ENCLOSURE N° 1

INTERUNIVERSITY CERTIFICATE OF HUMAN GENETICS

Continuing Education with University Certificate in Human Genetics

Rationale

Human genetics is a relatively young medical discipline which originated in the sixties with the demonstration of chromosomal anomalies in constitutional and acquired disorders. The discipline experienced a rapid growth with the development of DNA analytical methods which enabled the identification of several genetic, mainly monogenic, disorders. At present, human genetics experiences another growth spurt due to the development of genome-wide analysis tools, high capacity mutation detection methods leading towards complete human genome sequencing. This evolution leads to an ever increasing relevance within all medical disciplines. The current technologies not only enable to identify inherited Mendelian disorders, but also increase our understanding of complex diseases. Human genetics not only enables diagnosis, but is leading more and more to improved guidance and treatment.

From this ever increasing importance and complexity, the Belgian Society of Human Genetics identified the need for a course which provides a theoretical basis for human genetics at a postdoctoral level. The members of the society represent the eight Belgian human genetics centers as well as scientists and professionals involved in human genetics.

The postgraduate course in human genetics intends to fulfill the need of a growing number of professions in which a full theoretical basis of all aspects of human genetics is useful or required. In the industry, health care, diagnostics as well as in certain areas of research, such knowledge is needed. Within the Belgian genetics centers, the course will provide a uniform and adequate theoretical basis for all those taking up responsibilities in human genetics-related activities.

Aims

This permanent education in human genetics aims to

- Cover all aspects of human genetics
    - Clinical genetics
    - Molecular genetics
    - Cytogenetics
    - Biochemical genetics
- Bring an up-to-date program embedded within the current practices
- Deliver a certificate acknowledging a robust knowledge basis in human genetics

Target students

The course is aimed at

- Everyone taking up a responsible function in a genetic center
- Professionals in industry involved in or with human genetics
- Pharmaceutical industry involved in human genetics
- Postdocs/PhD students with interest in human genetics
- MDs involved in human genetics

Prerequisites

Participants hold

- A masters/licentiaats/license degree, or MD degree
- Some knowledge of molecular biology

Organisation

The course outline is based on the book Genetics in Medicine (Thompson & Thompson, Seventh edition). The course chapters will be tought by representatives of the 8 human genetic centers in Belgium, localized at or associated with 8 different universities. The courses will take place on the second Friday of each month, unless there are holidays. A final examination will take place on a 9th Friday. Each center for human genetics is responsible for the organization of the course at its University.

Evaluation and certificate

To obtain the certificate in human genetics the candidate will take an examination at the end of the course program. This written test will cover the different topics presented during the course. It will consist of 30-60 questions with multiple choices, no negative mark, but a correction for random errors (correct for 4/20 if randomly answering the 5 proposals of each question). Students obtaining 10/20 or more will pass. The jury is composed of the Program Organizing Committee (POC) which includes eight members, representing each Belgian Center of Human Genetics. The certificate will be approved by the BeSHG and will be delivered by the University at which the student registered.

Credit points (ECTS)

The course entails 60 contact hours + exercises in human genetics. The total course sums up to **10 ECTS (credit points)**

REGISTRATION

The registration cost of the course is **200 Euro.** Registrations are open in each university (except for the Ghent University) / human genetics center, from 11/9/2017 to 08/10/2017.

Registration Contacts:

- ULB : Damiano.Di.Stazio@ulb.ac.be, 02 555 6430
- VUB : cmg@uzbrussel.be, 02 477 6865
- ULg : genetique.humaine@ulg.ac.be, 04 366 8145
- KUleuven : rita.logist@uzleuven.be
- UCL : liliana.niculescu@uclouvain.be, 02 764 7490
- IPG : rina.davella@ipg.be, 071 44 71 39
- UA : bettina .blaumeiser@uantwerpen.be, 03 275 9774

For practical reasons, we can only accept 50 students. Registration will be effective when payment is received.

Course overview

DAY 1: KULeuven 13.10.2017

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

Basic concepts (Thierry Voet)

Introduction: The chromosome
The 3D nucleus
Mitosis
Meiosis

The human genome: gene structure and function (Gert Matthijs)
Gene structure and function
Gene regulation and activity

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

Mutational analysis (Harry Cuppens)
Sequencing (Harry Cuppens)
Molecular cytogenetics tools (Joris Vermeesch)
Bioinformatic tools: Human genome browsers & its applications to clinical genetics (Joris Vermeesch)

DAY 2: ULB 10.11.2017

Aud F.2-104, Campus Erasme, 808 Lennik St, 1070 Brussels

9:30-11:00 ***Patterns of single gene inheritance***
(Marc Abramowicz)
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
(Marc Abramowicz)
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 (François Fuks)

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 08.12.2017

Human gene mapping and disease gene identification

Mapping of human genes: principles and applications (Paul Coucke and Andy Willaert)

Practical exercises with lod score calculations (Paul Coucke and Andy Willaert)

The molecular, biochemical and cellular basis of genetic disease

General introduction (Paul Coucke)

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

Inborn errors of metabolism (Olivier Vanakker)

Mutations in developmental genes (Bert Callewaert)

Mutations in extracellular matrix proteins (Sofie Symoens)

Mutations in signaling pathways (Bart Dermaut)

DAY 4: IPG 12.01.2018

09:30-11:00 Disorders of the autosomes (cytogenetics/molecular abnormalities and clinical aspects) Damien Lederer and Stéphanie Moortgat
11:00-11:15 coffee break
11:15-12:45 Disorders of gonadal and sexual development (gonadal embryogenesis, cytogenetics/molecular abnormalities, and clinical aspects) Isabelle Maystadt
12:45-13:30 lunch
13:30-14:00 Foetopathology 1 Christian Dugauquier
14:00-15:00 Foetopathology 2 Christian Dugauquier
15:00-15:15 coffee break
15:15-16:45 Treatments of metabolic diseases Dominique Roland

DAY 5: UCL 23.02.2018

Salle de séminaire 42A
UCL - Faculté de Médecine (Cliniques universitaires Saint Luc),
Avenue Mounier, 51, B-1200 Brussels
(by metro: line 1 towards Stockel, ALMA station > Auditoires centraux)

9:00-17:30

GENETIC ASPECTS OF DEVELOPMENT (Thompson 7th ed chptr 17)

Introduction: Prof. Miikka Vikkula
Regulators of development: HOXs etc.: Pr. René Rezsohazy
Vascular anomalies and overgrowth syndromes: Pr. Nisha Limaye
Cleft lip and palate: Prof Nicole Revencu
Birth defects: approach to syndromology: Prof. Yves Sznajer
Q & A

CANCER GENETICS and GENOMICS (Thompson 7th ed; chptr 16)

Introduction to Cancer
Introduction: Miikka Vikkula
Molecular basis of oncogenesis: Pr. François Duhoux
Hereditary basis of cancer – specifics for genetic counseling: Dr. Anne De Leener

Hereditary cancers:
Inherited breast cancer: Dr. Anne De Leener
Other inherited cancer predispositions Dr. Anne De Leener
Inherited colon cancer: Dr. Anne De Leener
Q & A

Acquired cancers
Hematological malignancies: Prof. Hélène Antoine-Poirel
Paragangliomas and pheochromocytomas Pr. Alexandre Persu
Q & A

Cancer treatment
Theranostics in cancer treatment: Pr Jean-Pascal Machiels
Q & A

DAY 6: UA 09.03.2018

Genetics of common disorders with complex inheritance

Elementary concepts of multifactorial diseases
Bettina Blaumeiser
Concepts in complex genetics: from Fisher to GWAS
Guy Van Camp
Beyond GWAS
Erik Fransen
Osteoporosis as paradigm for studies into complex diseases
Wim Van Hul
Of mice and human genetics
Frank Kooy
Web resources and datamining in genetics
Geert Vandeweyer, Wim Wuyts

DAY 7: ULg 20.04.2018

Pharmacogenetics and pharmacogenomics

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

Clinical aspects of dysmorphology (Saskia Bulk).

The immune system

Immune genetics (Stéphanie Humblet (KULeuven), Sabine Franke)
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 18.05.2018

Prenatal diagnosis

Non-invasive testing
- Ultrasound (Prof W Foulon)
- Biochemistry (Dr E Ankaert)

Invasive testing
- Indications (Dr K. Keymolen)
- Methods (Prof W Foulon)
- Laboratory investigations
  - Cytogenetics (Dr Sci C. Staessen)
  - DNA (Dr Sci W. Lissens)
  - Biochemistry (Dr Sci W. Lissens)

Preimplantation genetic diagnosis (Prof K. Sermon, Prof I.Liebaers)

Genetic counseling and risk assessment

Indications for genetic counselling (Prof I. Liebaers)

Genetic counselling providers (Prof I. Liebaers)

Determining recurrence risks (Prof M. Bonduelle)
- Mendelian conditions
- Conditional probability
- Empirical recurrence risks

Molecular tools in determining recurrence risks (Dr Sci S. Seneca)

Managing the risk of recurrence in families (M Vanhorenbeeck, Nekkebroeck)

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.

FINAL EXAMINATION

08.06.2018

14.09.2018