Structuring European Biomedical Informatics to Support Individualised Health Care (INFOBIOMED) – Results achieved after 2 years of the project lifetime

Eich HP[1], Wenzel M[1], Diaz C[2], Sanz F[2] and the INFOBIOMED Consortium
[1]*Coordination Centre for Clinical Trials, Heinrich-Heine-University Düsseldorf, Germany*
[2]*Biomedical Informatics Research Group, Municipal Institute of Medical Research – IMIM, Barcelona, Spain*
eich@uni-duesseldorf.de

Introduction Biomedical Informatics (BMI) is the emerging discipline that aims to facilitate integration of Bioinformatics (BI) and Medical Informatics for the purpose of accelerating discovery and the generation of novel diagnostic and therapeutic modalities. The European-funded INFOBIOMED Network of Excellence (NoE) has been constituted with the main objective of setting a structure for collaborative approach at a European level. Initially formed by fifteen European organisations, the main objective of the INFOBIOMED network is therefore to enable the reinforcement of European BMI at the forefront of these emergent interdisciplinary fields [1,2]. This abstract summarizes the results achieved within the last 2 years of the projects lifetime.

Material and Methods The network has been structured by activities covering all the significant aspects that are relevant to both MI and BI and that have the potential to provide a space for synergy between them. These aspects are included in two separate blocks of activities, one for data interoperability and management, and the other for methods, technologies and tools. All the knowledge gathered in the framework of these 'horizontal' activities will be tested into four 'vertical' pilot applications that aim to cover the whole range of information levels from molecule to population.

On the other hand, a set of complementary activities are included for promoting integration of the research carried out in the fields of reference. These activities aim at spreading the excellence and attracting external researchers to the common space created by the network, reinforcing the BI field by creating and improving the European research capacity in the field, and providing platforms for a virtual collaborative environment. They encompass dissemination and communication activities and training and mobility programmes. Finally, the coordination and management of all of these activities is represented by separate tasks, which include assessment of progress and impact of the network according to its integrative objective.

Results As part of the horizontal activities mentioned above, reports have been assembled, which are a collaborative effort between all INFOBIOMED NoE partners towards a comprehensive review of the state-of-the-art in BMI research as related to "technologies, methods and tools" and to "data interoperability and management". Both reports are available for the public via the INFOBIOMED web site [3]. Beside this work, the horizontal activities give input to the development of the pilot applications. First demonstrators could already been build. The finalisation of the pilot applications is expected for mid to end of this year. An evaluation will follow beginning next year.

Pharma Informatics (pilot application 1) carries out research on the impact of BMI and pharmaceutical research. Research in this area focuses on establishing an information continuum pathology – pathway – target – ligand. This pilot is based in two case studies: 1.) The Complex Regional Pain Syndrome (CRPS) addresses the direction from pathology to ligand: a) from pathology to pathway all known pathways have been identified through literature data mining; b) from pathway to target commercial tools are in use (Collexis©, PathwayAssist™) to investigated both obvious and non-obvious interactions; c) from target to ligands / approved drugs compound / ligand databases are in use to identify approved drugs or ligands that are active against members of the associated or expanded pathway; d) the original population database is verified finally, if the found approved drugs are being used, what their indications are, whether it is possible to use them in CRPS or whether patients on these drugs have an altered incidence of CRPS. 2.) The Nuclear Hormone Receptors (NHR) addresses the direction from ligand to pathology: a) from ligand to target, relevant ligands and privileged structures are identified. Compound and structure data bases utilize this step. Presently, a literature database of pharmacological activities is in use; b) from target to ligand PathwayAssist™ is used to identify all pathways related to the targets and Collexis© to differentiate or expand them; c) from pathway / target to genetic variation and adverse events individual members of the identified pathway are linked to specific phenotypic information, i.e. genetic variants and deficiencies.

Genomics and Microbiology (pilot application 2): The work is focused on the study of host and pathogen genetic polymorphisms, protein interactions and transcriptional/translational control and how these impact on pathogen virulence and host immune responses to infection. To date in excess of 2000 viral and microbial genomes have been sequenced and genetic variation at the single nucleotide level of our genome is fast approaching eight figures. Comparative and functional genomic approaches combined with proteomic strategies are further helping to describe gene/protein interaction pathways. These recent advances are dependent on the use and development of novel bioinformatics tools. In medicine, the quantitative modelling of viral dynamics in patients treated with multi-drug regimes are gaining increasing effectiveness in treatment management. The determination of viral sequence variation for assessing escape mutants from therapeutic agents in individuals is fast becoming standard practice for instance in HIV infected patients. These advances require essential tools and new algorithm development in medical informatics. Fundamental to the biology and virulence of an infection is a clear understanding of the host-pathogen interactions at the systemic and cellular levels and which opens new challenges and opportunities for advancing anti-infective therapies. These challenges and opportunities will require biomedical informatics approaches. The general activities in this pilot are aimed at using pathway biology (of the interferon system) as a central hub for integrating bioinformatics and medical informatics. Two distinct clinical relevant pathogens, HIV and Cytomegalovirus, are used as exemplars in the pilot. Here, it will be necessary to further characterize a) the viral genome, load and dynamics at a given stage of disease and b) assess the host's genotype, e. g. polymorphisms in key genes defining the hosts innate resistance to viral infection and proliferation and those determining the efficacy of therapeutic drugs (and their combinations) in clinical use. Taking in account the higher complexity of the human genome, in this application the NoE concentrates on the interferon pathway, combining host and virus genotype data with clinical data in order to find new markers of host immunity and viral therapy resistance.

Genomics and chronic inflammation (pilot application 3): This pilot aims at investigating the complex susceptibility to adult periodontitis. About 10% of the adult population will develop severe forms of destructive, chronic periodontal disease (chronic periodontitis). This complex inflammatory disease is precipitated in susceptible subjects by infection of the periodontium (tooth supporting tissue) by Gram-negative, anaerobic, mostly commensal oral microorganisms. Moreover, the environmental factor smoking contributes importantly to disease severity. Modifying disease genes determine the susceptibility of periodontitis. However, still very little is known about the interplay and relative importance of genetic factors, bacterial pathogens and environmental determinants, like smoking and stress. There is a great need to gain more insight in the complexity of periodontitis, to design new treatment strategies and devise preventive measures. Periodontitis is an excellent model to study complex chronic inflammatory diseases because of its multifactorial etiology (genetics, bacteria, and environment), relative high prevalence and broad and easy access to diseased patients' and normal tissues, genomic DNA, and access to the history of infections and other relevant data through patient records. The aim of this pilot application is to build a periodontitis data warehouse based on patient information coming from different sources: genetics, infection, environment, intermediate phenotype and disease phenotype. This data warehouse will be explored by data analysis and data mining tools from the various partners.

Genomics and colon cancer (pilot application 4): This pilot targets at accumulating knowledge useful for the planning and organization of screening in families with a high-risk of developing colon cancer and supporting research on the subject. HNPCC (Hereditary Non Polyposis Colon Cancer) is a dominantly inherited colorectal cancer syndrome, with a lifetime risk up to 90% of developing colorectal cancer (CRC) for carriers of the genes. Furthermore there is an increased risk of developing endometrial cancer or cancers in the urinary tract. In this pilot application a general IT-infrastructure based on open XML standards for communication is build-up, to link different kinds of medical departments working together in an HNPCC register. These standards meet specific HNPCC needs (e.g. transmission of pedigrees including geno-phenotype), the needs of related fields (e.g. other onco-genetic diseases) and should be usable in several different countries. Existing international standards build a basis (e.g. HL7) for this purpose. In a proof of concept, the IT-infrastructure of the Danish HNPCC register is transformed from mainly isolated databases with paper-based communication amongst them to linked and interoperable databases with XML communication.

Training and mobility programmes have been developed and already installed. These programmes cover exchange of students between the single NoE

partners, special training courses called “training challenges” (up to 10 students) and an eHealth Summer schools together with two other NoE with up to 100 students in July this year.
Also available on the web site are an INFOBIOMED course database and an Biomedical Informatics Gateway with relevant upcoming conferences in this field.
Discussion Following an initiative of the European Commission, INFOBIOMED offers an innovative networking approach that intends to exploit synergies of established scientific disciplines for the empowerment of an emerging one. This structuring effort seeks to deploy the promised benefits of the genomic revolution to society by combining the expertise and experience acquired through the, up to now, independent development of both BI and MI. Past and present integration initiatives in that respect suffer from an excessive isolation or only address the problem partially; INFOBIOMED represents the global integrative vision and joint effort required to overcome the obstacles that are delaying the development of true genomic medicine.
Acknowledgements The INFOBIOMED Network of Excellence is funded by the European Commission within its FP6 Programme, under the thematic area “Information Society Technologies”, contract number 507585.

Literature

[1] Eich HP, de la Calle G, Diaz C, Boyer S, Pena AS, Loos BG, Ghazal P, Bernstein I. Practical Approaches to the Development of Biomedical Informatics: the INFOBIOMED Network of Excellence. Stud Health Technol Inform. 2005; 116: 39-44.
[2] Sanz F, Diaz C, Martin-Sanchez F, Maojo V. Structuring European biomedical informatics to support individualized healthcare: current issues and future trends. Medinfo. 2004; 11(Pt 2): 803-7.
[3] www.infobiomed.org / www.infobiomed.net