HYPERGENES
European Network for Genetic-Epidemiological Studies

softeco sismat information technology

Building a method to dissect complex genetic traits using essential hypertension as a disease model

HYPERGENES

Programme: HEALTH

Start date: February 2008

Coordinator: Università di Milano (IT)

Partners:
Katholieke Universiteit Leuven (BE)
Jagiellonian University Medical College (PL)
IBM Israel (IL)
IMS Istituto di Management Sanitario S.r.l. (IT)
Siberian Branch of Russian Academy of Medical Sciences (RUS)
INSERM (FR)
University of Warwick (GB)
University of Sassari (IT)
STMICROELECTRONICS SRL (IT)
University of Lausanne (CH)
Pharnext S.A.S. (FR)
Softeco Sismat S.p.A. (IT)
Shanghai Institute of Hypertension (CN)
Prague Charles University (CZ)
University of Padova (IT)
Medical University of Gdansk (PL)

Keywords:
gene, genetics, genetic traits, essential hypertension, genome, disease model, genotyping, sequencing, expression

COOPERATION

www.hypergenes.eu

www.research.softeco.it/hypergenes.aspx

Contacts

Enrico Morten
Phone: +39 10 6026 328
Fax: +39 010 6026 350
Email: enrico.morten@softeco.it

Stefano Bianchi
Phone: +39 010 6026 368
Fax: +39 010 6026 350
Email: stefano.bianchi@softeco.it

OVERVIEW

Most of the common-complex, chronic diseases, that have a high prevalence in our populations, arise through interaction between genetic, environmental and life-style factors. To understand the composite origin of these diseases, we need first to know the path from genotype to phenotype. A complex trait is phenotypically and genetically heterogeneous and thus requires a global genomic approach to understand its etiology and pathogenesis. Such a global approach has not been feasible until recently. So far, all experimental investigations dealt with "single" pieces (e.g., genes) of the whole pattern: however relevant the findings, we still lack a broader and comprehensive view of a complex disease per se.

To define a comprehensive genetic epidemiological model of complex traits, we propose to apply new, but already well-established technologies of high throughput genotyping, analyzed with sophisticated statistical-mathematical modelling, to already existing cohorts of subjects with essential hypertension (EH) and intermediate phenotypes of hypertension dependent/associated Target Organ Damages (TOD).

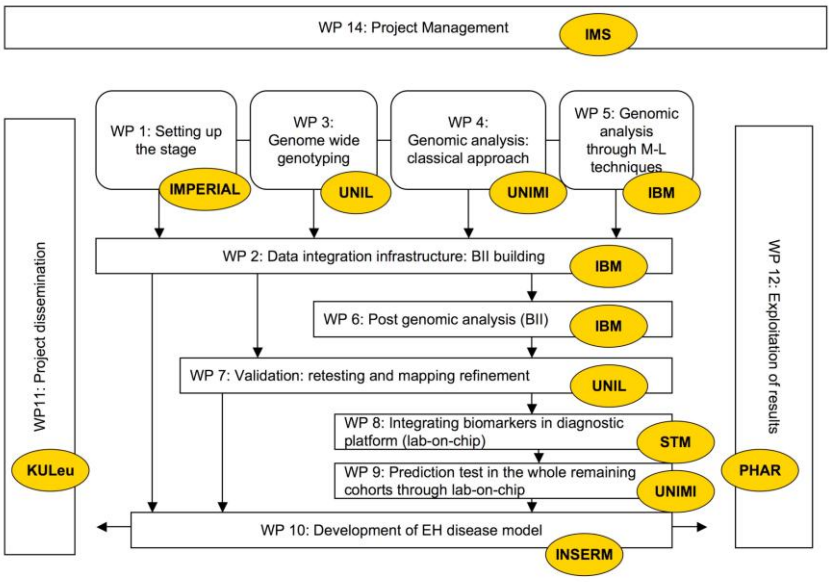
The aim of our integrated approach is to develop an exhaustive model to disentangle the genetic bases of a complex disease using population genetic epidemiology as a methodological tool. We have chosen EH as the disease model, both because of our long-term experience in investigating the genetics of EH and because the cardiovascular complications remain the major cause of death in the EU. Its impact in term of cost and disability are a devastating burden for patients, for their relatives and for the human potential of the EU. Designing a comprehensive genetic epidemiological model of complex traits will also help us to translate genetic findings into improved diagnostic accuracy and new strategies for early detection, prevention and eventually personalised treatment of a complex trait.

OBJECTIVES

- **Find genes responsible for EH and TOD, using a whole genome association/entropy-based approach**
- **Develop an integrated disease model, taking the environment into account, using an advanced bioinformatics approach**
- **Test the predictive ability of the model to identify individuals at risk.**

More specifically, Hypergenes' activities are meant:

- to identify the common genetic variants (e.g. SNPs, haplotypes) relevant for the pathogenesis of EH and EH-associated TODs in a case-control study of 4.000 subjects recruited from historical European cohorts, using whole genome association techniques;
- to design and implement a set of computational tools to support the deployment of the knowledge management needed to support the analysis and data mining related to the genetic, clinical and environment data across different populations;
- to develop a comprehensive Biomedical Information Infrastructure (BII) to store molecular, clinical, and environmental data that will help to build a comprehensive model of disease;
- to develop new methods, new protocols and new standards for genomic association analysis and related issues (power, replication, stratification), gene annotation and molecular pathways;
- to develop and test a set of specialised Decision Support Systems (DSS) tools combining multiple relevant information sources (genetic, clinical and environmental);
- to create a "Web-Based Portal" hosting the BII to allow knowledge dissemination;
- to develop a simple, inexpensive genetic diagnostic chip to be validated in the cohorts considered;
- to strengthen the existing clinician-basic scientist collaborative network on the genetic mechanisms of EH.
- to generate educational tools to support professional training on genetics and genomics of complex traits, favouring mobility of PhD students, post-docs as well as joint PhD programs on two sites.
- to implement successful dissemination actions through participation in scientific meetings, in teaching tutorial sessions, encouraging publication of project results in high-impact scientific journals and providing an interactive and scalable feedback mechanism serving the research community.



Softeco Sismat provides the Hypergenes Consortium with its renown expertise in data analysis and semantic aggregation, supporting IBM in the task of homogenizing the phenotypic information gathered from the cohorts considered for the discovery and validation phases (WP2 Data Integration Infrastructure) and providing the foundation for data analysis and correlation.

Softeco Sismat also operates the official project website www.hypergenes.eu.