

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

Project No. 316254

# **BASTION**

*“From Basic to Translational Research in Oncology”*

## Deliverable D1.1

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

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

## Introduction

Deliverable D1.1 corresponds to the task T1 (T1.1-T.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 2013 was planned via:

- a) 3 incoming visits (1 young researcher, 2 experienced researchers) of the foreign Partners' representatives to the MUW (3 months in total)
- b) 12 outgoing visits (2 young researchers, 10 experienced researchers) of the MUW staff to the foreign laboratories (26 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 each of the 16 twinning and networking tasks within WP1 the following goals were achieved in the first 18 months of the Project:

### 1. 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  |
|------------------------|---|--------------|
| <b>OUTGOING VISITS</b> | 1 young researcher 3 months (2013)              | yes, in 100% |
|                        | 1 experienced researcher 2 months (2013)        | yes, in 50%  |
| <b>INCOMING VISITS</b> | 1 young researcher 1 month (2013 or 2014)       | yes, in 50%  |
|                        | 1 experienced researcher 1 month (2013 or 2014) | -            |

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 | 17.06.-05.07.2013. | Department of Immunology, MUW |

Ad. visit 1:

Aleksandra Dudek is a 3rd year PhD student at the Cell Death Research and Therapy (CDRT) Laboratory, KU Leuven, Belgium. During her PhD, Aleksandra studies key molecular and immunological parameters underlying the process of immunogenic cell death (ICD) elicited by various chemotherapeutics, using metastatic melanoma as cellular/ in vivo model.

The main purpose of Ms Dudek's visit to MUW was to investigate the immunogenic properties of murine melanoma cells treated with various anticancer therapies in mice vaccination experiment. The Department guided by Prof. Golab has an immense experience in various mice experiments, thus it was a great opportunity for Aleksandra to acquire skills in mice handling and performance of the mice vaccination experiment. Moreover, during Ms Dudek's visit, she was shown how to measure cytokines by cytokine bead array (CBA) and performed few analysis on the crucial samples from in vitro-treated, dying cancer cells: dendritic cells co-cultures.

Furthermore, during her visit future collaborative experiments were discussed. Definitely, not only this scientific visit to the laboratory of Prof. Golab resulted in important advances in the PhD project of Aleksandra Dudek, but as well will have a consequence in the very close collaboration in the topic of immunogenicity of cancer cell death in the future.

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, MUW                           | 3-17.07.2013.      | School of Biomolecular & Biomedical Science, Conway Institute, University College Dublin       |
| 2     | Slawomir Gruca, MUW                         | 3-17.07.2013.      | School of Biomolecular & Biomedical Science, Conway Institute, University College Dublin (UCD) |
| 3     | Magdalena Gabrysiak, MUW                    | 11.09.-15.12.2013. | Cell Death Research and Therapy Laboratory, KU Leuven  |

Ad. visit 1 and 2:

Dr Pawel Gaj, a post-doc researcher and MSc Slawomir Gruca, an IT specialist from the bioinformatics group at the Department of Immunology (DoI) of Medical University of Warsaw (MUW), participated in the Twinning Programme of the BASTION project, held between 3<sup>rd</sup> and 17<sup>th</sup> of July 2013. The activities were conducted at the Conway Institute, University College Dublin (UCD), Ireland.

During their stay at UCD, they joined the research group of the School of Biomolecular & Biomedical Science led by Prof. William Gallagher. The main purpose of the visit was to become acquainted with the state-of-art imaging systems available in the twinning partner institution and used to acquire and analyze images of immunohistochemically (IHC) stained tissue samples. Using the slides stained by IHC in their home institution in Poland, the researchers had the opportunity to evaluate the modern digital pathology solutions from two different manufacturers. Apart from the IHC scanner hardware, also software for tissue image analysis, annotation and management were investigated - basic measurements on acquired images were performed. Acquiring the expertise in the digital pathology field has been vitally important for the visiting researchers, as an analogous digital pathology core facility is being created by Dr Radoslaw Zagodzón - a leader of the bioinformatics group at the DoI, which Dr Gaj and MSc Gruca are members of.

Collaboration between Dr Pawel Gaj and researchers from the Conway Institute was initiated prior to his visit in UCD. During the visit, the results of statistical analyses prepared by Dr Gaj for the co-investigated projects were presented and discussed, and also follow-up research directions were proposed. Furthermore, the subjects focusing the optimal data analysis pipelines for the Next-Generation Sequencing (NGS) application in gene expression studies were discussed. Some of that knowledge has already been used in the research conducted at the DoI.

Ad. visit 3:

The main goal of Magdalena Gabrysiak's visit to the Laboratory of Cell Death Research and Therapy (CDRT), KU Leuven, Belgium was to become familiar with techniques used to analyse different forms of cell death. She employed such techniques as flow cytometry (Annexin V staining, cell cycle analysis) and Western blotting to determine survival and cell death mechanisms in cells subjected to various treatment modalities such as irradiation, proteasome inhibitor (bortezomib) or photodynamic therapy (PDT). Moreover, she had the opportunity to learn exosomes purification with use of ultracentrifugation and to determine whether exosomes isolated from cells subjected to various treatments could induce cell death after incubation with untreated cells. Beside planning and performing experiments, Ms Gabrysiak had many opportunities to participate in scientific meetings held by the CDRT Laboratory and other groups, which enabled her to further broaden her knowledge in cell death field. Moreover, she had an opportunity to present and discuss her own results with the whole team, which resulted in developing new ideas that she could further apply in Poland.

| <b>Publications resulting from the collaboration between the twinning partners:</b>  |
|--|
| Garg AD, Martin S, Golab J, Agostinis P. Danger signalling during cancer cell death: origins, plasticity and regulation. <i>Cell Death Differ.</i> 2014; 21(1): 26-38.   |
| O'Leary P, Terrile M, Bajor MA, Gaj P, Hennessy BT, Zagodzón A, O'Connor DP, Brennan DJ, Connor K, Li j, Mills GB, Gonzalez-Angulo AM, Sun HD, Pu JX, Pontén F, Uhlén M, Jirström K, Nowis D, Crown JP, Zagodzón R, and Gallagher MW. Peroxiredoxin-1 protects estrogen receptor $\alpha$ from oxidative stress-induced suppression and is a protein biomarker of favorable prognosis in breast cancer (under second revision in <i>Breast Cancer Res</i> ). |

## 2. 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  |
|------------------------|--|--------------|
| <b>OUTGOING VISITS</b> | 1 experienced researcher 3 months (2013) | yes, in 100% |
| <b>INCOMING VISITS</b> | -  | -            |

Details of the executed incoming visits:

No incoming visit was planned for 2013.

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                      | 21.08.-16.10.2013. | Institute of Tumor Immunology, Cancer Research Center of Marseille, University of Mediterranean, Marseille |
| 2     | Malgorzata Bobrowicz                        | 14.10.-22.11.2013. | Institute of Tumor Immunology, Cancer Research Center of Marseille, University of Mediterranean, Marseille |

Ad. visit 1 and 2:

During these visits Dr Winiarska and Mrs Bobrowicz had a unique possibility to learn methods of isolation of NK cells and a vast series of methods used to study NK cell functions. They adopted assays measuring NK cells activation by assessing their degranulation, cytokine release and multiparameter analysis of NK cells surface antigens. What is more, they learned how to culture established NK cell lines and thanks to this collaboration they were able to acquire those cell lines for their future research in Poland.

Moreover, Dr Winiarska and Mrs Bobrowicz during their visits studied the influence of several drugs used in hematooncology on the activity of NK cells and ADCC process.

The aim of their project was to evaluate the influence of kinase inhibitors and histone deacetylase inhibitors on NK cells.

| <b>Publications resulting from the collaboration between the twinning partners:</b>  |
|--|
| Bojarczuk K, Siernicka M, Dwojak M, Bobrowicz M, Pyrzynska B, Gaj P, Karp M, Giannopoulos K, Efremov DG, Fauriat C, Golab J and Winiarska M. B-cell receptor pathway inhibitors affect CD20 levels and impair antitumor activity of anti CD20 monoclonal antibodies. <i>Leukemia</i> doi:10.1038/leu.2014.12                                 |
| Winiarska M, Bojarczuk K, Pyrzynska B, Bil J, Siernicka M, Miazek N, Zapala P, Dwojak M, Bobrowicz M, Zagodzón A, Krol M, Syta A, Podszycalow-Bartnicka P, Dabrowska-Iwanicka A, Juszczynski P, Efremov D, Slabicki M, Zenz T, Le Roy A, Olive D, Golab J. SRC family kinases are involved in the regulation of CD20 (manuscript submitted). |

### 3. Task 1.3.

MUW: Task leader – Dr Tomasz Stokłosa

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 leukaemia.

|                        | <b>PLANNED</b>                           | <b>CARRIED OUT</b>                    |
|------------------------|--|---------------------------------------|
| <b>OUTGOING VISITS</b> | 1 experienced researcher 2 months (2013) | yes, in 100% (subdivided in 2 visits) |
| <b>INCOMING VISITS</b> | 1 experienced researcher 1 month (2013)  | no, rescheduled for 2014              |

Details of the executed incoming visits:

No incoming visit was executed in 2013. As stated by Dr Stokłosa, his group twinning plan for 2013 has been realized in 50%, since there were two visits from MUW to University Hospital of Ulm, however visit of an experienced researcher from Ulm was not accomplished. This was due to the fact that 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 with extremely busy schedule. Although it was not possible to arrange his visit in 2013, his visit has been rescheduled for 2014.

Details of the executed outgoing visits:

| Visit | Name and family name of visiting researcher | Date of the visit | Place of the visit                                     |
|-------|---|-------------------|--|
| 1     | Eliza Głodkowska-Mrówka                     | 08.07-07.09.2013. | Department of Internal Medicine III, University of Ulm |
| 2     | Dr Tomasz Stokłosa                          | 22-31.08.2013.    | Department of Internal Medicine III, University of Ulm |

Ad. visit 1 and 2:

Group of Dr Stokłosa is focused on the molecular pathogenesis of haematological malignancies and twinning visits were extremely valuable to conduct their research projects. Specifically, Dr Stokłosa group is trying to dissect chronic myelogenous leukemia (CML) and chronic lymphocytic leukemia (CLL) pathogenesis. Recent publications proved that targeted treatment with tyrosine kinase inhibitors (TKI) can be effective in CLL, also in heavily-pretreated patients and in high-risk groups but it is still uncomparable to TKI effectiveness in CML. One of the reasons is that detailed mechanisms of action of TKI in CLL is not well understood. Also predictive markers to new targeted therapies are not known in CLL. Therefore major aim of their project is to discover gene signature and described genes involved in response to these promising novel therapies in CLL cells, in order to define a group of patients who may benefit from such treatments. Recently Professor Lars Bullinger's team launched new methodology to analyze gene expression profile - RNA sequencing on next-generation sequencing (NGS) platform. Twinning with Bullinger's laboratory enabled Dr Stokłosa group to analyze a cohort of CLL patient's samples in regard to their response to TKI. The planned 2 month visit of one experienced researcher from MUW was subdivided into two visits, one longer visit by Mrs Głodkowska-Mrowka, who performed majority of the experiments and second by Dr Stokłosa's who came to participate in data analysis. Thanks to such organization of the twinning, they were able to participate in data processing and analysis with dedicated software for NGS obtained by Prof. Bullinger's team.

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| <b>Publications resulting from the collaboration between the twinning partners:</b> |
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| none so far |
|-------------|

#### 4. 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              |
|------------------------|--|--------------------------|
| <b>OUTGOING VISITS</b> | 1 experienced researcher 2 months (2013) | no, rescheduled for 2014 |
| <b>INCOMING VISITS</b> | 1 experienced researcher 1 months (2013) | no, rescheduled for 2014 |

Details of the executed incoming and outgoing visits:

| Visit | Name and family name of visiting researcher | Date of the visit | Place of the visit |
|-------|---|-------------------|--------------------|
| -     | -   | -                 | -                  |

As stated by Prof. Zbigniew Gaciong, the leader of the T1.4 task, two visits planned for 2013 have been rescheduled for 2014. Dr Marzena Lazarczyk, a newly hired postdoctoral fellow, joined Prof. Gaciong's team in October 2013. After getting familiar with the research topics and organization of work in Prof. Gaciong's team she will proceed with all the planned visits to the laboratory of Prof. Cecilia Soderberg-Naucler at Karolinska Institutet in Stockholm.

| <b>Publications resulting from the collaboration between the twinning partners:</b> |
|---|
| none so far   |

## 5. 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 metalloproteases in prostate cancer.

|                        | PLANNED   | CARRIED OUT              |
|------------------------|---|--------------------------|
| <b>OUTGOING VISITS</b> | 1 young researcher 1 months (2013)              | no, rescheduled for 2014 |
|                        | 1 experienced researcher 1 months (2013)        | no, rescheduled for 2014 |
| <b>INCOMING VISITS</b> | 1 young researcher 1 month (2013 or 2014)       | no, rescheduled for 2014 |
|                        | 1 experienced researcher 1 month (2013 or 2014) | no, rescheduled for 2014 |

Details of the executed incoming and outgoing visits:

| Visit | Name and family name of visiting researcher | Date of the visit | Place of the the visit |
|-------|---|-------------------|------------------------|
| -     | -   | -                 | -                      |

As stated by Dr Wlodarski, his team program of exchanging staff between research institutions in Germany and Netherlands were not completed in 2013. Their plans failed due to the two main reasons: 1) the goal of the exchange was chiefly to train young researchers in the use of novel equipment and technology implemented to MUW by BASTION. Since the purchase of the equipment was synchronized with the construction of the new facility in the MUW, that has been delayed by 18 months by now, the hands-on training of our scholars with the experts was to be postponed; 2) planning to train young research personnel, Dr Wlodarski considered PhD students working in his laboratories as model candidates. Unfortunately, it turned out, that these candidates do not fulfill criteria of the exchange partners in BASTION. Therefore 2 of our PhD students in these projects, who were nominees to the twinning, were not eligible to participate.

In the next two years, Dr Wlodarski's group is planning to accomplish the schedule of the twinning. Firstly, their new facilities are about to be completed (spring 2014), and the microdissector will be placed at its destination room. Secondly, thanks to the newly acquired founding for the project, one of the former PhD students – Dr Radosław Maksym – will be part-time employed by the MUW, hence he will be eligible to the twinning with the Saarland University. Unfortunately, it will not be possible to employ the other former PhD student – Marek Janiak – who was the nominee to visit Prof. Schalken laboratory (Medical Center Nijmegen). In these circumstances, Dr Wlodarski is going to seek other financial resources to employ PhD students in the coming years and we will offer the training opportunities to the new members of our research group.

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| <b>Publications resulting from the collaboration between the twinning partners:</b> |
| none so far   |

## 6. Task 1.6.

MUW: Task leader – Dr Krystian Jażdżewski

Foreign Partners: University of Ferrara, Italy (Dr. 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              |
|------------------------|---|--------------------------|
| <b>OUTGOING VISITS</b> | 1 young researcher 1 months (2013)              | no, rescheduled for 2014 |
|                        | 1 experienced researcher 1 months (2013)        | no, rescheduled for 2014 |
| <b>INCOMING VISITS</b> | 1 young researcher 1 month (2013 or 2014)       | no, rescheduled for 2014 |
|                        | 1 experienced researcher 1 month (2013 or 2014) | no, rescheduled for 2014 |

Details of the executed incoming and outgoing visits:

| Visit | Name and family name of visiting researcher | Date of the visit | Place of the visit |
|-------|---|-------------------|--------------------|
| -     | -   | -                 | -                  |

As stated by Dr Jazdzewski, the visits in the partnering laboratories could not be completed due to the fact that both researchers with whom his group planned to hold collaborative projects, moved to American universities. Dr. Stefano Volinia is currently at the Ohio State University, Columbus, USA, and Dr. Sean Lawler moved to the Department of Neurosurgery, Brigham and Women's Hospital, Boston, Massachusetts, USA.

Since the European Commission does not allow for introduction of any changes to the partnering institutions, nor for collaboration with American Universities, Dr Jazdzewski's group was seeking new scientific partners at both the University of Leeds and University of Ferrara. Due to specificity of their research, it was necessary to identify laboratories working in the field of microRNA or thyroid.

During the search for new partnering scientists they found a new potential partner – Dr. Ramzi Ajjan, Associate Professor and Consultant in Diabetes and Endocrinology working at the Division of Cardiovascular and Diabetes Research of the Faculty of Medicine and Health, University of Leeds.

The current plan is to hold 2-month visits (of both the young and the experienced researcher) in the laboratory of Dr. Ajjan in July-August, 2014.

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| <b>Publications resulting from the collaboration between the twinning partners:</b> |
| none so far   |

### 7. 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              |
|------------------------|--|--------------------------|
| <b>OUTGOING VISITS</b> | 1 experienced researcher 6 months (2013) | yes, in 30%              |
| <b>INCOMING VISITS</b> | 1 experienced researcher 1 month (2013)  | no, rescheduled for 2014 |

Details of the executed incoming visits:

No incoming visit was executed in 2013 and was rescheduled for 2014.

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                         | 3.11.-22.12.2013  | Department of Medicine, Center for Molecular Medicine, Karolinska Institutet, Stockholm |
| 2     | Dr Oksana Kovtonyuk                         | 16.02. 2014 -     | Department of Medicine, Center for Molecular Medicine, Karolinska Institutet, Stockholm |

The collaboration that is supported by BASTION let Dr Religa to expand his research activity by implementation of new techniques in his group. They are mostly related to gene expression analysis by using modified cancer cells, genetically modified mouse models. They have been learning how to use digitalized techniques of image analysis.

As stated by Dr Religa, Dr Kovtonyuk (his new postdoctoral fellow) was able to fulfil just 30% of the planned for 2013 6-month stay in Karolinska Institutet. As Dr Kovtonyuk is of Ukrainian nationality, it turned out that due to the visa regulations she does not qualify to visit Sweden for 6 months . Thus, the remaining 18-week visit of Dr Kovtonyuk in Stockholm is rescheduled for 2014 and will be executed as several short-term stays fostering the continuous scientific collaboration between MUW and Karolinska Institutet.

Ad. visit 1:

The main goal of Dr Kovtonyuk's stay in Stockholm was to get acquainted with the research projects conducted by Prof. Cecilia Söderberg-Nauclér's team, get familiar with their laboratory techniques and to perform immunohistochemical staining of tissue samples from Poland with their further analysis. She had a possibility to learn and perform various laboratory techniques such as microtome sectioning, tissue fixation, immunohistochemical staining of different tissues, preparation of samples for cell analysis and cell sorting by flow cytometry. Moreover, she had a chance to get familiar with optimized immunohistochemistry protocols which can be used to identify viral proteins in tumors.

During her stay at Karolinska Institutet Dr Kovtonyuk had a unique possibility to participate in scientific meetings with many teams working in the Department of Medicine as well as with invited speakers from abroad. Her visit was a great time to discuss obtained results and to plan ahead for the future projects and collaboration.

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| <b>Publications resulting from the collaboration between the twinning partners:</b> |
| none so far   |

Ad. visit 2: the second secondments started on February 16<sup>th</sup>, 2014.

### 8. Task 1.8.

MUW: Task leader – Prof. Sławomir Majewski

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

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

|                        | <b>PLANNED</b>                          | <b>CARRIED OUT</b>       |
|------------------------|---|--------------------------|
| <b>OUTGOING VISITS</b> | 1 experienced researcher 1 month (2013) | no, rescheduled for 2014 |
| <b>INCOMING VISITS</b> | -                                       | -                        |

Details of the executed incoming and outgoing visits:

| Visit | Name and family name of visiting researcher | Date of the visit | Place of the visit |
|-------|---|-------------------|--------------------|
| -     | -   | -                 | -                  |

As stated by Prof. Majewski, the postdoctoral fellow planned to join his team was finally hired by Prof. Rafal Ploski in September 2013 and will execute all the planned secondments in 2014.

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| <b>Publications resulting from the collaboration between the twinning partners:</b> |
| none so far   |

### 9. 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  |
|------------------------|--|--------------|
| <b>OUTGOING VISITS</b> | 1 experienced researcher 2 months (2013) | yes, in 75%  |
| <b>INCOMING VISITS</b> | 1 experienced researcher 1 month (2013)  | yes, in 100% |

Details of the executed incoming visits:

| Visit | Name and family name of visiting researcher   | Date of the visit  | Place of the visit            |
|-------|---|--------------------|-------------------------------|
| 1     | Dr Gaetano Vattemi, University of Verona, Department of Neurology and Movement Sciences   | 26.10.-23.11.2013. | Department of Immunology, MUW |
| 2     | Dr Valeria Guglielmi, University of Verona, Department of Neurology and Movement Sciences | 26.10.-23.11.2013. | Department of Immunology, MUW |

Ad. visit 1:

During his visit Dr Vattemi was involved in research activities carried out by Dr Dominika Nowis and her group members. His collaboration with Dr Nowis arose from the common interest to study the biological effects of a proteasome inhibitor on skeletal muscle and primary myoblasts and myotubes. Dr Vattemi also had the opportunity to discuss with Dr Nowis the on-going collaborative project and plan some final experiments to conclude their joint study. Moreover, he got familiar with the research projects and laboratory techniques performed at the Department of Immunology, in particular he had a chance to follow some transfection experiments that have been performed on HeLa and primary human myoblasts. During his stay in Warsaw Dr Vattemi gave a seminar about his on-going research projects in order to share ideas and to find out possible common scientific interests with members of the Department of Immunology. Thanks to his visit to the MUW he got in touch with Dr Tomasz Stoklosa and Dr Rafal Ploski groups, who are developing next-generation sequencing platform at MUW. Thanks to this visit they are currently performing whole exome sequencing in some patients with skeletal muscle disorders with unknown causative mutation.

Ad. visit 2:

At the Department of Immunology, MUW Dr Guglielmi carried out research activities together with Dr Nowis and her group members, in particular with Dr Firczuk. Her four-week stay in Warsaw was a good opportunity to discuss with Dr Nowis, Dr Firczuk and Dr Vattemi on-going collaborative projects and to plan some final experiments to conclude their joint study. Moreover during her stay in Warsaw Dr Guglielmi was

involved in the research activity and laboratory techniques performed at the Department of Immunology. She got familiar with HeLa cell culture and transfection using the GeneJuice Transfection Reagent. In particular, she transfected HeLa cells with a previously prepared plasmid expressing wild type or mutated myotilin in order to evaluate the effect of the mutation on protein aggregation. Moreover, she worked at the cloning of the gene encoding sarcalumenin, a muscle-specific protein that play a role in the calcium reuptake from the cytoplasm to the lumen of the sarcoplasmic reticulum.

Details of the executed outgoing visits:

| Visit | Name and family name of visiting researcher | Date of the visit  | Place of the visit  |
|-------|---|--------------------|---|
| 1     | Dr Małgorzata Firczuk                       | 27.07.-10.08.2013. | University of Verona, Department of Neurology and Movement Sciences |
| 2     | Dr Dominika Nowis                           | 29.08-28.09.2013.  | University of Verona, Department of Neurology and Movement Sciences |

Ad. visit 1:

The main goal of Dr Firczuk two-weeks stay in Verona was to get acquainted with the research projects conducted by Dr Vattemi's group, get familiar with their laboratory techniques, and to discuss possibilities of common interests and future collaboration.

During her stay in Dr Vattemi's laboratory Dr Firczuk had an opportunity to assist or perform various laboratory techniques such as immunostaining of frozen sections of muscle biopsies, myoblasts cell culture, 2-dimensional electrophoresis of lysates from muscle tissue, preparation of samples for electron microscopy analysis.

Importantly, during broad discussions on their research interests Dr Firczuk and Dr Vattemi focused on a common topic involving the role of protein folding defects in pathogenesis and diagnosis of muscle disorders.

Ad. visit 2:

The main goal of Dr Nowis four-week stay in Verona was to perform final experiments for the joined project aimed at the evaluation of the influence of anti-tumor drugs on skeletal muscle structure and function. She had a chance to learn how to culture primary human skeletal myoblasts and how to differentiate them into multinuclear myotubes for subsequent experiments. Together with Dr Vattemi and Dr Guglielmi she also collected samples for further biochemical studies to be performed at the Department of Immunology, MUW. Moreover, Dr Nowis continued the work initiated in Verona by her post-doctoral fellow Dr Firczuk on evaluation of endoplasmic reticulum stress induction



and triggering of unfolded protein response in patients suffering from different types of myopathies.

During her stay at the Medical University of Verona Dr Nowis also had an unique opportunity to witness the diagnostic process of skeletal muscle disorders and to get familiar with biochemical and functional studies of skeletal muscles samples.

Moreover, she participated in several meetings with physicians (hematologists and neurologists) and scientists participating in their collaborative main research projects to thoroughly discuss the progress in the studies and to plan their future research and collaboration.

As stated by Dr Nowis, the two remaining weeks of a visit of an experienced researcher from MUW to the partnering institution have been rescheduled for 2014.

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| <b>Publications resulting from the collaboration between the twinning partners:</b> |
| none so far   |

### 10. 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.

As a new group leader within the BASTION project Dr Zagozdzon established a collaboration between his team and the Royal College of Surgeons Dublin for the purposes of the know-how exchange and technology transfer.

Brief description of Dr Zagozdzon’s collaborative research project and his foreign partner:

B-cell lymphomas are the most common subtype of non-Hodgkin lymphoma (NHL). They pose a significant social problem, especially since the occurrence of this type of cancer in the European population continues to grow. Importantly, although some of the subtypes of B-cell lymphomas initially respond well to the treatment, they frequently relapse as refractory disease, resulting in poor salvage therapy options and shortened survival. Further research is necessary to deepen the understanding of the molecular events underlying the classification and differential outcome between various types of B-cell lymphomas, especially in the context of the search for new therapeutic strategies. In the current project, Dr Zagozdzon proposes to evaluate the role of peroxiredoxins (PRDX) 1 and 2 along with the thioredoxin 1 (TXN) – thioredoxin reductase 1 (TXNR) [further in the application collectively referred to as 'the PTTR system'] as potential biomarkers in B-cell lymphomas. A part of their investigations is related to the assessment of the expression of the components of PTTR system in biological samples, i.e. cell lines and clinical specimens, using proteomic method.



The laboratory of Dr Bryan Hennessy is one of the pioneers of a state-of-art antibody-based proteomic technique, the reverse-phase protein assay (RPPA). Hence, under the twinning agreement of the BASTION project, Dr Zagozdzon intends to carry out the technology transfer between the two laboratories via short reciprocal visits of their team members in 2014 and 2015. This will allow him for generation of the collaborative results on the constituents of PTTR system in B cell lymphomas.

|                        | PLANNED | CARRIED OUT |
|------------------------|---------|-------------|
| <b>OUTGOING VISITS</b> | -       | -           |
| <b>INCOMING VISITS</b> | -       | -           |

Details of the executed incoming and outgoing visits:

| Visit | Name and family name of visiting researcher | Date of the visit | Place of the visit |
|-------|---|-------------------|--------------------|
| -     | -   | -                 | -                  |

**Publications resulting from the collaboration between the twinning partners:**

O’Leary P, Terrile M, Bajor MA, Gaj P, Hennessy BT, Zagozdzon A, O’Connor DP, Brennan DJ, Connor K, Li j, Mills GB, Gonzalez-Angulo AM, Sun HD, Pu JX, Pontén F, Uhlén M, Jirström K, Nowis D, Crown JP, Zagozdzon R, and Gallagher MW. Peroxiredoxin-1 protects estrogen receptor  $\alpha$  from oxidative stress-induced suppression and is a protein biomarker of favorable prognosis in breast cancer (under second revision in Breast Cancer Res).

**11. 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  |
|------------------------|--|--------------|
| <b>OUTGOING VISITS</b> | 1 experienced researcher 2 months (2013) | yes, in 100% |
| <b>INCOMING VISITS</b> | -  | -            |

Details of the executed incoming visits:

No incoming visit was planned for 2013.

Details of the executed outgoing visits:

| Visit | Name and family name of visiting researcher | Date of the visit  | Place of visit             |
|-------|---|--------------------|----------------------------|
| 1     | Dr Karolina Dzwonek                         | 24.06.-20.07.2013. | Science Business, Brussels |
| 2     | MSc Michal Gieraltowski                     | 26.08.-27.09.2013. | Science Business, Brussels |

The subject of task 1.11 of the BASTION project assumed the transfer of know-how and stimulation of innovation-driven research to bring research results from bench to the bedside. There was planned a 2-month internship by MUW employee at Science|Business office in Brussels, which was subdivided into two visits – one of Dr Karolina Dzwonek, BASTION Innovation Manager, and another one of Michał Gieraltowski, BASTION PR Manager. The secondment objectives comprised facilitation of collaborative innovation driven research between industry and academic centers of excellence in translational oncology and personalized medicine.

Science|Business, partnering organization in the project, is an SME that connects public researchers, private funders and policy makers in the European innovation community. It runs news service to help members of the research and innovation community find out about each other and organizes several events a year gathering top level professionals and decision makers, including members of European Parliament and European Commission representatives. The company, based in London and Brussels, is run by leading technology journalists, including former managing editors of the Wall Street Journal Europe and Nature.

Ad. visit 1:

Dr Karolina Dzwonek had been working at Science|Business office from June 24th until July 20th 2013. She was engaged in all activities of the company at the time of her stay, including networking, organizing events, data analysis and marketing. All new contacts and experiences she got during her stay will facilitate innovation driven research of BASTION project groups and can comprise a starting point of new initiatives. Dr Dzwonek has also started collaboration with one of the leading technology transfer units in Europe – Leuven Research & Development (LRD) at KU Leuven. She consulted Mr Olivier Lescroart, intellectual property specialist at LRD, about insights into technology transfer process at university. This experience can be extremely valuable in light of implementing technology transfer management schemes at Medical University of Warsaw.

Ad. visit 2:

Mr Michał Gieraltowski had been working at Science|Business office from August 26th until September 27th 2013. He was engaged in all company activities, including:

networking, organizing events, data analysis, marketing, online promotion activities. Organizing events which involves engaging key stakeholders was one of the Michał responsibilities during his twinning in SB. Such experience would be useful in any innovation project executed by the MUW. Managing key stakeholders would be crucial input of any big project. Unique know how regarding using multiple data bases and online promotion tools especially gained on the European level would be a unique know which would put any MUW initiative in to the next level. Above mention activities is only a sample of projects that Michał Gierałtowski was responsible during his twinning at Science|Business.

## **12. Analysis of added value**

As stated in the grant proposal one of the expected key benefits of the WP1 realization was transfer of scientific and experimental knowledge between MUW and partnering institutions. In fact, execution of Work Package 1 during first 18 months of BASTION project provided significant added value by bringing together experts from various disciplines willing to share their expertise and resources. This 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. In several of the twinning visits actual research and training program exceeded initial plans, the best example illustrating this fact is described in Task 1.3 (page 7-8) - twinning between MUW and University Hospital of Ulm allowed not only to learn but also to employ ultramodern technology of RNA sequencing on next-generation sequencing (NGS) platform instead of previously planned classical microarray analysis. Thus WP1 execution allowed increased scientific dialogue between partnering academic institutions and MUW and gave excellent training opportunity for the recruited staff, both at MUW and at the partnering organizations. Further continuation of twinning tasks and execution of the full WP1 plan will definitely enable new, joint opportunities in research projects for the scientists from MUW and partnering organizations.

## **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 centres 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) regarding twinning via secondments, which are being gradually cleared. This however, caused delays and rescheduling of some twinning visits for 2014. Despite the fact that not all the visits planned for the first 18 months of the project had been executed, those secondments, which were successfully accomplished were extremely valuable. 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**

| <b>PERSONNEL, TRAVEL, AND OTHER MAJOR DIRECT COST ITEMS FOR BENEFICIARY "1"<br/>M1 – M18</b> |                         |                         |   |
|--|-------------------------|-------------------------|---|
|  | <b>Item description</b> | <b>Amount<br/>[EUR]</b> | <b>Explanations</b>   |
| <b>Work<br/>Package<br/>1</b>  | Personnel costs         | 51 426,00               | Salaries of the WP1 leader, Co-leader and Task leaders (14,05 PM)   |
|  | Travel                  | 65 683,00               | Travel & accommodation - 12 outgoing missions and 3 incoming visits |
|  | Other direct costs      | 0,00                    | -   |
|  |                         |                         |   |

*/\* - exact costs for M1-M18 will be presented in the 1<sup>st</sup> Period Report and Form C (April 2014)*

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

Prof. Jakub Golab  
BASTION Project Coordinator

*Warsaw, February 2014*