MSc in Bioinformatics for Health Sciences

GPA. Applied Genomics: Genome-Phenome Analysis in Human Health

Syllabus Information

Academic Course: 2018/19

Academic Center: 804 - Official Postgraduate Programme in Biomedicine

Study: 8045 – Bioinformatics for Health Sciences - MSc

Subject: 32036 – GPA. Applied Genomics: Genome-Phenome Analysis in Human Health

Credits: 5.0

Course: 1st

Teaching languages: English

Teachers: Abel González-Pérez, Marina Brasó, Francesc Calafell, Ferran Casals and Arcadi Navarro

Teaching Period: 3rd term

Presentation

This subject focuses on the conceptual underpinnings and the bioinformatics tools that are used to learn about the genetic architecture of human interindividual phenotypic differences. The course, in short, is about linking genotypes and phenotypes. Obviously, the most relevant such differences are those relating to disease, such as the presence/absence of a certain condition or differential responses to treatments. However, other complex traits are also covered in the course. An emphasis is made on novel methods used to ascertain the causal genetic variants associated with complex diseases, which are currently being applied to study many diseases of great relevance for public health. Recent studies are used as illustrative examples.

Associated skills

General:

Instrumental:

1. Proficient reading/writing/listening scientific English related to the subject.
2. Knowledge of software to do quality scientific presentations and reports related to the subject.
3. Elements of Statistics: concepts of association, correlation, and interaction.
4. Elements of Genomics: genes, alleles, genetic variants, markers, phenotypes, expression, complex traits, genomes, exomes, causal variants, heritability

Interpersonal:

1. Group work.
2. Ability to solve by yourself a given problem.

Systemic:

1. Analysis and synthesis abilities.
2. Ability to search and manage information from different sources

Specific competences:

1. To understand the complex nature of the factors generating phenotypes.
2. To understand the concept of heritability.
3. To become familiar with the different forms of human genome variation.
4. To understand the concept of Mendelian Disease.
5. To understand the concepts of Complex Trait and Complex Disease.
6. To understand the genealogical and correlational structure of human genome variability.
7. To master the basics of Linkage Disequilibrium measures and testing.
8. To master the concept of genotype and haplotype.
9. To understand the concept of Linkage Mapping
10. To understand and apply the concept of Association Test.
11. To master different allele-disease association measures.
12. To understand what interactions are and how they can be tested
13. Ability to use extant genetic epidemiology software.
14. To understand the concept of multiple testing problems.
15. To master different methods to correct for multiple testing.
16. To get the essentials of Genome Wide Association studies
17. To master information retrieval from disease-related public databases.
18. To understand and use basic variant calling techniques
19. To understand how new technologies of sequencing have revolutionized the field
20. To understand the new challenges and limitations of high-throughput sequencing technologies

Prerequisites

Basic knowledge on genetics and molecular biology

Basic knowledge of statistics (the BDA subject in this MSc is a good starting point)

Contents

Contents Section1: Overview of Health, Disease and Genomics.

Concepts:

Health and disease. Diseases as phenotypes. Disease types: the Mendelian to complex spectrum.

Variation in the human genome. Types of variation. Dynamics of variation. Sequencing and Genotyping techniques. Copy number variation and disease.

Linkage disequilibrium: the genealogical basis of association between Disease Susceptibility Loci and Genetic Markers.

Quantitative trait loci (QTLs). Heritability concept.

The common variant/common disease paradigm.

Procedures:

To be able to obtain information from disease databases.

To be able to obtain information from variation databases.

To be able to compute linkage disequilibrium between markers. To be able to infer haplotypes from genotypes.

To be able to use the basic concepts of heritability to get a basic estimation of the contributions of genetic and environmental factors to a given trait.

To understand the diversity of possible genetic architectures of human traits.

Contents section 2: Family-based methods for disease mapping.

Concepts:

Family studies, adoption studies, twins.

Linkage analysis. Definition. Types. Properties.

The Transmission-Disequilibrium test and the Family Based Association Tests.

Procedures:

To be familiar with family-based inference.

To be familiar with basic linkage-mapping calculations.

To be familiar with basic TDTs.

Contents section 3: Methods and tools for disease gene mapping.

Concepts:

Association studies. From single polymorphisms in candidate genes to Genome-Wide Association Studies.

Population genomics. The 1kGP, WTCCC, Biobanking, dbGaP, EGA and other large-scale public initiatives.

2nd Generation Sequencing. Exomes and Full Genomes.

Functional annotation of genetic variants.

Functional interpretation of results.

Procedures:

To be able to perform different association tests.

To master information retrieval from disease-related public sources.

To be able to develop functional interpretations of gene mapping studies and to suggest further research avenues.

Contents section 4: Technical and computational challenges.

Concepts:

Shortcomings and challenges of large-scale association studies. Replications.

Multiple testing.

Interactions.

Study design.

Procedures:

To become aware of the importance of replication.

To be able to understand and implement different strategies for multiple test correction.

To understand the concept of interaction and to be able to deploy different strategies to detect interactions.

Being able to get a synthesis of the different methodologies for genotype-phenotype studies in a critical way.

Contents section 5: Examples of the Genomics of complex diseases.

Concepts:

Examples on the genetics of normal variation: skin color, eye color, personality traits.

Recent studies on the genetics of diseases.

Pharmacogenetics.

Procedures:

To be able to critically assess extant research on the genetic architecture of complex diseases.

To be able to pinpoint specific drawbacks related to different computational methodologies.

Teaching methods

Approach and general organization of the subject

The course has 5 ECTS credits, comprising 15/20 hours of plenary lectures, 8/10 hours of exercises and hands-on computer classes, 5-7 hours of students' presentations in seminars, 13/18 hours of reading and personal study, and 2 hours performing tests

The subject is based on the understanding of key methodological concepts and tools and on the application of common software found in the genetic epidemiology and statistical genomics labs around the world. As this is a completely incremental subject, the student is advised of the need of strong interaction with the lecturers and of

keeping the class material up to date. Thus, the methods used are strongly based on the good understanding of basic principles of computer programming and statistics.

The course includes classical lectures and hands-on exercises. Please, bring your own laptop for the hands-on sessions

Training activities

The subject focuses on practical implementation of different types of tools for simple genotype-phenotype studies. Exercises and tutorials are distributed previous to the corresponding sessions.

Hands-on exercises are based on the use of publicly available resources and software packages, so individual development beyond what is covered in the course can be easily achieved by the students.

Each student will present a short seminar of 20-40 mins on a scientific article of relevance for the field.

Evaluation

Assessment system

The competences that need to be achieved in the course will be evaluated by means of written and oral presentations during the course, and an exam at the end of term.

Grading system

Grades are between 0 and 10 and an overall 5 is needed to pass. The weight that is given to the presentations and the exam depends on the performance of the whole group.

A minimum of 4.0/10 in the final exam is needed to pass.

Bibliography and Information Resources

There is no text-book bibliography as such, but a wide selection of papers will be distributed during the course.

Also, these books are available in the library.

Evolution in health and disease / edited by Stephen C. Stearns and Jacob C. Koella

The Genetic basis of common diseases / edited by Richard A. King, Jerome I. Rotter, Arno G. Motulsky

Genetics and analysis of quantitative traits / Michael Lynch, Bruce Walsh

Handbook of medical informatics / J.H. van Bemmel, M.A. Musen, editors ; J.C. Helder, managing editor

Handbook of statistical genetics / editors, D.J. Balding, M. Bishop, C. Cannings

Human genome epidemiology : a scientific foundation for using genetic information to improve health and prevent disease / edited by Muin J. Khoury, Julian Little, Wylie Burke

Statistical methods in genetic epidemiology / Duncan C. Thomas