs describing the interplay between SRC kinase inhibitors and anti-CD20 antibodies.

Ad. visit 2:

From January 26th till February 6th, 2015 Mrs. Malgorzata Bobrowicz participated in the scientific exchange in Laboratory of Molecular Biology and Immunology of CLL in University of Cologne. This laboratory, led by world famous Prof. Michael Hallek – an acknowledged specialist in the field of biology and therapy of chronic lymphocytic leukemia (CLL), is a part of Cluster of Excellence in Aging Research, an innovative multidisciplinary research unit in University of Cologne. During her stay Mrs. Bobrowicz had a chance to be a part of a research team of Dr. Lukas Frenzel, a haematologist and active scientist whom she had met during ASH Conference in December 2014. At their first meeting at ASH Conference in San Francisco they had established the basis of their collaboration and defined common interests. The laboratory of Dr. Frenzel focuses mainly on the lipid modification of proteins involved in the pathogenesis of CLL with the aim to improve the therapeutic outcome of drug combinations in CLL. During Mrs. Bobrowicz stay in Cologne she learned the methods to assess the palmitoylation status of proteins and performed experiments aiming at establishing if CD20 protein, an important therapeutic target explored in CLL, can undergo this modification. What is more she learned the methods of culture and co-culture of the cells isolated from patients with CLL, as the team of Dr. Frenzel has very well optimized protocols in this field. The results obtained during her short stay inspired Mrs. Bobrowicz and Dr. Frenzel to plan future experiments aiming at evaluating the influence of inhibitors of depalmitoylation on the efficacy of the therapy with monoclonal antibodies, part of which Mrs. Bobrowicz will perform in her laboratory in Warsaw. Moreover, they established plans for their future collaboration. As a consequence, having performed initial experiments back in Poland, Mrs. Bobrowicz will visit Dr. Frenzel Laboratory once again for 2 months in summer 2015. What is more, they agreed that Mrs. Bobrowicz would apply for Etiuda scholarship funded by National Science Centre in Poland that would enable our future collaboration.

Ad. visit 3:

From May 9th until July 10th, 2015 Ms. Marta Siernicka was visiting the Centre for Infectious Medicine (CIM) at The Department of Medicine, Karolinska University Hospital Huddinge Stockholm, Sweden. The studies within the CIM are focused on the human immune system and infection-immunity in humans. Many of the groups within CIM are involved in the NK cell biology studies and all of them work in close collaboration. The team of Professor Karl-Johan Malmberg investigates the molecular and cellular basis for NK cell differentiation and repertoire formation in health and disease. Their main goal is to study the role of killer cell

immunoglobulin-like receptors (KIR) in function of human NK cells. The main focus of Ms. Siernicka visit was to get familiar with a multicolor flow cytometry and many sophisticated assays to determine NK cell functionality on the subset level. At the beginning of her stay Ms. Siernicka has learnt how to design and compensate multicolor staining panels, up to at least 14 colors within one sample. She participated in experiments regarding optimization of the NK cells expansion protocol for the Phase I/II clinical trial based on adoptive transfer of NK cells across HLA barriers. Ms. Siernicka has learnt new method to study NK cells proliferation with simultaneous analysis of NK cell degranulation, cytokine production, contents of lytic granules and phenotype within particular proliferating NK cell subsets. Moreover, she got acquainted with the analysis of flow cytometry data using FlowJo software. At CIM Ms. Siernicka started the optimization of the new combined functional and cytotoxicity assay, which could be very useful to analyze both NK cell functionality and killing of target tumor cells in one sample within one assay. She also tested the influence of selected cell signaling pathway inhibitors on NK cells proliferation and phenotype. All the methods she has learnt during her twinning she is currently applying to improve her current research at the Department of Immunology, MUW, Poland.

Ad. visit 4:

Between 20th June and 12th August 2015 Mrs. Malgorzata Bobrowicz revisited the Laboratory of Dr. Lukas Frenzel in University of Cologne. Just at the beginning of her stay she received excellent news concerning the Etiuda scholarship funded by National Science Center for which she applied in order to continue collaboration with Dr. Frenzel. Thanks to this scholarship she will continue the research project initiated during BASTION programme and come for a 3-months internship to Cologne in summer 2016. During Mrs. Bobrowicz second stay in Dr. Lukas Frenzel lab she performed experiments assessing the influence of palmitoylation on the efficacy of various anti-tumor modalities used in the therapy of CLL. She tested well established and commonly used therapeutics as well as novel drugs. Mrs. Bobrowicz focused mainly on the therapies that induced apoptosis, which she assessed with flow cytometry. Thanks to her colleagues from Dr. Frenzel Team she gained expertize in the analysis of apoptosis and she was also given a very valuable introduction on the technical aspects of this method. This experience increased her confidence in using flow cytometry in the analyses of cytotoxicity. Moreover, having identified the therapies influenced by the palmitoylation in CLL cells she performed experiments aimed at elucidating the mechanisms of sensitization of CLL cells to the selected modalities, mostly by Western blotting. What is more, by working with Dunja Baatout Mrs. Bobrowicz has learnt the methods of exosome isolation and assessed the influence of palmitoylation on the secretion of these complexes. Mrs. Bobrowicz stay in Dr. Frenzel laboratory, apart from work in laboratory, was for her an opportunity to participate in numerous scientific meetings and lectures describing biology of CLL, but also other topics of research performed in CECAD such as metabolism in aging, diabetes, DNA damage responses in age-related diseases and mitochondrial dysfunction in neurodegeneration. Those talks are source of inspiration for her future research.

Ad. visit 5:

Dr. Beata Pyrzynska participated in the Twinning Programme of the BASTION project between June 25th and July 24th, 2015. The visit took place at the Cancer Research Center of Marseille (CRCM), affiliated to Inserm and located in the campus of Institut Paoli-Calmettes (IPC). During her stay at CRCM she collaborated with Dr. Cyril Fauriat from the research group of Prof. Daniel Olive. Two main research goals were achieved during the visit of Dr. Pyrzynska's in CRCM:

1) Estimation of the effect of FoxO1 and FoxO3 transcription factors on the expression of ligands for both the activating and inhibitory receptors of Natural Killer cells (NK cells). The experiments were performed with Raji and SU-DHL-4 cells lines modified by knockdown of FoxO1 or FoxO3 using CRISPR/Cas9 technology. Level of ligands on the surface of tumor cells was analyzed using BD FACSCanto II Flow Cytometer.

2) Optimization of transduction protocol for NK cells in order to modify them with CRISPR/Cas9 technology. The vector pLenti-CRISPRv2 was used to produce the lentivirus and transduce the NK cells followed by puromycin selection.

Details of the executed incoming visits:

Visit	**Name and family name of visiting researcher**	**Date of the visit**	**Place of the visit**
1	Dr. Cyril Fauriat, Institute of Tumor Immunology, Cancer Research Center of Marseille, University of Mediterranean, Marseille	12.07.-10.08.2014.	Department of Immunology, MUW

Ad. visit 1:

The main goal of the visit of Dr. Cyril Fauriat to the MUW was to continue collaboration between his and Dr. Winiarska's research teams on studies of NK cell functions. The collaborative project concerns the biology of human NK cells and the function of certain RNA binding protein in NK cell functions. Dr. Fauriat had the opportunity to learn and train on biomolecular techniques and to perform experiments such as cloning, transformation and transfection. He has also had the opportunity to design future experiments, especially knockout experiments with a new technique (CRISPR) that he wished to import to his laboratory. Furthermore, interactions of the Institute of Tumor Immunology, Cancer Research Center of Marseille with the team of Dr. Winiarska were strengthened and resulted in i) advances with the prospect of over-expression of their proteins of interest and ii) fruitful designs and discussions about CRISPR technique that they will use to evaluate the function of these proteins.

Task 1.3.

MUW: Task leader – Dr. Tomasz Stoklosa

Foreign Partner: University Hospital of Ulm, Germany (Prof. Lars Bullinger)

Subject: Investigation of the potential targets and markers of sensitivity to tyrosine kinase inhibitors in chronic lymphocytic leukemia.

	PLANNED	**CARRIED OUT**
OUTGOING VISITS	1 experienced researcher 2 months (2014)	yes, in 100% (but in 2015); 5 weeks of outgoing visit was completed by Marcin Machnicki (partial change from experienced researcher to young researcher was approved by the BASTION project EU Officer) and 5 days of the final twinning visit by Dr. Tomasz Stoklosa. Additionally, three weeks of out-going visit of experienced researcher has been ceded to allow to extended the visit of Dr. Lech Trzeciak from Prof. Rafal Ploski group to the University of Cologne, Germany (Task 1.8).
INCOMING VISITS	1 experienced researcher 2 x 1 month (2014)	yes, in 100%, since eight weeks of in-coming visit of an experienced researcher was ceded to allow extended the visit of Dr. Jeff Palatini (Task 1.6) to the Medical University of Warsaw; the change has been approved by the BASTION project EU Officer

Details of the executed outgoing visits:

Visit	**Name and family name of visiting researcher**	**Date of the visit**	**Place of the visit**
1	Marcin Machnicki	04.05.-13.06.2015.	Department of Internal Medicine III, University of Ulm, Germany
2	Tomasz Stoklosa	22-26.08.2015	Department of Internal Medicine III, University of Ulm, Germany

Ad. visit 1:

Between May 4th and 13th June Mr. Marcin Machnicki visited the Department of Internal Medicine III in University of Ulm in Germany. His visit was a third visit of the members of Dr. Stoklosa research team at Ulm and was strictly connected with the realization of an ongoing research project. This project is focused on the most common type of leukemia in

adults - chronic lymphocytic leukemia (CLL) and its aim is to find markers of response of CLL cells to tyrosine kinase inhibitor dasatinib. Since the major tool used in this study is gene expression profiling, collaboration with an expert in the field of genetics and hematological cancers (including CLL) prof. Lars Bullinger and his team from Department of Internal Medicine III constitutes an invaluable improvement to Dr. Stoklosa group research. The main objective of Marcin Machnicki visit in Ulm was to analyze a new group of patient-derived RNA samples that, together with the results acquired previously (during dr Eliza Glodkowska-Mrowka twinning visit in Ulm), to allow assessment of the expression patterns related to dasatinib response or resistance. Therefore, with the help of Dr. Anna Dolnik, Mr Machnicki had the possibility to learn how to acquire high-quality cDNA libraries for RNA sequencing and prepare all the samples planned in our study. During his stay in Germany Marcin Machnicki also had additional opportunities to join scientific meetings of research teams at University of Ulm, hear invited speakers from abroad, but also to watch master thesis presentations of students working in prof. Bullinger's team. Finally, he could discuss the future plans for the analysis of all data gathered during Warsaw-Ulm collaboration. Twinning visit of Marcin Machnicki in May/June 2015 was followed by short visit of Dr. T. Stoklosa in Ulm in August 2015 to sum up the obtained results and participate in data analysis.

Unfortunately twinning plan of Dr. Stoklosa group for 2014 could not be executed exactly as planned. Major reason for this was the fact that Dr. Joanna Drzewinska-Chanko, postdoc hired in 2013 in BASTION project to Dr. Stoklosa team, went on maternal leave in August 2014 and due to health problems during pregnancy she had to take sick leave already from April 2014. This resulted in delayed realization of research projects and related plans conducted by Dr. Stoklosa team, including twinning visits. Nevertheless, all planned twinning visits for 2014 were executed in 2015. On the other hand, any visit of an experienced researcher from twinning laboratory from Prof. Lars Bullinger team from University Hospital of Ulm could not be accomplished for the same reason (since research project related to gene expression analysis in leukemia required simultaneous experiments in both laboratories, delays in one laboratory enforce rescheduling of the exchange of the research visits). As mentioned in the previous report, Prof. Lars Bullinger is not only the leader of scientific laboratory but also chief attending physician at the Department of Internal Medicine III in University of Ulm and in the last year he had reorganization of the laboratory in Ulm which additionally affected twinning plans. Therefore incoming visits were ceded to allow extend visit of Dr. Jeff Palatini to conduct Task 1.6. Additionally short-term visit of Dr. T. Stoklosa to Ulm in August has been added to speed up data analysis and conclude the results of the collaboration within BASTION. Such flexibility in twinning visits has been suggested by external evaluators, Dr. Ali Gure from Bilkent University and Prof. Christel Herold-Mende from University of Heidelberg during first evaluation meeting in January 2015. This allowed to complete the task within planned timeframe.

Task 1.4.

MUW: Task leader – Prof. Zbigniew Gaciong

Foreign Partner: Karolinska Institutet, Stockholm, Sweden (Prof. Cecilia Soderberg-Naucler)

Subject: Vascular mechanism of tumor dissemination.

	PLANNED	**CARRIED OUT**
OUTGOING VISITS	1 experienced researcher 2 x 2 months (2013-2014)	yes, in 100%
INCOMING VISITS	1 experienced researcher 2 x 1 month (2013-2014)	yes, in 100%

Details of the executed outgoing visits:

Visit	**Name and family name of visiting researcher**	**Date of the visit**	**Place of the visit**
1	Dr. Marzena Lazarczyk	23.10.-21.12.2014.	Karolinska Institutet, Stockholm, Sweden
2	Dr. Marzena Lazarczyk	30.01.-30.07.2015.	Karolinska Institutet, Stockholm, Sweden

Ad. visit 1:

From 23rd October till 21st December Dr. Marzena Lazarczyk visited Center for Molecular Medicine and performed experiments for the Cell and Molecular Immunology research team headed by Professor Cecilia Söderberg-Nauclér for mutual sharing of vision, ideas, scientific knowledge and laboratory experience. Dr. Lazarczyk had an excellent opportunity to get familiar with established laboratory techniques and fixed protocols to further implement them in her research project on chemokine CCL9 involvement in colon cancer progression. Throughout her stay Dr. Lazarczyk conducted in vitro experiments with the use of CCL9-overexpressing mouse colon cancer CT26 cell line generated at the host Laboratory. All the preliminary results she obtained constitute a part of her research project co-supervised by Dr. Piotr Religa and submitted to National Research Centre in Poland in December 2014 for Sonata competition. During her stay in Stockholm, Dr. Lazarczyk attended laboratory meetings, lectures and seminars as well as got valuable new information on laboratory space organization at international, excellent level.

Ad. visit 2:

From January 30th till July 30th 2015 Dr. Marzena Lazarczyk visited Cell and Molecular Immunology Department at Center for Molecular Medicine in Stockholm. Main goal of her research studies Dr. Lazarczyk performed within indicated period was to investigate the role of MIP-1γ (alternative name: chemokine CCL9) in colon cancer progression using transduced mouse colon cancer CT26 cell line displaying enhanced CCL9 expression. In vivo studies in mice with subcutaneous injection of modified and blank control CT26 cells revealed significant differences in tumour growth between experimental groups: animals receiving control cells developed much larger tumours than mice injected with CCL9-enhanced CT26 cells as measured by caliper every 2 days. In addition, tumours appeared two times more frequently in control group than in animals inoculated with CCL9-enhanced CT26 cells. Tumour tissues and organs with suspected metastasis were fixed in formalin and frozen for inflammatory cells and lymphatic vessel immunodetection as well as microarray analysis. Simultaneously Dr. Lazarczyk continued in vitro studies using generated cell lines, CCR1 receptor inhibitors and recombinant mouse CCL9 protein in several assays: MTT, wound healing assay, migration transwell system or invasion assay for evaluation by light/confocal microscopy. Apart from studies on CCL9 chemokine in cancer, Dr. Lazarczyk supported team members of Piotr Religa's group in their research describing CMV virus involvement in colon cancer performing RNA isolations, immunohistochemical staining of several markers: CD45, CD68, LYVE1 on paraffin sections. Furthermore, Dr. Lazarczyk coordinated several research projects submissions to Polish National Science Centre. The time she spent in Swedish science entity, being one of the world's leading medical research centers was very fruitful and gave Dr. Lazarczyk unique opportunity to broaden her knowledge and to get familiar with new scientific tools and methods.

Details of the executed incoming visits:

Visit	**Name and family name of visiting researcher**	**Date of the visit**	**Place of the visit**
1	Dr. Piotr Religa	07.02.-07.04.2015.	Department of Internal Medicine, Hypertension and Vascular Diseases, MUW

Ad. visit 1:

From February 7th 2015 till April 7th 2015 Dr. Piotr Religa visited the Department of Internal Medicine, Hypertension and Vascular Diseases, MUW. During his stay in Warsaw, as previously, Dr. Religa conducted research in the field of experimental medicine together with a research team led by Prof. Zbigniew Gaciong and Dr. Grzegorz Placha. Dr. Religa's visit was aimed at finalizing their collaborative research in the field of circulating tumor cells (CTCs) in the diagnostics of cancer, especially in patients with idiopathic thromboembolism (IT). Together with Prof. Gaciong team he developed cancer screening techniques in IT patients based on real time PCR. Briefly, they performed observational cohort study among

110 patients with idiopathic lung thromboembolism using estimation in blood of CTCs and markers measured by RT-PCR. As results, 17 patients had increase CTCs indicating cancer. 14 (12.7%) patients among them was diagnosed with cancer after lung surgery. The patients were followed for 2 years. Eventually, 2 patients developed cancer, 1 (50%) with originally increased CTCs count. 9 patients had increased CTCs count however were not diagnosed cancer in the following 2 years. In conclusion, application of CTC for cancer screening requires additional studies.

Task 1.5.

MUW: Task leader – Dr. Pawel Wlodarski

Foreign Partner: Radboud University Medical Center Nijmegen, the Netherlands (Prof. Jack Schalken), additional partner: Saarland University, Germany (Prof. Friedrich A. Grässer)

Subject: Inhibitors of metaloproteases in prostate cancer.

	PLANNED	**CARRIED OUT**	
OUTGOING VISITS	1 young researcher 2 x 1 month (2014)	yes, in 100%	Five weeks of out-going visit of young researcher and six weeks out-going visit of experienced researcher has been ceded to allow extended visits of prof. Krystian Jazdzewski (Task 1.6), prof. Rafal Ploski (Task 1.8) and Dr. Radoslaw Zagozdzon (Task 1.10) team members to the University of Ferrara, University of Cologne and the University College Dublin, respectively.
	1 experienced researcher 2 x 1 month (2015)	yes, in 100%	
INCOMING VISITS	1 young researcher 1 month (2014)	No	Four weeks of in-coming visit of young researcher and four weeks of in-coming visit of experienced researcher has been ceded to allow extended the visit of Dr. Jeff Palatini (Task 1.6) to the Medical University of Warsaw; the change has been approved by the BASTION project EU Officer.
	1 experienced researcher 1 month (2014)	yes, in 100%	

Details of the executed outgoing visits:

Visit	**Name and family name of visiting researcher**	**Date of the visit**	**Place of the visit**
1	Radoslaw Maksym	03.07.-16.07.2014.	Institute of Clinical and Experimental Surgery, Saarland University, Germany
2	Dr. Madgalena Banach-Orlowska	21.10.-01.11.2014.	Department of Virology, University Hospital, Saarland University, Germany
3	Tomasz Piecha	25.11.-29.11.2014	Radboud University Medical Center Nijmegen, the Netherlands

Ad. visit 1:

The major task of Radoslaw Maksym visit to the Saarland University was to get extensive training in the unique methods of analysis of angiogenesis in animal models and to train microsurgical skills. Mr. Maksym put his hands on the dorsal skinfold chamber technique of implantation of endometrial tissue enabling real time observation of angiogenesis *in vitro* without the need of animal scarification for further implantation of endometrial implants. Furthermore, he was trained in the animal research methodology (e.g. estrous cycle analysis) and husbandry routine implemented at the University of Saarland. Mr. Maksym learnt also the aorta ring assay that allows assessment of the influence of diverse biophysical and pharmacological conditions (i.e.: drugs, cytokines, miRNA on angiogenesis in an organotopic model. He also had an opportunity to watch and train operative procedures for induction of peritoneal and mesenteric endometriosis lesions. Moreover, Mr. Maksym was trained in the computed methods of acquisition and data analysis (*in vivo* microscopy, MRI, X-ray and high resolution ultrasonography). Finally, during his stay Mr. Maksym presented the results of his current research in endometriosis and techniques applied by Dr. Wlodarski team to nurture the collaboration between MUW and Saarland University in tumor and endometrial angiogenesis studies.

Ad. visit 2:

The main goals of Dr. Banach-Orlowska two-week stay in the Saarland University were: (i) to discuss with Prof. Grasser the common interests and possibilities of close collaboration; (ii) to discuss the main topics of her grant proposal on miRNome characterization in endometriosis, and (iii) to get familiar with laboratory techniques employed by prof. Grasser team. Prof. Grasser is an expert in the field of miRNA analysis. His work is currently focused on the problems of the cellular response to the infection with Epstein-Barr virus (EBV) particularly in terms of miRNA composition, as well as on the searching for the molecular mechanisms of viral - host interactions. Prof. Grasser has also contributed to the miRNA profiling in prostate cancer. During her stay in Prof. Grasser's laboratory, Dr. Banach-Orlowska had an opportunity to assist and perform various laboratory techniques such as: co-immunoprecipitation of complexes formed by Ago2 protein (proteins and miRNAs) from distinct cell lines, luciferase assays, Northern blot analysis. Importantly, during discussions on their research interests, Dr. Banach-Orlowska and Prof. Grasser focused on a common topic concerning the functional aspects of miRNA in pathogenesis. If they obtain promising results in the project concerning the searches for new miRNA/ isomiRNAs in endometriosis, Dr. Wlodarski and Prof. Grasser teams would broaden their collaboration.

Ad. visit 3:

Mr. Tomasz Piecha is a urologist working at MUW and a researcher closely collaborating with Dr. Wlodarski group on development of prostate cancer. His visit to Radbound University was planned to set up a new branch of the research, aiming at involvement of prostasomes (the extracellular vesicles (EVs) released into prostatic fluid by prostate epithelial cells) in prostate cancer development. The experience of Dr. Schalken's group in this field is outstanding and this twinning visits was expected to help Dr. Wlodarski research team to modify their initial project.

From November 25th till November 29th 2014, Mr. Piecha visited the Radbound Institute for Molecular Life Sciences (RILMS) at Radbound University Medical Center in Nijmegen, Nederlands. Professor Jack Schalken is the leader in the field of the biology of urological cancers at RILMS, and world-class expert on prostate cancer molecular biology and prostate cancer biomarkers. His research group focuses on the discovery of new prostate cancer biomarkers and new molecular-based treatment solutions for urological cancers. The aim of Mr. Piecha visit to RILMS was to learn research techniques that allow the isolation and analysis of prostate-derived exosomes. Moreover, during his visit he gained some knowledge on the use of exosomes as potential biomarkers and therapeutic targets in prostate cancer. Mr. Piecha stay in RILMS not only helped to establish new scientific contacts but also to plan further cooperation between Radbound Institute for Molecular Life Sciences and Department of Urology, Medical University of Warsaw .

Twinning with Dr. Wlodarski partners has been successfully conducted for young and experienced scientist from Poland, who visited his partners in Germany and Netherlands. However, despite numerous invitations, senior researchers from the partnering institutions were not able to visit Dr. Wlodarski laboratories in Warsaw. It is important to stress, that they have been always helpful in discussions that solved Dr. Wlodarski team problems on many occasions. Their help in this matter is undisputed.

Task 1.6.

MUW: Task leader – Prof. Krystian Jazdzewski

Foreign Partners: University of Ferrara, Italy (Prof. Stefano Volinia), additional partner: Leeds Institute for Molecular Medicine, University of Leeds, UK (Dr. Sean Lawler)

Subject: The role of microRNAs sequence variations in response to cancer treatment.

	PLANNED	**CARRIED OUT**
OUTGOING VISITS	1 young researcher 2 x 1 month (2013-2014)	yes, in 100%; change of the young researcher to an experienced researcher approved by the BASTION project EU Officer
	1 experienced researcher 2 x 1 month (2014)	yes, in 100%
INCOMING VISITS	1 young researcher 1 month (2014-2015)	yes, in 100%; change of the young researcher to an experienced researcher

		approved by the BASTION project EU Officer
	1 experienced researcher 1 month (2014)	yes, in 100%

Details of the executed outgoing visits:

Visit	Name and family name of visiting researcher	Date of the visit	Place of the visit
1	Prof. Krystian Jazdzewski	24.07.-25.08.2014.	University of Ferrara, Italy
2	Dr. Michal Swierniak	22.11.-06.12.2014	University of Ferrara, Italy
3	Monika Kolanowska	23.02.-22.03.2015.	University of Ferrara, Italy
4	Dr. Monika Maciag	11.04.-09.05.2015.	University of Ferrara, Italy
5	Dr. Michal Swierniak	30.05.-27.06.2015.	University of Ferrara, Italy
6	Dr. Anna Wojcicka	24.06.-19.07.2015.	University of Ferrara, Italy
7	Dr. Anna Wojcicka	22.07.-08.08.2015.	University of Ferrara, Italy

Ad. visit 1:

During Prof. Jazdzewski stay in Ferrara he had the great opportunity to discuss with Prof. Volinia the details of their current collaborative projects, and future plans of cooperation. Prof. Stefano Volinia is an expert in computational biology. He has been involved in developing bioinformatics applications since 1988 (identification of statistically anomalous oligonucleotides in DNA databases). Lately he has been responsible for developing in-house protocols for DNA microarrays and next-generation sequencing analysis. Prof. Jazdzewski and Prof. Volinia both are especially interested in genome-wide analysis of miRnome in human cancers. They were working together on novel ways of analysis of the next-generation sequencing data, and combining them with publicly available data from different platforms. They focused on single nucleotide mutations in microRNA genes, and the ways to prove their functional relevance. First, they went through the detection and annotation process of all known and yet unidentified miRs and their isoforms in pairs of cancer and unaffected tissue from the same individual, and in normal tissue from cancer-free controls. As result they obtained a complete dataset of RNA molecules and their changes as normal tissue develops into cancer. Then, they correlated the deregulated miRs with the results of mRNA decay analysis. Finally, they worked on using the obtained data for the analysis of genetic background of an individual patient, identification of various factors implicated in clinical outcome of the disease and the ways to use it for tailoring of potential targeted therapies.

Ad. visit 2:

During his 2-weeks stay Dr. Michal Swierniak was working on analysis of the Next Generation Sequencing (NGS) data of patients diagnosed with the acute myeloid leukemia (AML). His analyses were focused on detection and annotation of circular RNAs (circRNAs). Dr. Swierniak has tested several approaches to optimize several steps of circRNAs detection, including aligning reads to the human genome, splitting unmapped reads to obtain anchors

from both ends, filtering, annotating and normalizing obtained results. As Prof. Volinia is an expert with great experience in NGS analysis so, apart from the above research, Dr. Swierniak had great opportunity to discuss with him other kinds of NGS data based applications such as quality control, gene expression profiling, variant discovery, targeted resequencing and others.

Ad. visit 3:

From 23rd of February until 22nd of March, 2015 Ms Monika Kolanowska visited research group of Prof. Stefano Volinia at University of Ferrara, Italy. During her one month stay in Italy Ms Kolanowska was fortunate to be involved in two interesting projects. In the first she evaluated the synergistic action of microRNAs and chemotherapeutic drugs on melanoma cell lines. The team was able to point microRNAs which increases the effect of anticancer drugs on examined cells. Furthermore that experience let Ms Kolanowska to learn new methods related to cytotoxicity assays which she will consider to use in her studies in Warsaw. In the second project Ms Kolanowska prepared vectors expressing pre-miRNAs. She selected 8 microRNAs significantly deregulated in breast cancer and melanoma and cloned sequences of their precursors to pcDNA3 vector. Prepared plasmids will be used for further evaluation of microRNAs effect on increased or decreased activity of anticancer drugs. As Prof. Stefano Volinia is a great expert in Next Generation Sequencing, thus Ms Kolanowska also had the opportunity to learn from him appropriate designing of experiments with use of this technology.

Ad. visit 4:

From April 11th till May 9th, 2015 Dr. Monika Maciag visited research group of Prof. Stefano Volinia at the University of Ferrara in Italy. Prof. Volinia is an expert in computational biology and has been involved in developing bioinformatics applications since 1988. Recently he has been responsible for developing an in-house protocols for DNA microarrays and next-generation sequencing analysis. His laboratory group studies the role of microRNAs in the progression and invasiveness of melanoma and breast cancer. During her stay at the University of Ferrara, Dr. Maciag had opportunity to join the laboratory group of Prof. Volinia. She participated in the on-going activity of his laboratory team concerning the influence of several microRNAs on melanoma. Dr. Maciag performed series of experiments to elucidate the effect of transfection of different microRNAs and drugs on various melanoma cell lines. One of the aim was to find microRNAs that inhibit cell growth. Having analyzed the results of individual experiments the group of Prof. Volinia together with Dr. Maciag compared the outcomes of experiments performed in parallel by few laboratory researchers and spent some time on discussion on the final results. During laboratory work Dr. Maciag had occasion to compare and discuss with the laboratory team members the advantages and limitations of different methods used in their laboratories. Thus, they had great opportunity to exchange their laboratory experiences.

Ad. visit 5:

From May 30th till June 27th, 2015 Dr. Michal Swierniak visited the research group of Professor Stefano Volinia at the University of Ferrara, Italy. It was his second visit in Ferrara (the first was in the end of 2014) and he was continuing the project of detection, annotation and statistical analyses of circular RNAs from the Next Generation Sequencing (NGS) data of patients diagnosed with the acute myeloid leukemia (AML). After testing available tools for exploring circRNA Dr. Swierniak decided to create his own algorithm which allow to detect potential circRNAs in sensitive and specific way. During his stay in Ferrara, using his own algorithm, Dr. Swierniak analyzed 250 AML samples resulting in identification of over 1000 circRNAs expressed in AML samples. These circRNAs need to be analyzed statistically and validated on the independent group of samples.

Ad. visit 6 and 7:

Dr. Anna Wojcicka visited the group of Prof. Stefano Volinia at University of Ferrara, Italy, twice - between 24.06 and 08.07.2015 and between 22.07 and 08.08.2015. Prof. Stefano Volinia is an expert in computational biology. Lately he has been responsible for developing in-house protocols for DNA microarrays and next-generation sequencing analysis. Both labs are interested in developing novel pipelines for the identification and analysis of non-coding RNAs from next-generation sequencing data. Dr. Wojcicka stay was related to the collaboration between the Department of Genomic Medicine, MUW and University of Ferrara on large scale data analysis and its many uses for studies of human cancers. In addition, it was a follow-up of the twinning visit performed by Dr.. Monika Kolanowska. During her stay, Dr. Wojcicka also discussed with Prof. Volinia the possibilities of applying for joint EU grants offered within Horizon 2020. The grant applications are currently being drafted and they expect to apply for collaborative projects on the use of non-coding RNAs in diagnostics and therapies of human cancers.

Details of the executed <u>incoming</u> visits:

Visit	**Name and family name of visiting researcher**	**Date of the visit**	**Place of the visit**
1	Prof. Stefano Volinia	21.05.-19.06.2014.	Laboratory of Genomic Medicine, Chair of General, Transplant and Liver Surgery, MUW
2	Dr. Jeff Palatini	13.01.-17.08.2015.	Laboratory of Genomic Medicine, Chair of General, Transplant and Liver Surgery, MUW
3	Prof. Stefano Volinia	15.03.-31.03.2015.	Laboratory of Genomic Medicine, Chair of General, Transplant and Liver Surgery, MUW

As execution of in-coming visits planned within the BASTION project met abovementioned obstacles, we decided to cede the remaining weeks of in-coming secondments to extend the visit of Dr. Jeff Palatini (Task 1.6) and Dr. Rut Klinger (Task 1.10) to the Medical University of Warsaw. These changes have been approved by the BASTION project EU Officer.

Ad. visit 1:

Prof. Stefano Volinia visited the Laboratory of Genomic Medicine between May 20th and June 21st, 2014. His stay was connected with the on-going activity of the laboratory, concerning mainly large scale data analysis and its possible use in studies on human cancers. Dr. Jazdzewski and Prof. Volinia teams were mainly interested in developing a proper pipeline for identification of novel microRNAs in data obtained in next-generation sequencing analysis. They also discussed the possibilities of applying for joint EU grants offered within Horizon 2020. On May 23rd, 2014 Prof. Volinia gave a lecture on „The role of microRNAs in the progression and invasiveness of breast cancer", during which he told the audience about the novel findings and his own role in elucidation of molecular changes underlying breast cancer.

Ad. visit 2:

Dr. Jeff Palatini stayed at Prof. Jazdzewski's lab at the Medical University of Warsaw from 13.01.2015 until 17.08.2015. During his stay, Dr. Palatini participated in on-going research projects involving next-generation sequencing methods, including small RNA sequencing. Specifically, Dr. Palatini was involved with the planning and set-up of the next-generation sequencing facility at MUW. Initially, he presented a series of lectures and a number of presentations focused on developing a greater understanding of sequencing. Once the sequencing instrumentation was installed, Dr. Palatini began working with Prof. Jazdzewski's lab on both small RNA focused sequencing and trancriptome sequencing projects, which are continuing. The most recent project he has worked on is the implementation of pre-indexing DNA fragments for targeted re-sequencing in mutation analysis in germline patient samples. The overall goal is to use next-generation sequencing for population screening in cancer and other disorders, including non-invaisive prenatal testing (NIPT).

Ad. visit 3:

The second visit of Prof. Stefano Volinia to the Department of Genomic Medicine, MUW took place between 15th and 31st of March 2015. Both Prof. Volinia and Prof. Jazdzewski are mainly interested in developing an up-to-date, sensitive and specific pipeline for the identification and analysis of non-coding RNAs from next-generation sequencing data. Prof. Volinia stay was related to their collaboration on large scale data analysis and its many uses for studies of human cancers. During his stay in Warsaw, Prof. Volinia also discussed with Prof. Jazdzewski the possibilities of applying for joint EU grants offered within Horizon 2020. The arrangements resulted so far in two joint applications for Marie-Curie grants.

Further applications are being currently drafted. On March 18th, 2015 Prof. Volinia gave a lecture entitled „The role of microRNAs in the progression and invasiveness of breast cancer", during which he told the audience about the state-of-the-art and the novel findings in the elucidation of molecular changes underlying breast cancer. The lecture took place at the Medical University of Warsaw.

Task 1.7.

MUW: Task leader Dr. Piotr Religa

Foreign Partner: Karolinska Institutet, Stockholm, Sweden (Prof. Monica Nister)

Subject: Studies of circulating tumour cells in diagnostics of colon cancer.

	PLANNED	**CARRIED OUT**
OUTGOING VISITS	1 experienced researcher 2 x 6 months (2014-2015)	yes, in 100%; four weeks of out-going visit of experienced researcher has been ceded to allow extended visits of Dr. Dominika Nowis (Task 1.9) team member (Dr. Piotr Mrowka) to the KU Leuven.
INCOMING VISITS	1 experienced researcher 2 x 1 month (2014-2014)	yes, in 100%

The collaboration between WUM and Prof. Cecilia Naucler and Prof. Monica Nister/ Karolinska Institutet, Stockholm, Sweden was successful. Three researchers were trained during BASTION project Task 1.7. They obtained extensive training in tumor biology, virology, and techniques for biological material analysis. Prof. Naucler used animal facility that is based in WUM to execute her research projects. However, due to personal problems of Dr. Oksana Kovtonyuk, remaining 3 months of her out-going mission to the KI was not possible.

Details of the executed outgoing visits:

Visit	**Name and family name of visiting researcher**	**Date of the visit**	**Place of the visit**
1	Dr. Oksana Kovtonyuk	16.02.-12.04.2014.	Karolinska Institutet, Stockholm, Sweden
2	Dr. Oksana Kovtonyuk	30.05.-29.06.2014.	Karolinska Institutet, Stockholm, Sweden
3	Dr. Marzena Lazarczyk	30.01.-30.07.2015.	Karolinska Institutet, Stockholm, Sweden

Ad. visit 1:

During her second stay in Karolinska Institutet Dr. Kovtoniuk continued her research in the field of experimental oncology previously started in collaboration with Prof. Cecilia Söderberg-Nauclér's team focused on understanding cytomegalovirus (CMV) role in colon cancer development as well as on the evaluation of antiviral and anti-inflammatory therapy effectiveness in the treatment of CMV-positive colon cancer. The main goal of Dr. Kovtoniuk stay at CMM was to perform immunohistochemical staining of tissue samples collected at MUW with their subsequent analysis for chemokines expression and levels of the markers of inflammation. During her stay at Karolinska Institutet Dr. Kovtoniuk had a unique possibility to attend numerous scientific courses (e.g. "Tumor virology course" and a joint international course "Employing genome-wide technologies for functional regulation in development and disease" organized by the RIKEN Center for Life Science Technologies, Yokohama, Japan and Karolinska Institutet) followed by a unique series of forward-looking lectures given by world leaders in their fields.

Ad. visit 2:

The main purpose of the 3rd visit of Dr. Kovtoniuk to Karolinska Instituet was to perform staining of the extracellular matrix (ECM) components (namely elastin and collagen) in patients samples collected at the MUW. The patients were diagnosed with arteriovenous fistula (AVF) - an abnormal connection between an artery and a vein. Dr. Kovtoniuk focused on analysis of malignant tumor-associated AVFs. Following surgical excision, fixation, embedment and sectioning, AVFs samples from patients underwent three different stainings. Hematoxylin and eosin (H&E) staining was used to determine the general morphology of the blood vessels. Masson trichrome staining was used for determination of collagen in tissue, Verhoeff van Gieson (EVG) staining was used to determine the presence of elastin in tissues. Samples were then analyzed histologically for collagen and elastin content. The subsequent numerical analysis content was done using next-generation viewer software (NDP.view2). Results of the project are in preparation for publication.

Ad. visit 3:

The detailed description of Dr. Marzena Lazarczyk visit to the Karolinska Institutet is included into Prof. Gaciong team report on task T1.5 (this secondment was executed to fulfil WP1 tasks 1.4 and 1.7).

Details of the executed <u>incoming</u> visits:

Visit	**Name and family name of visiting researcher**	**Date of the visit**	**Place of the visit**
1	Dr. Piotr Religa	28.09.-30.11.2014	Department of Internal Medicine, Hypertension and Vascular Diseases

Ad. visit 1:

From September 2014 to November 2014 Dr.. Piotr Religa visited the Department of Internal Medicine, Hypertension and Vascular Diseases, the Medical University of Warsaw. During his stay in Warsaw, Dr. Religa conducted research projects in the field of experimental medicine together with a research team led by Prof. Zbigniew Gaciong and Dr. Grzegorz Placha. Our research was aimed at establishing of collaboration to study the role of cytomegalovirus in oncology by using equipment and facility that are available at the Medical University of Warsaw. Dr. Religa research project focuses on the use new approaches and technologies to study the relationship between cytomegalovirus (CMV) infection and progression of colon cancer. The rationale for the proposed research project is that CMV has been shown to be a common virus that occurs in 98% of human population and is associated with cancer progression. The mechanism, by which CMV affects progression of cancer is not evaluated in details. In his research Dr. Religa focuses on the analysis of clinical samples obtained from colon cancer patients and identification of CMV-related proteins in tumors to explanation the CMV-dependent mechanism of tumor progression. During his visit at MUW in 2014 Dr. Religa mainly focused on establishment of colon cancer and glioblastoma animal models indispensable for his future research.

Task 1.8.

MUW: Task leader – Prof. Sławomir Majewski / Prof. Rafal Ploski

Foreign Partner: University of Cologne, Germany (Prof. Herbert Pfister)

Subject: Molecular and genomic studies of HPV-associated carcinogenesis.

	PLANNED	**CARRIED OUT**
OUTGOING VISITS	1 experienced researcher 1 month (2014)	yes, in 100%
INCOMING VISITS	1 experienced researcher 1 month (2014)	yes, in 100%; four weeks of in-coming visit of an experienced researcher has been ceded to allow extended the visit of Dr. Jeff Palatini (Task 1.6) to the Medical University of Warsaw; the change has been approved by the BASTION project EU Officer.

As previously stated by, the postdoctoral fellow (Dr. Lech Trzeciak) planned to join Prof. Majewski team, was finally hired by Prof. Rafal Ploski form the Department of Genetics, MUW in September 2013 and participated in the execution of the task T1.8.

A visit of BASTION scientist (Dr. Lech Trzeciak) to the Institute of Virology, University of Cologne (Director prof. Herbert Pfister) was split into two parts, and the first part (20 days) took place in spring 2014 and the second part (6 weeks) - in summer 2015.
The twinning with the Institute of Virology in Cologne, Germany was originally planned to involve the Department of Dermatology, Medical University of Warsaw, headed at that time by prof. Sławomir Majewski. Later on Prof. Majewski was appointed as a Vice Rector for Science and International Relations of the whole University and vacated his position as the head of Dermatology, what resulted in profound shift of his duties and responsibilities. Consequently his role in BASTION changed and was partly overtaken by prof. Rafal Ploski, head of the Department of Medical Genetics, and the recruited postdoc Lech Trzeciak. Together with German partners we have developed a cooperation in the field of human papillomaviruses infections in susceptible humans (one manuscript is in preparation), thanks also to the personal involvement and support of prof. Majewski. The Department of Medical Genetics specializes in Next Generation Sequencing (NGS; whole exome/genome sequencing, methylation studies, RNA sequencing) and population screening and we were inviting our partners to take advantage of these capabilities that could be exploited, for example, in functional studies on cellular or animal models or in studies on HPV sequence variability. While initially it seemed promising, ultimately has not led to the reciprocal twinning visit. We can only presume that at this phase of research Institute of Virology team was - regrettably - not sufficiently interested in NGS studies.

Details of the executed outgoing visits:

Visit	**Name and family name of visiting researcher**	**Date of the visit**	**Place of the visit**
1	Dr. Lech Trzeciak	23.04.-11.05.2014.	Institute of Virology, University of Cologne and the German National Reference Center for Human Papilloma Viruses
2	Dr. Lech Trzeciak	03.06.-17.07.2015.	Institute of Virology, University of Cologne and the German National Reference Center for Human Papilloma Viruses

Ad. visit 1:

The main goal of Dr. Trzeciak visit to Prof. Pfister laboratory was to elucidate the meaning of a homozygotic splicing site change that according to *in silico* analysis would lead to splicing aberrations resulting in protein truncation. To better characterize the HPV infection in a suspected epidermodysplasia verruciformis (EV) case, Dr. Trzeciak has successfully performed an extensive genotyping of the course of HPV infection throughout 8 years of disease history of the suspected case, utilizing formalin-fixed paraffin-embedded tissues (FFPE) as a DNA source. He had gathered hands-on experience in DNA isolation from FFPE, broad spectrum PCR and nested PCR with detection on probe-coated beads using Luminex flow-cytometry-like assay, reverse hybridization assay (RHA) to the Inno-LiPA blots. These studies demonstrated a profile of infection consistent with the diagnosis of EV. Interestingly,

1) rare strain of HPV alpha continuously dominates in genital lesions despite of a clear exposure to the typical HPV16 strain in the past; 2) while patient's skin is coinfected with multiple beta HPV types at various locations (what is typical for EV), one strain prevails with quite stable viral loads 3) HPV beta viral loads seem to remain unaffected by transplantation of the body skin onto a genital area; so far there are no signs of the dominant alpha type spreading into the transplant, despite the recurrence of skin changes in this area 4) a dramatic increase of viral DNA of another HPV B type was seen in lesions histologically typical for EV. The research initiated by Dr. Trzeciak in Prof. Pfister laboratory was continued in summer 2015.

Ad. visit 2:

During the first part of his twinning in the Institute of Virology in Cologne Dr. Lech Trzeciak has performed an extensive genotyping of the course of HPV infection in an atypical case of EV resulting from yet-unreported mutation in *TMC8* gene. He observed frequent co-existence of two (or more) types of HPVs in various areas. His second visit to Cologne, as signaled in the report from the first part of the twinning, was therefore devoted mostly towards establishing an in-situ hybridization method (ISH) in order to gain a better insight into (co?)localization of HPVs in normal and diseased tissue. Additionally, Dr. Trzeciak also set to learn how to isolate and culture human keratinocytes that could be indispensable in functional studies of proteins involved in HPV infection leading to carcinogenesis. During his stay in Cologne Dr. Trzeciak also took an opportunity to participate in Leica Microscopy Workshop. The workshop and following hands-on demonstration focused on modern ultraresolution techniques: DLS, GSD and STED.

Task 1.9.

MUW: Task leader – Dr. Dominika Nowis

Foreign Partner: University of Verona, Italy (Dr. Gaetano Vattemi)

Subject: Targeting of proteostatic mechanisms with specific inhibitors of proteasome and protein folding in cancer and normal cells for patient-oriented, personalized and more effective cancer treatment.

	PLANNED	**CARRIED OUT**
OUTGOING VISITS	1 experienced researcher 2 weeks (2013)	yes, in 100%
	1 experienced researcher 2 months (2014/2015)	yes, in 100%
INCOMING VISITS	1 experienced researcher 1 month (2014)	yes, in 100%; the visit of Dr. Valeria Guglielmi took place in 2013 and its description was included in the previous report (D1.1)

As stated by Dr. Nowis in the previous report, the two remaining weeks of a 2013 visit of an experienced researcher from MUW to the partnering institution were rescheduled for 2014 and executed by Justyna Chlebowska, a member of Dr. Nowis team. Due to Dr. Nowis maternal leave (June 12th, 2014 –June10th, 2015) and Dr. Gaetano Vattemi sabbatical to the USA (June 2014 - June 2015), the remaining 8-week visit to Verona has been rescheduled for 2015 and executed by Dr. Piotr Mrowka who in 2015 visited twice the laboratory of Prof. Patrizia Agostinis at the KU Leuven, Belgium.

Details of the executed outgoing visits:

Visit	Name and family name of visiting researcher	Date of the visit	Place of the visit
1	Justyna Chlebowska	26.05.-06.06.2014.	University of Verona, Department of Neurology and Movement Sciences
2	Dr. Piotr Mrowka	20.04.-14.06.2015.	Cell Death Research and Therapy Laboratory, KU Leuven
3	Dr. Piotr Mrowka	05.07.-09.08.2015.	Cell Death Research and Therapy Laboratory, KU Leuven

Ad. visit 1:

During her stay at the laboratory of Dr. Vattemi Justyna Chlebowska learned numerous laboratory techniques such as primary human myoblasts culture, immunostaining of frozen sections of muscle biopsies, 2-D electrophoresis and preparation of samples for transmission electron microscopy (TEM) analysis. Together with Dr. Vattemi and Dr. Valeria Guglielmi they analyzed results obtained from whole exome sequencing of samples collected from patients suffering from facioscapulohumeral muscular dystrophy (FSHD) and planned experiments to elucidate the pathogenesis of this disease. They also performed several immunostainings of proteins which structure and/or function could be impaired in FSHD. Moreover, Justyna Chlebowska and Dr. Vattemi spent some time on discussion and final analysis of the data obtained during the implementation of the joint project of the Medical University of Warsaw and University of Verona on musculotoxicity of anti-cancer chemotherapeutics.

Ad. visit 2:

Dr. Piotr Mrowka visited the Laboratory of Cell Death Research and Therapy (CDRT), KU Leuven, Belgium from April 20th till June 14th, 2015. During his stay in Leuven, Dr. Mrowka conducted research projects in the field of experimental oncology together with a research team led by prof. Patrizia Agostinis. His visit was a continuation of previous fruitful scientific exchange between the Medical University of Warsaw and CDRT, KU Leuven. Prof. Agostinis' research interests include molecular mechanisms of resistance of cancer cells to the therapy, autophagy, cell death pathways, endoplasmic reticulum stress, immunogenic cell

death and oxidative stress. During his stay in prof. Agostinis' lab Dr. Mrowka participated in the on-going project concerning the role of BNIP3 protein in melanoma cells biology and its potential to activate immune response. He was directly co-operating with Erminia Romano, a PhD student in prof. Agostinis group, and was responsible for both planning and performing experiments elucidating the influence of BNIP3 activation and silencing on melanoma cells itself and on immune cells response in contact with melanoma cells or their secretion products. Dr. Mrowka work in CDRT Laboratory enabled him to learn and practice several laboratory techniques that were not performed in his home laboratories before, including cell migration assay, phagocytosis assay, colony forming assay, just to name a few. Thanks to the experience he gathered during his stay at KU, Dr. Mrowka will be able to introduce some of new techniques in his home laboratory. Apart from a valuable experience in laboratory procedures, Dr. Mrowka also participated in scientific meetings held by the CDRT Laboratory and other groups in Campus Gasthuisberg that were focused on discussion of the results obtained by their team and others. He also participated in Oncoforum conference at KU Leuven. Moreover, Dr. Mrowka had a unique opportunity to observe organization of the work in laboratories and facilities at KU Leuven. Taken together, Dr. Mrowka visit to the KUL was a great opportunity to make progress in his research, learn new techniques, exchange ideas and to tighten cooperation between our teams.

Ad. visit 3:

Dr. Piotr Mrowka revisited the Laboratory of Cell Death Research and Therapy (CDRT), KU Leuven, Belgium from July 5th till August 9th, 2015. As during his first visit in CDRT Dr. Mrowka continued his fruitful cooperation with Erminia Romano on a project concerning the role of BNIP3 protein in melanoma cells biology and its properties to potentially modulate immune response to melanoma cells. To achieve that goal they were using BNIP3 knock-down cells and cells with induced BNIP3 when cultured under hypoxia. They were looking for changes in immune response to these cells when compared to control cells with basal BNIP3. One of the major experiments Dr. Mrowka had a chance to participate during this short stay was immune cells migration/attraction test in zebrafish model in vivo. Melanoma cells were injected into the yolk sac of transgenic zebrafish embryos 3 days post fertilization with labeled neutrophils and macrophages emitting green and red fluorescence, respectively. Localization and eventual migration of the immune cells to the place of deposition/injection of melanoma cells were observed under the fluorescent microscope. This unique opportunity to learn zebrafish model of immune system response to cancer cells will be hopefully very rewarding in Dr. Mrowka future scientific work.

Task 1.10.

MUW: Task leader – Dr. Radoslaw Zagozdzon – new group leader

Foreign Partner: Royal College of Surgeons Dublin, Ireland (Dr. Bryan Hennessy)

Subject: Evaluation of peroxiredoxins 1 and 2 along with the thioredoxin-thioredoxin reductase system as potential biomarkers in B cell lymphomas.

	PLANNED	**CARRIED OUT**
OUTGOING VISITS	2 experienced researchers 2 x 2 weeks each (2014 - 2015)	yes, in 100%
INCOMING VISITS	1 experienced researcher 2 x 2 weeks (2014-2015)	yes, in 100%

Details of the executed outgoing visits:

Visit	**Name and family name of visiting researcher**	**Date of the visit**	**Place of the visit**
1	Dr. Malgorzata Bajor	30.06.-13.07.2014.	Department of Oncology, Molecular Medicine Laboratories, Beaumont Hospital, Royal College of Surgeons in Ireland, Dublin, Ireland
2	Slawomir Gruca	04.11.-20.12.2014.	Bioinformatics Laboratory, University of Leeds, UK; this change in the twinning schedule has been approved by the BASTION project EU Officer
3	Dr. Malgorzata Bajor	06.05.-20.06.2015.	Cancer Biology and Therapeutics Lab, Conway Institute, University College Dublin
4	Dr. Malgorzata Bajor	01.07.-31.07.2015.	Cancer Biology and Therapeutics Lab, Conway Institute, University College Dublin
5	Agata Zych	01.07.-31.07.2015.	Cancer Biology and Therapeutics Lab, Conway Institute, University College Dublin
6	Joannna Stachura	05.07.-02.08.2015.	Cancer Biology and Therapeutics Lab, Conway Institute, University College Dublin

Ad. visit 1:

The main goal of Dr. Malgorzata Bajor two-weeks stay in Dublin was to use under the supervision of Prof. Hennessy the reverse phase protein arrays (RPPA) platform to study PRDX1 and PRDX2 protein expression in panel of different type cancer cell lines. Prof. Hennessy is an international leader in the application of (RPPA) for quantitative protein profiling to interrogate predictive and prognostic markers in breast, colon and other cancers, and has established this technology at RCSI. Prof. Hennessy is a clinician scientist whose research team has had considerable impact on the fields of kinase signaling and 'BRCAness' research in cancers including gynecological and breast cancers. He is a consultant of the

medical oncology at Beaumont Hospital, senior lecturer in the RCSI and adjunct professor in the Division of Cancer Medicine at the University of Texas, M.D. Anderson Cancer Center. With help of Prof. Hennessy group members, Clare Morgan and Dr. Mattia Cremona, Dr. Bajor had an opportunity to learn the whole RPPA method, starting from sample preparation, printing denatured protein lysates on nitrocellulose-coated slides, followed by probing with appropriate antibodies to detect signal by colorimetric reaction ending-up with data analysis. Using RPPA method Dr. Bajor has determined the levels of PRDX1 and PRDX2 proteins in breast cancer cell lines. Moreover, she performed the RPPA analysis for other types of cancer cell lines including lymphoma, leukemia, myeloma, and ovarian cancer cell lines. These analyses were performed in collaboration with Dr. Dominika Nowis, member of BASTION project team.

Ad. visit 2:

The detailed description of Slawomir Gruca visit to the University of Leeds is included into Prof. Golab team report on task T1.1.

Ad. visit 3:

Between 6th and 20th, May 2015 Dr. Malgorzata Bajor visited Laboratory of Prof. William M. Gallagher, working at the Cancer Biology and Therapeutics Lab, Conway Institute, University College Dublin, Dublin, Ireland. A major focus of the CBT Lab is the identification and validation of molecular determinants of tumor progression in breast cancer and melanoma. Moreover, the CBT Lab has a particular interest in the identification and validation of candidate prognostic and predictive biomarkers in oncology, with emphasis on the translation of transcriptomic and proteomic datasets into clinically relevant assays. The main goal of Dr. Bajor two-week stay in Dublin was to study effects of dysfunction of thiol-dependent antioxidant enzyme system on the oncogene-dependent signaling in breast cancer under the hypoxic conditions. During her stay Dr. Bajor had an opportunity to discuss her experimental plans with Prof. Cormac Taylor, a Principal Investigator in Systems Biology Ireland, and Professor of Cellular Physiology in UCD School of Medicine & Medical Science at University College Dublin, who is a leading authority in the field of hypoxia research. Dr. Bajor set up experimental conditions and carried out preliminary studies for her ongoing project related to the determination of the role for thiol-dependent antioxidant enzymes in estrogen-receptor positive breast cancer. The most valuable benefit of Dr. Bajor visit to the UCD was an opportunity to consult the research plan with Prof. Gallagher and Prof. Taylor. Furthermore, the visit helped to strengthen scientific contacts and plan further collaboration between Conway Institute, University College Dublin and Department of Immunology, Medical University of Warsaw.

Ad. visit 4:

Dr. Malgorzata Bajor visited the Cancer Biology and Therapeutics Laboratory headed by Prof. William M. Gallagher at the Conway Institute, University College Dublin, Dublin, Ireland in July 2015. During her one month stay in Ireland Dr. Bajor was working in the field

cancer biology continuing a research initiated during her first visit in the CBT Lab. She performed detailed study of effects of dysfunction of thiol-dependent antioxidant enzyme system on the oncogene-dependent signaling in breast cancer under the hypoxic conditions. Obtained results will be included in the publication focusing on the determination of the role for thiol-dependent antioxidant enzymes in estrogen-receptor positive breast cancer.The visit in the Prof. Gallagher laboratory helped Dr. Bajor to strengthen scientific contacts and plan further collaboration between Conway Institute, University College Dublin and Department of Immunology, Medical University of Warsaw.

Ad. visit 5:

From 1st till 31st July 2015, Ms Agata Zych visited the Cancer Biology and Therapeutics Laboratory of Prof William M. Gallagher. The main field of interest of CBT lab is the identification and validation of molecular determinants of tumor progression in breast cancer and melanoma. Moreover, they focus also on identification and validation of candidate prognostic and predictive biomarkers in oncology. Ms Zych stay in Dublin was strictly connected with the previous visit of another team member of our group – Dr. Malgorzata Bajor, who had investigated effects of dysfunction of thiol-dependent antioxidant enzyme system on the oncogene-dependent signaling in breast cancer under hypoxic conditions. The main goal of Ms Zych visit to the UCD was to interrogate the effect of PRDX 1 or PRDX 2 deficiency in the oncogene-dependent signaling in ER positive breast cancer cell lines under hypoxic conditions. During her stay at the UCD Ms Zych had also an opportunity to participate in CBT lab meetings, where she could listen to other researchers and their projects, which enabled her to further broaden her knowledge about breast cancer.

Ad. visit 6:

From July 5th till August 2nd Ms Joanna Stachura visited Professor William Gallagher Cancer Biology and Therapeutics Laboratory at Conway Institute, University College Dublin. One of the research area that Professor W. Gallagher group focuses on is identification and validation of candidate biomarkers of breast cancer and melanoma as well as preclinical evaluation of novel anti-cancer agents. The main goal of Ms Stachura visit to the UCD Conway Institute was to investigate mechanisms of action of anti-cancer drug lenalidomide under normoxic and hypoxic conditions. Lenalidomide is an immunomodulatory agent with still not well known mechanism of action on cancer cells. During her visit Ms Stachura had an opportunity to determine lenalidomide impact on vascular endothelial growth factor production and phosphorylation of its receptor in cancer cells. Performed experiments allowed her to gather preliminary date and broaden her knowledge in the field of hypoxia research. Moreover, Ms Stachura participated in scientific meetings and discussed her results with CBT Lab team.

Details of the executed incoming visits:

Visit	Name and family name of visiting researcher	Date of the visit	Place of the visit
1	Dr. Rut Klinger	08.12.2014.-	Department of Immunology, MUW

		05.01.2015.	
2	Dr. Rut Klinger	18.07.-11.08.2015.	Department of Immunology, MUW

Ad. visit 1:

The overall scientific goal of Dr. Klinger's stay in the Department of Immunology, MUW was to generate a hydrogen peroxide reporter system utilizing a HyPer3-based fluorescent marker. Dr. Zagozdzon has been working for several recent years on oxidative stress-related mechanisms in cancer. He has focused specifically on peroxiredoxin (PRDX) protein family and has recently published his work on PRDX1 in breast cancer in collaboration with Dr. Klinger's home research group (O'Leary et al., 2014). 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 H2O2 levels. Dr. Klinger has 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.

Ad. visit 2:

Between the 18th of July 2014 and 11th August 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 overall scientific goal of Dr. Klinger's stay was to generate a cysteine-tagged PRDX1 overexpression systems utilizing mammalian viral vectors. Dr. Zagozdzon has been working for several recent years on oxidative stress-related mechanisms in cancer. He has focused specifically on peroxiredoxin (PRDX) protein family and has recently published his work on PRDX1 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 H2O2 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 PRDX1 expressing constructs with cysteine-tags added on both gene ends using molecular cloning approaches. These would 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 could be used to efficiently purify PRDX1 proteins for subsequent analyses. Dr. Klinger has been cloning cys-tagged PRDX1 gene insert into HIV-based SFFV 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 added her expertise and participated in work regarding other stable genetically modified cancer cell models (such as breast cancer MCF7-based models) related to Dr. Zagozdzon's research in the area.

Task 1.11.

MUW: Task leader – Dr. Tomasz Stoklosa

Foreign Partner: London Genetics and Science|Business Publishing

Subject: Transfer of know-how and stimulation of innovation-driven research to bring research results from bench to the bedside.

	PLANNED	**CARRIED OUT**
OUTGOING VISITS	6 short visits	yes, in 100%
INCOMING VISITS	6 short visits	yes, in 50% (3 out of 6)

Details of the executed outgoing visits:

Visit	**Name and family name of visiting researcher**	**Date of the visit**	**Place of visit**
1	Prof. Jakub Golab	06-08.10.2014.	ACES/the Innovation Connection, the 2014 Science|Business Annual Summit, Berlin, Germany
2	Prof. Jakub Golab	16-18.02.2015.	Science|Business, Brussels, Belgium
3	Dr. Karolina Dzwonek	16-18.02.2015.	Science|Business, Brussels, Belgium
4	Prof. Zbigniew Gaciong	21-25.03.2015.	Science|Business, Brussels, Belgium
5	Dr. Karolina Dzwonek	21-25.03.2015.	Science|Business, Brussels, Belgium
6	Iwona Drozdowska-Rusinowicz	21-25.03.2015.	Science|Business, Brussels, Belgium

Ad. visit 1:

The ACES are the only pan-European awards for spin-outs from universities and public research institutes. The nominations for ACES Award come from all sectors, disciplines and countries in Europe and are judged upon key quality criteria, e.g. novelty, fundraising, market

potential, and impact on society by the Science|Business Innovation Board, a not-for-profit association created to improve the climate for innovation in Europe. The ACES are celebrated annually on the occasion of the Science|Business annual conference. The winners of the ACES 2014 were celebrated in Berlin on 7 October 2014. The Awards are given in the following categories: Green Award, ICT Award, Life Sciences Award, and Global Innovation Award. The Summit consisted of two discussion sessions and The ACES 2014 winners conference. The ACES awards programme was established in 2008 by Science|Business to recognize entrepreneurship at academic institutions. The morning session: 'How Europe can lead the world in innovation' started with an Opening welcome from Christian Thomsen, President, TU Berlin, and was followed by introductions by Richard L. Hudson, CEO & Editor, Science|Business and an interview with Jose Manuel Barroso, President of the European Commission. Then a discussion on the secrets to fostering global champions has taken place. Each speaker was asked to provide one secret way to achieve success in the innovation technology and had only 2 minutes to introduce it. This part was followed by a moderated debate and audience participation. The following participants were engaged in the discussion: Javier Gimeno, Professor of Strategy, INSEAD; Ramon A. Wyss, Vice President for International Affairs, KTH Royal Institute of Technology, Stockholm; Frank Salzgeber, Head of Technology Transfer Programme Office, European Space Agency and Raymond Hegarty, Managing Director, Intellectual Ventures International Licensing. Another panel discussion was entitled: "Can European VC survive? What's gone wrong and how to fix it". A flash report from a Science|Business study underway at Aalto University was presented and a discussion on overcoming the funding crisis and new ways to finance innovation has taken place with the following speakers: Gunnar Muent, Director, Innovation and Competitiveness, European Investment Bank; Anne Glover, Chief Executive and Co-founder Amadeus Capital Partners; Candace Johnson, President, European Business Angels Network (EBAN) and Mmboneni Muofhe, Deputy Director General: Technology Innovation, Department of Science and Technology, Republic of South Africa. Then, the Meet the finalists - Innovators' elevator-pitches took place followed by the session: Challenging the status quo - Germany's innovation machine takes on Silicon Valley. Detlef Dauke, Head of Innovation IT and Communications Innovation and Technology, German Federal Ministry of Economic Affairs and Energy was the main speaker.

Ad. visit 2 and 3:

Jakub Golab, BASTION project coordinator and Karolina Dzwonek, Innovation Manager, during their short visit at Science|Business in February discussed current issues concerning MUW-Science|Business collaboration. Together with Science|Business management they discussed the remaining project tasks of Science|Busienss experts. It appeared that there was a need to modify the tasks of Ms Gail Edmondson so BASTION team members proposed the following amendment to the contract signed on 28-05-2013 by and between the Medical University of Warsaw, and Ms Gail Edmondson: "Subtask 1 (15 working days in total) is being changed into: preparation of guidelines for Medical University of Warsaw for efficient technology transfer and IP management, based on KULeuven and university's technology

transfer office - KU Leuven Research & Development (LRD) history and best practices. The expert will take an interview with the Rector of KULeuven and one of the leaders of the LRD in order to identify strategies, solutions and management schemes that could be implemented by MUW authorities in order to facilitate translational research at the university. These guidelines could be used by MUW authorities in setting up the technology transfer unit within the structure of the university, financing it at the beginning of its activity, engaging the right human resources, building relations (inside the university and outside - identifying key partners). The expert will present a case study of successful commercialization of a technology developed at KULeuven, pointing key success factors of the enterprise. The new subtask 1 will be submitted in a form of a report, that includes two interviews, the summary of KULeuven technology transfer experience, guidelines for MUW authorities and a case study." During the meeting BASTION team members discussed with Science|Business upcoming event – Pharma Day 2015, to be organized within WP5 in the Spring 2015.

Ad. visit 4:

On March 25th Science|Business in partnership with the Axa Research Fund organized a private roundtable (The Future of Healthcare Systems: Challenges for the 21st Century) to explore how mega trends will affect healthcare systems in developed countries. Prof. Zbigniew A. Gaciong, Group leader in BASTION project, Head of Department of Internal Medicine, Hypertension and Vascular Diseases, Medical University of Warsaw, participated in this workshop. This event was an opportunity to discuss with a selected group of senior academics, industry executives and policy experts, and share the expertise on how welfare systems in developed countries may evolve in future decades, how emerging trends will change healthcare systems, and how to best understand and prevent related risks. The discussion was focused specifically on demographic and economic trends, new healthcare technologies such as synthetic biology or artificial intelligence and sociological trends including urbanisation and disintegration of extended families. This event was co-organised by the AXA Research Fund, the philanthropic organization of the AXA Group, which aims at supporting scientific research to better understand and prevent environmental, life, and socio-economic risks; and Science|Business,as a media and communications company specialized in EU innovation policies. The outcome of the discussions will help define the 2015 research agenda of the AXA Research Fund, whose commitment to academic research amounts on average €17 million a year.

Ad. visit 5 and 6:

Iwona Drozdowska-Rusinowicz, Project Manager, and Karolina Dzwonek, Innovation Manager, during the short visit at Science|Business, attended the conference that featured the different parts of the Horizon 2020 programme, with the participation of key European Commission officials to draw lessons from the results 14 months after the launch of the programme. During the conference, a breakout session of interest to the BASTION representatives was dedicated to Disease prevention. Dementia, Cardiovascular disease, Oncology. There were over a hundred participants from different EU countries and

organizations, including leaders of the ERC, Maria Sklodowska-Curie grants and SMEs. The meeting was inspiring and enabled reaching out to representatives of European universities, pharmaceutical companies and private capital units. It was important for MUW and BASTION – partners of Science|Business network - to participate in the meeting and to be involved in the discussions on challenges that research funding and development is facing nowadays, especially in light of upcoming Horizon2020 perspective. During their stay in Brussels Dr. Dzwonek and Ms. Drozdowska visited Science|Business office in order to discuss future collaboration, common Events planned for the last year of the project and to meet project experts.

Details of the executed incoming visits:

Visit	Name and family name of visiting researcher	Date of the visit	Place of visit
1	Florin Zubascu	23-27.04.2014.	MUW
2	Florin Zubascu	23-25.04.2015.	MUW
3	Shane McCollam	23-25.04.2015.	MUW

Ad. visit 1:

Florin Zubascu, journalist working for Science|Business, Brussels paid a 4-day visit in Warsaw due to Pharma Day which took place on April 25th. Florin assisted BASTION team in organization of the event, prepared press release about the meeting and ran interviews with participants.

Ad. visit 2 and 3:

Florin Zubascu and Shane McCollam joined Pharma Day on 25th April 2015 within Task 1.11 of BASTION project. They have prepared a summary of event and they ran two interviews with Pharma Day participants. The materials were published on Science|Business web site:

http://www.sciencebusiness.net/news/77050/Poland-making-moves-to-lift-barriers-to-investing-in-drug-discovery

http://www.sciencebusiness.net/news/77057/Patents-can-make-or-break-drug-discovery-in-Poland

Analysis of added value

Execution of Work Package 1 during second reporting period (19-36 months) of BASTION project was a great opportunity for researchers from MUW to gain know-how from partnering Institutions and was a chance to bring together experts from various disciplines willing to share their expertise and resources. What is more important during second reporting period,

twinning became really fruitful in the terms of more than a dozen of publications in peer-reviewed, international journals (12 original articles so far) . In several examples execution of twinning visits was the key element to finish some projects and publish the results already in the duration of BASTION project (all publications are listed in deliverable D1.3). Several manuscripts are either in the review process or in preparation, therefore total number of publications which resulted directly from execution of WP1 should exceed 20.

Additionally, twinning visits enabled researchers from MUW and partnering institutions to widen the scope of their scientific projects, beyond what is available within their own institution and to combine the available technologies. Unfortunately, some obstacles prevented full execution of planned twinnings as it was planned. They were mostly unpredictable and related to either personal issues (such as sick or maternity leave, job change) or institutional issues (administrative obstacles). Another problem related mostly to incoming visits of researchers from partnering laboratories was their extremely busy schedule.

Thanks to helpful remarks from external evaluators obtained during first evaluation round in January 2015 initial twinning plans were successfully rescheduled to complete all the tasks (as described in details above). In summary, WP1 execution during second reporting period allowed to continue scientific dialogue between partnering academic institutions and MUW, gave again several excellent training opportunity for the recruited staff, both at MUW and at the partnering organizations and resulted in important scientific discoveries in the field of oncology as proved by original publications. It must be emphasized that BASTION project covered only the costs of visits. The research activities were covered by own funds of each of the partnering institutions.

Conclusions

Work Package 1 comprises of exchange of know-how and best practice through twinning. Major goal of those bilateral visits was to bring together a highly skilled and complementary assembly of European researchers from academic and clinical centers and researchers from MUW participating in BASTION. Similarly to other large-scale projects there were several, initially unresolved and unforeseen, issues (in most cases of administrative type, in some cases personal issues such as sick leave or maternity) regarding twinning via secondments, which are being gradually cleared. This however, caused some delays and rescheduling of selected twinning visits for 2015. Implemented changes, such as rescheduling/dividing of the visits, exchanges of the twinnings between BASTION teams as well as allowing several young researchers to participate in the twinning allowed to complete all the visits important for the BASTION project for 19-36 months.

Therefore we can conclude that execution WP1 was successfully accomplished and

MILESTONE M6 -"Completion of secondments during the second reporting period" has been achieved.

Not only each researcher was given practical training in new technologies provided either locally or via visits to partnering laboratories, but also in many situations, there were unexpected benefits of such efforts such as new collaborations and new research projects undertaken as a result of this collaborations. In summary, research work of majority of groups complemented one another, and this synergy should be even more enhanced by further exchange of know-how between BASTION and partnering institutions.

Corresponding estimated/* budget

PERSONNEL, TRAVEL, AND OTHER MAJOR DIRECT COST ITEMS FOR BENEFICIARY "1" M19 – M36			
Work Package 1 (T1.1-T1.11)	**Item description**	**Amount [EUR]**	**Explanations**
	Personnel costs	45,066.85	Fees of the WP1 leader, Co-leader and Task leaders (11,08 PM)
	Travel	212,984.65	Travel &accommodation – 42 outgoing missions and 12 incoming visits
	Other direct costs		-
TOTAL DIRECT COST		258,051.50	

/ - exact costs for M19-M36 will be presented in the 2nd Period Report and Form C (October 2015)*

Dr. Dominika Nowis
WP1 Leader
Dr. Tomasz Stokłosa
WP1 Co-leader

Prof. Jakub Golab
BASTION Project Coordinator

Warsaw, August 2015