Project Deliverable

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Abstract:

The present socio-economic analyse measures economic outcomes referring to the technological market of **Human Genetics and Genomics**. The analyse covers European and Middle East Asian regions that develop referenced technologies.

It also describes societal trends and indicators impacting on the further development of such technologies.

The report contributes to developing next project activities namely twinning activities and reinforcement of USJ international cooperation capacities.

It consists in 5 sections:
1. Human Genetics and genomics. Definition. Application and technological challenges
2. Research and development landscape
3. Industrial landscape
4.Socio-economic impacts
5.Conclusion and recommendations

Table of Content

1. Introduction

1.1. Outline

The socio-economic analysis (SEA) includes research and reports on the socio-economic effects of technological domain **"Health-human genetics and genomics[1]"**, with particular emphasis on analyses from the perspective of research and development potential.

This analysis is one of the operational tasks of the Work package 2 of the LEB'IN project. Accordingly to the project contract,

[Socio-economic analysis of relevant Lebanon, Mediterranean and European needs will be done. Collection of data will take into account both the geographical and the R&D and SME/Industries' dimension. The necessary information will be acquired by the analysis of relevant documents, including strategic research agenda of main ETP, oriented in HEALTH-research; and by 10+ face-to-face or phone interviews with experts in the HEALTH-field, both in Lebanon, in Mediterranean and in Europe. A small scale round table may be organised.
The obtained results of the study will allow the detection of main priority sectors for USJ R&D and training in the field of HEALTH. Recommendations will be provided at the end of the Socio-economic analysis exercise]

In respect with the contract, the methodological approach is based on the bibliographical analysis of the relevant documentation (list provided in the chapter 1.4 *Data sources*) and interviews curried out with the experts in the Health-field within the task 2.1 SWOT analysis of the USJ (the list of experts interviewed is provided in the chapter 1.4).

The analysis has been lead by inno with assistance of the Institute Saint-Joseph, the project coordinator and University of Marseille.

1.2. Objectives

The present SEA is a tool for assessing the potential of human genome research and development. Its key objective is to clear up state-of-the-art of the research & development in the field of **human genome technologies** and to highlight their importance for the economy and society.

Additional objective is to assess the overall balance of technical challenges impact on society and demands of society on scientific and technical challenges.

The operational objectives are as following:

- **Provide current state-of-the art :**
    - R&D landscape,

[1] *Hereinafter referred to as "reference field"*

- Market landscape;

- **Identify technological trends**;
- **Assess major impacts** of technological development in human genome:
  - Impact on public health,
  - Impact on basic research in other domains
  - Impact on economy and society (growth, employment, life conditions).

Important note
Given the breadth of the referenced field that comprises numerous aspects **the report does not have the ambition to be complete or to cover all aspects referred to the field of the human genome**. The idea is to identify most important trends in the field and to give them as examples for presenting human genome technologies to a wider public (as a report is public) to provoke a discussion which addresses societal and economic expectations and concerns and to help the project teams with a formulation of main priorities for Saint Joseph University's R&D directions.

1.3. Geographical focus

- **Study Sub-Area 1 - Europe;**
- **Study Sub-Area 2 - MEDA (Morocco, Tunisia, Egypt) ;**
- **Study Sub-Area 3 - Middle East Asia including Lebanon.**

1.4. Data sources

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List of internet data sources employed in the report:

- World Health Organization. The global burden of disease: 2004 update. http://www.who.int/healthinfo/global_burden_disease/2004_report_update/en/
- index.html

- World Health Organization. The Grand Challenges in Genomics for Public Health in Developing Countries: http://www.who.int/rpc/grand_challenges.pdf

- OMIM (Online Mendelian Inheritance in Man): http://omim.org/

- ORPHANET: http://www.orpha.net/national/LB-EN/index/homepage/

- GOLDEN HELIX: http://server.goldenhelix.org/lebanese-old/

- REVUE MEDITERRANEENNE DE GENETIQUE HUMAINE: http://www.rmgh.org/

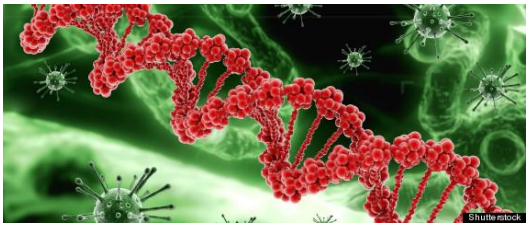
Interviews with experts in the field for the purpose of the WP2 tasks

Category	Interviewed experts
Internal USJ	* Prof Kamal **Kallab**, Neurologist – Medical faculty - USJ * Prof. Georges **Aoun**, Vice-president of research - USJ * Prof. Jean **Tamraz**, Professor of Neurosciences - PTS Pôle Technologie Santé USJ * Dr Michele **Kosremelli Asmar**, searcher at the Institute of Health Management and Social Protection - USJ * Dr Elie **Rizkallah**, Medical director of the Hôtel-Dieu de France

	hospital (attached to USJ)
Lebanon and MEDA	* Prof Tobie **Zakhia**, President of the Administrative Council of the Social Security in Lebanon * Dr Walid **Khoury**, Director of the Institut de gestion de la santé et de la protection sociale, Lebanon * Prof Vanda **Barakett**, Former director of the central laboratory of the Health Ministry and Director of laboratories at Hôtel-Dieu de France hospital, Lebanon * Dr Ali **Bazarbachi**, Professor of Medicine/Hematology and Oncology and Associate Dean for Basic Medical Research - American University of Beyrouth, Lebanon * Dr Fawaz **Fawaz**, Scientific advisor - CNRS Lebanon * Dr Walid **Abou Khalil**, Director - CCIAB Beirut & Mount Lebanon * May **Ghorayeb**, Algorithm pharma company, Lebanon * Nabila **Haddad**, Health project manager - Agence française de développement, Lebanon * Rami **Jisr**, General Manager at Audi Saradar Investment Bank, Lebanon * Yasmine **Laveille**, Chargé de mission for the university cooperation – French Embassy, Lebanon * Gilles **Thuaudet**, Attaché de coopération culturelle et technique scientifique – French Embassy, Lebanon * Roger E. **Khayat**, Economic advisor to the President - CCI, Lebanon * Prof Salim **Adib**, Professor of Epidemiology and Public Health, Egypt * Prof Hamadi **Ayadi**, General Director of the Biotech center of Sfax, Tunisia
EU and USA	* Prof Gerard **Lefranc**, Professor emeritus in immunology – University of Montpellier, France * Prof Andoni **Urtizberea**, Geneticist - MPR Hôpital Marin, France * Dr Cristina **Sobacci**, ITB CNR, Italy * Prof Raif **Geha**, James L. Gamble Professor of Pediatrics, Chief, Division of Allergy/Immunology/Rheumatology/Dermatology, Children's Hospital of Harvard Medical School, USA

2. Human Genetics and Genomics. Definition. Application and Technological challenges

2.1. Definition of the research domain "Human Genetics and Genomics"



Human Genomics refer to all studies related to a better understanding and knowledge of the Human Genome. It is defined as the systematic study on a whole genome scale for the identification of genetic contributions to human conditions The **Human Genome** is the complete set of deoxyribonucleic acid (DNA), packed in 23 pairs of chromosomes and in mitochondrial DNA, and containing all the genetic information from one individual. The human genome contains approximately 3 billion of DNA base pairs, of which, about 1% constitute the 30 000 genes, which encode proteins, essential components of our cells.

Human Genetics is the science, which studies the transmission of genes in individuals and mostly how variations in genes, called mutations, can lead to a disease, called hereditary disease. Genetic research is designed to advance our understanding of the human genome and the role of individual genes or groups of genes in human health.

LEB-IN project is more precisely dedicated to **developing strategies for better diagnosis and treatment of rare autosomal recessive hereditary diseases, based on the results from gene identification studies in large consanguineous families at the post genome era, i.e. by using High Throughput Screening strategies such as massive parallel sequencing**.

2.2. Application and technological challenges

In its latest report, World Health Organization (WHO) statistics indicate that the global burden of disease is shifting from infectious to non-communicable diseases (http://www.who.int/healthinfo/global_burden_disease/2004_report_update/en/index.html), many of which are genetically influenced and thus, enter our field of research: "Human Genomics and Genetics". The responsible genes can be identified using population resources and tools now at hand. However, the statistics from OMIM, the "Online Mendelian Inheritance in Men" database (http://omim.org/), a well-known online catalogue of Human genes and genetic disorders, widely used by physicians and geneticists, clearly show that there is still a huge work in the field of gene identification. Indeed, of the mean 30,000 genes composing the human genome, less than 10% (2966 genes, 22 February 2013 update) are known to be responsible for a specific phenotype (i.e., in our case, genes which have (a) mutation(s) causing a disease). These genes cause less than 5,000 (4,847) phenotypes: here, phenotypes refer to single-gene mendelian disorders, traits, some

susceptibilities to complex disease and some somatic cell genetic disease. The identification of disease-causing genes is usually based on the study of index cases and kindreds, through the segregation of genetic markers and sequencing of candidate genes by traditional Sanger sequencing methods. Although very reliable, these methods are costly and time-consuming.

In the last few years, the rise of Next-Generation Sequencing technologies (NGS), also known as massively parallel sequencing, has considerably sped up the researches in our field, allowing faster identification of disease-causing variants. In particular, Exome Sequencing is a technique used to selectively capture and sequence the coding regions of all annotated protein-coding genes. Coupled with NGS, it enables the analysis of functional regions of the human genome with unprecedented efficiency (Goh & Choi, 2012). Since its first reported application (Choi *et al.*, 2009, Ng *et al.*, 2009), Exome Sequencing has emerged as a powerful and popular tool for researchers elucidating genetic variants underlying human diseases, despite certain limitations. Indeed, there are still a lot of problems and issues in the analysis, sorting and interpretation of the thousands of genomic variants generated by Exome Sequencing, and NGS more generally. Ethical issues must not be forgotten, as NGS and Exome sequencing allow the emergence of a so-called "personalized medicine", with many possible misuses. Despite all these limitations, NGS has emerged as a revolutionary genomic tool, and like other new genomic technologies, NGS techniques will provide radical insights and change the landscape of Human Genomics.

Moreover, it is very important to notice that most of the successful Exome Sequencing studies published, to date, were realized in patient from consanguineous families such the ones that we study in this project. Indeed, the Southern and Eastern rims of the Mediterranean basin have among the highest levels of consanguinity in the world (Ozcelik *et al.*, 2010). In Lebanon, consanguinity rate is estimated at about 25% in Lebanon, but recent confident data are lacking (Khlat, 1988). Consanguinity has a direct impact on the frequency of recessive diseases. As a direct consequence of consanguinity, the prevalence at birth of severe congenital genetic disorders in the eastern Mediterranean is among the highest in the world: >65 affected children per 1,000 live births. By contrast, consanguinity on the northern rim of the Mediterranean basin is generally low. Coupled with the large family size, that is characteristic of the southern rim of the Mediterranean and the Middle East, this statistic results in increased frequency of recessive disease, creating human and medical challenges, but also the scientific opportunities to address them. Diseases inherited in a recessive pattern have traditionally been highly amenable to genetic analysis, due to the fact that homozygous variants are easily detectable. Previously, if a large family with many affected members was available for pedigree analysis, we were performing linkage analysis by genotyping family members in order to identify relatively short genomic intervals, homozygous by Descent in the affected individuals. Candidate genes in this interval were then screened for mutations. Direct interrogation of entire genomes for homozygous variants is now possible with NGS technologies, and public datasets can be used to exclude common variants that are less

probable to be disease-causing Identifying recessive variants is especially straightforward if the proband is a product of a consanguineous marriage. In short, families from Eastern and Southern rims of the Mediterranean basin should be eligible to benefit from the unprecedented technological revolution, which has begun in the field of genomics at the post-genome era. Unfortunately, this is not really the case, although most of the mutations published in genes using NGS methods are large consanguineous families (http://www.ncbi.nlm.nih.gov/pubmed/?term=exome).

In 2001, the Science article "Harnessing Genomics and Biotechnology to Improve Global Health Equity" hypothesized a 2010 World Bank report on *The Health Genomics Divide* lamenting how an unfolding revolution in treatments and interventions based on genomics-related biotechnologies in rich countries has been denied to people in developing countries (Singer & Daar, 2001). No such revolution has been unfolding, and the World Bank has not published such a report (Marshall, 2011). Truly, the last decade has however exposed a large gap between developed and developing countries in their capacity to carry out biomedical research, and with the vast majority of genomics research being carried out in the context of Western countries' genetic and environmental variation to address public health needs in these countries. If this trend continues, the health genomics divide is inevitable (http://www.who.int/rpc/grand_challenges.pdf). In the area, in which we are interested (Eastern Mediterranean and Middle East), there is, however, some hope that this "genomic fracture" might not occur.

According to currently available statistics, more than 1,500 laboratories perform genetic tests in the EU, and the annual growth in testing is close to 300%. With a population size comparable to the EU, the development, harmonization, validation and standardization of genetic testing services is a high-priority area in the Mediterranean basin. The implementation and delivery of services through national health systems is not easy, but the large and diverse populations of the Mediterranean basin have access to excellent universities, institutes and clinics. In many parts of the region, medical genetics is a recognized clinical specialty or sub-specialty, strengthened by highly trained dysmorphologists, pediatricians and human geneticists. Close collaboration with the European Society of Human Genetics, the American Society of Human Genetics and the American College of Medical Genetics has led to many national and regional congresses, workshops, and symposia focused on training, education, and workforce planning in medical genetics. The Mediterranean basin is also the home of the European Genetics Foundation, which organizes regular courses in genetic medicine, attended by more than 6,000 students over the last two decades (http://www.eurogene.eu/).

To address the **standardization and harmonization of genetics services**, Mediterranean geneticists have taken active roles in projects such as EuroGenTest (http://www.eurogentest.org/), MedGenMed and MedGeNet (http://www.eurogene.eu/), through which resources for assessing and addressing ethical, social and legal issues are also available (http://www.cags.org.ae/ctga_search.html). Finally, progress in the computational use of

medical and genomic data is reflected in genetic and genomic databases of Mediterranean populations that have already been launched (Tadmouri *et al.*, 2006) . We predict that these assets will be crucial for the integration of genetics research into the delivery of health outcomes in the region and the world.

In Lebanon, the network of universities is dense, with old, recognized universities, such as Saint-Joseph University, American University of Beirut and The Lebanese University.
In this context, the two partners from the LEB'IN project are mostly eligible to be major actors of this genomic revolution in the Eastern Mediterranean and Middle-East. Indeed, AMU and USJ, the two partners from the LEB'IN project, more precisely the team "Genetics and Physiopathology of Hereditary Peripheral Neuropathies", headed by Dr. Valérie Delague from AMU (Marseille, France) and The Medical Genetics Research Unit (UGM), headed by Pr André Mégarbané at Saint-Joseph University in Beirut (Lebanon) have a long and outstanding expertise in the field of Human Genomics and Genetics. More precisely, both have a strong expertise in the identification of disease-causing genes in large consanguineous families, with patients affected with autosomal recessive diseases. Finally, both partners have a long-lasting collaboration (UGM is an Inserm International Associate Laboratory, associated to Inserm UMR_S 910 research Unit in Marseille), and the project leader from AMU has a deep knowledge of the medical cultural, social and economical context in Lebanon and the Middle-East.
UGM, in Lebanon, has established a rich and solid network of collaborations outside Lebanon, namely in France.

Lebanon (under the leadership of UGM) is part of Orphanet, with a specific homepage (http://www.orpha.net/national/LB-EN/index/homepage/). Orphanet is the reference portal for information on rare diseases and orphan drugs, for all audiences. It aims at is improving the diagnosis, care and treatment of patients affected with rare diseases, by offering access to validated information about genetic diseases for both patient and health professionals, as well as a catalogue of laboratories performing genetic testing for specific diseases. Furthermore, all of the mutations identified in Lebanon by the UGM team are listed in a database available for all the scientific community (http://server.goldenhelix.org/lebanese/)(Megarbane *et al.*, 2006). The Golden Helix Institute of Biomedical Research has been established in 2003 as an international non-profit scientific organization with interdisciplinary research and educational activities in the field of genome medicine. The Institute's activities focus mainly in Europe and also in the Middle East, Asia, and in Latin American countries. The Golden Helix Institute of Biomedical Research has devoted a significant amount of effort to develop the Golden Helix Server, where a number of National/Ethnic Genetic databases are hosted: the Lebanese National Mutation Frequency database is one of them and is useful tool for all researchers from the area working on the same diseases.
In addition, the UGM Research Unit in Lebanon is Member, since 2005 , of the Arab-Bureau for the Gathering of Genetic Data (Dubai, CAGS) (http://www.cags.org.ae/index.html) and is contributing

to the CTGA: the database for genetic disorders in Arab populations (http://www.cags.org.ae/ctga_search.html)(Tadmouri *et al.*, 2006).

In parallel to the research conducted by UGM in the field of Human Genomics and Genetics, UGM has contributed to the development of a ''third cycle training/diploma'', based on the researches conducted in the laboratory; as well as the establishment of a ''doctoral'' school in Science and Health". Furthermore, UGM has set-up thematic training programs in Human Molecular Genetics including theoretical education and practical courses, including the latest techniques. The courses are provided by local and international specialists in the field, and have attracted more than 100 participants (students, doctors, biologists, laboratory technicians…) from Arab and Mediterranean countries such as Egypt, Jordan, Lebanon, Syria, Algeria, Morocco and Tunisia. Some participants from other countries such as France, Romania and Canada have also attended the previous courses. A diploma is delivered at the end of each school. The last training school took place on May 2012, and was focused on neuromuscular disorders, while the next one, scheduled in April 22-26, 2013 will focus on "Intellectual Deficiency".

Finally, Pr André Mégarbané and Dr Valérie Delague, both team leaders in the LEB'IN project are editors of an **online French-speaking scientific journal** (http://www.rmgh.org/) dedicated to free of charge diffusion of knowledge of results from genetic studies in the Mediterranean area. The journal will soon be available in the English language for more wide diffusion.

However, other centers of excellence exist in our field of research in the **Mediterranean area**, and a group of researchers (including Pr Mégarbané) have proposed a genomics initiative, following discussions held during the Mediterranean Medical Genetics Meeting (MediMedGen) at Bilkent University in Ankara in June 2009 (Ozcelik *et al.*, 2010). They propose *an International Collaborative Center of Excellence for Genomics Research in the Mediterranean region*, supported by international and national funding agencies and suggest that this Center of Excellence be geographically decentralized and function as a network of researchers and genomics research centers whose primary remit would be to support and facilitate joint research proposals. Members of the Center would include scientists from the region and those supporting the development of genomics in the region. They would engage in projects centered in Mediterranean laboratories whenever possible, and involving transfer of technology and training, to make the Mediterranean focus increasingly realistic with time. There is much greater strength in using resources to support science in existing institutions rather than creating a new physical structure. A decentralized, international, collaborative, investigator-initiated model alleviates hurdles of bureaucracy and facilitates international decision-making.

We fully support their views and this proposal but suggest more independency regarding fundings for the projects conducted by this international collaborative **Center of Excellence for Genomics Research in the Mediterranean region**. Funding from North America only would bias the balanced development of all the labs, which would be part of this Center of Excellence. We believe that

work to facilitate the generation of whole genome sequence data from representative Mediterranean populations, and the discovery and characterization of genes based on well-defined phenotypes in large kindreds and/or consanguineous families, should be scientifically and socially attractive to funding agencies within and beyond the Mediterranean. The role of EU here is of major importance.

3. Research and development landscape

3.1. Key research institutions

Note: this chapter presents the key European and Mediterranean research institutions involved in the cooperation with LEB'IN partners: USJ and AMU.

3.1.1. Sub-Aria 1: European Union

THE CYPRUS INSTITUTE OF NEUROLOGY AND GENETICS , NICOSIACYPRUS
Key research area: Genomes, Genomics, Neurology, Myology
Applications: diagnosis, Treatment, Therapy, Clinical Trials

BEIJING GENOMIC INSTITIUTE, COPENHAGEN, DENMARK
Key research area: Next Generation Sequencing
Applications: exome sequencing, genome sequencing

UMR_S 910, FACULTÉ DE MÉDECINE DE LA TIMONE, MARSEILLE, FRANCE
Key research area: Human Genetics and Genomics
Applications: diagnosis, Treatment, Therapy, Clinical Trials

INSTITUT DE MYOLOGIE, HÔPITAL LA PITIÉ SALPÊTRIÈRE, PARIS (FRANCE)
Key research area: Human Genetics and Genomics (Neuromuscular disorders)
Applications: diagnosis, Treatment, Therapy, Clinical Trials

IMAGINE, INSTITUT DES MALADIES GÉNÉTIQUES PARIS (FRANCE) (DIRECTOR : Pr Alain Fisher)
Key research area: Human Genetics and Genomics
Applications: diagnosis, Treatment, Therapy, Clinical Trials

WELCOME TRUST SANGER INSTITUTE, UNITED KINGDOM
Key research area: Genomes, Genomics
Applications: Sequencing, databases (Ensembl:www.ensembl.org)

BEIJING GENOMIC INSTITIUTE, COPENHAGEN, DENMARK
Key research area: Next Generation Sequencing
Applications: exome sequencing, genome sequencing

LABORATOIRES GÉNÉTHON, EVRY (FRANCE)

Key research area: Human Genetics and Genomics (neuromuscular disorders)
Applications: diagnosis, Treatment, Therapy, Clinical Trials

3.1.2. Sub-Aria 2: MEDA

INSTITUT PASTEUR DE TUNIS, LABORATOIRE DE GÉNOMIQUE BIOMÉDICALE ET ONCOGÉNÉTIQUE, TUNIS (TUNISIA) (RESP : SONIA ABDELHAK)
Key research area: Human Genetics, Oncogenetics

DÉPARTEMENT DE GÉNÉTIQUE, FACULTÉ DE MÉDECINE DE TUNIS, TUNIS (TUNISIA) (RESP : PR. HABIBA CHAABOUNI)
Key research area: Human Genetics

DÉPARTMEMENT DE GÉNÉTIQUE MÉDICALE, FACULTÉ DE MÉDECINE ET DE PHARMACIE, RABAT (MAROC) (Resp : Pr. Abdelaziz Sefiani)
Key research area: Cytogenetics, Human Genetics

LABORATOIRE D'INVESTIGATIONS MOLÉCULAIRES DES MALADIES GÉNÉTIQUES, INSTITUT PASTEUR MAROC, CASABLANCA, MAROC (Resp : Abdelhamid Barakat)
Key research area: Human Genetics

3.1.3. Sub-Aria 3: Middle East Asia including Lebanon

MEDICAL GENETICS UNIT, SAINT-JOSEPH UNIVERSITY BEIRUT (LEBANON) (RESP: Pr André Mégarbané)
Key research area: Human Genetics

American University of Beirut (Lebanone)
Key research area: Molecular Genetics, Proteomics

Lebanese American University (Lebanone)
Key research area: Hman Genetics

Genetics Research laboratory of the Chronic Care Center (Lebanone)
Key research area: Human Genetics (new genetic test strategies)

Qatar Foundation for Education, Science and Community Development (QF), Qatar

Key research area: Pediatric Genetics

It is to be noted the research projects in human genomic undertaken by the Joint Genome Research Center at King Abdulaziz City for Science and Technology (KACST), Saudi Arabia.

4. Industrial landscape

4.1. Key industrial players in the field of Human Genetics and Genomics

The aim of the research is to provide a better knowledge in the field of Human Genetics and Genomics, in order:

1. To improve the diagnosis and provide the patients with a diagnosis, and genetic counselling
2. To develop treatments and therapies.

The research domain "Human Genetics and Genomics" is not of great interest for big pharmaceutical firms, especially for the research in the field of genetic diseases, as we study some of the rarest, usually called orphan diseases. There is no market as such, however, we develop translational research, with many applications in the domain of molecular diagnosis.

This is particularly true, for NGS technologies, where we develop a lot of strategies toward a better molecular diagnosis.

Therefore in this chapter we put focus exclusively on sequencing industry represented by a few number of big companies such as Illumina, Life Technologies, Complete Genomics and Pacific Biosciences, which deliver a battle of truly mammoth proportions over the potentially enormous market for sequence-based diagnostics.

Some of them are listed below. As for MEDA and Middle East regions, any company hasn't been identified.

- **Integragen, Evry (France)**

Web-site: http://www.integragen.fr

IntegraGen's operates the establishment of the link between innovations derived from molecular research and medical practise, by developing biomarkers for autism and oncology specifically intended for clinical use, and subsequently to make its genomics services available to practitioners and researchers thanks to its exceptional technological and scientific know-how. The company has an extensive experience in NextGen sequencing and SNP genotyping.

- **Illumina, Cambridge (UK) and Eindhoven (the Netherland)**

Web-site: www.**illumina**.com

US company – key competitor of Life Technologies company - which applies innovative technologies for studying genetic variation and function, making studies possible that were not even imaginable just a few years ago. These revolutionary tools for DNA, RNA, and protein analysis are enabling rapid advances in disease research, drug development, and the

development of molecular tests in the clinic. Cambridge and Eindhoven units work on commercialization of Second Generation Sequencers.

Illumina recently launched HiSeq instrument that is rapidly becoming the platform of choice for genome facilities around the world, and it also has purchased exclusive distribution rights to exonuclease sequencing, a third-generation technology being developed by the intriguingly stealthy Oxford Nanopore.

- **Applied Biosystems (Live Science), US**

Web-site: www.**appliedbiosystems**.com

Applied Biosystems develops products for resequencing and gene expression analysis. The company is a part of a Global Life Science Company, a world leader in applied research in cell biology, genetic analysis and molecular biology. Life Technologies already owns a second-generation sequencing platform – the SOLiD system – but has been struggling to compete against the current market-dominating technology from Illumina. Numerous purchases realised by the company in recent past illustrates a serious investment in sequencing industry.

It is to be note that USJ has recently signed a contact with Applied Biosystem for the training of the Middle East criminologists on the genetic forensic tests.

- **Ion Torrent (Life Technologies), US**

Web-site: www.lifetechnologies.com

Bought by Life Technologies for an impressive US$375 million in cash and stock, Ion Torrent made a splash with its Advances in Genome Biology and Technology. The company has developed a sequencing technology based on measuring the flow of hydrogen ions (produced as new letters are added to a DNA strand) through tiny pores in a semiconductor chip. With existing second-generation sequencing platforms, Ion Torrent has a few key advantages: it's cheap ($50,000 per machine and $500 per run, according to the promotion material at AGBT), quick, has a small footprint on the bench (especially compared to the mammoth Pacific Biosciences machine) and has potential for further development. In particular, its reliance on semiconductor technology means that developers can leverage rapid advances in that trillion-dollar industry to wring more and more bases out of the platform over time.

- **Agilent technologies, Berkshire, UK**

Web-site: http://www.home.agilent.com

UK-based company specialized in Life Sciences & Chemical Analysis, Instruments & Systems, namely in development of sequence capture kits

- **NimbleGen, Switzeland and UK**:

Web-site www.nimblegen.com

Array and solution based targeted genomic enrichment. High resolution microarrays in multiple formats for multiple genomes. Instruments, sequence capture kits and software.

5. Socio-economic impacts

The human genetics research programs sought to create benefits for humankind by illuminating the fundamental molecular processes governing life. It was expected that the resulting advancements in genomics knowledge and technologies would impact on human healthcare, energy, and multiple other fields. The significant development of genomics technologies during last decennia propelled the growth of new markets by commercialization of these technologies and formed the ground for a highly active genomics-based industry. This is a particularly valuable for Unites States and Europe. The figure below extracted from the report of Battelle Memorial Institute (US) that aimed to assess the economic impact of sequencing in US provides an interesting map of economic and functional impacts of the Human Genomic Sequencing. LEB-IN focus will be put in this chapter on Public health, basic research, economic and social impacts.

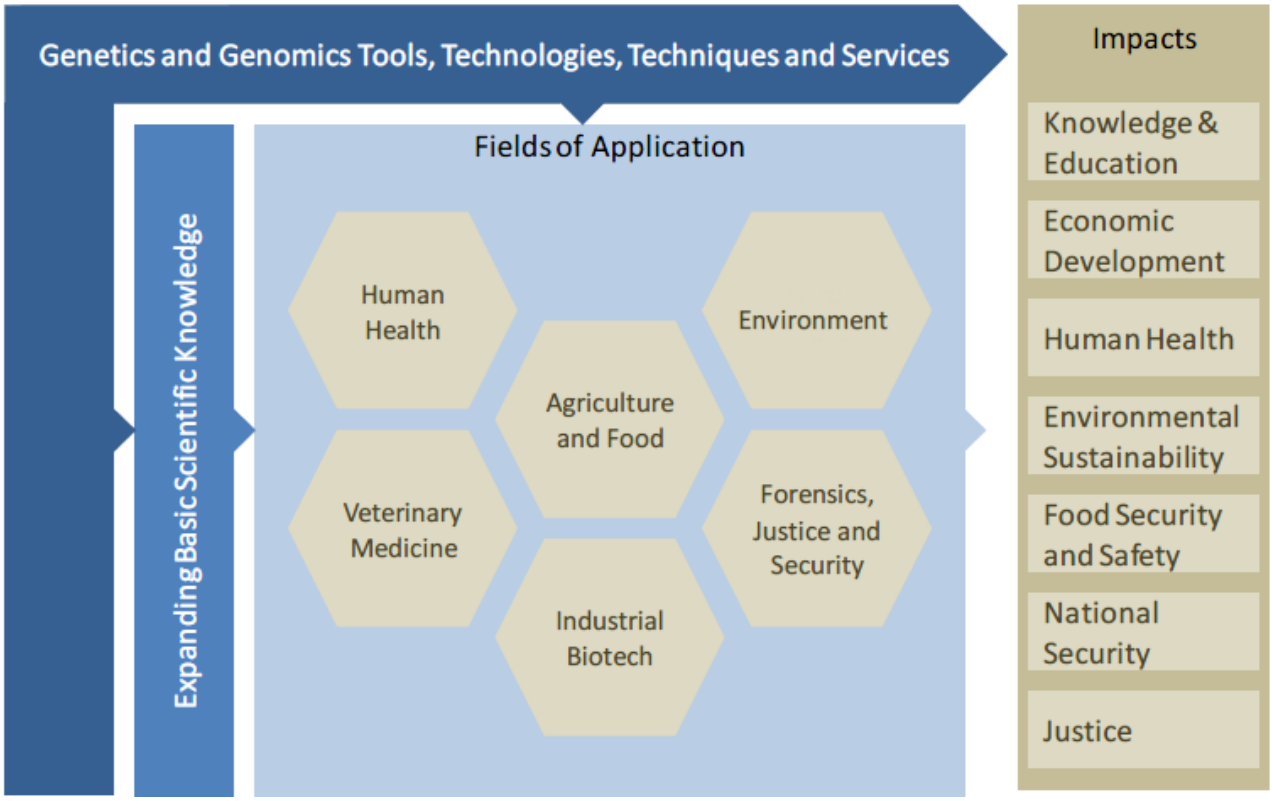


Figure 1: The Structure of Functional Impacts Associated with the Human Genome Sequencing**,** source: Economic impact of the Human Genomic project, Battelle, May 2011

5.1. Impact on public health

Measurement of impact on public health

Indeed, it is difficult to exactly measure the impact of research in the field of genetics/genomics, but discussion on it is very high among health professionals. Whereas some say that genomic

medicine will revolutionize clinical practice[2], some health professionals have argued that the discovery of genes and their association with disease will have only limited impact on clinical medicine and public health.[3, 4]

This is why some professionals have conducted a study in order to evaluate genetics tests available for clinical, research, and public health purposes in terms of their public health impact (measured by the number of people who could potentially be tested). Conclusions have shown that **about 10% of the genetic tests** listed[5] **are highly relevant to public health** (greater public health impact). The majority of genetic tests are used in diagnosis and/or genetic counselling for rare, single-gene disorders for a limited number of people. However, they conclude that the impact of genetic testing on public health is likely to increase, as more tests are being considered for newborn screening and associations between genes and common diseases are being discovered.[6]

Impact on public health resulting from research on rare diseases

Indeed, research on rare diseases (RD) is often linked to research on genetics[7]. The aim is to find genetic disorders that may be the source of rare disease and as thus find new solutions for treatment.

For example, "the Sandhoff disease is a rare disorder that progressively destroys nerve cells (neurons) in the brain and spinal cord caused by mutations in the HEXB gene; its frequency varies among populations. This condition appears to be more common in the Creole population of northern Argentina, the Metis Indians in Saskatchewan, Canada and people from Lebanon."[8]

> "Lebanon has a high incidence of common and rare genetic diseases, due probably to the mosaic different ethnic origins and the high rate of consanguineous marriages in certain communities. (…) Recorded genetic diseases, some characteristic of ethnic group or particular to a geographic region include familial paroxysmal polyserositis, familial hypercholesterolemia, hypothroidism, the Dyggve-Melchoir-Clausen syndrome, Sandhoff disease, and various genetic hematologic diseases."[9]

Although individually inherited disorders are rare, in aggregate, they represent approximately 5% of the total disease burden in the world population.[10] This is a number that shouldn't be

[2] Collins FS, McKusick VA. Implications of the Human Genome Project for medical science. JAMA 2001;285:540–544.
[3] Holtzman NA, Marteau TM. Will genetics revolutionize medicine? N Engl J Med 2000;343:141–144.
[4] Vineis P, Schulte P, McMichael AJ. Misconceptions about the use of genetic tests in populations. Lancet 2001; 357:709–712.
[5] GeneTests database, http://www.genetests.org/
[6] Paula W Yoon, Bin Chen, Andrew Faucett, Mindy Clyne, Marta Gwinn, Ira M Lubin, Wylie Burke and Muin J Khoury, *Genetics in Medicine* (2001) **3**, 405–410.
[7] NB: "Rare diseases are diseases which affect a small number of people compared to the general population and specific issues are raised in relation to their rarity. In Europe, a disease is considered to be rare when it affects 1 person per 2000", http://www.orpha.net/national/LB-EN/index/about-rare-diseases/
[8] US National library of Medicine, http://ghr.nlm.nih.gov/condition/sandhoff-disease
[9] Dr. Vazken M. Der Kaloustian, Josette Naffah, Jacques Loiselet, John M. Opti, Genetic diseases in Lebanon, American Journal of Medical Genetics Volume 7, Issue 2, pages 187–203, 1980.
[10] Rimoin DL, Connor JM, Pyeritz RE, editors. Principles and practices of medical genetics, 3rd ed. London: Churchill Livingstone, 1997:31.

underestimated – and this is the same for impact on public health resulting from research in this field.

Impact on public health is however not limited to the fact that rare diseases represent 5% of the total disease burden: results taken from research in rare diseases bare more and more potential of transferability to wide-spread diseases. For example, it was possible to transfer conclusions taken from research on rare diseases to the treatment of more common diseases:

"Research on rare diseases has proven to be very useful to better understand the mechanism of common conditions such as obesity and diabetes, as they often represent a model of dysfunction of a single biological pathway."[11] Research on specific RDs has given much insight in pathophysiology of more prevalent diseases, like migraine for example[12].

Furthermore, when companies develop a technology for the treatment of a RD, this may be used for developing treatments for other rare or more prevalent diseases.

In general, "history shows that a substantial part of the universal medical knowledge did start with a model of a RD and helped understanding more common diseases. Genetic mapping of some RDs has identified previously unknown or under-appreciated normal biological processes, e.g. in immunological self-tolerance (AIRE) or in primary cilia (defective in polycystic kidney disease)."[13]

This means that impact on public health through research on genetics shouldn't only be measured through results from research on rare diseases, but also the impact through transferability of results has to be taken into account.

Impact on public health in common complex diseases

Common complex diseases such as cancers and cardiovascular disease result both from interactions between many low-penetrant genes and from impact through environmental factors; this limits the possibility to test individuals for genetic susceptibility and to tailor interventions. However, tests on genetic variants, such as those that predispose for example to familial adenomatous polyposis and hereditary nonpolyposis colorectal cancer, when used appropriately, can detect important disorders, lead to appropriate treatment and as thus reduce morbidity and mortality[14,15]. Furthermore, as the understanding of gene-gene and gene-environment interactions increases, genetics will become an integral part of most, if not all, areas of medicine. Impact is then to be considered very high.

The US National Cancer Institute states "Behavioural and social sciences are needed to assess how genetic information can be used to effect behaviour change to reduce the burden of cancer. As importantly, delivery research on clinical utility, effectiveness, and economics of genomics-based health care applications are needed to assess their added value in cancer care and prevention.

[11] COM (2008) 679 Communication from the Commission to the European Parliament, the Council the Economic and Social Committee and the Committee of the Regions on RDs: Europe's challenges.).

[12] Vries B, et al. (2009) Molecular genetics of migraine. Hum. Genet. 2009 Jul; 126 (1): 115-32.

[13] D Mathis and C Benoist 2007; A decade of AIRE. Nat Revs Immunol. 7, 645-50). (http://www.eurordis.org/sites/default/files/publications/why_rare_disease_research.pdf

[14] Rabelo R, Foulkes W, Gordon PH, Wong N, Yuan ZQ, MacNamara E, Chong G, Pinsky L, Lasko D. Role of molecular diagnostic testing in familial adenomatous polyposis and hereditary nonpolyposis colorectal cancer families. Dis Colon Rectum 2001; 44:437–446.

[15] Renonene-Sinisalo L, Aarnio M, Mecklin JP, Jarvinene HJ. Surveillance improves survival of colorectal cancer in patients with hereditary nonpolyposis colorectal cancer. Cancer Detect Prev 2000; 24:137–142.

Genomics and related fields will also affect surveillance, dissemination and diffusion research as well as evaluation of cancer progression and survivorship. (...) NCI's mission is to integrate genomics into public health cancer research, policy, and programmes. Its vision is to use genomic knowledge to reduce the burden of cancer."[16]

Experts state that applying what we know today in hereditary breast/ovarian cancer, Lynch syndrome and familial hypercholesterolemia has the potential to affect thousands of people in the US population every year. Enhanced partnerships between genetic and nongenetic providers of clinical medicine and public health are needed to overcome the challenges for implementing genomic medicine applications both now and in the future.[17]

Given that gene-environment interactions underlie almost all human diseases, the significance to public health of genomic research on common diseases with modifiable environmental risks is based not necessarily on finding new genetic "causes", but on improving existing approaches to identifying and modifying environmental risk factors to better prevent and treat disease. Such applied genomic research for environmentally caused diseases is important, because 1) it could help stratify disease risks and differentiate interventions for achieving population health benefits; 2) it could help identify new environmental risk factors for disease or help confirm suspected environmental risk factors; and 3) it could help our understanding of disease occurrence in terms of transmission, natural history, severity, etiologic heterogeneity, and targets for intervention at the population level. While genomics is still in its infancy, opportunities exist for developing, testing, and applying the tools of genomics to clinical and public health research, especially for conditions with known or suspected environmental causes. This research is likely to lead to population-wide health promotion and disease prevention efforts, not only to interventions targeted according to genetic susceptibility.[18]

Impact through genomic technologies

Next-generation genomic technologies allow clinicians and biomedical researchers to drastically increase the amount of genomic data collected on large study populations.[19] When combined with new informatics approaches that integrate many kinds of data with genomic data in disease research, allowing researchers to better understand the genetic bases of drug response and disease.[20]

Indeed, genomic technologies will revolutionize medicine by increasing the proportion of medicines aimed at the causes of disease rather than the symptoms. "We're looking at what the medication is doing to a particular part of the body at a genetic level," says Mark Gessler, president and CEO of Gene Logic, Inc., a provider of genomic information. "As we get more

[16] http://epi.grants.cancer.gov/phg/

[17] Bowen MS, Kolor K, Dotson WD, Ned RM, Khoury MJ., Public Health Action in Genomics Is Now Needed beyond Newborn Screening, Public Health Genomics. 2012; 15(6):327-34. doi: 10.1159/000341889. Epub 2012 Sep 11.

[18] Khoury MJ, Davis R, Gwinn M, Lindegren ML, Yoon P., Do we need genomic research for the prevention of common diseases with environmental causes? Am J Epidemiol. 2005 May 1; 161 (9):799-805.

[19] Feero, W. Gregory; Alan E. Guttmacher, Kathy L. Hudson (2011-09-15). "Genomic Medicine: Genomics, Health Care, and Society". *The New England Journal of Medicine* 365 (11): 1033–1041.

[20] Feero, W. Gregory; Alan E. Guttmacher, Christopher J. O'Donnell, Elizabeth G. Nabel (2011-12-01). "Genomic Medicine: Genomics of Cardiovascular Disease". *The New England Journal of Medicine* 365 (22): 2098–109.

samples, we'll be able to select an individual drug and patient and get genetic insights from real human samples." That approach will eventually open the way to personalized medicine, with the drug and the dose tailored to the individual patient and his or her condition.[21]

Outreach for future impact

Public health practice has to date in particular focused on environmental or social determinants of health and disease and has paid few attention to genomic variations within the population. The advances brought about by research on genomics are changing these perceptions. In the long run, the knowledge gained through genomics will enable health promotion messages and disease prevention programmes to be specifically directed at susceptible individuals and families, or at subgroups of the population, based on their genomic risk profile; personalised healthcare will be possible. As the controversial discourse in science and health politics shows, the integration of genomics into public health research, policy and practice is one of the major challenges that the health-care system is currently facing.[22]

The integration of genomics into the aims of public health is called Public Health Genomics (PHG) and is defined as "the responsible and effective translation of genome-based knowledge and technologies into public policy and health services for the benefit of population health".[23, 24] So far there has been no systematic integration of genome-based knowledge and technologies into public health research, policy, and practice. Thus, the public health agenda demands a vision that reaches beyond the research horizon to arrive at application and health impact of these innovations. The Public Health Genomics European Network (PHGEN) aims to fulfil this task in Europe.[25]

Whereas medicine is currently undergoing remarkable developments "from its morphological and phenotype orientation to a molecular and genotype orientation", promoting the importance of prognosis and prediction, the discussion about the role of genome-based information for epidemiological research and public health still is at the beginning. Public Health Genomics (PHG) contributes to this discussion by focussing on the use of genome-based information for epidemiological research, surveillance systems, health policy development, individual health information management and effective health services.[26]

[21] Peter Gwynne, Guy Page, Technologies in Genomic Research: the sequel, http://www.sciencemag.org/site/products/sequel.xhtml

[22] Brand A, Brand H, Schulte in den Bäumen T., The impact of genetics and genomics on public health. Eur J Hum Genet. 2008 Jan; 16(1):5-13. Epub 2007 Oct 24.

[23] Brand H, Brand A., Public Health Genomics. The integration of genome-based knowledge into public health research, policies and health services, Bundesgesundheitsblatt Gesundheitsforschung Gesundheitsschutz. 2007 Feb; 50 (2):135-44.

[24] Burke W, Khoury MJ, Stewart A, Zimmern RL; Bellagio Group., The path from genome-based research to population health: development of an international public health genomics network, Genet Med. 2006 Jul; 8(7):451-8.

[25] Brand A, Rosenkötter N, Schulte in den Bäumen T, Schröder-Bäck P., Public health genomics. The future is built today! Bundesgesundheitsblatt Gesundheitsforschung Gesundheitsschutz. 2009 Jul; 52(7):665-75. doi: 10.1007/s00103-009-0875-8.

[26] Boccia S, Brand A, Brand H, Ricciardi G., The integration of genome-based information for common diseases into health policy and healthcare as a major challenge for Public Health Genomics: the example of the methylenetetrahydrofolate reductase gene in non-cancer diseases, Mutat Res. 2009 Jul 10;667(1-2):27-34. doi: 10.1016/j.mrfmmm.2008.10.003. Epub 2008 Oct 21.

Example from abroad
Australia has a multicultural society that has arisen from continuous migration. While the population is relatively small, just over 20.7 million, it is genetically diverse and is spread over a large land mass. (...) Population genetic screening occurs throughout Australia predominantly as newborn screening programmes and to identify pregnancies at risk of chromosomal and neural tube defects, while carrier screening programmes are essentially ad hoc. Despite inevitable tensions between federal and state policies, there is increasing evidence of the development of national policy in a range of genetic issues, not least in newborn screening, genetic testing, and health professional education. Impact on public health arising from genomic testing being considered important, its integration as public health genomics has been started. However, further work is necessary to establish frameworks for the regulation and funding of new genetic tests across state/federal boundaries, which will be crucial to the establishment of a national approach to public health genomics policy.[27]

5.2. Impact on Basic research

The impact of sequencing of the human genome on human health is extremely important but its benefits extend into areas of far beyond human health. Indeed, sequencing of the genome has been a paradigm shifting event in genomics and in whole biology sciences, but it greatly impacted on a broad range of other sciences, namely on information sciences and mathematics which are now closely interlinked as sequencing of the genome sowed that biology is fundamentally an information science. New scientific fields have been raised such computational biology, systems biology, bioinformatics. Indeed, without the progress made in the latter part of the 20th Century in computer processors, data storage and computational analysis methods, the sequencing of the human genome would not have been possible.

Some most relevant new disciplines that have been emerged from the development of three primary branches of Genomics disciplines (Structural Genomics, Comparative Genomics and Functional Genomics) are briefly present below:

• The '**Omics'** – a series of disciplines that are an outgrowth of genomics and its discoveries, generally grouped by the term 'Omics'. They comprise:

- Proteomics – The study of the set of proteins encoded by a genome
- Metabolomics – The study of the complete collection of metabolites present in a cell or tissue under a particular set of conditions
- Transcriptomics – The study of all RNA molecules, including mRNA, rRNA, tRNA and non-coding RNA in an organism or specific cell.

• **Computational Biology** – based on mathematical and computational approaches this discipline addresses theoretical and experimental questions in biology. Its sub-discipline "computational

[27] Metcalfe SA, Bittles AH, O'Leary P, Emery J., Australia: public health genomics, Public Health Genomics. 2009; 12(2):121-8. doi: 10.1159/000160666. Epub 2008 Oct 2. Copyright 2008 S. Karger AG, Basel.

genomics" performs statistical analysis on the data generated by gene sequencers and microarray technologies to evaluate gene and gene products expressed by various cell types.

• **Bioinformatics** – often viewed as the applied twin of computational biology, the Sanger Institute's glossary (UK) provides the following definition of this discipline "Science of using computer technology to gather, store, analyze and merge biological data. Dealing with billions of data points, research centres request high-speed computers, powerful large-scale computing clusters and data storage centres. Many genomics researchers today agree that **cloud computing** is the future compute model that can provide the elastic scale needed for DNA sequencing.

One of the investigations of the LEB'IN consortium concerns the practical interconnection between the ICT and genomics research. The promises are significant but a large degree of uncertainty remains. The consortium will try to promote via dissemination and twinning activities the new strategies of information networking between European and Lebanon research centres operating in these two fields.

• **Evolutionary Developmental Biology** (EvoDevo) – deals with the origins and evolution of embryonic development. This field outgrew of the existing discipline "Embryology" has been empowered by data contained in genome sequencing of human and model organism cells.

• **Metagenomics** –investigates the communal genome contained within an environmental sample. It enables the study of the symbiosis and interactions of organismal genomes and genetic products as a biological system.

We can mention also the impact on the development of other disciplines, such as Bio-archaeology, Anthropology, Agricultural and Environmental Sciences. For example, European research centres are working on edible vaccines for incorporation into food products (food security) and investigate on the genomes of multiple non-pathogenic microbes for use in the environmental waste remediation, energy productions, carbon cycling, and biotechnology applications.

The fundamental advancement of scientific knowledge embodied in the human genome sequencing is also well illustrated by the broad variety of major research projects that have been funded by the European Commission under FP7 some of them we mentioned above.

5.3. Impact on economy and society

5.3.1. Economic impact

For patients with autosomal recessive hereditary disorders, diagnosis has historically presented a serious problem. Primary care physicians and paediatricians may never have encountered a specific type of monogenic disorder that presents in a patient, and unfamiliarity with a rare

disorder can lead to an incorrect diagnosis, the wrong treatment, negative side effects from the wrong treatment, and ongoing suffering from the disorder or disease. It is particularly difficult for a physician to diagnose a rare disease when its symptoms may mirror another more common disease. Without definitive genomic tests, physicians are often running practically blind; having to use one-size fits all approach to their diagnoses and treatments. Research centres involved in LEB-IN project greatly contribute to refined understanding of the human genome and related cellular processes that are the basis for effective gene therapy. Their discoveries embodied in human genome sequencing are being directly applied to address progress in the diagnosis and treatment of autosomal recessive hereditary diseases. The diagnosis and treatment stimulated and facilitated by the Next Generation Sequencing technologies help to move from "prescribe and hope" medicine to personalized, data-driven medicine in which the efficacy of a treatment regime is known in advance. As for pharmaceutical market, achievement in genomic medicine impacts on the development of the rational drug design that relies heavily upon computer modelling and genomics to design a new generation drug that will interact specifically with a selected molecular target important in disease progression.

Progress in genomic medicine and screening technologies become vital for human health improvement and for modern economies as good health of population is an investment in economic growth. The economic benefits are numerous, among the most relevant are cost saving opportunities that genomic medicine will provide across multiple fronts in healthcare. Over time, advancement in gene therapy will allow disorders and diseases to be completely averted, while already preconception genomic tests can provide advice to potential parents regarding risk of devastating illness to their children, thus providing actionable information to avoid the heartache and cost of fatal childhood congenital diseases.
Research on rare diseases carried out by LEB'IN partners presents remarkable interest both for EU and Lebanon sides: rare diseases can serve as models for more common diseases and the complexity of rare diseases often requires multidisciplinary innovative approaches. Successful models exist to support research on rare diseases in Europe, but funding dedicated to research on rare diseases, both at national and European level, remains limited with regard to the number of different rare diseases, and the current generally poor availability of diagnostic and therapeutic options. An implementation of successful models, potentially adapted to fit the state of the art in each region, would benefit the rare diseases international community.

To date, a very limited number of so-called orphan drugs are marketed, leaving the majority of rare diseases without any effective treatment. In order to translate research results into the marketing of orphan drugs for the benefit of patients, it is important that the pharmaceutical industry participates in the development process. This requires strengthening the links between academia and industry, so that industry better capitalises on academic research results to translate these into new diagnostic tools and therapies.

A lot of question linked to the short- and long-term economic impact of the human genome research still remain open and we need to work with economists to understand better the

economic factors that will determine whether and how genomics is translated into practice. What will be financial costs and societal benefits of integration of genomics into health care? Will society ultimately save money through increased productivity of a healthier population? How can we ensure that all benefit from genomic medicine and that it is not exclusive?

5.3.2. Labour Force Profile

Human genetics encompasses a variety of overlapping fields including: classical genetics, cytogenetics, molecular genetics, biochemical genetics, genomics, population genetics, developmental genetics, clinical genetics, and genetic counselling. The profiles of the specialists are extremely various and composed of a great number of employment categories. The sector requests to pursue a cross-disciplinary education. Research challenges in human genomics are too broad to be solved by specialists trained in only one discipline.

Next generation and third generation sequencing technologies have started making big impacts on biological research. Despite increasing read lengths and accuracy, multiple pre and post sequencing challenges remain and can be addressed by complementation with parallel technologies. Therefore, more job opportunities are expected in this field.

In regard to the burgeoning drug industry based on genomics, the Consulting Resources Corporation's for biotechnology professionals expects the job growing trends in new genomics, proteomics, and bioinformatics technologies to dominate developments in therapeutics by greatly improving the efficiency and speed of the entire drug discovery, testing, and approval process.

To propel human genomics technologies forward, the theoretical scientists should work in tandem with industrial scientists and especially with those having engineering knowledge and firsthand experience with the technology. In either case, appears a shortfall between the industrial request for technology and underexploited pool of research excellence. Europe knows well such a scheme when two worlds have existed separately.

The "bridge" role in linking research and industry is played by **"gatekeepers", emerging innovation agents specialised in creating new technology and boosting it to the economic growth**. Their ability and skills to work with researchers, investors, industrials and even political is vital in the context of modern cross-sectorial technologies and interactive networks.

Example from abroad
In "The advanced material revolution", Sanford L Moskowitz[28] shows interesting results of a survey of 50 successful high-technology firms involved in development of advanced materials products. The figures show that percentage of these firms succeeded primarily because of the actions of each of the professional groups listed. The last two categories (gatekeeper team /

[28] The advanced materials revolution : technology and economic growth in the age of globalization, Sanford L Moskowitz, Hoboken, N.J. : John Wiley, ©2009.

gatekeeper individuals) distinguish between multidisciplinary individuals and the teams composed of individuals specialised in different fields who effectively coordinate these disciplines into a closely integrated unit. The striking conclusion from this survey is that the vast majority (90%) of successful firms must operate in an integrated multidisciplinary environment. No one discipline, not even engineering or venture capital, dispute their importance can "go it" along. They must be linked within a network of interconnected and mutually reinforcing jobs.

Finally, the availability of appropriate human capital depends not only on the aggregate numbers of personnel, but also on the mobility of labour. To address the mobility challenge, international research community pays particular attentions to issues aiming at attracting and promoting young scientists graduated in the field of human genomics. Rapid development of different genomics applications for health, security, agriculture, military, and space exploration push genomics science in new and profitable direction that creates an important dynamic for human capital supply.

5.3.3. New Business Growth

As stated above, the interest of pharmaceutical firms for the research outcomes in the field of orphan diseases is very moderate comparably to other disciplines in Human Genetics and Genomics. The market is very limited; however there are some niches in particularly in translational research that offers many applications in the domain of molecular diagnosis. This is particularly true, for NGS technologies, where LEB'IN partners develop a lot of strategies toward a better molecular diagnosis.

5.3.4. Ethical issues

The research on Human genome is a particular sensitive field where ethical aspects play a primordial role.

When doing research in this field, the following aspects should be considered:

- **Access to genetic information**: *Who should have access to personal genetic information, and how will it be used?*
- **Privacy and confidentiality** of genetic information: *Who owns and controls genetic information?*
- **Reproductive issues** including adequate informed consent for complex and potentially controversial procedures, use of genetic information in reproductive decision making, and reproductive rights.
- **Clinical issues** including the education of doctors and other health service providers, patients, and the general public in genetic capabilities, scientific limitations, and social risks; and implementation of standards and quality-control measures in testing procedures:
  - *How will genetic tests be evaluated and regulated for accuracy, reliability, and utility?*
  - *How do we as a society balance current scientific limitations and social risk with long-term benefits?*
- **Uncertainties** associated with gene tests for susceptibilities and complex conditions (e.g., heart disease) linked to multiple genes and gene-environment interactions.

- **Conceptual and philosophical implications** regarding human responsibility, free will vs genetic determinism, and concepts of health and disease.
  - *Do peoples' genes make them behave in a particular way?*
  - *Can people always control their behaviour?*
  - *What is considered acceptable diversity?*
  - *Where is the line between medical treatment and enhancement?*

Indeed, impact relating to ethics can arise in particular in the field of Human Genome, as the subject is considered sensible and is frequently debated. Even though research in this field can bring high benefit for public health (see relevant chapter), especially the aspects of privacy and the potential risk of misuse is discussed.

As such, genetic testing has become also the subject of policy debates at different institutional and international levels. Recent work took place at the European Parliament- through the work of the "Temporary Committee on Human Genetics and Other New Technologies in Medicine"-, at the Council of Europe – through the "Working party on Human Genetics", preparing a preliminary Protocol on Human Genetics – at the European Group on Ethics in Science and New Technologies - who held a debate on ethical issues of genetic testing in the workplace – and at the OECD - through the Working Party on Biotechnology which established a Steering Group (including several EU countries, Japan, Canada and US) to survey the situation of genetic testing world-wide and to issue recommendations for an international and mutually recognized approach for quality assurance in genetic testing.

In this context, the European Commission – DG Research - has supported a series of research projects, networks and studies aimed at improving the quality of genetic services, analyzing the ethical, legal and social aspects and providing support for the development of related responsible policies. The present study is an example to illustrate some aspects of the complex research at the core of genetic testing.

In Lebanon, an Ethic Council exists and has to be addressed for approval of any project related to Health. In addition, the different institutions (Université Saint-Joseph, American University of Beirut) have internal Ethics Committees with strict regulations to be considered.

6. Conclusion and recommendations

We remain that the present report does not have the ambition to be complete and to cover all aspects referred to the field of the human genome. The idea is to identify most important trends in the field and to give them as examples for presenting human genome technologies to a wider public (through public report) to provoke a discussion which addresses societal and economic expectations and concerns and to help the project team with a formulation of main priorities for Saint Joseph University's R&D directions.

The findings clearly demonstrate the importance of human reference genome and the technologies of modern genomics for human medicine. Moreover, the research conducted in the field has significantly affected science and applied technology deployment in multiple fields outside of human medicine. Disciplines including veterinary medicine, agriculture and food production, environmental science, industrial biotechnology, biosecurity and forensics are all beneficiaries and users of the knowledge and technological advancements made possible by the human genome programs. The application of genomics across the above fields and disciplines generates a broad variety of impacts at economic and social levels.

Based on the bibliographic analysis and interviews with European and Lebanon experts, we conclude that the primary impact area includes Human Genome & Molecular Genetics fields - the most advanced fields pursued by scientists to address chronic and congenital disorders.

With respect to the LEB-IN partners' medical focus (orphan diseases) we put forward the fact that the specificities of rare diseases - limited number of patients and scarcity of relevant knowledge and expertise - single them out as a distinctive domain of very high European added-value.
In this context, European cooperation with Lebanon ensures that scarce knowledge can be completed and resources combined as efficiently as possible, in order to tackle rare diseases effectively across both regions.

Recommendation 1 :
Enhance existing EU-Lebanon research collaboration in the field of genetics of rare non-communicable diseases

From a regional perspective, programs that address recessive diseases have a high priority and need to go beyond gene identification to the characterization of the mutational spectrum relevant to each locale, and to the provision of community-based medical genetics services. This extremely sensitive issue, owing to its ethical, legal and social aspects, can best be addressed by professionals from the same cultures as the affected families, and this is most likely to lead to clinically effective outcomes. A concentrated effort to solve the genetic bases of non-communicable diseases will have an important public health impact far beyond the specific alleles identified in the first families to be studied. The genetic dissection of well characterized disease phenotypes in large kindreds will reveal genes that underlie complex, heterogeneous diseases. Indeed, pathways relevant to common diseases are often identified through genes responsible for related rare disorders.

As we also stated in the SWOT analysis (see D2.2 Report on SWOT analysis of USJ) the most promising path to integrate Lebanese research in Human Genome & Molecular Genetics fields into

ERA is a cooperation of European and Lebanese Health clusters. However, given the youth of the USJ's Health Technopole, it should be placed in a mid-/long-term perspective since such cooperation requests from the USJ to develop the Health Technopole towards an international node of knowledge and innovation.

The immediate actions to start an integration process should refer to the existing twinning collaboration schemes. The cooperation should further consolidate the major efforts initiated by LEB'IN and other similar projects. In respect to the new orientations given by the Europe 2020 Strategy, these schemes should involve partners/experts from the EU and the Lebanese health industry.

Recommendation 2 :
Promote the Lebanese leading role in quality of Genetics research knowledge platform for Middle East

The European interest in developing the Lebanese medical genomic research is important. To emphasise the economic and social impact of the research in human genomics, there is a need for adequate coordination of European and Lebanese efforts in order to optimise the resources and synergies. One of the possible opportunities will be to create a platform of knowledge in the Middle East area lead by Lebanese research centers. Indeed, the Middle East market is quite difficult to access from EU, in terms of geographical and cultural distance and language barriers. However, Lebanon could play a hub function for access to this region, as close collaboration already exists that could be the linking nod with Europe.

It should be noted that USJ is a leader of the project aiming at the "Creation of a center for training researchers in Medical Genetics in the Middle East," that was funded by the Francophonie University Agency (AUF). Funding organizations took into account the scientific value and impact of such a project on Lebanese research excellence. Joint research projects (such as recent collaboration of the USJ with Qatar on Lebanese, Quatrain, Tunisian, and Saudian genome sequencing) can play consolidation role for the knowledge platform setting up.

Lebanon's leading position in forensic genomic tests can be also a point for the potential Middle East knowledge platform. The future action can be inspired by recent USJ's activities aiming at delivering the training sessions dedicated to genetics professionals on genetics forensic tests for justice purpose: criminology, paternity…. To be noted that in the world there are only three centers that deliver this specific training: one in France (Europe), one in Russia and one in Lebanon (USJ).

Recommendation 3 :
Support young researchers: investment in the future

The EU-Lebanon cooperation may be reinforced by encouraging young researchers' mobility and their more intensive implication in joint research projects. There is a bilateral programme for exchange of students, which is working well. However, in order to strengthen the cooperation, more international programmes with participation of young researchers (e.g. post-docs) should be developed. There is much work to be done in this domain as this is not structured and efforts need

to be encouraged. Higher salary rates for young graduates in business in comparison with the salaries in the academia exist in Lebanon. This impedes the involvement of more students in the R&D field. The number of students has to be increased by better wage level in research, but this is an issue to be addressed by the Lebanese government. Integration of Lebanon to the ERA should be the way to attract the bright Lebanese undergraduate or master's students for carrying out research in the country. This could be a countermeasure to reduce the brain drain phenomena. One of the important actions of the USJ is to organize a **Human Molecular Genetics School** for students, genetics, doctors, and biologists, laboratory technicians, which aims at providing latest theoretical and practical knowledge in the domain. This annual school attracts student participants from Lebanon, Mediterranean partner countries, EU and the Middle East. As thus, besides providing extensive knowledge, it also serves as a networking platform for the future generation of human genetics specialists.
This positioning of the USJ as a regional and inter-regional center of excellence for training will be helpful to enhance the collaboration schemes involving young researchers.

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The present findings will be discussed by the LEB'IN partners and scientific reference team experts during the upcoming consortium meeting in April 2013 in Beirut (Lebanon) in order to integrate the most relevant of them into Strategic Development Plan of the USJ and orient the project exist strategy.