LE GOUVERNEMENT
DU GRAND-DUCHÉ DE LUXEMBOURG

MINISTÈRE DE L'ÉCONOMIE
ET DU COMMERCE EXTÉRIEUR

MINISTÈRE DE LA CULTURE,
DE L'ENSEIGNEMENT SUPÉRIEUR
ET DE LA RECHERCHE
Recherche et innovation

MINISTÈRE DE LA SANTÉ

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Jeannot Krecké, Minister of the Economy and Foreign Trade:

"Rationale of the project and economic perspectives"

General Context:

- The burst of the stock market bubble in 2000 has increased the awareness about risks inherent to the monolithic structure of Luxembourg's economy. In 2004 **the Luxembourg Government has therefore committed to pave the way for the so-called Lisbon strategy** - i.e. to favor the emergence of a knowledge-based economy - by encouraging new, research-based, innovative activities; among others in the biomedical field.

- Health care industry is a particularly interesting subject area: a challenge in terms of public spending, because of steadily increasing expenditures (9% of GDP in average in OECD countries), but also an engine for employment and economic growth, and a key sector for R&D activities.

Against this background the Government has elaborated a ***Health Technologies*** action plan, presented in April 2007. Focus of this plan:

- Establishing Luxembourg as a prime location for high-end research and commercial activities in niche areas, by leveraging existing industrial and research competences

In this context, it has been decided **to take a strategic and common approach**, with the minister of Research and the minister of Health, in order to maximize chances of success and potential returns for Luxembourg.

The overall project

Today we are very pleased to be able to share with you the outcome of this common effort, namely **a major initiative in the field of molecular diagnostics and personalised medicine**. This involves **strategic partnerships** with two major US research institutes:

- Translational Genomics Institute (TGen), Phoenix (AZ), led by Dr. Jeffrey Trent;
- Institute for Systems Biology (ISB), Seattle (WA), led by Dr. Leroy Hood;
- and with the Partnership for Personalized Medicine (PPM), an initiative led by Dr. Lee Hartwell

The **central piece** of the initiative is the **creation of a biobank**, in collaboration with TGen. The **second part** is a **partnership with the ISB**, which aims at creating a centre of excellence in systems biology. And the **third** and last **part**, consists in **a research project with the PPM on lung cancer**.

The undertaking obviously has a strong research emphasis - Minister F. Biltgen will elaborate on this aspect -. This is what we wanted, because we feel that research efforts need to be strengthened in order to be able to play a role as a country in this very dynamic and promising field.

The economic perspectives

This being said, positive economic impacts can be expected in a fairly short period of time. Indeed, the **biobanking capacities** that will be developed **as well as the competences which will be acquired** through the research projects **are very valuable to the health care industry**:

- First concrete opportunities for creating for-profit entities, directly linked to the overall initiative will be explored in the coming months.

Further important dimension in terms of economic development and diversification:

- The three projects are heavily tilted towards both information and communication technologies and material sciences. Synergies are hence expected with these domains, in which Luxembourg already has some strengths and competencies.

Finally:

- The technological know-how of our American partners can help Luxembourg to carve out a privileged position in the field of molecular diagnostics.

Let me conclude by quoting a statement of Luxembourg's national plan for innovation and full employment: "*The ultimate objective of the Government is to achieve and maintain a high and sustainable quality of life for the population of the country. Economic competitiveness will consequently be a tool for men and women living and working in Luxembourg*".

This project certainly aims at fulfilling such an objective because:

- it is expected to have a strong leverage effect which will allow accelerating the development of a centre of excellence in a niche area of the health sciences and technologies, by attracting researchers, companies and investors;
- but also, and beyond, because it will serve the interests of the general population as the healthcare system could benefit from research finding – as Minister Di Bartolomeo will tell you in a moment –.

François Biltgen, Minister for Culture, Higher Education and Research:

"Boosting Luxembourg's research efforts through strategic partnerships with key US research institutes"

In 2004 the Government agreed to:

- Encourage establishment of **scientific and technological centers of excellence** –i.e. concentrate efforts on a **limited number of state-of-the-art sectors**, which have an international dimension and which will benefit the country at large, in the framework of **public-private partnerships**; in 2007 these priority areas have been retained by the Government following the Foresight initiative of the National Research Fund, **translational research on chronic and infectious diseases** ranks high on this priority list,
- **Increase public spending on R&D** while **maximizing efficiency** of expenditures for research, both fundamental and applied.
- **Encourage synergies between the University and the Public Research Centers**, as well as **scientific collaborations** and the **mobility of researchers**.

The scientific background of the projects presented today is that of molecular diagnostics, namely a personalized diagnostics, which is made possible by genomics and proteomics applications.

The initiative, which consists of **three complementary projects** - the creation of a biobank, and two research projects which will use the biobank's services – is very much **in line with the objectives set by the Government with regard to public research** mentioned above.

This initiative fits very well with the national research policy for the following reasons:

- It represents a **substantial research effort in a cutting edge domain** – molecular diagnostics and offers the essential ingredients for successfully developing a real center of excellence.
- In addition, the research **topics** of this initiative **reflect national research priorities and fit well with existing research efforts;**
- It is organized as an **integrated approach**: biobank as research infrastructure to support Hood's and Hartwell's projects (provision of samples).
- It constitutes a **sound mix between fundamental approach** (understand mechanisms of a pathology), **applied research** (validate biomarkers for clinical use) **and technological developments** (improve analytical tools).
- There are also **strong synergies and cooperation between Luxembourg research actors.** Biobanking operations will be set up through a joint venture of the 3 CRPs and the Universiy ;

- Finally, **partnerships with well-known institutes** and scientists will allow to **reinforce Luxembourg's research base** and to **increase its visibility internationally**.

Molecular diagnostic is at the intersection of biomedical research, software engineering, and materials science. The following presentations will show that Luxembourg can **leverage the existing competences in these areas**.

This initiative offers extraordinary **development perspectives in 3 different areas: research, public health and economic development**. Upfront this initiative focuses mainly on a considerable research effort. Thus the overall **success** of this initiative is **highly dependent on the good performance of the research part**. Therefore I have asked the services in my ministry to follow this part of the initiative with special care.

The **overall investment is quite substantial: some 140 M€ over the next 5 years**. A large part of this investment focuses on **personnel** expenditures. Thereby, this initiative addresses a typical issue of research in smaller countries, i.e. that of reaching **critical mass**. It is expected to develop through this initiative the critical mass of expertise to further the development of the field of molecular diagnostics in Luxembourg.

It is of equal importance that **public money is well spent**, we shall ensure this through:

- **linking public spending to clearly defined activity programmes and detailed business plans**
- setting up **robust evaluation procedures** for carefully following the progress of work
- ensuring **permanent and close coordination among the three ministries** involved

MINISTÈRE DE LA SANTÉ

Mars Di Bartolomeo, Minister of Health:

"Links with and expected returns for Luxembourg's healthcare system"

The health sector is today and will remain in the future an important growth area:

1. The **progress realized by medicine and technology offers a strong potential to improve the heath care system by developing new and better-targeted treatments**. It will be a major contribution to increase the quality of life.

2. Recent developments in research show that **the health sector can be in the future, even more than today, an important factor for economic growth**.

3. Concerning employment the **health sector is very dynamic and generates good and secure jobs**.

The organizational an financial **structure of the health care system in Luxembourg is designed in order to deliver high standard of patient care and to give free and equal access to all medical services regardless of the income**. We do have a viable health-care system because it is financed by an obligatory health insurance model built on the principles of solidarity and by a significant public co-financing.

From the Ministry of Health's point of view, **one important added value of the two common projects "Biobank" and "Lung Cancer" will be to increase resources allocated to clinical research**. Only by allocating additional resources and creating new partnerships in the health field in general and especially in clinical research we can reasonably improve patient care.

We are very confident, that **the econometric study of biomarker's project will mainly contribute to improve the cost-efficiency of healthcare expenditures**.

We are furthermore **convinced that by investing in clinical research we will fill new gaps**. There is "no time to lose" if we want Luxembourg to become an actor in this area. The returns on our investment should be evaluated in terms of additional benefits for the patients.

On the one hand, this goal will be reached by developing individualized diagnostic through "personalized medicine: give the right drug, at the right person, at the right moment, at the appropriate dose."

On the other hand, early detection of diseases remaining a major public health concern like lung cancer can save lifes and be of a tremendous benefit for the patients and their families. Not to forget that avoiding tobacco is the best prevention of lung cancer.

"**The best medicine you can imagine will always be the one you will never have to take**." This means, that even if personalized medicine will provide precious pieces of information to our medical and clinical actors in order to improve the medical treatment, **our national health policy will focus on developing prevention and early diagnostic campaigns**.

The involvement of the Ministry of Health in project design and execution has been strong and will give guarantees covering some important themes including:

- patient rights,
- informed patient consent,
- data protection,
- questions for the committee for ethics,
- application of strictest ethical and quality standards,
- health care and public health priorities before commercial interests.

Dr Jeffrey M. Trent (Translational Genomics Research Institute) & Dr Jean-Claude Schmit, CRP Santé

"Create a world-class biobank to support research efforts and evidence-based medicine"

Literature:

1. The Importance of Biobanking

Biobanking Basics

The practice of biobanking—the collection, storage, processing and distribution of biological specimens, as well as the data that accompany them—has become a tool of critical importance to biomedical research today. Biobanks, alternately known as *biorepositories* or *tissue banks*, usually refer to those entities that work with human tissue and associated clinical data, although the term may also apply to institutions working with animal tissues, cell and bacterial specimens, or samples of environmental materials.

Modern biobanks exist under many different organizational "umbrellas:" academic medical center establishments, universities, pharmaceutical companies, biotechnology firms, or dedicated research institutions. Biobanks typically exist connected to or within a clinical environment, where the ability to conduct vital research on human disease depends on the success of recruiting donors, collecting tissues, and obtaining information on donors from clinical patient or doctor interviews, as well as from donors' medical records. Additionally, biobanks may offer other services, including logistical support (e.g., transportation and storage of specimens) and laboratory processing.

The Evolution of Biobanking

The importance of biobanking is becoming more evident, especially since the 2003 completion of the sequencing of the human genome (the complete hereditary information contained within the 23 thread-like chromosomes of the human species' DNA). The availability of biological specimens, or *biospecimens*, obtained through biobanking can now help researchers to better understand human disease at the molecular level.

Banked tissues facilitate the comparison between the unique molecular information in a given tissue sample to what is known clinically about the progression of a disease (that information having been garnered from the donor's medical history). In fact, the usefulness of information gleaned from either alone diminishes greatly without the comparative melding of molecular data with clinical outcomes. In short, clinical data without genomic data, and vice versa, can make it difficult "to see the forest for the trees." As an example, the most frequent causes of mortality in the developed world are cardiovascular and cerebrovascular diseases and cancer. The combined power of genomic data and medical outcomes will help combat these and other diseases afflicting the world's populations.

The Next Generation of Biobanking

The next generation of biobanks will help address significant diseases by working to improve the capability to prevent, diagnose, and treat each at a more personalized level. Biobanks of the 21st Century, together with institutions and investigators worldwide who consider the bank an invaluable resource, will work to address critical issues to enable the implementation of personalized and evidence-based medicine.

The biobanking of human tissue samples can assist in identifying and corroborating specific targets for drugs, and in developing newer and more accurate screening tests by exploiting the specific physical traits of DNA, called *biomarkers.* Using these characteristic regions of the genome allows the pinpointing of the mechanisms (how the disease process "works") that both cause a disease and contribute to its progression, the gauging of the likelihood of effectiveness a particular therapeutic has on an individual, and, ultimately, the determination of the best course of treatment for a patient.

These new biobanks will aim to function as **biobanking, biotechnology,** and **bioinformatics** organizations. They will collect, store, analyze, and redistribute biospecimens while preserving the confidentiality of the donor's data. Beyond "traditional" biobanking activities, the biobank of the 21st Century, through integrated, world class research technology, will support basic and clinical research activities by providing the necessary bioinformation, technology platforms, and scientific expertise to advance the knowledge for the prevention, diagnosis and treatment of disease.

This banking of biological specimens has become instrumental in accelerating the new discipline of *personalized medicine*, where treatment no longer follows an "off-the-shelf, one-drug-fits-all" paradigm, but rather utilizes diagnostics and drugs that recognize each person's individual genetic makeup, thus allowing the design of a "custom-fit" treatment regimen attuned specifically to it.

Over time, the worth of the information gathered through such biobanking, biotechnology, and biomedical informatics initiatives increases, as each biospecimen undergoes examination against a specific group of "core technologies."

Biobanks are an essential resource for the new era of disease research grounded in the realm of the molecule. The specimens obtained through the generosity of donors are an absolute necessity in the evolution of new life-saving diagnostic tools and treatments for diseases once believed to be hopelessly intractable. Above all, the research knowledge achieved through the contributions of these new biobanks will help to make possible the foreseeable end to ineffective treatments—or, perhaps, more importantly, to those treatments where the "cure" might do more harm than good.

2. The Integrated Biobank of Luxembourg: A Biobanking, Biotechnology, and Biomedical Informatics Initiative

The promise of personalized medicine and the discoveries of the Human Genome Project have produced an explosion in genomic research; however, the utility of this research is limited without the ability to correlate genomic data with clinical outcomes. A critical step in harnessing the power of this research, and the development of subsequent clinical treatments, will be the comparative melding of molecular data and clinical outcomes.

The Integrated Biobank of Luxembourg (IBBL), a collaborative organization developed by the Grand Duchy of Luxembourg, a number of key stakeholders from the Luxembourg political, economic, healthcare, and research and education sectors, and the Translational Genomics Research Institute (TGen), in Phoenix, Arizona, is attempting to do just this.

The IBBL represents a new generation of biobanking that goes far beyond simple collection of specimens. The IBBL will be an academically-oriented resource that will blend the faculty of Luxembourg (its universities and research institutions) and TGen with key international partners to address the critical issues blocking the implementation of personalized medicine. The IBBL will work to bring personalized and evidence-based medicine to improve healthcare in Luxembourg and beyond. The IBBL will support molecular-based research by amassing an extensive network of expertise in biology and pathology, informatics and information technology infrastructure, laboratory operations, transportation, legal matters, and ethics. Moreover, the IBBL will critically support both disease-based and population-based advanced research studies, bolstering biospecimen availability with clinical data, all coordinated by a world-class informatics capability.

The IBBL will serve as a true resource to foster cooperation between research and clinical investigators with pre-eminent international and Luxembourg scientists, clinicians, research organizations, hospitals, and other biobanks. Using advanced technology platforms to analyze biospecimens and capture relevant information, the IBBL will support the building of a growing and data rich environment. The IBBL will create a comprehensive framework for sharing and comparing research results through a robust, flexible, scalable, and secure bioinformatics system that supports the collection, processing, storage, annotation, and distribution of biospecimens and data using standard operating procedures based on best practices. Critically, the information generated within the IBBL as part of the “core technology” center, will also begin to increase in its utility over time, and with expansion of Luxembourg's clinical research infrastructure.

The IBBL has the promise to become an advanced European hub for biobanking, biotechnology and biomedical informatics services, setting the stage for molecular-oriented therapeutic decisions and the realization of personalized medicine.

Biobanking

The IBBL will develop a centralized human specimen repository that will oversee the acquisition of appropriately consented, standardized and rigorously collected biospecimens, including their transport and preservation. The goal will be to collect a sufficient breadth and depth of samples to support a wide variety of research studies. Top priorities include

recruitment of donors with a wide variety of demographic and genetic backgrounds, with health status on a continuum from healthy to gravely ill.

The IBBL will strive to continuously improve reliability of samples by implementing a common set of standards and harmonization guidelines in sample acquisition, preservation and analysis. The IBBL will also provide outreach and education to collaborating healthcare stakeholders and potential donors.

Biotechnology

The IBBL will house capabilities for molecular analyte production, core genomics technologies (e.g., DNA sequencing and genetic mapping), and will partner with other institutions for more advanced technologies (e.g., proteomics), thus rendering the IBBL a comprehensive biotechnology resource. The IBBL will be a source of high quality molecular analyte extracts of biosamples (DNA, RNA and protein) for investigator initiated studies. The IBBL will develop tissue microarrays for use in validation of molecular markers in clinical samples, discovery of potential diagnostic markers, optimization of screening assays and detection parameters, and analysis of the frequency of molecular alteration in different tissue types. The IBBL will also include powerful cell sorting technology for separation of solid tumor types into distinct cell populations.

The IBBL will primarily focus on mature technologies in the areas of genomics and proteomics (among others). Leading-edge technologies will be housed at Luxembourg-based and international research organizations, allowing the IBBL will support and leverage these advanced research technologies. Applying mature technologies, IBBL will provide molecular analysis and high throughput genomics tools to its customers. Initially, capillary-based DNA sequencing will be available, with a directed plan to introduce next generation sequencing technologies incorporated into standard practice. Gene Expression, and a broad spectrum of array analyses including visualization, statistical analysis, SNP, copy number, and informatics will also be available through the IBBL. High-Throughput SNP Genotyping will provide access to the complete gamut of single nucleotide polymorphism (SNP) genotyping technologies, including whole genome analysis (linkage or association), fine-mapping and candidate gene studies.

Bioinformatics

IBBL will incorporate advanced bioinformatics and computational biology capabilities. This technology provides computational resources, biomedical informatics support, biostatistics and knowledge-based data management systems. The development of faculty and staff in computational biology, linked internationally to colleagues at other research centers in applying state-of-the-art information technology to manage the large amounts and varied types of data is critical to the IBBL's success. Considerable sophistication in efficient data storage, retrieval, and mining and the ability to convert the many different representations of data used in medicine to a common format is required. Analytical staff will help apply strong mathematical models of biology to understand the complex relationships in gene action and failure to act, that start and sustain disease.

Moreover, the IBBL will be underpinned by an advanced information technology system. Each component of the IBBL will require and utilize an information management system to automate its operational processes, link clinical data, track samples and derivatives, and

compile internally or externally-derived data. Furthermore, IBBL will securely acquire data, distributed from its partners, integrate clinical and sample data, and disseminate the integrated data for research. Secure communication is necessary between the information management systems with each IBBL unit to ensure seamless exchange of samples and data using standardized protocols, formats, and vocabularies. An integrated clinical genomics data warehouse, which compiles the complete set of historical data on donors, samples, derivatives, experimental results, research outcomes, and other annotations on related events, enables scientists to perform and accelerate their research with complete and accurate information. Such a system will create an environment that enables scientists to discover and validate rules that map donors' molecular characteristics with targetable biomarkers and drug agents, as well as allowing physicians to gain a better understanding of combining traditional and molecular characterizations of donors when choosing a course of therapy.

Dr Leroy Hood (Institute for Systems Biology) & Dr Rolf Tarrach (University of Luxembourg)
"Develop a center of excellence in systems biology through two ambitious research projects"

Literature:

1. Systems Biology: The 21st Century Science

The biggest challenge for biology and medicine in the 21st century is one of complexity. Biology is now uniquely positioned to resolve the problems of biological complexity with new research strategies (a systems view of biology and medicine), an integrative view of biology (as an informational science), and new technologies, including computational and mathematical tools, for dealing with the ever increasing complexity of biological data. The ability to manage biological complexity will allow us to solve many fundamental problems of humankind from healthcare and nutrition to agriculture, energy, and the environment.

As the name suggests, systems biology is the study of biological systems as a whole. Instead of analyzing individual components of a system—genes or proteins—systems biology analyzes an entire system, such as the immune response, by tracing the connections between genes, proteins, and a system's behavior. Systems biology emerged as the result of the genetics "parts list" (that is, the sequence of the human genome) provided by the Human Genome Project; the ability of the Internet to store and distribute massive amounts of information; the development of cross-disciplinary interactions where biologists work with computer scientists, mathematicians, physicists, and engineers; and the development of new technologies with the potential to transform science.

Traditional biology has focused on identifying individual cells, proteins, and genes and studying their specific functions. As scientists have developed the tools and technologies that allow them to see deeper and deeper into the units of biological information—DNA and its genes and proteins—they have learned that these components almost never work alone. They interact with each other and with other molecules in incredibly complex ways, similar to the networks of computer interactions that constitute the Internet. Systems biology seeks to understand these networks and their interactions. These are the keys to understanding life.

Whereas traditional biology is a science of description and classification, systems biology is an informational science. It is defined and driven by the digital information contained in the genome, the source code of life, which specifies the informational units of life—genes and their proteins. The individual and collective behavior of proteins and other molecules in networks is determined by the interplay of the digital information of the genome and environmental information from outside the genome (or "nature and nurture"). Looking at all of this information together—acquiring it, analyzing it, and modeling its networks—is what we mean when we say we are studying a system.
Studying biological systems at the level of genetic information will allow scientists to develop the knowledge that will ultimately transform our understanding of wellness, health, and disease. Systems biology will have a profound effect on the practice of systems medicine, making it possible not just to react to a disease that is already present but to eventually prevent its onset.

2. Research Projects to be conducted with the University of Luxembourg and the Center for Systems Biology Luxembourg

Overview

The Institute for Systems Biology (ISB) will collaborate with the University of Luxembourg (UL) and the Center for Systems Biology (CSBL, which will be created by ISB and UL in collaboration with CRP Gabriel Lippmann, CRP Henri Tudor, and CRP Santé) to conduct two basic research projects designed to allow greater insight into the identification of disease and to enable more effective treatments:

Project 1: Personal Genome Sequencing and Systems Genetics

This project is designed to pioneer the development of an integrated system of genomic technologies and methodologies that will serve as the foundation for the practice of systems medicine in which the emphasis is on prevention and where patients and physicians have access to technologically advanced and informative scientific knowledge for improved treatment and care.

This project will have a number of key components: 1) the development of a new approach called "systems genetics" that will create new methods for the analysis of the genome and the understanding of the heritability of traits important to health and disease, 2) the development of new methods to determine individual genome sequences inexpensively and completely, and 3) the integration of this sequence information with health characteristics and with data on blood protein markers (Project 2) to understand the role of genetic variations in the diagnosis, treatment, and prevention of disease.

The project will evaluate diverse new sequencing technological approaches and develop and refine the related analytical methods. ISB will apply its genetic and systems biology tools and techniques first to study model organisms such as mice to determine how best to analyze in an innovative and more powerful manner the human genetic data to be obtained. New computational and mathematical tools will be developed to facilitate these large-scale genome analyses.

Project 2: Personal Blood Proteomics, RNA, and Cell Analysis

This project is designed to pioneer the development of integrated systems proteomics technologies and methodologies that will serve as the foundation for systems medicine in order to more precisely analyze patient health as well as more efficiently diagnose disease. ISB has begun to develop the tools to analyze patterns of blood proteins, or "fingerprints", and single-cell characteristics that can report on the physiological state of the body's 50 major organs.

This project will focus on developing the science and technology to use these blood fingerprints to analyze the underlying cellular networks in the body and determine how the network's characteristics relate to types and stages of diseases. Both the analytical techniques and devices to read the fingerprints from a drop of blood will be developed. This will lead to powerful early diagnostic approaches to disease and the ability to monitor the effects (e.g., effective responses or adverse reactions) on individuals undergoing treatment with existing drugs and participating in clinical trials of new drugs.

Integration of the Two Projects

The effective impact of the research efforts depends critically on the computational integration of the data from the two projects. The creation of a shared Computational Analysis Group will be essential to devise the mathematical and software approaches to the difficult and multi-faceted problem of data integration and interpretation. As tasks are undertaken for each project, the advantages gained by one from the other will multiply. For example, it is the systems genetics work described in Project 1 that will in turn enable the understanding and integration of data from Project 2 and enable the long term impact on health and disease from this work.

Integration with Luxembourg

Luxembourg's interests in developing its presence, capabilities, and collaborations in the area of life sciences and health-related industries for the purpose of creating economic growth, health-sciences research growth, and improved health care and scientific education align with those of ISB, and through the two research projects, create an opportunity to establish an enduring strategic partnership for the advancement of mutually held and mutually beneficial longer-term scientific goals, such as:

- Fostering a deeper understanding of the pathobiology of diseases common among the population of Luxembourg, other EU countries, and the United States
- Supporting the development of new diagnostic tools and technologies which will in turn improve the prevention, diagnosis, management, and treatment of illnesses
- Supporting the development of a database and related computational and mathematical approaches to store and analyze the enormous amounts of information to be generated
- Supporting the development of intellectual property which can be commercialized or licensed and the related value captured for the benefit of Luxembourg and ISB to be jointly determined

- Supporting the adoption of new approaches to medicine across the Luxembourg and U.S. health care systems
- Exploring collaborations within Luxembourg at all levels of research (sequencing, information technology, etc.) and related medical applications, to promote and stimulate shared learning for the replication of these approaches in other systems and environments
- Encouraging other research and education-related cooperative activities related to the improvement of the Luxembourg and U.S. research infrastructures.

ISB's and Luxembourg's interests, therefore, share a mutual alignment that provides both parties with the opportunity to work toward creating a long-term strategic partnership for the development of mutually beneficial outcomes. This collaboration will impact the Luxembourg health sciences and technologies capabilities, ISB's own research and technology development agenda, and the quality and progress of biomedical research and health care across the world.

Dr Lee Hartwell (Partnership for Personalized Medicine) & Dr Guy Berchem (CRP Santé)

"Validate biomarkers for lung cancer and simulate economic impact on health care system"

Literature:

1. The Partnership for Personalized Medicine

The Urgent Need

By several measures, health care spending continues to rise at the fastest rate in our history. In 2005, total national health expenditures in the United States rose 6.9 percent—roughly two times the rate of inflation—with total annual spending reaching $2 trillion, or 16 percent of the US Gross Domestic Product (GDP). By 2015, health care spending is expected to reach $4 trillion, or 20 percent of GDP.

Given the significantly greater costs of advanced disease, there is a critical need for diagnostics that will enable the timely and effective implementation of treatment and prevention strategies, and thus contain the health care burden at an individual country and global scale.

Early detection is the most egalitarian form of health intervention, since it supports better health for all citizens at the earliest stage and the lowest cost, unlike expensive therapeutic regimens or interventional technologies that are unaffordable and hence inaccessible to poorer patients.

In addition, a limitation of many current therapies lies in the inability to match patients with appropriate treatments. This results in the broad application of very expensive technologies that benefit only a subset of patients. Significant cost savings could be realized if treatments were administered only to those patients most likely to respond and least likely to experience adverse reactions. Diagnostic tests that reveal those at higher risk for disease permit the selective application of prevention strategies only to those who will benefit, reducing costs and the number of adverse events.

The Promise of Diagnostics

If persons at highest risk for diseases such as heart disease or diabetes can be identified for high intensity prevention, or if diseases such as cancer can be detected at an early highly curable stage, society will realize the benefits of a much healthier population.

The ability to detect and measure biomarkers in blood or tissue samples provides a powerful way to diagnose diseases. Some biomarkers of molecular or physiological processes have already been identified and are currently used in disease management. The vast majority of such biomarkers remain to be discovered.

Diagnostics can enable the selection of more cost-effective therapies through the identification of disease and/or the prediction of treatment response. For example, testing of creatine kinase, myoglobin, and troponin for rapid detection of heart attack in the emergency room yields a 30 percent savings in hospital costs. However, proteins will be much more informative than DNA or RNA as the basis for diagnostic tests and can be applied to a broader spectrum of diseases.

The greater utility of proteins arises from several key features, including:

- Proteins change in response to variations in physiological conditions since they are the agents that mediate physiology. Proteins therefore can reveal the consequences of life-style and environmental exposures for disease risk, in contrast to DNA, which reveals only hereditary disposition.

- A single gene can produce a family of 10 to 100 variant proteins. This variation adds to the amount of information revealed by the spectrum of proteins present in a disease state.

- Proteins from diseased tissue are found in the bloodstream, whereas DNA and RNA molecules must be obtained by biopsy of the diseased tissue itself. The availability of proteins in blood samples allows clinicians to measure specific protein biomarkers in human blood, thereby sampling diseased processes throughout the body by a method that is much less invasive than tissue biopsy.

- Although blood contains an estimated 100,000 different proteins, very few have been validated for disease diagnosis and management.

The most definitive diagnostic tests will remain those based on visualizing the disease within the anatomy of the body. The discovery of new protein diagnostics will empower developments in imaging technologies, including X-rays, nuclear magnetic resonance imaging (MRI), ultrasound, and positron emission tomography (PET).

A New Initiative

A new model that employs a collaborative approach to the development and validation of new diagnostics is desperately needed.

The Partnership for Personalized Medicine is a major health care research initiative that unites contributions from two leading Arizona-based philanthropic organizations: The Virginia G. Piper Charitable Trust ($35 million) and the Flinn Foundation ($10 million) with leadership and research capabilities from Fred Hutchinson Cancer Research Center,

the Translational Genomics Research Institute, and the Biodesign Institute at Arizona State University.

The Partnership will initially unite the efforts and capabilities of TGen and the Biodesign Institute at ASU, without replicating existing resources but rather leveraging them to generate the greatest impact per dollar of initial investment. The Partnership also will link in other Arizona institutions and initiatives, including the Arizona Protoemics Alliance (AzPA) and Arizona's Clinical Translational Science Award (CTSA).

The Partnership is a broad-based effort to develop new, protein-based diagnostic tools to improve human health and reduce health care costs. The Partnership aims to develop, test, and validate personalized diagnostic tools for a wide range of diseases and then obtain approval for clinical use of these tests that would be reimbursed by health care systems. The result of this effort will be an entirely new approach to medicine that offers more accurate assessments of disease risk; better predictions of responses to treatment; and safer, more effective treatments.

The goals of the personalized medicine initiative are several, including developing new medical strategies that will advance the translation of cutting edge research into tangible changes in patient care based on individualized diagnosis, treatment, and prevention. The benefits expected to be generated are improved patient outcomes, reduced long-term health care costs, and avoidance of the costs associated with decreased productivity due to illness and disease. For example, improved diagnostic tools will enable earlier assessment of disease risk and application of preventative measures that will improve human health and avoid much of the suffering and cost associated with disease and disease treatment. Such tools also will improve the sensitivity and specificity of diagnoses, allowing for earlier, more accurate detection of disease. In doing so, these tools will enable patients to avoid the negative health impact and costs that result when diseases go undetected and untreated.

Combining these far-reaching benefits will usher in a new era of individualized therapies that are safer, more effective, and more cost-efficient.

2. Overview of Project Lung Cancer

The Rising Cost of Health Care

The persistent cost escalation associated with medical treatment seriously threatens the viability of today's healthcare systems, limits treatment options, and impedes access to the vast majority who need care. Current data suggests that by 2015, health care spending in the United States will reach $4 trillion, or 20% of GDP and by 2020, spending will double in Organization for Economic Co-operation and Development countries. Luxembourg's health care system ranks among the top G8 in the world, with the government sustaining 90.2% of all costs. As a publicly financed, universal access system, Luxembourg must look to the future on how to sustain support to provide high quality health care to its citizens, while managing health care costs administered via the

Ministry of Social Security's Union of Sickness Fund programs.

The Grand Duchy of Luxembourg, responding to a call for action by the European Council's Lisbon Strategy (developed in 2000), initiated the Luxembourg Health Sciences and Technologies Plan, to transform Luxembourg into a research and technology hub for the EU and beyond. From this arose the concept of the Integrated Biobank of Luxembourg (IBBL), of which Luxembourg Project Lung Cancer will be the first demonstration project.

Luxembourg Project Lung Cancer

Luxembourg Project Lung Cancer provides a unique opportunity to invigorate and revolutionize health care by capitalizing on the efforts of the U.S.-based Partnership for Personalized Medicine (PPM), led by Nobel Laureate Dr. Lee Hartwell. By employing high-throughput genotyping, expression profiling, and proteomics, the PPM plans to develop new molecular diagnostics for health care that Luxembourg's bioscience and medical entities can leverage to accelerate research and transfer knowledge. The proposed initiative begins with the development of specific molecular diagnostic test(s) with a focus on lung cancer, an important public health issue for the Luxembourg population. Depending on the type of diagnostic developed, a successful test may decrease the number of persons diagnosed with advanced stage lung cancer, improve the efficiency and accuracy of diagnosis, increase cure rates, and/or improve surveillance strategies to detect recurrent disease. Luxembourg will engage in this initiative as it moves forward with the country's vision to improved research within its academic community as well as to build and expand its infrastructure to support clinical research that will improve the health of its citizens.

Local and regional clinicians specializing in lung cancer support the value of such an approach as well as the benefit of improving their ability to diagnose risk, provide early detection and to match therapies to specific biomarkers.

Working through the Ministries, the National Laboratory of Health, and the CRP Santé, clinical sites will be identified in Luxembourg where blood and tissue samples can be obtained from patients with lung cancer and individuals at high risk for lung cancer with appropriate informed consent and privacy. Additionally, as Luxembourg moves toward launching its new electronic medical records system, it will be poised to capture patient characteristics and treatment as well as track patient outcomes, creating a solid infrastructure on which to build a patient informatics infrastructure.

We believe this sea change in approach is possible by realigning science to meet the needs of health care. Luxembourg has a unique opportunity to accomplish this vision as it creates and builds its research infrastructure across the country. The promise of personalized medicine to improve health care outcomes and reduce health care costs, however, will not be manifest by the marketplace without the implementation of novel initiatives such as the PPM and Project Lung Cancer.

Project Lung Cancer has identified four objectives that underpin planned activities and

support the anticipated outcomes of our comprehensive efforts:

a) **Risk assessment:** Identifying individuals at greater risk for lung caner, thus enabling implementation of preventive measures that could eliminate suffering and the costs associated with treatment. Identifying high-risk individuals is also essential to initiate cost-effective screening programs for early detection and the potential for behavior modification.

b) **Early detection:** For many diseases, particularly lung cancer, early state diagnosis increases the likelihood of effective treatment and cure. For example, for individuals at higher genetic risk for lung cancer, early detection can lead to a possible cure at a fraction of the cost of ineffective treatments for late-stage disease.

c) **Definitive diagnosis and improved treatments:** The diagnosis of many diseases is challenging due to a lack of distinctive symptoms and the fact that many different diseases can have similar presentation. Improved diagnostics will allow more rapid and effective implementation of appropriate treatments for those who will benefit from them, while preventing adverse side effects and the costs of treatment for those who will not. Additionally, access to information that better describes the lung cancer or its subsets of disease allows physicians to better treat their patients by more precisely matching therapies and, in terms of clinical management, determining those patients who may relapse.

d) **Reduced health care costs:** Overall treatment-related medical care costs should be reduced based on earlier diagnosis and intervention that includes more targeted treatment of specific diseases given the ability to identify lung cancer as well as distinguish different disease types.

A Novel Opportunity to Revolutionize Health Care

Project Lung Cancer establishes a solid foundation that enables Luxembourg patients to live healthier, more productive lives while reducing the overall costs of health care. Additionally the project will yield economic models for use by Luxembourg in other disease areas. Finally the project establishes a true translational research infrastructure that assures the application of important research outcomes into the clinic.