INTER UNIVERSITY COURSE MEDICAL GENETICS

(Based on book *"Genetics in Medicine"* by Thompson and Thompson. Eight edition)

DAY 1 : , KULeuven

9:30-11:00 ***The human genome and the chromosomal basis of heredity***

Basic concepts

Introduction: The chromosome
The 3D nucleus
Mitosis
Meiosis

The human genome: gene structure and function

Gene structure and function
Gene regulation and activity

16:30-17:30 ***Tools of human molecular genetics***

Mutational analysis
Sequencing
Molecular cytogenetics tools
Bioinformatic tools: Human genome browsers & its applications to clinical genetics

DAY 2 : ULB

9:30-11:00 ***Patterns of single gene inheritance***

Monofactorial genetic diseases. Penetrance, expressivity. Dominant, recessive, and X-linked inheritance, and why these models are approximations. Incidence and prevalence. Pseudoautosomal inheritance. Lyonisation (partly). Mitochondrial inheritance (partly). Anticipation. New mutations. Germ-line and soma. Somatic mosaics, germ-line mosaics. Pedigrees. Intrafamilial and interfamilial variation. Genetic background.

Consanguinity, chances of homozygosity by descent. Consanguinity as common traditional practice. Inbred communities. Pseudodominance. Founder effect, overdominance. Uniparental disomy.

Genetic variation in individuals and populations: mutation and polymorphism

The life and death of a highly penetrant mutation (hemophilia). Wild type alleles, mutated alleles. The concept of neutral polymorphisms and minor mutations. Blood groups as an example of polymorphism. SNPs. CNVs. Hardy-Weinberg equilibrium, and factors that disturb it. Metapopulation. Mutations and diversity by change. Meiosis and diversity by assembly. Biological fitness. Positive and negative selection. Divergence and diversity.

The history of DF508. Most recent common ancestors. Coalescence. A schematic overview of the ascent of man. Gene tree, species tree. Trans-species polymorphisms. The "common disease, common variant" hypothesis. Haplotype blocks. HapMap. Effective population size. The special case of the Y chromosome.
Incidental findings.

Epigenetics

1. Chromatin structure

1.a. Notions of chromatin structure.
1.b. Post-translational modifications of histones
1.c. DNA methylation: definition
1.d. Biological significations of epigenetics

2. Epigenetics : mechanistic insights

2.a. Crosstalks between histones modifications et DNA methylation: the histone code hypothesis
2.b. Targeting and regulation of DNA methylation

3. Epigenetics and human diseases

3.a. DNA methylation and cancer
3.b. DNA methylation and neurodevelopmental syndromes (Rett and ICF)
3.c. Deacetylase and DNA methyltransferases inhibitors as anti-cancer epigenetic drugs

Last session = 16:30-17:30

DAY 3: , Ugent

Human gene mapping and disease gene identification

Mapping of human genes: principles and applications

Practical exercises with lod score calculations

The molecular, biochemical and cellular basis of genetic disease

General introduction

Examples of monogenic diseases caused by mutations in different classes of proteins:

Inborn errors of metabolism

Mutations in developmental genes

Mutations in extracellular matrix proteins

Mutations in signaling pathways

DAY 4: IPG

Clinical cytogenetics: disorders of the autosomes and the sex chromosomes

Sex chromosomes and their abnormalities:

Cytogenetics and molecular cytogenetics of X and Y chromosomes
Molecular diagnosis of X and Y chromosomes

The treatment of genetic disease

The treatment of genetic disease (

DAY 5: UCL

9:30-17:30

GENETIC ASPECTS OF DEVELOPMENT

Introduction:
- Birth defects: approach to syndromology
- Vascular anomalies
- Cleft lip and palate

GENETICS OF CANCER

Introduction to Cancer
- Introduction to Oncogenesis

Hereditary cancers :
- Breast and ovarian cancer
- Colon cancer

Acquired cancers
- Introduction to somatic mutations
- Hematological malignancies

DAY 6: UA

Genetics of common disorders with complex inheritance

Elementary concepts of multifactorial diseases

Concepts in complex genetics: from Fisher to GWAS

Beyond GWAS

Osteoporosis as paradigm for studies into complex diseases

Of mice and human genetics

Web resources and datamining in genetics

DAY 7: ULg

Pharmacogenetics and pharmacogenomics

Pharmacogenetics

course will be based on 2 updated papers :

Inheritance and Drug Response by Richard Weinshilboum. New England Journal of Medicine, 2003.

Pharmacogenomics - Drug Disposition, Drug Targets, and Side Effects by WE. Evans, and HL. McLeod, New England Journal of Medicine, 2003.

- metabolic enzymes and polymorphisms.
- Polymorphisms and drug transporters and targets.
- Genetic conditions generating unexpected side effects.
- Ethnic differences and clinical consequences.

Birth defects

Clinical aspects and nosography

Illustration of genotype-phenotype relationships and a way from the birth defects to pathophysiologic mechanisms

1 - helicase-deficient syndromes

2 - example of two dermatological conditions : lipodystrophies and cutis laxa syndromes

The immune system

Immune genetics

The HLA complex .

inherited immune defects.

Gene therapy in relation with immune defect.

acquired alterations of IGH and TCR loci in lymphoproliferative disorders.

DAY 8: VUB

Prenatal diagnosis

Non-invasive testing

- Ultrasound
- Biochemistry

Invasive testing

- Indications
- Methods
- Laboratory investigations
  - Cytogenetics
  - DNA
  - Biochemistry

Preimplantation genetic diagnosis

Genetic counseling and risk assessment

Indications for genetic counselling

Genetic counselling providers

Determining recurrence risks
- Mendelian conditions
- Conditional probability
- Empirical recurrence risks

Molecular tools in determining recurrence risks

Managing the risk of recurrence in families

ADDITONAL WORK

Students must contact the Program Organizing Committee (POC) member at the institution where they registered. Each student must produce a personal work on a genetic subject, under the supervision of a member of the Teaching College from his registration center. The contents should be equivalent to a publication in a peer-reviewed scientific journal as first author, or to a thorough review of a genetic topic presented to an interdisciplinary seminar. The additional must produce a written report. The additional work amounts to 2 ECTS.