ReProForce
FP7-REGPOT-2009-1

REINFORCEMENT OF THE RESEARCH CAPACITY OF THE BULGARIAN INSTITUTE "BIOLOGY AND IMMUNOLOGY OF REPRODUCTION"

FRAMEWORK PROGRAMME
THEME CAPACITIES – RESEARCH POTENTIAL

Activity 4.1 Unlocking and developing the research potential in the EU's convergence and outermost regions

Grant agreement for: **Coordination and support actions (Support)**
Project acronym: **ReProForce**
Project full title: **Reinforcement of the research capacity of the Bulgarian Institute "Biology and Immunology of Reproduction"**

Grant agreement no.: **245641**

Beneficiary Number *	Beneficiary name	Beneficiary short name	Country	Date enter project	Date exit project
1(coordinator)	Institute of Biology and Immunology of Reproduction – Bulgarian Academy of Sciences	IBIR-BAS	Bulgaria	1	42

FINAL REPORT

1. EXECUTIVE SUMMARY

The ReProForce project has been an important mean for the Bulgarian Academy of Sciences Institute of Biology and Immunology of Reproduction (IBIR-BAS) to increase its scientific and technological capacity and to further integrate the European Research Area. It had allowed the creation of favourable conditions for the reinforcement of IBIR research potential in order to restore its leading positions in the field of biology and immunology of reproduction.
Activities have been supported by 7 European research performing organisations, which have leveraged the training and scientific knowledge transfer to IBIR-BAS researchers and Institute management.

The implementation of the project has led to the following visible results that have strongly supported the research capacity building at IBIR:
Up-grade of equipment consisting of the purchase of 13 new items and the up-grade of 4 IBIR-BAS laboratories: Laboratory for proteome analysis, Laboratory for cell culture, physical and chemical analyses, Laboratory for in vitro fertilization and embryo transfer and the Laboratory for confocal and light microscopy. The laboratories have been widely presented to stakeholders from Bulgaria and abroad. The strengthened technical capacity of IBIR-BAS has led to the following:

- Increased research efficiency expressed in the publication activities of IBIR's researchers (new **100** publications and **10** books for the period 2010-2012, among which 51 having an Impact Factor (international journals: for animal reproduction(AR) -12, for human reproduction(HR) - 37; national: AR -19, HR-32);
- Attraction and involvement of students in development of Bachelor and Master Theses at the Institute Departments (**12)** ;
- Attraction and involvement of researchers from other Research Institutions and Universities for conducting PhD thesis programs (**10)** ;
- Attraction and involvement of researchers from other Research Institutions and Universities for joint experiments (**26)** ;
- Additionally, 2 researchers from other Research Institutions and Universities have been attracted under external Research Projects and Grants - **2** ;

Two-way mobility of scientists and knowledge transfer activities have been implemented which has led to:

- Organization of 10 scientific and methodological seminars.
- Participation at 3 European Networks: ESDAR, AETE, ESRADI and at 8 Conferences (Annuals' Conferences of AETE-3; of ESRADI-3; of ESDAR -2).
- Establishment of closer relationships with 10 National Actors: **5** Universities; **3** Public Scientific Institutions; **2**Business partners in reproductive medicine.
- Establishment of IBIR-BAS Reproduction Network extended to 18 new partners from EU (and SEE) Research Institutions, European Industry Partners and Innovation and Technology Transfer Partners.

Strengthening of scientific capacity trough recruitment of researchers from abroad (3) and enhancement of the qualification of staff: 4 PhD candidates have defended research theses; **4**

Associate Professor degrees and **2** Professor Degrees were conferred; **5** researchers are in procedures for conferring Associate Professor Degrees; **1** member of ReProForce project got a research fellowship from DAAD, Germany for 3 months training in Jena.
The implementation of the activities has contributed to significant knowledge increase through mobility and seminars given as well as participation at Conferences where it is fundamental that knowledge transfer and sustainability of participation are maintained. The project has attracted new expertise but also allowed open and easy access to important scientific literature. It has allowed the purchase of cutting-edge technology and equipment strengthening though the scientific leadership position of IBIR at national level. IBIR will build now on its new technological and research capacity to attract further young researchers but also develop and explore deeper its innovation capacity and links with the private sector. Since support and scientific collaboration are of primary importance for effective research, IBIR will further enhance its scientific activities through strong partnership developed under ReProForce.
To ensure sustainability and greater impact of the project tasks and deliverables, the Institute has developed, based on external peer review, a RTDI Strategy for IBIR-BAS for 2014-2020, accompanied by a robust action plan.

2. SUMMARY DESCRIPTION OF PROJECT CONTEXT AND OBJECTIVES

The reproduction is of basic quality and function of living organisms which makes it an object of intensive studies for a number of decades. The Institute of Biology and Immunology of Reproduction – Bulgarian Academy of Sciences (IBIR-BAS) is an ambitious and fast developing research centre in the field of reproduction of both humans and animals. It has a long standing 70 years history of successes in research of reproduction. The "reproductive immunology" as a unique field of research has been created and developed within this Institute. IBIR-BAS had many achievements at national and European level at the start of ReProForce in terms of scientific collaboration, contacts with industry, participation in European networks and platforms etc. However, despite all this, the development of the research potential in the convergence regions of EU, meets important difficulties. Structural support is missing due to lack of a national strategic framework for research and innovation for the last years with the exception of a draft Innovation law, under validation and the Scientific strategy for R&I 2020 which does not provide any binding provision and therefore commitment at national level.
Indeed, the financial shortage during the last years restricts:

- the deepening of the research in reproduction
- the opportunity of IBIR-BAS researchers to upgrade their qualification in leading research centres and exchange their experience;
- the access to International symposia;
- the successful participation, particularly in the capacity of coordinator of EU research projects, particularly within FP7 and cooperative investigations;
- the attraction of talented and perspective researchers
- the wide dissemination of the scientific results among all relevant stakeholders

Againts this backdrop, IBIR-BAS proposed under ReProForce a comprehensive set of measures to address its weaknesses and to strenghten and exploit better its research potential and thus disseminate better its result.

The main objective of the ReProForce was to set out the necessary and favourable conditions for the reinforcement of IBIR-BAS's research potential and to restore its leading positions in the field of biology and immunology of reproduction.

To achieve this, ReProForce team has elaborated a detailed and robust action plan, based on the following operational objectives:

- Enhancing IBIR-BAS's scientific and research capacity in the targeted scientific sectors by means of mobility and knowledge exchanges with excellent research EU institutions, participation in and organization of scientific events, hiring of experienced researchers, organization of methodological trainings and others;
- Reinforcing IBIR-BAS's technological capacity by means of purchasing thirteen new apparatus and up-grading four laboratories, subscribing membership in to online scientific database;
- Strengthening of European partnerships by means of creation of partners' network and build-up of a strong long-term collaboration with research organisations and enterprises from EU and SEE, organization of International conferences, participation in European conferences, establishment of closer relations with industry, cooperation with national labs, organizing workshops with farmers, performance of roundtable with patients, local events.
- Visibility rising by means of wider dissemination campaign and performance of open days, seminars, visits at IBIR-BAS, preparation of website, leaflets and other dissemination materials and wide public targeted dissemination efforts.
- Independent evaluation of IBIR and ReProForce implementation and developing a strategy for research and innovation supported by a robust action plan to ensure sustainability and increased visibility of IBIR in the European Research Area (ERA) till 2020.

3. DESCRIPTION OF THE MAIN S&T RESULTS/FOREGROUNDS

Through its collaboration with 7 European partners, the implementation of the ReProForce activities for the whole project period can be graphically presented as follows:

Specific objectives	Activities	Measurable outputs	Impact
Strengthening of the research capability of IBIR-BAS	• Two ways mobility visits with 7 outstanding European research partners • Strengthened employment strategy in view of attracting back experimented researchers and	• 21 visits in total (9 junior/12 senior outgoing) – 21 individual knowledge transfer reports, 6 incoming visits • Recruitment of researchers from scientific units abroad (2), Researcher Technicians (1), Technician (1), part-time employee assistant manager (1) ; • Enhancement of the qualification of staff: 4 PhD	New knowledge developed New collaboration started in view of tackling jointly European research priorities and achieving

	provide necessary boundary conditions for career path development • Organisation of methodological trainings	candidates have defended research theses; 9 Associate Professor degrees and 3 Professor Degrees were conferred; 1 member of ReProForce project obtained a research fellowship from DAAD,Germany for 3 months training in Jena. • 10 methodological trainings and training courses were implemented in collaboration with local and international partners	greater excellence in research Transfer of knowledge on new methodologies and technologies
Strengthening of the research and technological capacity of IBIR-BAS	• Acquisition of new equipment & Reorganization and up-grade of 4 laboratories and an animal facility • Subscription and membership to online scientific data and journals	• 13 new items purchased and distributed between 4 laboratories • Renovated and registered facility for experimental animals • 11 technical trainings performed by the equipment providers and/or by visiting Professors. 6 Indirect events related to promote the work at IBIR-BAS, notably by using the new equipment. • 10 new subscriptions (both print and online), including membership in 8 online databases	• Mastering modern research techniques • Attracting research and business stakeholders for increased collaboration, including students and junior researchers to perform scientific career at IBIR-BAS
Becoming an Institute of prior interest for Bulgarian and SEE end-users and **further integrating the European research Area**	• Establishing closer relationship with local partners and wider stakeholder community (Strengthened relationship with 10 national scientific/academic institutions and 2 business partners in reproductive medicine)	• 17 new joint publications with international partners in European scientific journals, 1 scientific books published abroad • 60 new joint publications with national partners, 8 scientific books (5 published in Bulgarian editions and 3 published abroad) • attraction of interest from 12 students to develop Bachelor and Master theses in IBIR • attraction of 10 PhD students	• New collaboration started to efficiently tackle major societal challenges, poor resources and exchange best practices • Increased

	• Participation to and organisation of European-wide events (Participation to 8 European conferences and Networks: ESDAR, AETE, ESRADI; Organisation of 2 Balkan (EU-wide) Training courses, 2 International Symposiums, 1 International workshop; 4 support-partners meetings) • Increased dissemination and promotion activities (Organisation of 1 scientific seminar and round-table discussion 3 Open doors event, business networking, media coverage, social and education awareness (see annex on promotion materials description) 3 stakeholders meetings and questionnaire survey for stockholders in animal and human reproduction)	from other institution to develop their thesis in IBIR • attraction of researchers under 2 external Research Projects and Grants • attraction of 30 researchers to conduct joint research at IBIR . • attraction of funding for research - 4 projects under National science found (220 000eu) and 1 under Operation programme "Human resources" for PhD students support (400 000 eu) • developing of the RTDI Strategy of IBIR till 2020 • http://ibir.bas.bg • http://reproforce.ibir.bas.bg	international collaboration with outstanding research centres • Increased visibility and therefore attractiveness of IBIR (e.g. for collaboration, conduct research, private investment etc.) • Greater interest at scientific career in Bulgaria and social awareness since very early stage on the main problems and current challenges in the field of both human and animal reproduction

1) Strengthening the research capability of IBIR-BAS

The objective of scientific knowledge increase was mainly pursued through mobility visits and trainings.

Exchange of know-how by mobility visits

27 mobility visits were implemented out of which 21 outgoing and 6 incoming.
Mobility visits contributed to the objective of know-how exchange and transfer of knowledge, thus improving the research potential at IBIR-BAS and reinforcing the established collaborative links with leading European institutions in the field of reproductive biology and immunology.
All planned visits achieved its goal: deepening of the partner's contacts, obtaining of new knowledge and of valuable exchange of experience and know-how. IBIR staff had acquired new competences as well as research knowledge valuable for the advancement of their particular research at IBIR.
In parallel, ReProForce support partners were acquainted with the research performed in IBIR-BAS, the newly purchased modern equipment and therefore gained better impression and acquaintance on the level of local research that would be very beneficial for future collaboration and better know-how transfer.
Mobility visits have naturally led to the strengthening of the network for collaboration within ReProForce as to attract also new partners for future scientific contacts and participation in a network of European partner organizations working on the problems of biology and immunology of reproduction.
The results from collaborative research during the mobility visits were discussed in details with the partner's institutions as a basis for preparation of possible joint European research projects.

Extensive methodological training of scientists from IBIR-BAS

10 methodological trainings have been implemented, with the participation of local stakeholders community, Institute's staff and its ReProForce national and international research partners.
The trainings allowed the successful application of new methods in reproductive biology and immunology by using the new purchased equipment and the upgraded technical resources of IBIR.
The methodological knowledge transfer from ReProForce EU partners (training and discussions) given during the two-way mobility exchanges of junior and senior researches has additionally contributed to the optimal utilization of the new equipment and, hence, increased research potential of IBIR's scientists.

Recruitment of new researchers

The establishment of a better research environment within the Institute made it attractive for former Institute PhD graduates with international research experience who have naturally chosen to rejoin their colleagues and transfer back their knowledge on new methodologies and technologies. Two researchers that had defended their PhD theses at IBIR with experience gained at US Research Institutions in practical medicine in the field of reproductive health have returned and are willing to help boosting the research potential of the Institute. Indeed, IBIR has fostered its reputation at an international scale amongst both young scientists and experienced researchers. It is to say that the return (and overall awareness) has been facilitated

by the online publishing and dissemination of the new job opportunities provided by ReProForce.
2 researchers have been employed on permanent basis and one on an ad-hoc basis within the scope of the implementation of ReProForce.
Open positions and job description have been published on both IBIR-BAS website and EURAXESS.
In addition, an "Open Door" policy was established, especially for young PhD students, involving support on their research projects trough brainstorming conversations, or methodology (good practices) know-how transfer. This policy also envisages for a prospective Master degree biology/immunology student to undergo training in IBIR's Laboratories in the form of Master Thesis with Lab research work and Thesis manuscript preparation.

As a result of the implementation of the above activities, the following outcome has been achieved:

Deepening of the partner's contacts: Mobility led to the establishment of thematic teams in view of ensuring the sustainability of the scientific work and the preparation of joint projects and publications.

- **Knowledge transfer:** The reinforcement of the research potential of the Institute through mobility visits contributed to the creation of new generation of high quality scientists. This reflects also in the enlarged publication activity of IBIR (49 publications in international journals and 51 in national journals) for the period 2010-2012. Additional publication of 10 scientific books was realized: 6 in Bulgaria and 4 in abroad.

- **Joint activities with other international partners** resulted in 13 collaborative publications in peer reviewer international journals as well as 1 scientific books published abroad.

- **Strengthening of the network for collaboration:** IBIR researchers got acquainted with up-to-date methods on operation with new apparatus, enabling them to work in respect of the standards of outstanding European research organizations. Within the implementation of ReProForce and with a view to further develop collaboration with research partners, the ReProForce team **has been enlarged with 19 new organizations in** the field of biology and immunology of reproduction.

- **Detailed knowledge of the technical resources in the partners' organizations** during the mobility visits created possibilities for discussions of joint experiments using the unique equipment they have at their disposal. Contacts have been already established with the School of Biological Sciences, Imaging Unit and Proteomics Unit, University of Essex, Wivenhoe Park, Colchester CO4 3SQ, Essex, UK and research experiments with the participation of PhD students and young researchers from IBIR

were done. Some of the results will be included in 1 PhD thesis and others in 4 joint ready for publications research papers.

- **Acquaintance with the experimental** base in the partner's organizations during the mobility visits created possibilities to use their experience for optimization of the work in the animal house of IBIR as well as a discussion on the problems related to the fulfilment of the European regulations of the conditions for breeding of "happy" animals. The IBIR animal house was fully renovated and registered under Bulgarian Veterinary Law.

- **Future possibilities for exchange of PhD students and young researchers** working on similar problems were planned in details during the meetings with students and young researchers from partner institutions as well as working meetings for the exchange of experience in research.

- **Strengthening of the international visibility** of IBIR due to visiting professors from leading top European research centres; Presentation of IBIR scientific results at 83 international scientific forums; Presentation of IBIR's scientific results at partners Laboratory seminars.

- **Three new projects within FP7 were developed in collaboration with European partners** in results from collaborative research activity during the mobility visits and the network-building process. Mobility allowed for in-depth discussion on joint projects opportunities (as well as analysis on submitted proposals). This includes assessment on Institute's and partners network strengths and weaknesses for which an important basis constituted the rejected for funding KBBE proposal 'REPROPIG', fruit of collaboration between ReProForce partners. Further opportunities and strengthened argumentation and working modalities were discussed for future FP7 and Horizon 2020 call for proposals.

- **Last but not least,** increased knowledge contributed to the resolution of issues related to natural resources, reproductive health, and quality of life; tightening the contacts with the medical and farm and agricultural communities, in favour of economical beneficence of the results produced in IBIR-BAS; support to the implementation of Government programs targeted to demographic problems prevention, and continuous development of the country natural resources. The Institute developed and applied biotechnology for cryopreservation of gametes, embryos and reproductive tissues, which is part of the National programme for genetic resources preservation at a new high –class level.

<u>Strengthening the research and technological capacity of IBIR-BAS</u>

Purchase of new equipment reorganisation of IBIR-BAS laboratories

- The equipment planned for the modernization of the Institute's four research Laboratories has been delivered and put into operation within the first six months of the project.

Theoretical and practical trainings have been held according to the contracts with the companies providers

- In the course of the re-organization and the up-grade of the four laboratories EU standards and recommendations for high level efficiency and safety were taken into consideration.
- The new re-organized laboratories were done in a way to present multifunctional features hence allowing systemic and detailed studies in the field of reproductive biology and immunology and providing a creative basis for high-level education and training of young researches, Ph.D. fellows and undergraduates.
- To ensure greater visibility and impact of the new technical potential of IBIR-BAS, a list of the purchased and present equipment, accompanied by illustrations of the equipment and the laboratories, was presented to the Bulgarian Academy of Sciences to be promoted to its scientific structures. This was also reflected on IBIR-BAS's website to increase its visibility and raise awareness on the new possibility for high level research present at IBIR.
- During the Open Doors Days within the project, the upgraded laboratories were presented to the visitors (more than 100 people) and opportunities were explored for the joint use by scientists from other institutes of the Bulgarian Academy of Sciences, universities and etc.
- In parallel, important communication and networking activities were organized. Technical experts from the relevant scientific fields have presented at the occasion of several methodological and theoretical trainings, an up-date on the latest techniques and scientific methods.

In conclusion, the results obtained from research experiments with the new equipment are at a level comparable to that of other outstanding European centres, which can be supported by the latest IBIR's scientists publications in internationally recognised scientific peer-view journals with high impact (**Carcer Chemother.Pharmacol**., 67,13-25, 2011. ISSN: 0344-5704; IF 2.654; **Neuropeptides**, Vol. 44, Issue 6, 485-489 (2010). ISSN: 0143-4179. IF – 2.176; Journalof **Obstetrics and Gynaecology Research**, Vol.37, Issue 6, 511–519, 2011, ISSN: 1447-0756; IF- 0.777; . Reproductive Bio Medicine Online, Vol. 21, 304– 311 (2010); **Photochemical & Photobiological Sciences**, 10, 91-102 (2011) ISSN: 1474-9092. IF – 2.708; **Cancer Chemother Pharmacol** - in press, doi: 10.1007/s00280-010-1273-5 ISSN: 0344-5704.IF 2.654; . **Fertil.Steril.,** - in press, doi:10.1016/j.fertnstert.2010.04.034. ISSN: 0015-0282 IF - 3.970; **Tech Immunoassay**, Open Access publisher of Scientific Books and Journals (in press).

As a consequence, the new equipment and labs' reorganization have made the Institute an attractive place for scientific career for young students and scientists, preventing though at long term the phenomena of "brain drain" to foreign countries, in particular within the EU or other industrialized countries (e.g. USA).

Membership to on-line scientific databases and journal subscription

According to the work programme, subscriptions to two online databases have been planned as follows: HINARI and SCOPUS. However, at the time of the project negotiations, the Bulgarian Academy of Sciences has provided free access to SCOPUS for all its members,

which gave the possibility for IBIR to subscribe to other, non initially planned scientific journals and database. This has further facilitated the access to knowledge of IBIR staff and hence impacting on potential new publications and research contacts. The HINARI (http://www.who.int/hinari/en/) database itself enabled IBIR researchers to gain access to one of the world's largest collections of biomedical and health literature. The programme contributed to improved health research within the Institute in addition to the allowed access to data.
An additional element to increase the research capacity of the Institute was the **subscription to some very important online scientific reviews,** providing access to research quotations and publications, such as Biology of Reproduction, Stem Cells, Theriogenology, and Nature Immunology etc

During the project period the scientists in IBIR-BAS had access to **SciVerse ScienceDirect and SciVerse Scopus supported by Elsevier Publishing, as well as Science Direct, Thompson Reuter Web of Science, SpringerLink, DOAJ-Direction of open access journals, Research Gate and High Wire Press.**

Additionally, training on (open) access has been provided such as the organised in 2012 course on "**What is new in the data base of ScienceDirect and Scopus"** with the presence of representatives from the Ministry of Education and Science.

Finally, the subscription to the main leading scientific journals and online databases in the field of Human and Animal Reproduction Communities ensured the direct access of Institute's staff to up-dated information on novelty achievements on the problems of different processes and mechanisms of the reproductive process.

3) Integrating the European Research Area by increased dissemination and network building

Network Building

To establish a common vision and collaboration plan with ReProForce partners, four meetings of the ReProForce network took place and have defined the existing scientific problems at EU and global level to identify strategic areas of cooperation and to develop a common plan for future cooperation. The network was expanded to new national and European partners and led to defining clearer guidelines on funding programmes and future priorities (notably under Horizon 2020). Minutes of the meetings have been transmitted to the external ReProForce reviewers to be further taken in consideration when defining IBIR-BAS RTDI strategy 2014-2020.

Establishing closer relationships with national laboratories, business and local actors

The network buidling activities had raised significantly the awareness and trust building on IBIR-BAS which have developed scientific and practical agreements for cooperation in

research of reproductive problems in humans and animals with the most prominent national public and private institutions:

- The Faculty of Veterinary Medicine, Thracian University, Stara Zagora
- Agro-biological Faculty, Thracian University, Stara Zagora
- Agrarian University, Plovdiv
- The Research Institute of Mountain stockbreeding and agriculture, Troyan
- The Agriculture Institute, Shumen
- The Institute of Animal Sciences, Kostinbrod
- Agricultural Experimental Institution-Sredez
- Department of Biology, Medical University, Sofia
- Biological Faculty, University in Sofia
- The Veterinary faculty of Sofia, Forestry University
- Center for Obstetrics and Gynecology "Wiara-Dr Genov"
- Center for Obstetrics and Gynecology "Reproductive Health"

The concluded scientific and practical agreements for development of educational programs and exchange of know-how and experience between IBIR-BAS's and Bulgarian scientists stimulated the collaborative participation in elaboration of funding projects under the European framework programs, the Operative programs and other international and national organizations. Efforts are ongoing and are expected to lead to new joint experiments and publications, presentations at scientific meetings

Finally, the private sector has been also involved and collaboration gave birth to an important national protect with the Center of Genetics and Biotechnology, Sofia on the "Genetic improvement of the sheep breeds in Bulgaria through the application of innovative product for optimization of the biotechnology for in vitro conservation of male gametes

The overall scientific collaboration with national partners for the period of 2010-2013 resulted in:

- 28 National partners' participation at the scientific events organized by IBIR under ReProForce Project;
- 35 Publications as a result of collaborative investigations with national partners (scientific and academic institutions) and **8** scientific books**:** (5 in Bulgarian and 3 in international editions**);**
- 25 Publications with national industry partners;
- 47 Joint presentations at international congresses and symposia;

Participation at European Conferences

IBIR staff has participated at **8 leading European Conferences** and Networks **(ESDAR, AETE and ESRADI)** and presented the Institute scientific achievements to the wide European scientific community. By the same, IBIR's researches received an up-dated training on the most actual topics of their research. As a result also, new interpersonal professional connections were endured and new knowledge - acquired in the field of biology and immunology of reproduction. Participants in the Conferences took hold of the new possibilities for further partnership development and hence discussed Institute's collaborative investigations on important for IBIR and at global level topics such as:

- **Studies on decidual stromal cells**, presented at the Joint 10th International Congress of the American Society for Reproductive Immunology (ASRI) and the European Society for Reproductive Immunology (ESRI.
- **Studies on localization of matrix metalloproteinases–2 and -9 in ejaculated, capacitated and acrosome-reacted human spermatozoa cells,** presented at the 10th International Congress of ESRI with Prof. M. Kurpisz, the President of ESRADI from Poland.
- **Isolation of mesenchymal stem cells from placenta (pMSC)** presented during a visit at Jena Partner's center, Germany (Placenta-Laboratory, Department of Obstetrics, Friedrich-Schiller-University) on the occasion of the 3rd Jena InTReST satellite event of 10th International Congress of ESRI.
- **Participation at the 9th Congress of ESRADI** was followed by suggestions for future collaboration in the field of **technologies for microarray analysis of single cells** (Prof. Udo Markert). Presentations provoked also interest on the issue of **visualization of receptors participating in the innate immune response** where **Prof. Nelson Fernandes** offered possibilities for future mutual work**. Prof. E.R. Barnea** suggested mutual scientific work on the **preimplantation factor PIF in embryonic and fetal tissues from pigs with the purpose of establishing PIF as commercial product for early diagnostics of pregnancy in human and animals**.

Participation at the **28th Congress of European embryo transfer association** (AETE) has led also to further collaboration and submission of joint FP7 KBBE proposal. Finally, IBIR-BAS was invited to take part at the **COST Action FA1201** - Periconception environment as an epigenomic lever for optimising food production and health in livestock.

The European Conferences also gave the opportunity to establish **contacts with some business representatives** working in the field of reproduction i.e. the German producer of cattle embryos MASTERRIND GmbH and the Swedish company NidaCon International AB, responsible for developing, manufacturing and selling of Medical Devices for the Assisted Reproduction Technology.

Participation in EU conferences and networks resulted in 14 scientific publications out of which - **five** are with Impact Factor.

Dissemination of IBIR-BAS's scientific results

IBIR-BAS has widely disseminated project activities and deliverables during all project duration with the aim to further develop and create joint collaborations with all project partners thus increasing the quality of research on molecular mechanisms of reproductive process and elaborating new biotechnologies to be applicable in human medicine and agriculture practice.

Six scientific events at major international scale were organised and offered the opportunities for exchanging knowledge and new ideas for future work in the fundamental and clinical aspects of reproduction. They also opened the gate for new strategic research and innovation more focused partnerships in the field of biology of reproduction and particularly on modern practical applicable embryo transfer technologies and gametes mitochondrial functions.

The events are briefly listed below:

- Organisation of 2nd Conference of **Balkan Network for Animal reproduction** biotechnology "European achievements in Biotechnology in Animal reproduction" with Supporting Workshop, 24/25 March 2011, IBIR-BAS, Sofia, Bulgaria.
- Training Course for Farmers, Breeding Associations Representatives **"Biotechnology of Embryo Transfer in Farm Animals"**, 25-28 September 2011, in collaboration with the Institute of Mountain Agriculture and Stock-breeding (IMSBA), Troyan, Bulgaria - the national partner of IBIR in the ReProForce project.
- Organization of Workshop "**Mitochondria and Reproduction**", joint event with COST Action FA0602, at IBIR-BAS on 2-3 June, 2010.
- Organization of the **13th International Symposium for Immunology of Reproduction**
- **Round Table on the problems of assisted reproduction techniques**.
- Scientific seminar "**Immunological problems of human reproduction**", organized by IBIR-BAS on 5th November 2011.

Overall, all the organized events ensured wide dissemination of IBIR's scientific results to European scientists, creating though opportunities for joint collaborations with partners working on modern reproductive biotechnologies for sustainable breeding and management of animal resources at European level.

The Network building process for reproduction investigations supported the young generation of scientists in this research field and consolidated the efforts of the scientific institutions to develop reproductive biotechnologies as a perspective approach for ensuring healthy off spring and animal resources in the region as well as in wide Europe.

Finally, the activities during the organized events contributed to the strengthening of IBIR's cooperation with veterinary medicine practice and industry partners which took part in the scientific programs of the events.

4)Evaluation of the IBIR and ReProForce and development of IBIR-BAS RTDI strategy by independent experts

The activities undertaken to increase IBIR-BAS's research and technological capacity, including dissemination efforts, have been thoroughly evaluated by 3 independent experts, in view of preparing a comprehensive RTDI Strategy for IBIR-BAS 2014-2020.

Evaluation of ReProForce deliverables

According to the experts, IBIR-BAS has successfully implemented the action plan described in the ReProForce work programme and covered well the five mandatory measures, namely, i) exchange of know-how and experience, ii) recruitment of experienced researchers, iii) acquisition of research equipment and upgrading of laboratories, iv) organisation of workshops and conferences and v) dissemination and promotion.

The project activities have reinforced and improved the RTDI potential of the IBIR-BAS. It has provided some of the tools necessary for tackling the problems in human and animal reproduction in Bulgaria and better integration of IBIR-BAS in the ERA.
The project has provided some tools which can contribute to national and regional economic and social development provided that further inputs, especially the funding, are made available.
The increase in capability, capacity and networking has improved the potential of IBIR-BAS to participate in European Framework as well as other programmes. In fact, during the life of ReProForce 2 projects were submitted under FP7 calls which were, unfortunately, rejected.

RTDI Strategy for the IBIR development till 2020

All of the experts conclusions have been considered for the preparation of the RTDI Strategy for IBIR-BAS 2014-2020 with an overall objective to steer IBIR – BAS along the way of strengthening its research potential and network of partners, and positioning itself as a true player in the European Research Area.
The RTDI strategy builds upon the findings of diversified activities undertaken in the period

The strategy identifies both the research and the development priorities of IBIR – BAS until 2020. It spells out four development priorities, which are further diversified into strategic goals and measures, the performance of which will be measured through specific indicators for each measure.
Priorities include:

- Scientific research in view of further alignment to European and global scientific priorities
- Education and training in the area of biology and immunology of reproduction employing the life-long learning approach, thus focusing on the career development of young researchers with high research potential on the one hand, mobility of senior researchers, as well as on enhancing the qualifications of the staff for their research and practical activities.
- Technology transfer, where given the societal importance of the research carried out by IBIR–BAS for both the human and veterinary medicine, the transfer of the research achievements into practical applications will be of high priority in IBIR's future activities.
- Enhancing the research and innovation cooperation and networking in the country and abroad, encompassing conducting joint research, joint research projects under national and European programmes, joint organisation and joint participation in seminars and conferences. This is why this priority is of a horizontal nature, i.e. it will support the attainment of the strategic goals of the preceding 3 priorities.

The strategy should be implemented through bi-annual action plans, which encompass concrete tasks per measure.

4. POTENTIAL IMPACT AND MAIN DISSEMINATION ACTIVITIES AND EXPLOITATION RESULTS

Direct impact

ReProForce has been planned and conducted with the main goal to reinforce IBIR-BAS's research potential to restore its leading position in the field of reproduction biology and immunology. To reach this goal the project has focused on obtaining new laboratory equipment (WP2), conducting mobility visits of junior and senior scientists of IBIR to its ReProForce partners in Europe (WP1), hiring new and trained staff (WP1), organizing meetings and workshops (WP3/4), and finally increasing the awareness on all the above within the wider scientific community .

The new equipment purchased at the start of ReProForce was used to provide four key laboratories of IBIR (proteome analysis lab, cell culture lab, IVF / embryo transfer facility, confocal/light microscopy facility) with cutting edge technology to perform competitive research in reproduction biology and immunology on an international level (D2.1). Subsequent training courses with the new equipment (D1.1) and the recruitment of new scientists and technicians (D1.2) experienced in using the new tools / techniques allowed the successful establishment of new assays. This did attract not only scientists from Bulgaria but also from other European countries including Germany, the Netherlands and the United Kingdom to visit and collaborate with IBIR scientists.

Several of the senior and junior scientists visited the labs and scientific departments of ReProForce partners (D1.1). These visits strengthened the ties between the partner

laboratories, initiated additional collaborations between IBIR scientists and their partners, expanded the laboratory skills of IBIR-BAS's scientists and led to an increase of publications in international journals. In addition, the recruitment of new scientists from US laboratories did not only have a significant impact on the scientific output at IBIR but did also motivate other Bulgarian scientists working in top laboratories abroad to return back to Bulgaria and train IBIR-BAS's staff.

Scientists from IBIR-BAS had also the opportunity to attend regional and international conferences and present/discuss their scientific results with their colleagues from abroad. Interaction with other scientists during those conferences gave the possibility for future collaborations with other laboratories working in reproduction biology and immunology (D3.2), as well as for expanding contacts and develop projects with the private sector. In addition, IBIR scientists were also very active in networking with other research institutions, but also with industry partners ((D3.1, D3.3) within Bulgaria and abroad. By organizing several scientific meetings on the national, regional (Balkan), and international level (D.3.4), IBIR could increase its visibility and demonstrate its productivity to a broad audience leading to additional collaborations and strategic partnerships within Bulgaria and internationally.

Indirect (mid-term) impact

The RTDI strategy for IBIR-BAS 2014-2020, developed with international peer reviewers has a significant role in defining the mid-term impact and sustainability of the project.

Through diversifying its research agenda and developing also its innovation potential IBIR – BAS strives to become by the year of 2020 an important and renowned research centre in the field of human and animal reproduction in the European Research Area.

Following the priorities of its RTDI strategy IBIR – BAS will manage to concentrate its efforts on enhancing its research activities and improving the overall performance of the educational activities as well.

The implementation of the strategy will allow for strengthening the research capacity of the institute through interdisciplinary PhD programmes and the recruitment of qualified young researchers. The strong competition at both the national and European levels demands from scientists to be at the same time good researchers and good research managers. Hence, the strategy focuses on developing the complementary skills of the research staff i.e. research and innovation management, knowledge on IPR, technology transfer.

The implementation of the strategy will also help IBIR – BAS to considerably expand its partnership networks not only in Bulgaria, but in the European Union and internationally as well.

The attainment of the strategic goals will help IBIR – BAS to become a centre of excellence in its scientific domain with:

- Contemporary research agenda.
- Multidisciplinarity of research and complementarity of skills.
- High-level and high-standing researchers.
- Conducting competitive research.
- High international visibility.

- Strong networking and connectivity with the scientific and business communities.
- Dynamic exchange of qualified researchers.
- Stability of funding and diversified financial resources.

MAIN DISSEMINATION ACTIVITIES

The main objectives of project dissemination was to facilitate communications between IBIR-BAS and a wide scientific and non-scientific community aimed to better integration in ERA and to disseminate achievements of reproduction science in the society in view of increasing visibility of the research activities of IBIR-BAS and improving their responses to socio-economic needs of the country.

Targeted groups consisted of students, scientists specialised in biology, veterinary and human medicine and scientific centres in Bulgaria and abroad, but also the entire society, relevant NGOs in the field, national administration and final beneficiary of the research activities of IBIR-BAS (farmers, veterinary and human doctors, people with infertility problems and others).

Activities consisted in popularisation of IBIR-BAS and development of a creative concept on increasing IBIR visibility and its wide recognition in society. Communication support activities consisted in advertising and presentation materials, photo and video materials, brochures and invitations, media including pres releases, publications of articles in national and international magazines, templates for presentation at scientific and business meetings was realized.

Dissemination materials were distributed on the occasion of visits to national stakeholders, organizators and/or participation to various scientific and methodological events (of both national and international nature), the open doors days, visits to schools as well as contacts with business partners.
A dedicated **web-site** supported the on-line presence and visibility of ReProForce

Preparation of IBIR-BAS's website
An Institute website was established during the 1st Reporting Period of the project aiming at the popularization of the science activities of IBIR among both national and international scientific area and society. It was accompanied by a separate website for ReProForce presentation in June 2010.

Activities included:
- Overview of existing web sites of different institutions, design consultations and endorsement of a new form for renovation of the site of IBIR-BAS according to European requirements and other competitive websites.
- Preparation of of the information on administrative structure, IBIR laboratories, current

research topics, scientific achievement, published papers, information on past and future scientific events and business meetings, career opportunities, links to similar pages and organizations (presented in both English and Bulgarian).
- Addressing target groups, listed in the task objectives, as follows : scientific communities (biologists, chemists, morphologists, medical doctors, veterinary doctors), undergraduate students, MS students, PhD students, young researchers, research centers in the country and abroad; national administrative structures; general public; beneficiaries from studies done by IBIR (medical doctors, individuals with reproductive problems).
- Maintenance of the website with regularly up-dated information on IBIR state of play and activities, including all important scientific events in the field of biology and immunology of reproduction.
- Specific link to the page of ReProForce project page and the uploaded Information booklets and bulletins concerning the progress of the project.
- Preparation of a photo gallery for illustration of the scientific achievements of the Institute and its current updating.

Address of the project public website : http://reproforce.ibir.bas.bg
Internet web site of IBIR-BAS (http://ibir.bas.bg)

"Open Doors" at IBIR-BAS
3 open doors event have been organized each year to present the ReProForce activities and outcomes; expose posters and film presentation for the scientific and applied science achievements of the Institute; followed by a presentation on the scientific and applied science achievements of IBIR in the last 5 years

The Open doors days attained a great success and the Institute's achievements were exposed to more than 100 attendants every year**,** including scientists from different institutes and universities, private clinics and reproductive centers, business representatives, schools and students, journalists and interested citizens.
The events attended also a very high level participation: Advisory Board Representatives from Bulgarian Academy of Sciences, from Ministry of education and sciences and from Union of Bulgarian Scientist.

The **Open Days Events** in IBIR gave possibilities for:
- Increasing the visibility of the results from the activities of the FP7 ReProForce project.
- Increasing the visibility of the results from the research activity in IBIR in the field of biology and immunology of reproduction.
- Demonstration of the high technology base for fundamental and applied science studies.
- Attraction of new partners from the scientific and business communities in the field of biomedicine and animal breeding

Dissemination activities were conducted actively during all events organised by IBIR-BAS, but also at the occasion of participation in mobility visits, European Conferences and

Networks, contacts with industry and research performing organisations at national and European level and any other occasion with relevance to ReProForce tasks and deliverables (i.e. Extra Joint activities with the Bulgarian Union of Scientist, Bulgarian Universities, Medical and Agriculture Entities)

These activities resulted in:

Attraction and involvement of 12 students in development of Batchelor and Master Theses at the Institute Departments

1. Michaela Orlinova Dacheva - Diploma student, Sofia University – Expression of survivin in cell lines and tissues from malignant tumors. 2010.
2. Ralica Plamenova Petkova - Diploma student, Sofia University – Comparitive charakterization of human mesenchymal stem cells from adipose tissue and mouse embryonic fibroblasts for maintenance of plasticity of human embryonic stem cells. 2010
3. Sonja Dimitrova Dimitrova - Diploma student, Sofia University – Study of the expression of MMP-2 and 9 and ADAMs family members in breast carcinom samples. 2010-2011
4. Natalia Spasova - Diploma student, University Hospital "Ts. Yoanna", ISUL, Clinic of Cardiology. Quantitative determination of Lp-PLA2 (lipoprotein-associated phospholipase A2) in human plasma. 2011.
5. Bozidar Krustev, Diploma student, University Hospital "Ts. Yoanna", ISUL, Clinic of Cardiology. HSP 70 and MPO expression in cancer patients before and after therapy. 2011.
6. Elena Markova, Diploma student, University of Chemical Technology and Metallurgy, Department of Biotechnology. - A non-invasive RT-qPCR assay for oocyte competence assessment using cumulus cells specimens as a diagnostic source. 2011
7. Daniela Gruning – Diploma student, University of Mainz, Germany – Identification and localization of RUVBL1 in different tissues including testis, pancreas and brain. 2012-on
8. Vladislav Lazarov, Diploma student, University of Sofia – Expression of stress proreins in reproductive tissues. 2012
9. Kalina Belemezova – Student in Sofia University - Isolation, culturing and characterization of human endometrium stem cells. Decidualization. 2011- on
10. Tankica Timcheva – Diploma student, Student in Sofia University – Obtaining of human induced pluripotent cells. 2011 – on
11. Ahmed Abdelwanees Abdelhameed Moustafa – Diploma student, ERASMUS Programme, University of chemical technology and metallurgy - Mesenchymal stem cells effect the proliferation of prostate cancer cell line PC3. 2011
12. Svetlana Bojkova. Diploma student, University of Sofia, Biological Faculty. – Oxidative stress and antioxidant protection in preovulatory follicle. 2012.

Attraction and involvement of 10 researchers from another Research Institutions and Universities for conducting PhD thesis programs:

1. Dora Marinova, PhD student, Pulmonary Diseases Clinic, Medical University – Sofia,

PhD Thesis: Expression of low-molecular stress-proteins in small cell and non-small cell pulmonary carcinoma. 2010-2011

2. Petko Mladenov, PhD student - Agro Bio Institute, Academy of Agrcultural Sciences - Proteomic analysis of the plant Haberlea rhodopensis cultivated in normal conditions and in draught stress conditions. 2010-2011
3. Iliana Bateva Hristova, PhD student, Medical University of Sofia, Medical Faculty, Department of Biology, PhD Thesis: Investigations on the effect of low molecular stress proteins on fertilization and pregnancy in mammals. 2011-2012
4. Dimitrina Georgieva – PhD student, University of Sofia – PhD Thesis: Drosophila mutants lacking their sole fragile X mental retardation 1 (FMR1) family member (dfmr1). 2011-2012
5. Radostina Cherneva, PhD student, Medical University of Sofia, Medical Faculty, Department of Internal Medicin. PhD Thesis: Investigation on humoral immune response against alphaB-crystallin in operated-on non-small-cell lung cancer patients. 2011-2012
6. Boryana Ruseva, PhD student, Medical University - Varna, PhD Thesis: Use of selenium supplementation in treatment and prevention of cardiovascular diseases. 2011-2012
7. Neselina Kostadinova, PhD student, The Stephan Angeloff Institute of Microbiology, Bulgarian Academy of Sciences, PhD Thesis: Investigations on new temperature sensitive (cold-active) enzyme SOD, isolated from strain *Aspergillus glaucus* 363. 2012-on
8. Uliana Rainova, PhD student, Institute of Organic Chemistry, Academy of Sciences, PhD Thesis: Characteristic of hemocianine in Helix pomacia, 2012-on
9. Despina Pupaki, Assist. Prof., PhD student, Veterinary Faculti, Sofia, Foresty University. PhD Thesis: Role of endopeptidases in pathogenesis of dog breast carcinoma. The period of the realization of the studies: 2012 – on
10. Tsvetomir Ivanov. PhD student, University of Sofia, Biological Faculty, Metalloproteinasis in canine breast cancer. 2012 –on.

3. Attraction and involvement of 26 researchers from another Research Institutions and Universities for collaborative Joint Research Experiments

1 Assoc Prof. Nedka Trifonova, Medical University of Sofia, Medical Faculty, Department of Biology - Investigations on expression of low molecular stress proteins during embryogenesis. The period of the realization of the studies: 2010-on

2 Dobroslav Kyurkchiev - Laboratory of Clinical Immunology, St. I. Rilski University Hospital, Medical University Sofia - Characterization of mesenchymal stem cells from different sources. Immunoregutory effect of progesterone. The period of the realization of the studies: 2010 - on

3 Ekaterina Ivanova Ivanova-Todorova - Laboratory of Clinical Immunology, St. I. Rilski University Hospital, Medical University Sofia - Characterization of mesenchymal stem cells from different sources. Immunoregulatory effect of progesterone. The period of the realization of the studies: 2010 – on

4 Emil Sapundjiev, Assoc. Prof., Veterinary Faculti, Sofia, Foresty University- Morphological Characteristics of the Canine and Feline Stomach Mucosa. The period

of the realization of the studies: 2010 – on

5 Despina Pupaki, Assist. Prof., Veterinary Faculti, Sofia, Foresty University- Morphological Characteristics of the Canine and Feline Stomach Mucosa. The period of the realization of the studies: 2010 – on

6 Assoc Prof. Nedka Trifonova, Medical University of Sofia, Medical Faculty, Department of Biology - Expression of stress proteins in reproductive organs. The period of the realization of the studies: 2011-on

7 Assoc Prof. Dobroslav Kyurkchiev - Laboratory of Clinical Immunology, St. I. Rilski University Hospital, Medical University Sofia - Effect of Progesterone on Human Mesenchymal Stem Cells. The period of the realization of the studies: 2011 - on

8 Assoc Prof. Ekaterina Ivanova Ivanova-Todorova - Laboratory of Clinical Immunology, St. I. Rilski University Hospital, Medical University Sofia - Effect of Progesterone on Human Mesenchymal Stem Cells. The period of the realization of the studies: 2011 – on

9 Assoc Prof. Georgi Dimov, Agro Bio Institute, Academy of Agro Sciences, Influence of selected seminal plasma proteins on mitochondrial integrity of ram sperm stored at low temperature. The period of the realization of the studies: 2011 – on

10 Assoc Prof. Vasil Gersilov. Agrarian University, Plovdiv. Repriductive biotechnologies in animals. The period of the realization of the studies: 2012 – on

11 Assoc Prof. Emil Sapundjiev, Veterinary Faculti, Sofia, Foresty University- Role of endopeptidases in pathogenesis of dog breast carcinoma. The period of the realization of the studies: 2012 – on

12 Vanya Mantareva, PhD, Institute of Organic Chemistry with Centre of Phytochemistry, Bulgarian Academy of Sciences. Photodynamic efficacy of water-soluble Si(IV) and Ge(IV) phthalocyanines towards Candida albicans planktonic and biofilm cultures.The period of the realization of the studies: 2011 - on

13 Stefka DelimitrEra, Assoc. Prof. Medical University of Sodia, Medical Faculty, Department of Biohogy. The period of the realization of studies: 2011-on

14 Raliza Zhivkova. Assoc. Prof., Medical University of Sofia, Medical, Faculty, Department of Biology The period of the realization of studies: 2012 – on

15 Raliza Skrobanska Assist. Prof., University of Sofia, Biological Faculty, Department of Cytology, Histology and Embriology. The period of the realization: 2012 – on

16 Bochev Ivan -Ob/Cyn Hospital "Dr. Shterev" Isolation, culturing and charachterization of human endometrium stem cells. Decidualization. The period of realization of studies: 2011- on

17 Isura Sainova,PhD, Institute of Experimental Morphology and Antropology, Bulgarian Academy of Sciences. The period of the realization of the studies: 2011- on

18 Ginka Genova, Prof. Ujiversity of Sofia, Biological Faculty, Department of Genetics. The period of the realization of the studies: 2012 – on

19 Yosif Dimitrov, AG Center "Yosif Dimitrov „ Melatonin Receptor Type MT1 Expression in Human Ejaculated Spermatozoa". The period of the realization of the studies: 2011- on

20 Stoyno Stoynev, Assist. Prof., Institute of Molecular Biology, Characterization of DNA fluorescence dye. The period of the realization of the studies: 2012- on

21 Boris Antonov - University Hospital “Tsaritsa Yoanna” – ISUL, Effect of the implant on mesenchymal stem cells from bone marrow proliferation and osteogenic differentiation. 2012-on

22 Veselin Vassilev, Assist. Prof., Veterinary Faculty, Sofia, Foresty University. Immunochemical characterization of vipoxin in the reproductive system. The period of the realization of the studies: 2012- on

23 Assist. Prof. Tsvetanka Stefanova, The Stephan Angeloff Institute of Microbiology, Bulgarian Academy of Sciences, Department of Immunology. The role of Nitric oxide on survival and apoptosis of granulose cells. The period of the realization of the studies: 2012– on

24 Assist. Prof. Radoslav Abrashev, The Stephan Angeloff Institute of Microbiology, Bulgarian Academy of Sciences, Department of Micology. Role of oxidative stress and antioxidant defense in ovarian function. The period of the realization of the studies: 2012– on

25 Assoc Prof. Plamen Georgiev, Depatment of Obstetrics, Reproduction and Reproductive Disorders, Faculty of Veterinary Medicine, Trakia University. Immuno endocrine regulation of reproductive processes in cats and dogs. The period of the realization of the studies: 2012– on

26 Assoc Prof. Stanimir Yotov, Depatment of Obstetrics, Reproduction and Reproductive Disorders, Faculty of Veterinary Medicine,Trakia University. – Immuno endocrine regulation of reproductive processes in Bulgarian Murrah buffalo. The period of the realization of the studies: 2012– on.

4. Attraction and involvement of researchers from another Research Institutions and Universities for joint experimental research work under external Research Projects and Grants.

1 Irina Alexandrova, Ph.D. Institute of Molecular Biology, BAS - Re integration grant N982763, NATO financed. “Mitotic Exit Regulatory Networks in Human Cells and Cancer Development.” The period of the realization of the studies: The period of the realization of the studies: 2010 - 2011

2 Vanya Bogoeva, Ph.D. Institute of Molecular Biology, BAS. The work related to 5 9ears Work programme o& ICGEB, Tries4e, Italy. Project N CRP/BUL07-02: Hydrop`obic bindin' of tumour specific galactins and anti-cancer effects of their synthetic lagans on tumour cell lines. The period of the realization of the studies: 2010-2011.

5. ADDRESS OF PROJECT PUBLIC WEBSITE AND RELEVANT CONTACT DETAILS

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