



Universitat de Lleida

DEGREE CURRICULUM **MOLECULAR PATHOLOGY AND THERAPEUTICS**

Coordination: BOIX TORRAS, JACINT

Academic year 2017-18

Subject's general information

Subject name	MOLECULAR PATHOLOGY AND THERAPEUTICS			
Code	14700			
Semester	1st Q(SEMESTER) CONTINUED EVALUATION			
Typology	Degree	Course	Typology	Modality
	Master's Degree in Biomedical Research	1	COMMON	Attendance-based
ECTS credits	4			
Groups	1GG			
Theoretical credits	0			
Practical credits	0			
Coordination	BOIX TORRAS, JACINT			
Department	CIENCIES MEDIQUES BASIQUES,MEDICINA,MEDICINA EXPERIMENTAL			
Important information on data processing	Consult this link for more information.			

Teaching staff	E-mail addresses	Credits taught by teacher	Office and hour of attention
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Learning objectives

1. The development of an integrative and molecular view of the human cell in disease.
2. The identification of cell death phenotypes and other degenerative or infectious cytopathic traits.
3. The description of molecular entities that regulate and execute apoptosis and other types of cell death.
4. The molecular characterization of the tumor cell phenotype, the cell heterogeneity in neoplasia and the invasive and metastatic potential.
5. The understanding of the tumor resistance to hypoxia and therapy mechanisms.
6. The performance of translational approaches, diagnostic, prognostic or therapeutic based on the molecular mechanisms stated before.

Competences

CB1 Possessing knowledge and understanding that provide a basis or opportunity for originality in developing and /

or applying ideas, often within a research context.

CB2 Being able to apply the acquired knowledge and have the ability to solve problems in new or unfamiliar environments within broader (or multidisciplinary) contexts related to their field of study.

CB3 Being able to integrate knowledge and handle complexity, and formulate judgments based on information that was incomplete or limited, include reflecting on social and ethical responsibilities linked to the application of their knowledge and judgments.

CB4 Being able to communicate their conclusions, and the knowledge and rationale underpinning these, to specialist and non-specialist audiences in a clear and unambiguous.

CB5 Acquiring the learning skill to study in a self-directed and autonomous way.

CG1 Knowing how to select and apply different analytical methods molecular, biochemical, cellular, genetic and phenotypic for the diagnosis and study of disease.

CG4 Capacity for critical and creative thinking with your work and that of other researchers.

CE3 Identifying and assessing the implications of the phenomenon of cell death in the pathogenesis of multiple diseases and the therapeutic rational basis that provides.

CE4 Recognizing the high performance techniques (high throughput) and the use of bioinformatics tools for data analysis.

CT1 Having a correct oral and written expression

CT4 Respect the fundamental rights of equality between men and women, to the promotion of human rights and the values of a culture of peace and democratic values

Subject contents

The molecular mechanisms that cause the pathological phenotypes in the cells and their pharmacological modulation are the main subject of this course. Physical agents like radiation, chemical or biological ones like mutagens, viral infections, etc. converge in generating degenerative phenotypes that will precede cell death or, alternatively, oncogenic transformation characterized by proliferative expansion, loss of cell differentiation and resistance to hypoxia and therapy. Cell death by apoptosis, autophagy and, even, necrosis occur by an ordered activation of molecular mechanisms. Tumoral progression, cell heterogeneity in neoplasia, tissue invasion and metastasis are the result of specific molecular disruptions. As an example, the dysfunctions in the expression regulatory networks defined by microRNAs (miRNAs). A better understanding of these mechanisms and events will allow the identification of therapeutic targets and strategies, diagnostic resources and valuable prognostic parameters.

Methodology

Lectures (Topics), Seminars, Scientific conference

Development plan

1. LECTURES

TOPIC 1. CELL NECROBIOLOGY

(Prof. J. Boix)

- Cell death: Terms, concepts and types.
- Cell death studies: A historical perspective.
- Cell death phenotypes: Apoptosis versus necrosis.
- The genetics of apoptosis: The *C. elegans* model.

TOPIC 2. CASPASES

(Prof. J. Boix)

- The discovery of caspases.
- The targets of caspases.
- The cell death phenotype resulting from caspase activation: Apoptosis.
- IAPs: Physiological inhibitors of caspases.

TOPIC 3. THE REGULATION OF CASPASE ACTIVATION

(Prof. J. Boix)

- The extrinsic pathway.
- The intrinsic pathway.
- Mitochondrial outer membrane permeabilization (MOMP).
- Mitochondrial inner membrane permeabilization (MIMP).

TOPIC 4. THE BCL-2 FAMILY OF PROTEINS

(Prof. J. Boix)

- Bcl-2 a new type of oncogene.
- Bcl-2 protein structure and homology domains.
- Functional classification of the members of the Bcl-2 family.
- Regulation of MOMP by the Bcl-2 family members.
- BH3-only proteins as sensitizers or activators of MOMP.
- BH3-only proteins as transducers of cell stress.

TOPIC 5. AUTOPHAGY

(Prof. C. Cantí)

- Characterization of the phenomenon.
- Molecular mechanisms of autophagy.
- Regulation by Bcl-2 proteins.
- Cell death by autophagy or with autophagy?
- Implications of autophagy in oncogenesis and cancer treatment.

TOPIC 6. MECHANISMS OF CANCER INITIATION

(Prof. X. Matias-Guiu)

- Oncogenes and tumor suppressor genes.
- Genetic and epigenetic changes in cancer.
- Familial versus sporadic cancer.

TOPIC 7. MOLECULAR MECHANISMS FOR CANCER PROGRESSION

(Prof. X. Dolcet)

- Cancer Progression.
- Angiogenesis.
- Features and phases of metastasis.
- The epithelial-to-mesenchymal-transition in invasion.
- Genes involved in blood travelling and establishment of metastases.

- The TGF- β signaling in metastasis.

TOPIC 8. MODELING CANCER IN VIVO AND IN VITRO

(Prof. X. Dolcet)

- Animal models in cancer biology
- Mouse models of cancer
- In vitro study of cancer.
- Modeling morphogenesis and oncogenesis in 3D cultures.
- Endometrial and mammary 3D cultures.
- Xenotransplanting tumors in mice.

TOPIC 9. STEM CELLS IN CANCER

(Prof. X. Dolcet)

- What is a stem cell?
- Stem cells versus cancer stem cells.
- Cancer stem cells and multidrug-resistance.

2. SEMINARS

SEMINAR 1. APOPTOSIS AND VIRAL PATHOGENESIS

(Prof. J. Boix)

- Viral mechanisms to disrupt cell apoptosis.
- Apoptosis induction by the immune system.
- Apoptosis in the pathogenesis of AIDS.

SEMINAR 2 and 3. CELL DEATH AND MOTONEURON DISEASE

(Prof. J. E. Esquerda)

- Clinical forms of motoneuron (MTN) disease: Amyotrophic Lateral Sclerosis (ALS) and Spinal Muscular Atrophy (SMA).
- Mechanisms for selective MTN vulnerability.
- Cell dysfunction and death in MTN disease.
- Involvement of glutamate mediated excitotoxicity.
- Involvement of neuroinflammatory processes.
- Animal models and therapeutic strategies.

SEMINAR 4 and 5. CELL DEATH IN CARDIAC DISEASE

(Prof. D. Sanchis)

- Role of cell death in heart failure.
- Apoptosis versus necrosis: molecular pathology and experimental evidences.
- Non-apoptotic role of the apoptotic machinery in development.
- Alternative signaling to apoptosis in adult myocyte death.

SEMINAR 6. CYTOPROTECTIVE AUTOPHAGY

(Prof. C. Cantí)

- Beneficial versus detrimental roles of autophagy.
- The role of constitutive autophagy in the heart.

- Autophagy in myocardial Ischemia/Reperfusion.
- Autophagy in hypertensive heart disease.
- Blockage of autophagy in lysosomal storage disorders.

SEMINAR 7. MOLECULAR PATHOLOGY OF MELANOMA

(Prof. R. M. Martí)

- Classification.
- Molecular alterations.
- Therapeutic strategies.

SEMINAR 8. MOLECULAR PATHOLOGY OF ENDOMETRIAL CARCINOMA

(Prof. X. Matias-Guiu)

- Classification of endometrial carcinomas.
- Genetic molecular alterations of endometrioid carcinomas.
- Transition of endometrial hyperplasia to endometrial carcinoma.
- Alterations in non-endometrioid carcinomas.

SEMINAR 9. MICRORNA (miRNA)

(Prof. J. Ribas)

- Discovery. Biogenesis. Localization. Microprocessor, Dicer and RISC. Stability. Function: transcription vs translation.
- MiRNAs and disease. MiRNAs in cancer: OncomiRs.
- MiRNAs as diagnostic markers.
- MiRNAs as therapeutic targets.

SEMINAR 10. MOLECULAR TARGETS IN ANTI-TUMOR THERAPY

(Prof. X. Matias-Guiu / Prof. Boix)

- Principles of targeted therapies.
- Pharmacological modulation of p53 function.
- Exploiting oncogene addiction in tumors.
- Exploiting non-oncogene addiction in tumors.

3. CONFERENCE

- There will be one conference performed by an invited scientist.
- The subject and author of the conference will be announced along the course.

Evaluation

- Attendance to all sessions will provide the 50% of the course mark. Each unjustified nonattendance will imply the loss of a 2%.
- There will be some exercises based on the practical analysis, interpretation and discussion of experimental results, either preliminary (from the bench to the classroom) or published in a scientific journal. This will provide the 30% of the evaluation.
- Conference will be evaluated by writing a summary about its content (minimum 300, maximum 500 words). Scientific journal style in the abstract is suggested. The summary/abstract will provide the 20% of the evaluation.

Bibliography

Specific and general bibliography will be provided. Students will get PDF files related to the subjects approached in the course by connecting to their master folders in the UdL network.