Universitat Autònoma de Barcelona

2020/2021

Mutagenesis

Code: 101980
ECTS Credits: 6

Degree	Type	Year	Semester
2500890 Genetics	OB	2	2

The proposed teaching and assessment methodology that appear in the guide may be subject to changes as a result of the restrictions to face-to-face class attendance imposed by the health authorities.

Contact

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Use of Languages

Principal working language: catalan (cat)
Some groups entirely in English: No
Some groups entirely in Catalan: Yes
Some groups entirely in Spanish: No

Prerequisites

There is not any official prerequisite more than those needed for the access to the degree.

Objectives and Contextualisation

The Mutagenesis course does refer to the nature of the mutational changes, to the different factors and mechanisms involved in the induction of genetic damage and to the relation between mutations and different diseases, in special cancer and those syndromes associated with chromosomal instability and defects in DNA repair. The course also serves to introduce the assays more employed in the genotoxic/mutagenic evaluation and that they are currently used in the standard testing batteries. Likewise, it establishes the links between the fundamentals of the systems of mutagenic evaluation, their role in the mutagenicity analyses and its application to the studies of biomonitoring of human populations. It is a course that has both basic and applied aspects, integrating different levels, from the molecular to the individual and populational levels. The subject of Mutagenesis is in the second course and develops basically the following aspects: molecular basis of mutagenesis, physical and chemical mutagens, detection of mutations, systems of mutagenic evaluation, mutations and diseases, human biomonitoring.

Competences

- Be able to analyse and synthesise.
- Define mutation and its types, and determine the levels of genic, chromosomal and genomic damage in the hereditary material of any species, both spontaneous and induced, and evaluate the consequences.
- Develop self-directed learning.
- Reason critically.
- Use and manage bibliographic information or computer or Internet resources in the field of study, in ones own languages and in English.

Learning Outcomes

1. Be able to analyse and synthesise.
2. Describe the basics of the main methods of mutagenic evaluation.

3. Describe the different types of genic and chromosomal mutation and their somatic and germinal consequences.
4. Describe the molecular bases of mutations and repair mechanisms in prokaryotes and eukaryotes.
5. Develop self-directed learning.
6. Reason critically.
7. Recognise the application of the main methods of mutagenic evaluation in biomonitoring studies.
8. Use and manage bibliographic information or computer or Internet resources in the field of study, in ones own languages and in English.

Content

Unit 1. INTRODUCTION

Brief introduction to the developmental history of Mutagenesis. Basic and applied aspects. His paper in both Genetics and Genetic Toxicology disciplines. Importance of Environmental Mutagenesis.

Unit 2. GENE MUTATION

The mutations. Types of mutations. Gene mutations. Phenotipic effects of mutations. Types of mutants. Reversion and supression. Spontaneous mutations. Endogenous and exogenous causes of mutations. Molecular basses of gene mutations. Mechanisms that contribute to the spontaneous mutation.

Unit 3. CHROMOSOME MUTATION

Main types of chromosome aberrations. Cell cycle and expression of structural chromosome changes. Paper of single and double strand breaks in the genesis of chromosomal alterations. The fragile points. Aneuploidy and chromosome loss. Causes and consequences of chromosome non-disjunction.

Unit 4. MECHANISMS OF REPAIR

Repair and mutagenesis. Mechanisms of repair. Reversion of the induced damage. Base excision repair. Nucleotide excision repair. Mismatch repair. Tolerance to the genetic damage. Regulation of mutagenesis in eukaryotic cells.

Unit 5. CHEMICAL AND PHYSICAL MUTAGENS

Nature of physical and chemical mutagens. Chemical mutagens that require metabolic activation. Chemical mutagens that are activated by the light. Direct mutagens. Indirect mutagens. Intercalating agents. Base analogs. Ionizing radiation. Ultraviolet light. Fibers.

Unit 6. CARCINOGENESIS

The nature of cancer. Clues about the origin of cancer. The genetic basis of cancer. Oncogens. Tumour supressor genes. Growth distortion in cancer cells. Carcinogenesis as a multicausal, multigenic and multistage process. Some important genes in the clinical of cancer. Cancer Stem Cells.

Unit 7. PHARMACOGENETICS

Genetic variability in the biotransformation of xenobiotics. Polymorphismsof enzymatic loci involved in the biotransformation. Cytochromes P450. Glutathione S-transferases. N-acetyl transferases. Other enzymes involved in the metabolism of drugs and foreign chemicals. Pharmacogenetic polymorphisms and diseases susceptibility. Factors that influence the metabolism of xenobiotics.

Unit 8. INHERITED SUSCEPTIBILITY TO MUTATION

Mechanisms of inherited susceptibility to mutation. Hereditary diseases characterized by defects in DNA repair: xeroderma pigmentosum and Fanconi's anaemia. Hereditary diseases characterized by cell deficient responses to the genetic damage: ataxia telangiectasia and Bloom's syndrome. Other diseases with possible defects in the processing of DNA damage.

Unit 9. MUTAGENICITY ASSAYS

Assays in bacteria: the Ames test. Assays in cultured mammalian cells: gene mutation, chromosome mutation, micronucleus and sister chromatids exchanges. *In vivo* asays with *Drosophila melanogaster*: sex-linked recessive lethal mutations, and somatic mutation and recombination events. Common *in vivo* mammalian assays: genotoxicity and germ cell mutations.

Unit 10. NEW TECHNIQUES IN MUTAGENICITY ASSAYS

Detection of adducts in DNA and proteins. The single cell gel electrophoresis assay (Comet test). Use of fluorecence *in situ* hybridization techniques. Detection of aneuploidy. Utilization of transgenic animals for measuring genetic events.

Unit 11. DEVELOPMENT OF ASSAYS BATTERIES

General philosophy. Matricial (batteries) and hierarchical (tiers) systems. Approaches to the development of assays batteries. Basic recommendations. Interpretation of the data of the assays batteries. Importance of the controls.

Unit 12. BASIC PRINCIPLES OF BIOMONITORING

Environmental monitoring. Biological monitoring. Human monitoring. Biomarkers. Biomarkers of exposure to genotoxins. Biomarkersof genotoxins-DNA interactions. Biomarkers of irreversible genetic damage. Molecular epidemiology. Epidemiologic correlations.

Unit 13. BIOMONITORING OF HUMAN POPULATIONS

Mutational spectra in exposed and non-exposed populations. Populations environmentally exposed. Populations occupationally exposed. Populations medically exposed.

Unit 14. INTRODUCTION TO THE GENETIC RISK ESTIMATION

Basic considerations and definition of genetic risk. Strategies for the qualitative risk characterization. Organisms and relevance to humans. Categorization of risk. Quantitative characterization. Dose- response extrapolation.

Unless the requirements enforced by the health authorities demand a prioritization or reduction of these contents.

Methodology

The development of the formative activities of the course is based in: theory lectures, solving problems and case analysis sessions, and seminars. These activities will be done following his specific methodology and will be complement with tutorials.

Lectures will address in a formal and systematic way the main ideas and applications of the different topics. Students should expand and confront autonomously as a personal work. The content of different units will be explained by the professor using visual material. Students must bring this material in class as a guide.The lectures are conceived basically as a unidirectional method of knowledge transmission but the professor will motivate the participation of students.

The solving problems and analysis of cases are devoted to apply the knowledge acquired from the lectures and personal study to the resolution of representative problems and practical cases, previously stated. The students culd work in small groups, developing the capacities of interaction, analysis of data and synthesis of the results.

Seminars: : Students will choose a topic related to mutagenesis and will make a presentation to the rest of the students.

Classes to orient the autonomous learning: They will serve principally to advise for the search of consistent scientific information and for bibliographic queries, as well as to establish effective learning strategies.

Tutorials: His objective is multiple: resolution of doubts, bibliographic orientation and use of the virtual tools. These sessions will not serve to advance matter, they will be of support.

The proposed teaching methodology may experience some modifications depending on the restrictions face-to-face activities enforced by health authorities.

Activities

Title	Hours	ECTS	Learning Outcomes
Type: Directed			
Lectures	26	1.04	3, 2, 4, 6, 1
Preparation of works	10	0.4	3, 2, 4, 5, 6, 7, 1, 8
Self-directed learning	3	0.12	5, 6, 7, 1, 8
Seminars	5	0.2	6, 7, 1, 8
Type: Supervised			
Group tutorials	4	0.16	5, 6, 7, 1, 8
Type: Autonomous			
Problem classes and seminars	10	0.4	3, 2, 4, 5, 6, 7, 1, 8
Problem resolution	20	0.8	6, 7, 1, 8
Study	65	2.6	3, 2, 4, 5, 6, 7, 1, 8

Assessment

The competences of this subject will be evaluated as follows:

1.- Examinations

Examinations include the evaluation of the contents of both the theoretical lessons and the problems.

Two midterm written exams will be done. To pass the exam the students must get at least a mark of 5. It is possible to compensate from 5.

To improve the mark, or to surpass a mark inferior to 5, the students can do the reassessment exam. To be eligible for the retake process, the student should have been previously evaluated in a set of activities equaling at least the two thirds of the final score of the course. Thus, the student will be graded as "No Avaluable" if the weighthing of all conducted evaluation activities is less than 67% of the final score.

The qualification obtained in the exams will represent the 75% of the final mark.

2.- Participation

The qualification of the team work represents the 5% of the final mark. It does not be necessary a minimum mark of this part in order to pass the subject.

3.- Individual work

The oral presentation, the writing, the structure, the quality, the clarity, and the consistence of the individual work will be considered. The qualification of this module will represent the 20% of the total mark.

Final considerations:

For a positive evaluation of the course, the students must obtain at least 5 in the final mark.

The students that can not attend an examination for justified causes can address to the Degree Coordinator in order to find an alternative date.

Student's assessment may experience some modifications depending on the restrictions to face-to-face activities enforced by health authorities.

Assessment Activities

Title	Weighting	Hours	ECTS	Learning Outcomes
Active participation	2%	0	0	5, 6, 1
Exams	75%	7	0.28	3, 2, 4, 6, 7, 1
Seminar	23%	0	0	5, 6, 7, 1, 8

Bibliography

Álvarez, E., Cunha, R.(Editors) DNA Adducts. Formation, Detection and Mutagenesis. Nova Biomedical Press (2010).

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Dhawan, A., Bajpayee, M. (Editors) Genotoxicity Assessment. Methods and Protocols. Humana Press (2013).

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Wilson, S.L., Suk, W.A. (Editors) Biomarkers of Environmentally Associated Disease. Technologies, Concepts and Perspectives. Lewis Publishers (2002).

Web links:

www.mutagenesisambiental.com/

www.eems-eu.org/

www.ems-us.org/

www.ukems.org/