



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

PROJECT SUMMARY

The project is focused on the definition of a comprehensive genetic epidemiological model of complex traits like Essential Hypertension (EH) and intermediate phenotypes of hypertension dependent/associated Target Organ Damages (TOD).

To identify the common genetic variants relevant for the pathogenesis of EH and TODs, we will perform a Whole Genome Association (WGA) study of 4.000 subjects recruited from historical well-characterized European cohorts.

Genotyping will be done with the Illumina Human 1M BeadChip.

Well-established multi-variate techniques and innovative genomic analyses through machine learning techniques will be used for the WGA investigations. Using machine learning approach we aim at developing a disease model of EH integrating the available information on EH and TOD with relevant validated pathways and genetic/environmental information to mimic the clinician's recognition pattern of EH/TOD and their causes in an individual patient.

Our statistical design is with two samples run in parallel, each with 1,000 cases and 1,000 controls, followed by a replication/joint analysis. This design is more powerful than replication alone and allows also a formal testing of the potential heterogeneity of findings compared to a single step (one large sample) design.

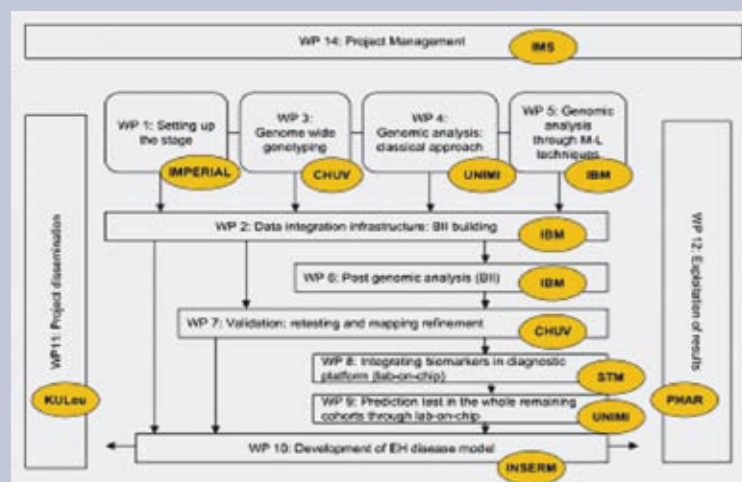
The results represent the source to build a customized and inexpensive genetic diagnostic chip that can be validated in our existing cohorts (n=12,000 subjects).

HYPERGENES is in the unique position to propose a ground-breaking project, improving the methodology of genetic epidemiology of chronic complex diseases that have a high prevalence among EU populations. 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 personalized treatment of a complex trait.

The ultimate goal will be to promote the quality of life of EU populations.

SCIENTIFIC AND TECHNOLOGICAL OBJECTIVES

- ▶ To identify the common genetic variants relevant for EH and TOD.
- ▶ To design and implement appropriate computational tools.
- ▶ To develop a comprehensive Biomedical Information Infrastructure (BII).
- ▶ To create a "Web-Based Portal" to allow access to the BII in order to allow dissemination of knowledge.
- ▶ To develop new methods, protocols and standards for genomic association analysis, gene annotation and molecular pathways.
- ▶ To develop a set of Decision Support Systems tools combining genetic, clinical and environmental information.
- ▶ To develop a simple, inexpensive genetic diagnostic chip, that can be validated in our existing well-characterized cohorts.
- ▶ To strengthen the existing clinician-basic scientist collaborative network on the genetic mechanisms of EH.
- ▶ To generate educational tools to support professional training on all aspects of the project, favoring mobility of PhD students and post-docs.
- ▶ To disseminate HYPERGENES achievements through scientific meetings, teaching in tutorial sessions, publication in high-impact scientific journals etc.
- ▶ To exploit the results in a traslational scenario



HYPERGENES CONSORTIUM



HYPERGENES TIMING

HYPERGENES planned duration is 42 months.

The Project started on 1 January 2008.

The Project is structured in three steps:

STEP 1: DISCOVERY (from month 1 to month 27)

STEP 2: VALIDATION (from month 18 to month 39)

STEP 3: DISSEMINATION AND RESULT

EXPLOITATION (from month 1 to month 42)

PARTNERS

- ▶ UNIVERSITA' DEGLI STUDI DI MILANO, Milano, Italy - Project Coordinator
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- ▶ THE JAGIELLONIAN UNIVERSITY MEDICAL COLLEGE, Krakow, Poland
- ▶ IBM ISRAEL - SCIENCE AND TECHNOLOGY LTD, Haifa, Israel
- ▶ REFORM E.C., DRUZBA ZA MEDNARODNO TRGOVINO, D.O.O., Nova Gorica, Slovenia
- ▶ I.M.S. - ISTITUTO DI MANAGEMENT SANITARIO SRL, Milano, Italy
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- ▶ INSERM - INSTITUT NATIONAL DE LA SANTE' ET DE LA RECHERCHE MEDICALE, Paris, France
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- ▶ CHARLES UNIVERSITY IN PRAGUE, Prague, Czech Republic
- ▶ UNIVERSITA' DEGLI STUDI DI PADOVA, Padova, Italy
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