**New Virtual Physiological Human Projects (ICT-2009.5.3)**

**INBIOMEDvision – Promoting and Monitoring Biomedical Informatics in Europe**

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**M**edicine is undergoing a revolution today. Sixty years ago, we barely understood the genetic basis of heredity. Today, we can sequence an entire human genome in six minutes, at a similar cost to an MRI scan (around $1000). Within a few years, the cost of doing so will be no more than a hundred U.S. dollars. Meanwhile, progress in drug development has significantly slowed down. The time spent today from drug discovery to marketing is around 12-15 years; it was 8 years in 1960. Moreover, conventional approaches to drug design are foundering within the pharmaceutical industry, reflected by a very substantial reduction of new products developed over the past decade. Diseases are diagnosed by general clinical representation, while treatments are based on molecularly targeted drugs. Little wonder a large number of candidate drugs fail at various stages of clinical trials, and drugs are only effective in a fraction of patients. Running clinical trials is becoming more costly, with continually increasing levels of complexity and bureaucracy introduced by regulatory bodies. Furthermore, assuming a given “blanket” therapy, which targets some nominal average person, to be optimal to a population group having the same disease, is no longer satisfactory with today’s advanced capabilities in next-generation sequencing and developments in computational biomedicine. All these considerations have paved the way for the emergence of preventive, predictive and personalised medicine, which promises to specifically tailor medication and treatments to a person’s specific genome or metabolism, hence improving the quality of outcomes and reducing the chances of relapse.

While some researchers argue that one’s genetic blueprint holds the answers to future medical conditions, others consider the nonlinear interactions between genes, and between genes and proteins, as equally important. Beyond that, gene expression is strongly dependent on environmental factors, which determine genetic activity as much as genes directly govern phenotype. Other “levels” of biological activity – sub-cellular, cellular, tissue, organ, and higher functions -- may all be crucial in varying degrees, and cannot be seen as simply controlled by the molecular level DNA “blueprint”.

In practice, as a result of tighter funding in the current global economic climate, healthcare priorities are more aligned with delivering frontline patient services that can be quickly and directly mapped into patient outcomes, which are seldom congruent with longer-term requirements supplied by research and its supporting infrastructure in relation to the vision of personalised medicine. The reality is that much of the medical data on patients, held in hospitals is still paper-based. Even when electronic data are available, formats are not standardised, sometimes even within one hospital, let alone between healthcare trusts, districts or countries. The legal ownership of medical data is still an open question, where security, ethical, and privacy concerns are critical as sensitive data on individuals are involved. Various models of data management exist today, centralised, federated and third party provision of compute and storage data cloud services. IT governance remains unclear not only to clinicians but also to researchers who usually pre-suppose that all data will reach them in electronic format.

INBIOMEDvision is a two-year Coordination and Support Action (CSA) project, funded by the European Commission 7th Framework Programme of ICT under the Virtual Physiological Human (VPH) flagship, and aims to address these questions along with various others, through collaborative efforts of a wide range of experts. It was funded as a CSA for VPH because the molecular level is rather largely ignored by much of existing VPH-I activity, which has led to the identification of a gap between basic biomedical research and clinical practice, which INBIOMEDvision aims to bridge and strengthen. We aim to promote Biomedical Informatics (BMI) throughout Europe and beyond, by means of permanent monitoring of the scientific state-of-the-art approaches, methods and existing activities in the area, prospective analysis of the emerging challenges and opportunities, and wide dissemination of knowledge and resources in the field. In INBIOMEDvision, 7 partners from 4 European countries, with complementary expertise in bioinformatics, text and data mining, medical informatics, and computational biomedicine, have dedicated themselves to bridging the gap between the bio- and medical informatics communities. This is being realized by the integrative management and synergic exploitation of wide-ran-
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ging and inter-related information generated and required in healthcare settings, as well as in the biomedical research institutions and health-related industry.

Three invitation-only Think Tanks were organised in June and October 2011, on the “Re-use of Clinical Information in Research” (Figure 1), “Translational Systems Biology and Bioinformatics”, and “Genotype-Phenotype Resources” (Figure 2). The Think Tanks were followed by the preparation of consensus-view strategic reports aimed at the European Commission as well as the wider scientific community. The first Think Tank report stated that a “digital vision” and agenda are needed within Europe, to cover the next five years and beyond. EU member states are urged to commit significant resources to this effort, and to adopt clear and fully aligned legal positions to allow the optimum re-use of data in research and to support clinical decision-making. This would substantially facilitate the digital revolution in healthcare provision that is urgently required. It is important to involve Internet-savvy “expert patients” and their families not only in their own treatment, but to actively contribute to basic biomedical research into their conditions. Areas covered included data, IT security, information governance, and legal issues with regard to clinical data. The second Think Tank report saw potential in sub-cellular (or molecular) systems biology approaches to biomedicine, as compared to conventional methods of drug design. Despite these approaches being at an infant state, and a vast amount of research remains to be done, they may be able to assist in more personalised approaches to drug treatment, for example in the use of multi-target therapy, for finding genotype association to risk of disease and drug response. For translational systems biology to make a major impact, the whole system of data access (including access to medical records) needs to be transformed into one based on more openness and sharing of information between hospitals, academia and industry. Various societal structures currently impede this development. Regulatory and funding agencies must be involved to overcome these obstacles.

The third Think Tank report addressed prospects for the development and application of genotype-phenotype resources and considered these to be very promising. Establishing clear relationships (correlations) between increasing amounts of genotypic information available from clinical studies (e.g. as provided by genome wide association studies (GWAS)), and similarly of phenotype information at the population level, is still largely impossible today. Also, assuming that the genotype controls the phenotype in all cases is unlikely to be correct. Indeed there are rather general grounds for thinking that, making any trivial correlations will always be fraught with difficulty. This could also assist in “stratification” — instead of rejecting so many drugs, it could be that several existing ones will work well for sets of patients on genetic grounds.

Figure 1. Integration of large-scale heterogeneous clinical information (genomics data, X-ray images etc.) and enabling their re-use in research can elucidate management of diseases such as lung disease. (Courtesy of ISCI, Spain).

Figure 2. Linking Genotype to Phenotype Resources. (Courtesy of ISCI, Spain).
Other INBIOMEDvision objectives are to:
- compile the existing knowledge on genotype and phenotype data resources, providing an overview of methods and models that connect biological systems at the molecular level with the clinical physiopathology
- produce periodic state-of-the-art reviews and perform prospective analyses on these themes
- generate a permanently updated and electronically accessible catalogue of initiatives and resources in the field
- consolidate a BMI community of researchers by congregating and promoting the interaction between them (available via our Researcher Directory Tool)
- organise community building activities (Think Tanks, scientific meetings etc.), and (website, newsletter) to develop and carry out activities (INBIOMEDvision Training Challenge) to train new generations of scientists and professionals having a BMI perspective and skills.

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INBIOMEDvision Consortium: University College London [UK], Pompeu Fabra University [Spain], Mar Institute of Medical Research Foundation [Spain], Technical University of Denmark [Denmark], Erasmus University Medical Centre [The Netherlands], Technical University of Madrid [Spain], and Institute of Health Carlos III [Spain].

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Synergy-COPD: Modelling and simulation for systems medicine

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Figure 1. Understanding schema of systems function.

The Synergy-COPD project is developing a clinical decision-support system (CDSS) and a simulation environment aiming at enabling the deployment of systems medicine. The project focuses on patients with chronic obstructive pulmonary disease (COPD), which is a major public health problem and a complex, heterogeneous and multi-component disease.

The Synergy-COPD project began in February 2011 and ends 31 January, 2014. The project consortium is led by Barcelona Digital Technology Centre of Spain, a European leader in health informatics. The consortium includes four universities (Karolinska Institutet, University of Oxford, University of Birmingham, and Technical University of Budapest) and one research institute (Consorci Institut d’Investigacions Biomèdiques August Pi i Sunyer), each with very strong clinical links. As well as these academic partners, the consortium includes three SMEs (Biomax Informatics AG, Linkcare Health Services SL, and Infermed Ltd.), ensuring the necessary clinical inputs and the industrial backing to move the final results forward into prototypes and industrial deployment.

In the current framework, in which a change of focus from acute care to integrated and continuous care is under way, primary-care clinicians (or general practitioners, GPs) take a greater part of the responsibility in treating complex chronic diseases. As new evidence becomes available and new assessment techniques are introduced, best practices are revised, new treatments become available, and the rules for treating a disease are updated. And GPs face a harder time on being up to date with new research developments in many diseases.

Synergy-COPD CDSS assists GPs and non-specialist clinical staff in the diagnosis, assessment and management of COPD, and delivers up to date support. In particular, Synergy-COPD CDSS will have the following features: