Project Title:

Reinforcing IPT capacities in Genomic Medicine, Non Communicable Diseases Investigation and international cooperation

Project acronym: **GM_NCD_in_Co (GENOMEDIKA).**

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Outline

Executive Summary

The aim of the proposal is reinforcing IPT capacities in genomic medicine, with applications in Non Communicable Diseases (NCD) investigation, and in International Cooperation activities.
The project targets Institut Pasteur de Tunis, a more than centenary institution considered as a national and regional centre of excellence. To answer to the new challenges of the epidemiological transition, IPT has developed new activities related to the investigation of the genetic basis of monogenic and multifactorial diseases. Reinforcing these promising activities has a great potential to benefit EU research institutions through new international cooperation activities. The consortium includes Institut Pasteur in Paris a nonprofit research organization and 1 SME Synbea, specialized in strategy, organization and innovation consulting.
To achieve the project objectives the following specific actions were proposed: 1) Setting and implementing training modules, 2) Planning and implementing two pilot projects, 3) Establishing a communication plan, 4) Performing exchanges of visits between Tunisia and European Institutions and vice versa, for young and confirmed researchers, 5) To build IPT business plan and the associated strategy of valorization and technology transfer activity in the frame of EU/Tunisian R&D cooperation.
Results: Two trainings on international project setting in the frame of European Framework Program were ensured. These trainings included theoretical and practical sessions on H2020 project setup.
Ten national and International advanced courses and theoretical and practical workshops in various aspects of structural and functional genomics, bioinformatics and next generation sequencing technologies have been organized.
Two pilot projects have been planned. The first pilot project aimed to determine the Tunisian genetic landscape. We have also analysed genomic regions in relation with the susceptibility to breast cancer.
For the second pilot project, we evaluated NGS for disease gene identification in patients with various phenotypes. Preliminary analysis of exome data showed very promising results for some phenotypes.
Exchanges of visits between IPT, IP Paris and other EU laboratories working on relevant field were planned and implemented to improve networking capacities and acquire new competencies in genomic medicine.
Dissemination and networking activities were performed via the project website, social Media, newsletters, organization and participation to meetings and brokerage events.
A strategic development plan for IPT research results valorisation, in particular in the field of genomic medicine has been elaborated as a sum of business units on bio-banking, diagnosis, bioinformatics and training services. Two supporting units have also been proposed one for R&D and one platform for rare disease research and support to patients and their families. Recommendations are proposed at the institutional and organizational, level. These include promotion of scientific excellence, better definition of the research priorities, mutualisation of the resources, strengthening and sustaining strategic partnership and adapting the ethical, regulatory and legal framework to better conduct genomic research and international cooperation activities
In the frame of this project, we have reinforced the activities of the National Contact point and the Health Thematic Contact point in a synergistic way with other EU projects.
The project contributed to acquire and generate new knowledge this will conduct to better diagnosis of rare diseases and consequently better prevention and therapeutic

measures. The project helped also to introduce new topics in the university curricula and to improve the employability of young researchers.
The ultimate goal of this project is to integrate Tunisia, a Mediterranean Partner Country (MPC), into ERA, which is one of the priorities of EU's European Neighbourhood Policy (ENP).
The project duration is 36 months.

Project context

Major non-communicable diseases (cardiovascular diseases, cancer, chronic respiratory diseases and diabetes), represent the predominant health problem of the 21st century. Prevention and control of chronic diseases is the priority of the WHO, the United Nations and European Union Council.
Chronic diseases affect all age groups. They are the world leading cause of disabling and mortality, even in low- and middle-income countries.
Non-communicable diseases (NCDs) include chronic common multifactorial diseases caused by complex gene-environment interactions and rare genetic diseases. The Council of the European Union has adopted a series of actions and recommendations for rare diseases. Because of the high rate of consanguinity, genetic diseases are relatively frequent in Tunisia and in the region.
Since the end of the Human Genome Project (HGP) in 2003, there has been much progress in genomics. Advances in genomics generate foundational knowledge about the structure and function of the human genome and about the genetic contributions to human health and disease.
In Southern Mediterranean countries, despite advances in institutional and national health research capacities, there is a lack of competencies and a huge gap in the field of genomic medicine.
Genomedika project targets Institut Pasteur de Tunis, an independent governmental institution, under the tutorship of the Tunisian Ministry of Health. This more than centenary institution is considered as a national and regional centre of excellence in particular in the field of infectious diseases. With the increase of prevalence of NCDs, IPT has developed new activities related to the investigation of the genetic basis of monogenic and multifactorial diseases. Reinforcing these promising activities has a great potential to benefit EU research institutions through new international cooperation activities. The consortium includes Institut Pasteur, a non-profit research organization and 1 SME Synbea, specialized in strategy, organization and innovation consulting.

Project main objectives

The general objective of Genomedika is reinforcing the capacity of the Institut Pasteur de Tunis (IPT) (i) in genomic medicine, with applications in Non Communicable Diseases (NCDs) investigation, and (ii) in International Cooperation activities. This project will facilitate joint science and innovation related activities between European and Tunisian researchers in the field of NCDs. Indeed, at the national level, the objectives of the project are to increase the research activities in the field of NCDs and cooperation capacities and facilitate the participation of Tunisian researchers in relevant topics in the health.

To achieve these aims the following actions are structured within 5 work packages (WP) and are proposed as follows:

1- Strengthen IPT competencies in international cooperation and project setting in order to enhance participation of researchers to international FP projects. This will be achieved via specific training modules (WP2).

2- Reinforcing IPT scientific research and technical capacities in the field of genomic medicine and new molecular tools for the investigation of the genetic basis of NCDs. This specific objective will be achieved through:

- Setting up and implementing professional trainings via advanced courses and workshops in IPT (WP2), four advanced courses and theoretical and practical workshops in various aspects of structural and functional genomics are planned as well as on genomic research valorisation.
- Exchange of visits between IPT, IP and other EU laboratories working on relevant fields are also planned to improve competencies in genomic medicine (WP3) and networking capacities as well (WP4).
- Two pilot projects are programmed, one on a preliminary description of the genetic landscape of Tunisian population and one on disease gene identification using next generation whole exome sequencing . The pilot projects will help stimulate cooperation, identify potential bottlenecks and propose improvements (WP3).

3- To stimulate collaboration between Tunisian and EU researchers in topics of mutual interest in the field of NCD with networking and dissemination activities (WP4).

4- To build IPT business plan and the associated strategy of valorisation and technology transfer activity (WP5). The development plan will serve to increase IPT visibility, regional coverage and to improve its response to socio-economic needs, in particular, to increase job opportunities.

5- The project coordination is ensured by IPT (WP1).

The project results will be analyzed and recommendations drawn to the national authorities on how to increase participation of Tunisian researchers in ERA, to tackle common regional challenges for health systems.

The ultimate goal of this project is to integrate Tunisia, a Mediterranean Partner Country (MPC), into ERA, which is one of the priorities of EU's European Neighbourhood Policy (ENP).

Main S & T results/foregrounds

Training activities

The aim of the training activities is to strengthen IPT competencies in:
- International cooperation and project setting in order to enhance participation of researchers to international FP projects
- Genomic medicine and new molecular tools for the investigation of the genetic basis of NCDs
- R&D valorization, technology transfer and IP.

To reach this goal training modules were developed and training on project setting and professional training were realized.

1-Project set up training

The main objectives of the trainings on project setting were:
- Raise researcher's awareness about the opportunities and benefits of participation in European and international collaborative projects.
- Enable researchers to acquire or improve their expertise in setting up and management of international research and cooperation projects in the field of Health.
- Initiate work on concrete project ideas (practical part of the training).

The trainings targeted Tunisian researchers and research organizations in the domain of health and in particular researchers from Institut de Pasteur de Tunis interested to set up or integrate research or cooperation projects at the European or the international level attended this training.
The trainings were implemented in French in order to fit better the local needs as it is the working language of all the researchers.
Two trainings on project set up have been held in Institut Pasteur de Tunis:
- A first theoretical and practical course took place on 27th-28th June, 2012.
- A theoretical and practical training on H2020 project setup was organized on 15th May 2014.

In addition an infoday on H2020 was organized on 20th September 2013 with the valuable support of experts from PASRI, the Europe Aid project for the support of the National System of Research and Innovation (*Programme Appui de Soutien au Système National de Recherche et Innovation*).

The theoretical courses were attended by more than 80 participants and were organized as 20 to 30 minutes presentations by Genomedika team from IPT and Synbea. The programs included presentations on:
- Collaborative projects: objectives, potential impacts, difficulties and challenges.
- Engineering and life cycle of collaborative projects.
- Administrative and financial aspects of European project management.
- Presentation of funding opportunities for MPC (Mediterranean Partner Countries).
- Presentation of tools allowing the monitoring of funding opportunities

The theoretical courses were followed by practical sessions for a limited number of participants. The program of the first practical workshop included presentation of project ideas by the participants and working on project ideas.
Team members of Synbea ensured the first practical training.
The second practical training was ensured by Dr Frank Heemskerk from Research & Innovation Management Services bvba (RIMS) with the help of Mrs. Najet Hadhri (IPT) and included the following topics:

- Registration on the participant portal platform.
- Choice of a call in Health, demographic change and wellbeing societal challenge.
- The structure of a proposal and proposal writing exercise.

2-Professional trainings

Several professional training programs have been established and implemented during Genomedika project.
In order to strengthen the IPT scientific research and technical capacities in the field of genomic medicine, several theoretical and practical professional trainings have been programmed and implemented (WP2).

- 1st International course on "Genomic Diversity and Health of Populations" held at IPT on April 16 to 24, 2012.

The workshop has two main objectives: initiate young researchers to human genomics and different methodologies for human genome analysis and raise awareness among young researchers to the impact of genomics on research in biology and human health. More than 70 students and young researchers working in the field of human molecular genetics attended the theoretical training.
Twenty-four students working in the field of human molecular genetics and who needed to learn laboratory techniques and sequence analysis attended the technical part of the workshop.
During the practical workshop, participants learned about several molecular techniques applied in the field of human genetics including sequence analysis of mitochondrial DNA and Y chromosome STRs profiles and their application in population genetics and forensic, and on next generation sequencing.

- Theoretical and practical course on "Sequencing and genotyping: Novel technologies at the service of human genetics" held at Institut Pasteur, Paris on March 04th to 08th, 2013. This training on Next Generation Sequencing technologies and associated bioinformatic analysis targeted twelve young researchers working in the field of human molecular genetics in order to become themselves trainers in this field.

- Four hybrid courses have been organized in collaboration with the Euro-Mediterranean Centre in Bologna, Italy, with a remote transmission of a theoretical course and a practical course organised locally in IPT. The courses allowed the training of more than 30 participants from Institut Pasteur

de Tunis, the Faculty of Science of Tunis and the Faculty of Medicine of Tunis.
The main objective of the first hybrid course, held on 13th-16th May 2012, was to initiate young researchers to statistical tools applied in the field of molecular genetics and consanguinity.
The second and third hybrid courses were on "Next Generation Sequencing" were held in IPT on 17th-20th May 2013 and May 06th-10th, 2014.
In parallel with the theoretical part of the hybrid courses, the young researchers, members of the Genomedika team, who were trained in Institut Pasteur, conducted a local workshop.
The practical workshop was conducted on bioinformatics tools for NGS data analysis in particular Whole Exome Sequencing data analysis for the identification of disease causing genes.
A fourth hybrid course on "Medical Genetics" was organized in collaboration with the European School of Genetic Medicine and the European Society of Human Genetics on 11th-15th, May 2014. Twenty Tunisian students and researchers from the Institut Pasteur de Tunis and the Faculty of Medicine Tunis, working in the field of molecular genetics and interested by Medical genetics attended the course. The presented topics were grouped on sessions that covered, introduction to Human genome analysis, approaches to clinical and molecular genetics, therapy and gene regulation.
The hybrid courses were the occasion to test a new way of conducting courses via Internet and to increase the visibility of Genomedika project and Team.

- International course on "Functional Genomics" from March 31st to April 4th, 2014 place in Institut Pasteur de Tunis. Forty-eight participants attended the course. Thanks to the support of the network of Institut Pasteur, Algerian and Moroccan students and researchers have attended this course in addition to Tunisian young researchers. In addition to speakers from Institut Pasteur, speakers from other European Institutions contributed to the course e.g. International Centre for Genetic Engineering and Biotechnology (ICGEB), Italy and Medical Center for Molecular Biology, Slovenia.
Several topics were presented including omic approaches in biomarker Discovery, functional studies of splicing mechanism and therapy, Exome sequencing, nano-bodies design and potential applications in immunotherapy, neurological and neuro-sensitive disease study, gene environment and gene-gene interaction.
In parallel with the theoretical course, members of the Genomedika and H3ABionet team conducted a local workshop on bioinformatics applied to NGS data analysis.

- Course on "Introduction to biostatistics and phylogeny" from April 14th to 18th, 2014 was organized in Institut Pasteur de Tunis by young researchers belonging to Genomedika team that have been trained as trainers. About 30 participants from LGBMO and two collaborators from Algeria attended the

course, which took place in Institut Pasteur de Tunis from April 14th to 18th, 2014. This practical course was not programmed initially, and was conducted for adequate implementation of the pilot projects, as there was a crucial need for acquiring competencies in biostatistics applied to population genetics and genomic medicine. The program of the workshop included an introduction to Linux, descriptive and analytical biostatistics, genotyping data analysis using «R» and mitochondrial sequence analysis and phylogeny.
This was again the occasion for young researchers trained in the frame of Genomedika to transmit their knowledge and communicate on the project and its results.

- Practical training on research activities valorization was held on 13-14 May 2014, in IPT. This training was held as a coaching to Genomedika team in order to work on business units with the ultimate goal to prepare a business plan for genomic medicine activities in Institut Pasteur de Tunis.
The main objective of the practical training on research valorization was to help young researchers to improve their skills and acquire soft skills in order to create and manage a small enterprise. In addition, the Genomedika team was training on writing a project of a business unit for the activities to be included in the institutional business plan. M. Jacques LOUIS (Synbea) ensured the training.

- A symposium on “Consanguinity and hereditary rare diseases: Challenges and perspectives in post-genomics” was held in Institut Pasteur de Tunis from September 22nd-27th 2014. The training was organized with the support of the French Foundation for Rare Diseases and The World Academy of Science FFRD/TWAS.
The main objective of the symposium was to initiate young researchers from the region to the use of high throughput data to investigate several aspects related to consanguinity.
A total of 111 researchers from 8 countries and 12 different nationalities participated to the symposium. Speakers from Institut Pasteur (Beneficiary 2) as well as from other distinguished institutions such as Institut de la Vision, International Centre of Genetic Engineering and Biotechnology (ICGEB) and University of Bologna contributed to the symposium.
Theoretical and practical sessions focused on the following themes: new tools and strategies for molecular investigation of genetic diseases with examples from infertility, neurological and neuro-sensorial diseases and consanguinity and health impact. After the theoretical course, Genomedika team has organized a workshop on biostatistics and bioinformatics. The trainers used genotyping and exome data generated by the pilot projects conducted in the frame of Genomedika.
It was an occasion to disseminate on Genomedika activities and to increase the networking of Genomedika team among the community working on rare diseases.

In conclusion, all the training activities planned in Genomedika were successfully organized and positively evaluated by the attendees.

Pilot projects

Two pilot projects have been pre-identified in the frame of Genomedika: one on the preliminary investigation of the genetic landscape of Tunisian population and one on the use of Next Generation Sequencing (NGS) for disease gene identification. A detailed planning has been established during the first period of the project and adjusted according to the challenges identified during their implementation.
The pilot projects have been submitted to the institutional review board for ethical approval. The studies were conducted according the Helsinki declaration. All study subject, or their guardians for minors, gave their written informed consent.
Several challenges have been identified during the first phase of the implementation of pilot projects:
1- Absence of a structured bio-bank and associated clinical and biological database.
2- Lack of adequate platform for high throughput genotyping and sequencing and high cost of genotyping.
3- Lack of adequate Information Technologies (IT) environment (appropriate servers for data storage, analysis and management, skilled personal in particular IT Manager, etc.).

We tried to find short, middle and long-term solutions for each challenge according to the local environment and to the potential offered by international cooperation activities.

- For the first challenge, there is a need of institutional commitment. It is currently planned to set up an institutional bio-bank in IPT and a national bio-bank at the biotechnology park of Sidi- Thabet.

- For the second challenge, we have interacted with various companies Illumina, Agilent, Life Technologies and Affymetrix, among others. The process of purchase and setting up of new platforms is particularly long and difficult. In addition, genotyping technologies, despite the reduction of the cost, are still very expensive at the population level and needs access to adequate platform. Consequently, genotyping of 500 individual at high coverage is not feasible currently.
Several groups have published recently on population genomics in North Africa. These groups allow access to genotyping data for new analysis to test novel hypothesis. Consequently, combination of generating our own data on a relatively small subset of individuals to data collected from the literature and from various databases is the solution to circumvent the aforementioned challenges.
In addition, in collaboration with Prof Lotfi Chouchane, from Weil Cornell Institute in Qatar, we have generated data on 100 individuals from urban regions of Tunis and from some parents handling founder mutations. These

data of genotyping have been generated using an Affychip SNP6.0 (over 600,000 SNPs and 600,000 CNV). These data have not been analysed from the population genetic point of view and not compared to other populations. We have agreed to re-analyse the data by selecting markers of pharmacogenetic relevance or corresponding to natural selection markers. The data mining parts are, particularly, time consuming and necessitate acquiring new competencies in biostatistics and bioinformatics.
In addition to these short-term solutions to conduct the project on time and according to the planned activities, discussions with the Director General allowed to identify the institutional middle and long-term vision for the set up of technological platforms.

- For the third challenge, we have started collaboration with the Group of Bioinformatics and Mathematical Modelling in IPT. We are involved with this group in an institutional international project H3Bionet that aims to reinforcing capacities of African Researchers in genomic data analysis.
In parallel to these key elements, and in addition to nascent collaborative projects, new opportunities have been identified, in particular collaboration with Prof Christine Petit from Institut de la Vision, Collège de France and Institut Pasteur, Paris, on the identification of genes involved in neuro-sensorial diseases and Prof Odile Tanguy from the Department of Pediatric Neurology in Hôpital Robert Debré in Paris on the identification of genes involved in Leucodystrophies.

During the second phase of the project, we pursued the two pilot projects and advanced on data analysis.
For the first pilot project, meta-analyses have been performed in order to determine the Tunisian genetic landscape based on maternal and paternal lineages, as well as bi-parental molecular markers. Independently from their type, genetic markers indicated high genetic affinities among North African populations with some outliers. Several analyses are still needed to exploit the data generated on Tunisian population. These analyses are going to be performed in collaboration with the team of Prof Marco Seri at University of Bologna in the frame of a short site visit made by Majdi Nagara.
For genes involved in response to drugs, the information content of the used chip was relatively limited. This was also the case for natural selection markers and for paternal and maternal lineages that were poorly informative compared to STR or to HVS1 and 2 mitochondrial sequences. For these reasons, thanks to the new collaborations set with our European partners, we found alternatives to circumvent this difficulty. Indeed, in the frame of exchanges of visits, new collaborations have been set, in particular with University of Montpellier, the IDIBAPS (Institute of Biomedical Investigations in Barcelona, Spain) and with the University of Bologna, these would allow to use adequate platforms for genotyping and NGS sequencing for whole mitochondrial genome sequencing. This would also allow us to generate new data and to improve our competencies in the large-scale genome data analysis.

Part of the results of the first period of pilot projects is now published:

Kefi R, Hsouna S, Ben Halim N, Lasram K, Romdhane L, Messai H, Abdelhak S. Phylogeny and genetic structure of Tunisians and their position within Mediterranean populations. Mitochondrial DNA. 2014 Feb 3. [Epub ahead of print] PubMed PMID: 24491098.
Hammami W, Kilani O, Ben Khelifa M, Ayed W, Abdelhak S, Bouzouita A, Zhioua F, Amouri A. Prevalence of Y chromosome microdeletions in infertile Tunisian men. Ann Biol Clin 2014; 72(3): 331-6 doi:10.1684/abc.2014.0962

For the second pilot project, we evaluated NGS for disease gene identification in patients with various phenotypes. Preliminary analyses of exome data showed very promising results for some phenotypes. Indeed, we identified new mutations responsible for deafness, cardiomyopathies and Xeroderma pigmentosum in Tunisian population.
Besides the families investigated in collaboration with Prof McElreavey, other families have been studied in collaboration with Prof Christine Petit. This work has been performed thanks to the exchanges of visits that allowed completing the training of a PhD student Zied Riahi.
This work was published in Plos one under the following reference:
Zied Riahi, Crystel Bonnet, Rim Zainine, Malek Louha, Yosra Bouyacoub, Nadia Laroussi , Mariem Chargui , Rym Kefi, Laurence Jonard, Imen Dorboz, Jean-Pierre Hardelin, Sihem Belhaj Salah , Jacqueline Levilliers, Dominique Weil, Kenneth McElreavey, Odile Tanguy Boespflug, Ghazi Besbes, Sonia Abdelhak, Christine Petit. **Whole exome sequencing identifies new causative mutations in Tunisian families with non-syndromic deafness**. *Plos One.* 2014 Jun; 9(6): e99797.
A second open access publication has been recently accepted:
Zied Riahi, Crystel Bonnet, Rim Zainine, Saida Lahbib, Yosra Bouyacoub, Rym Bechraoui, Jihène Marrakchi, Jean-Pierre Hardelin, Malek Louha, Leila Largueche, Salim Ben Yahia, Moncef Khairallah, Leila Elmatri, Ghazi Besbes, Sonia Abdelhak, Christine Petit. **Whole exome sequencing identifies mutations in Usher syndrome genes in profoundly deaf Tunisian patients**. (Submitted to Plos One, October 2014).
Zied Riahi the PhD student who conducted this work, defended his thesis in August 2014. This was the first PhD in the laboratory, which included results of investigations using next generation sequencing technologies for disease gene identification.
Two other PhD thesis have included NGS results of pilot projects in their dissertation, one by Majdi Nagara on renal disease investigation and one by Yosra Bouyacoub on ocular genetic disease investigation. Currently, six PhD thesis are being conducted and will integrate NGS data analysis in their projects.

Following the success of this collaborative study, that was possible thanks to the pilot project and to the exchanges of visits, this collaboration is going to be pursued and two young researchers from Genomedika team, Zied Riahi and Yosra Bouyacoub are now going to join the laboratory of Prof Christine Petit for a postdoc.

General conclusion on pilot projects, recommendations and future directions

In conclusion, one of the most important achievements in the pilot projects is the introduction of NGS use in research and diagnosis activities of IPT. Indeed, the pilot projects allowed us to enter into the second genomic era.
As the Tunisian population has not been sequenced and North African population either, except Mozabite, gaining new expertise in a group of populations not investigated before opened new opportunities for international collaborations.
We established a database with a collection of data generated on Tunisian population either by Genomedika team or by others.
These data still need further analysis and will be completed with new data generated in the frame of new collaborations which has been set during this project: e.g.:
- data on natural selection genomic markers and on mitochondrial DNA whole sequence with the team of Donata Luiselli in the University of Bologna
- proteomic and transcriptomic data generated with Radovan Komel from University of Ljubljana
- exome data generated with Odile Boespflug Tanguy from INSERM
- exome data generated with Christine Petit from Institut de la vision Paris
- exome data generated with Anu Bashamboo in the frame of an ACIP project
- exome data generated with Thomas Bourgeron in the frame of ACIP project on Mediterranean Autism.
- exome data to be generated in the frame of the Project RARE-MED “Setting up a Mediterranean Research Network for the study of rare diseases in the Mediterranean area” Coordinated by Pr Nicolas Lévy, recently accepted following the call for proposal A*midex Aix Marseille call “Méditerranée”.
With the ongoing and future projects, we intend to extend the studied populations to other Mediterranean countries and thus increase the impact of our project.
The pilot projects combined to the training activities attracted young scientists from the region for training activities.
In addition, we are shifting from genetics to epigenetics with new projects set with IDIBAPS and we are also shifting from structural genomics to functional genomics and to system biology.
A preliminary impact assessment in terms of competencies and skills acquired, shows the following: in the beginning of the project, no one of the team members had expertise about genome wide or exome data analysis. At the end of the project not only Genomedika team are now able to analyse these data but more than 50 young researchers from the region are able now to do so. During University Year 2014-2015, we have introduced the teaching of genome data analysis into 3 master programs in Tunisian universities. We have also raised awareness in the whole region about the genomic gap that needs to be tackled.

In conclusion, WP3 implementation was indeed challenging but very enriching not only for Genomedika team but also for several young researchers from the region. We anticipated that the proposed pilot projects will help to build IPT capacities and develop competencies in genomic research and would

create the ground for setting future international collaborative projects. The acquired new expertise in genome analysis with new generation technologies allowed not only to the IPT but also to other institutions in the region to “jump” in the post-genomic era.

Dissemination activities

In order to have a clear vision of our dissemination activities and its goals, a dissemination plan was established, thus mapping the general course of action that should be undertaken by all partners.
The first step of this plan is to identify the different objectives and targeted groups (research community, innovation community, Institutional community, financial community…) of our communication. The second step is to define our different communication channels and tools (cooperation with other EU projects, website, web media, press relations, events, brochure, newsletter…) in accordance with their efficiency and impact on the target public, and our objectives. The third step of the dissemination plan is to describe our actions according to each targeted group, how we are going to make them (implementation plan), and how to evaluate them, to see if our objectives are reached and if they have to be reevaluated.
A project website (www.genomedika.org) has been created and social Medias (Facebook, LinkedIn etc.) were also used thus giving to the project a continuous visibility on the web, and a tool to receive feedbacks and suggestions on the project activities.
The website reputation-vip who measures the e-reputation of institutions, names, brands… gave to Genomedika the score of 100. That is the sign of a very good visibility and positive e-reputation.
The results of Genomedika have been presented during the IPT Scientific board annual meeting (may 2014), representatives of the Ministry of Health were very impressed by the project results and by its potential long term national impact, as the Minister of Health has put the fight against chronic and genetic diseases as a priority in the next years.
In November 2014, a conference on « Consanguinity and hereditary rare diseases: Current situation in the region and perspective » has been presented by the members of the project during the meeting of the Regional Network of Institut Pasteur (MATI network, Maroc, Algérie, Tunisie, Iran).
In this conference, we presented the project results to policy makers and scientists of 6 countries (Morocco, Algeria, Tunisia, Iran, France and Greece).
In December 15th, 2014, during the first National Days on Research and Innovation, the project was also presented as an example of success story of FP7 projects to various stakeholders.

Genomedika team in Tunis has performed 46 exchanges of visits, training and participation to international meetings.
During these events, we shared contacts and expertise and we were able to cross-fertilize networks, ideas and projects and create a positive dynamic within Genomedika project.

Furthermore, we have organized eleven exchanges of visits of senior European scientists, from Institutions other than those who are part of Genomedika beneficiaries.
We tried to capitalize on existing networks and on local and regional initiatives, such as FP7 projects Mediterranean Innovation and Research coordination Action MIRA, he Mediterranean Science, Policy, Research & Innovation Gateway MEDSPRING, the Health NCP network, the Fit for Health network, European Tunisian Cooperation ETC and Future European Tunisian Research and Innovation Cooperation FETRIC.
We also developed new collaborations on local and regional initiatives.
The exchanges of visits were achieved successfully and allowed to:
- Increase the institutional visibility in the field of medical genomics and non-communicable diseases,
- Acquire new competencies and expertise not only scientific and technical but also other skills like communication and managerial,
- Benchmark with other institutions at the regional and international level.
- Initiate the set up of new collaborative projects,
- Ensure dissemination and networking activities with all stakeholders in RDI and international cooperation activities,

IPT business plan and deployment strategy

The aim of this WP is to build IPT business plan and the associated strategy of valorisation and technology transfer activity in the frame of EU/Tunisian R&D cooperation
In the frame of Genomedika activities a business plan and associated deployment strategy have been proposed.
The principal axes of the BP are the following:
Axis 1: Structuring and developing activities within the IPT
Axis 2 - Increasing the flow of collaborative R & D and innovation projects
Axis 3: Enabling entrepreneurship projects: start up activities or existing SMEs
The business plan has been elaborated in 4 steps:
STEP 1: Model and analyse the Genetics and Genomics Ecosystem (value chain)
STEP 2: Identify and characterize activities and projects
STEP 3: Focus on projects and activities carried out:
STEP 4: Attract interest, support and assistance of partners:

- Promotion of projects & activities toward financial, institutional, and other economic stakeholders
- Supporting Project Teams in promoting and fund raising activities

The business plan has been structured as the sum of four business units and two supporting activities:

- Business unit: Bio-informatics
- Business unit: Diagnosis
- Business unit: Bio-banking
- Business unit: Training
- Supporting activities: Research and development
- Supporting activities: Rare disease Alliance

In parallel with the business plan pilot fund raising instructions have been set in order to allow IPT and GENOMEDIKA teams to optimize fund searching for the various activities described in the business plan including services, research and social / societal component.
Funding sources are either public or private and can take very different forms (donation, grant agreements, contracts, investment funds, ...).
Thanks to the coaching of Genomedika team, and to the training on project set up, several projects have been elaborated and submitted to national, regional and international projects. Over 14 mobidoc projects have been submitted and 13 projects have been accepted for funding by the Europe-Aid Programme of Support to National Research and Innovation System (PASRI). Three projects have been accepted for funding by the Network of Institut Pasteur (Action Concertée inter-pasteurienne) and two H2020 projects have been submitted.
Genomedika team entered in a competition launched by the World Academy of Science and the French Foundation for Rare diseases in order to organize an international symposium on consanguinity and rare diseases and won (only one project selected among 19).
Genomedika team contributed also to the setting up of a project of Clinical Investigation Centre (CIC) on neurological and neuro-cognitive diseases in a call for proposals launched jointly by the Ministry of Higher Education and the Ministry of Health in August 2014. The project has been evaluated positively and its implementation is going to start in March 2015.

Final recommendations

In order to elaborate the final recommendations for IPT strategic plan for the valorisation of its activities in the sector of genetics, genomics and associated services, the main results of Genomedika project including the business units and supporting activities have been presented and discussed with experts from different institutions and communities. The discussions were conducted either in face-to-face meetings or during national and international events.
During the test and validation process of the business plan, some challenges have been identified. At the level of Institut Pasteur de Tunis (IPT), there is a loose definition of the research priorities, a fragmentation of existing resources and difficulties of distinguishing between research and diagnosis activities.
At the level of the external level (policies and governing bodies), there is an absence of adequate regulatory and legal framework in several aspects of the Research and Innovation value chain.
Recommendations are proposed at the level of Institut Pasteur de Tunis (IPT) or at the external institutional, national organizational, level.

Recommendations at the level of IPT:

- **R1: Promotion of scientific excellence**

Scientific excellence is the pillar for R&I activities. This should be maintained and promoted via life long learning programmes in several fields including omics, bioinformatics, etc. towards 4P medicine.

Scientific excellence could be strengthened via mobility programs (exchanges of visits and training activities) for all the actors of R&I.

- R2: Better definition of the research priorities

Currently the research activities in IPT on genetics, genomics cover several thematics including rare diseases, Neuro-sensoriel, Neuro-developmental and neuro-cognitive diseases, Onco-genetics, Diabetes and its complications, Anthropology, Forensic.

Strategic choices of the thematic on which to focus should be made according to the scientific excellence, integration into networks of excellence and availability of resources.

- R3: Separation between diagnosis and research activities

Some of the current tests performed for research purpose, should be shifted to the IPT portfolio of services. Introduction of a quality control program is in progress but needs additional human resources. Shifting some tests into routine services needs also setting the adequate environment in order to ensure timely delivery of results.

- R4: Mutualisation of the resources and creating shared infrastructure and services

This recommendation has been already discussed since several years in the Scientific Advisory board.

Joining European networks in the frame of H2020 infrastructure program or existing European networks would help accelerate this process.

- R5: Strengthen and sustain strategic partnership:

Strategic partnerships identified during Genomedika projects should be consolidated to ensure the success of the identified business units.

Recommendations at external institutional level:

- R6: Define, adapt and reinforce the ethical, regulatory and legal framework:

Genomics and genetic investigation and analysis, raise several Ethical, Legal, and Social issues (ELSI).

This is also true for the establishment of bio-banks and associated registries. The legal framework for preclinical and clinical research and for protecting personal data as well as defining the conditions for access and sharing of those data is currently being set in Tunisia.

Specific projects and programs for capacity building on ELSIs related to genomics should be set, in particular in the frame of the European Program H2020.

The legal framework related to the recruitments in the public sector and the status of all the actors of R&I should be also better defined. Indeed, some jobs and carrier profiles are still not recognized (e.g. Communication Officer, Research Engineers etc.).

Despite the existence of some encouragements for the creation of spinoffs, public private partnership regulatory framework in Tunisia needs further improvements.

In conclusion, despite the challenges that have been identified, the Genomedika project was highly structuring on the genetics and genomics activities in Institut Pasteur de Tunis and associated valorisation. With the experience acquired by the IPT Genomedika team, the relative recent improvement of the general climate of the country and the strong will at the level of the Ministry of Health of creating the adequate environment for preclinical and clinical R&I activities, Genomedika business units could be deployed successfully.

Potential impact

The potential impact of the project results is the following:

- Contribution to R&D capacity building and management in Tunisia.

The project has contributed to build capacities in specific areas of health research and internalizing advances in technology as well as in international collaborative projects management.
The project will help better identification of research priorities for Tunisia and at a wider extent to the Mediterranean and MENA regions (Middle East and North Africa) in the field of health.

- Enhanced participation of Tunisian researchers in the H2020 Program.

The specific training in EU project setting, interactions between EU/Tunisian scientists and dissemination and networking activities achieved during this project will enhance participation of Tunisian researchers to H2020, in particular the societal challenge health, demographic change and wellbeing.

- Increased visibility and scope (regional coverage, subjects, and activities) of IPT with increased linkage with economic and social environment.

The networking and dissemination activities have increased the visibility of IPT and raised awareness in the region about the importance of medical genomics and associated economic activities.
Thanks to the strong network that has been built at the regional level with Mauritania, Morocco, Algeria and Libya (for the later, this depends strongly on further evolution of the situation in the country), together with various European partners, it is expected that the project would have a wider regional impact.

The results of the pilot projects will help to increase the use of next generation sequencing and genotyping techniques in health research and to improve the

health of populations and decrease the burden of non-communicable diseases.

It is expected that thanks to the project new services related to genomic medicine, bioinformatics and omics in general will be developed in Tunisia and in the region.

- Networking with other research centres in Member States or Associated Countries (mobilising the human and material resources existing in a given field, disseminating scientific information as well as the results of research, facilitating communication between the centres having similar scientific interest).

Several new collaborations have been set during Genomedika project implementation. This will improve cooperation between Europe and Tunisia. A measurable increase in the effective collaborations is expected, as well as improvement in the mutual understanding of the respective research systems in Europe and in Tunisia.

- Increased job opportunities that encourage gender equality in the country, in particular for young scientists (measures to avoid 'brain drain' phenomena: better career opportunities, better work conditions, access to research infrastructures).

Young researchers have acquired new competencies, improved their curricula, consequently, they have better and new career opportunities.
Synergies between the various work packages in particular training activities, pilot projects and dissemination activities act as multipliers to increase employability.
The pilot projects raised awareness about the importance of next generation genomic tools for the investigation of the genetic basis of diseases. Introducing these tools in health research will benefit population health and economies. Concretely medium term expectations are the creation of SMEs proposing various services related to genomics and bioinformatics.

- Spreading excellence, exploiting results, disseminating knowledge:

Each member of Genomedika has contributed to the dissemination of the project, at each event (workshop, meeting, conference…), in the context of the project or in any another context, provided a good occasion to communicate on the project, particularly to cover all stakeholders in the research and innovation value chain.
For the majority of these dissemination activities, communication material were given or presented (brochure, powerpoint presentations, posters…).

In addition to these dissemination activities, regular communication on the project and its thematic (genomic medicine and non communicable diseases) was provided through the project website www.genomedika.org, the Institut Pasteur de Tunis website and the project social Medias, on facebook (More than 300 followers) and linkedin (More than 50 members), which gave to the project a continuous visibility on the web, and a tool to receive feedbacks and suggestions on the project activities.

The project consortium decided to be more present on the web by creating other social acoounts (Twitter, pinterest, slideshare…). It gives to the project a bigger and more positive visibility. The more the project communicate by himself on the web, the more the message belongs to the project, and is positive and true.

The website reputation-vip who measures the e-reputation of institutions, names, brands… gave to Genomedika the score of 100. That is the sign of a very good visibility and positive e-reputation.

We also decided in the second phase of the project to follow the recommendations of the European Commission in terms of communication for H2020 projects: ” new emphasis on open access to research publications and experiments with open access to other results”. That is why we created an account on the principal platform of curation, scoop-it. Curation means “gathering, organizing and online presentation of content related to a particular theme or topic ». In case of our project, the NCD and the activities of the project. More than 1300 visits on the Genomedika scoop-it page have been noted. In addition to curation, our politic of open access, which is in line with the Institut Pasteur de Tunis institutional communication strategy, is to let people read, share and use our documents. Slideshare is a good tool for this purpose, and the many visits we noted on our documents on slideshare is the sign that there is a interest on the activities of project and on european projects in the health domain. The documents we put on slideshare are quite often read. Some of them have been read more than a 1,000 times.

The multiple training activities and the project events were the occasion to share the knowledge acquired during the project at the national and regional level. In addition, the preliminary results of the pilot projects have been published in international scientific journals.

The project website: www.genomedika.org

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