VNIVERSITAT DE VALÈNCIA

Course Guide
33151 Regulation of cellular proliferation and destination

COURSE DATA

Data Subject	
Code	33151
Name	Regulation of cellular proliferation and destination
Cycle	Grade
ECTS Credits	7.5
Academic year	2021 - 2022

Study (s)

Degree	Center	Acad. year	Period
1109 - Degree in Biochemistry and Biomedical Sciences	Faculty of Biological Sciences	3	First term

Subject-matter

Degree	Subject-matter	Character
1109 - Degree in Biochemistry and Biomedical Sciences	12 - Biomedicina molecular	Obligatory

Coordination

Name	Department
FARIÑA GOMEZ, MARIA ISABEL	21 - Cellular Biology and Parasitology
IGUAL GARCIA, JUAN CARLOS	30 - Biochemistry and Molecular Biology

SUMMARY

"Regulation of proliferation and cell fate" is a compulsory subject taught in the first quarter of the third year of the degree in Biochemistry and Biomedical Sciences and corresponds to 7.5 ECTS credits. This course is part of the theme block "Cell fate and development" which includes, in addition to this subject, that of "Developmental Genetics". The course pursues a detailed study of the molecular mechanisms that control the process of cell division and proliferation in eukaryotes, and the mechanisms that regulate cell fate, differentiation, senescence, and cell death. Cell proliferation is essential for the construction and viability of organisms, and defects in its regulation underlie cancer. The same applies to regressive cellular processes whose disruption also leads to pathologies such as cancer or degenerative and autoimmune diseases. Therefore, this field of molecular and cellular biology is of major interest in the study and current research in biology and biomedicine. Furthermore, the regulation of cell differentiation processes is fundamental during the construction of the organs during embryogenesis and for stem cell-based tissue renewal in adult organisms. The study of these issues has implications in understanding the aging process, as in the development of strategies for regenerative medicine and tissue engineering. This

subject has, in terms of content, important links to the course of "Functional histology" and "Genetics of development". Consideration will be given to the knowledge acquired in the course "Intracellular dynamics and signaling" that is taught during the second year.

PREVIOUS KNOWLEDGE

Relationship to other subjects of the same degree

There are no specified enrollment restrictions with other subjects of the curriculum.

Other requirements

Knowledge of the basic aspects of the subjects of Biochemistry, Genetics and Molecular Biology and Cell Biology.

OUTCOMES

1101 - Degree in Biochemistry and Biomedical Sciences

- Comprensión de los mecanismos moleculares básicos que controlan los procesos de división, proliferación celular, diferenciación celular, apoptosis y senescencia.
- Comprensión de las bases celulares y moleculares del establecimiento de patrones de destino celular y la morfogénesis.
- Conocimiento de las bases moleculares del cáncer.
- Comprensión de los procesos de renovación y reparación tisular a nivel celular y molecular.
- Conocimiento de los organismos modelo fundamentales en el estudio del ciclo celular, diferenciación y desarrollo.
- Conocimiento de la conservación de procesos esenciales en el control de la división celular, diferenciación celular y desarrollo.
- Conocimiento del método científico. Desarrollo de la capacidad de entender y razonar la base experimental del conocimiento.
- Comprensión y manejo de los sistemas experimentales y métodos utilizados en la investigación de las materias de estudio.
- Capacidad para la organización de la información (esquemas, diagramas, mapas conceptuales) y la preparación de exposiciones públicas.
- Capacidad de aprendizaje autónomo.
- Conocimiento y manejo de diversas fuentes de información.

LEARNING OUTCOMES

- Understanding the molecular mechanisms that control cell division and proliferation, cell differentiation, cell death, and oncogenic transformation, as well as their integration.
- Understanding the cellular and molecular basis of cell fate and tissue repair and renewal and their relationship to pathology.
- Knowledge about the basic model organisms in the subjects studied.
- Understanding evolutionary conservation of essential mechanisms and molecules in the control of cell division and differentiation.
- Understanding the rationale of complex cellular processes from its molecular regulation. Understanding basic experimental approaches and solutions to cell fate problems.
- Understanding experimental approaches in this field, their limitations and interpretation of derived scientific results.
- Knowledge about how understanding basic regulation of complex cellular processes contributes to biomedical science.
- Developing skills of observation and capacity for integration of molecular, genetic and functional data to achieve an integrated view of the functioning of tissues, organs and organ systems as well as their development and pathological changes.
- Becoming familiar with the main bibliographical sources in the field, strengthen the capacity for analysis and synthesis and the ability to organize, integrate and present information with scientific criteria.

DESCRIPTION OF CONTENTS

1. INTRODUCTION TO THE CELL CYCLE

Basic properties of the cell cycle. The logic of the cell cycle. Main features of the cell cycle during embryogenesis. The maturation promoting factor (MPF). Discovery of cyclins. A cell cycle engine. The somatic cell cycle. Yeast as a model system to study the cell cycle. Genetic approach to the study of the cell cycle. The mutant cdc28 and START in the cycle of Saccharomyces cerevisiae. The cdc2 mutant and control entry into mitosis in the cycle of Schizosaccharomyces pombe. A universal cell cycle engine.

2. CELL CYCLE REGULATORS

The family of kinases CDKs and cyclins. Regulation of CDK activity. Regulation by binding of cyclins. Regulation by phosphorylation: proteins involved. Regulation by binding of CDK inhibitors. Pathways of protein degradation involved in cell cycle control. Transcriptional regulation in cell cycle control. The control system of the cell cycle.

3. The S. cerevisiae CELL CYCLE

CDKs and cyclins of S. cerevisiae. Meaning and description of START. G1 cyclins: synthesis and degradation Cln1, Cln2 and Cln3. The transcriptional program in the initiation of the cell cycle. Coordination of cell cycle with growth. Clb cyclins. Control of replication: the role of the CDK inhibitor Sic1. Oscillations in the Cdc28-cyclin kinase activities during the cell cycle. Exit from mitosis.

4. THE MAMMALIAN CELL CYCLE

Study of the mammalian cell cycle. The restriction point. The G1/S transition: CDKs, cyclins and CKIs involved. Transcription regulation during the cell cycle. The function of the Rb protein. The G2/M transition. Cancer and cell cycle.

5. REGULATION OF DNA REPLICATION

DNA replication and the cell cycle. Regulation of initiation by CDK: the S phase promoter factor (SPF). The licensing factor model. Pre-replication complex. The blockade of the re-replication: alternating S phase/M phase.

6. CHECKPOINT MECHANISMS

The concept of checkpoint. Mechanisms of response to DNA damage and incomplete DNA replication. The p53 protein and its role in checkpoints. Cell cycle arrest in response to spindle defects.

7. SIGNALLING PROCESSES INVOLVED IN CELL PROLIFERATION

Growth factors. Receptors with Tyr kinase activity. Receptors with Ser-Thr kinase activity. Cytokine receptors: JAK Tyr kinases. Modules of protein-protein recognition. The Ras and MAP kinase pathway. The PI3K and AKT kinase pathway. Phospholipases and protein kinase C. Activation of transcription by growth factors. The SRF-TCF system and the transcriptional factor AP-1. Smad proteins. STAT transcription factors. The control of proliferation by the transcriptional factor Myc. Cancer and cell proliferation control mechanisms.

8. CELLULAR SENESCENCE

Causes and mechanisms of cellular senescence. Effectors in cellular senescence: p53 and p16/p19. Telomerase, telomeres and replicative senescence. Oxidative stress and genomic damage. Premature senescence. Senescence caused by oncogenes. Markers of senescence. Non-autonomous effects of senescent cells. Senescence in vivo.

9. CELL DEATH

Types of cell death. Cell death in physiological and pathological conditions. Causes, characterization and functional significance of the various types of cell death. Apoptosis: cascade of proteolytic enzymes and regulation of apoptosis. Survival factors and death signals. Extrinsic and intrinsic apoptotic pathways. Necroptosis and other forms of cell death.

10. CELL SPECIFICATION AND DIFFERENTIATION

General mechanisms of mammalian development. Genome equivalence (totipotency and pluripotency) and regulation of differential gene expression. Stem cell concept and potential. Progressive restriction. Lineage and cell fate. General stages of differentiation. Levels of control of cell differentiation. Models and strategies for generating cell diversity. Inductive interactions. Lateral inhibition. Regulation of division mode. Fundamentals and applications of cellular reprogramming.

11. CELL AND TISSUE RENEWAL

Renewal of differentiated cells. Renewal by duplication. Stem cell renewal. Stem cells and transit-amplifying progenitor cells. Self-renewal and multipotentiality: molecular regulation. Niche concept. Epidermal, intestinal, hematopoietic and neural stem cells. Regeneration.

12. CANCER BIOLOGY

Types of tumors. Tumor cell biology. Environmental factors and cancer. Oncogenes. Tumor suppressor genes. Defects in DNA repair. Chemoresistance. Cellular basis of tumor progression. Cell tumor markers. Cancer stem cells. Angiogenesis. Metastasis: matrix remodelling and epithelial-mesenchymal transitions.

13. AGING

Aging and cellular senescence. Genetic syndromes of premature aging. Genetic basis of longevity. Ageing and metabolism. Stem cells and aging. Aging and disease.

14. Laboratory experiences

Practice 1. PERIODIC EXPRESSION OF Clb2 cyclin and Sic1 inhibitor in S. cerevisiae.
Practice 2. CHARACTERIZATION OF STEM CELL DIFFERENTIATION.

WORKLOAD

ACTIVITY	Hours	% To be attended
Theory classes	55,00	100
Laboratory practices	16,00	100
Classroom practices	4,00	100
Development of group work	10,00	0
Development of individual work	5,00	0
Study and independent work	30,00	0
Preparation of evaluation activities	31,00	0
Preparing lectures	26,50	0
Preparation of practical classes and problem	10,00	0
TOTAL	**187,50**	

TEACHING METHODOLOGY

The development of the subject is divided into:

Lectures. Presentation and discussion of previously announced selected topics. Teaching and bibliographic resources will be available to students in multimedia. The teacher will present the basics of the subject, devoting more time to highly complex issues, and will guide the students in the integration of the contents with related issues of other subjects.

Laboratory practical classes. A program of laboratory experiences will connect theoretical classes with research approaches in the field. Attendance is compulsory.

Seminars, conferences or other activities. Their purpose is to allow students to expand their knowledge on the subject by preparing presentations or by attending conferences of invited scientists. One of these activities will be the critical analysis of scientific papers selected by the teachers of the subject. This activity aims at training the students in the reading and discussion of scientific papers (which necessarily involves reading technical English), bringing them closer to the original scientific literature and facilitating the observation of new current advancements in biomedical sciences. This activity mandatory, will be organized jointly with the other subjects in their third year, corresponding to each subject between 3 and 6 items, depending on number of credits. The preparation, presentation, and discussion (30 minutes) of the selected papers will be carried out in groups of 2 students and supervised by the teacher through the tutorials. In addition, seminars will be given by researchers in the field of study of the subject, as a way of exposing the students to current research in the topics covered by the program. Additional activities may be carried out, specially if new scientific developments take place.

Tutorials. There will be two one-hour tutorials, each one associated with each of the blocks of the course. During the tutorials, the progress of the course will be discussed. An additional tutorial will be dedicated to discuss the development and results of the laboratory practical classes.

EVALUATION

A **single exam** including questions with different formats (multiple choice, developmental, problem solving questions) will be used to evaluate the knowledge and understanding acquired by the students as well as their ability to use specific scientific language in an appropriate way. The grade obtained in this test will represent **80% of the final grade**.

The evaluation of the **lab work** will be based on the preparation of an **activity report** and will represent **15% of the final grade** of the subject. In addition, questions about the practical work can be included and graded in the exam.

The **evaluation of the activity** consisting in the critical analysis of scientific papers will take into consideration the degree of understanding of the information contained in the articles, the correct use of terminology and the presentation skills during the oral debate with the rest of the group. If the student does not reach the minimum required score in this activity, he/she will fail the subject. If the activity is adequately accomplished, the mark obtained will represent **5% of the final grade in each of the subjects of the third ye**ar that participate in this activity. Also, the participation of other students in the presentation and discussion sessions may be taken into account by the teacher to modulate their final score.

To pass the subject, it will be necessary to attend the practical classes, to participate in group activities, to obtain a minimum score of 4,5 out of 10 in theory test and a final score of no less than 5 out of 10 in the journal club activity. In case of not passing the subject in the first call, the note of the examination of one of the parts can be kept until the second call of the same course if the grade is equal to or higher than 4,5.

REFERENCES

Basic

- Alberts, B., A. Johnson, J. Lewis, M. Raff, K. Roberts y P. Walter (2008). Molecular Biology of the Cell. 5ª ed, Garland Science, New York.
- Lodish, H., A. Berk, C.A. Kaiser, M. Krieger, M.P. Scott, A. Brestcher, H. Ploegh, y P. Matsudaira (2008) Molecular Cell Biology. 6ª ed. Freeman and Co., New York.
- David O. Morgan (2007) The Cell Cycle. Principles of Control. New Science Press Ltd. Oxford University Press.
- Robert A. Weinberg (2006) The Biology of Cancer. Garland Publishing Inc.

- Lanza, R. (ed.) (2009) Essentials of Stem Cell Biology. 2ª ed. Academic Press
- Becker, W.M., L.J. Kleinsmith y J. Hardin. (2006). The World of the Cell. 4ª ed. Benjamin/Cummings Publishing Company.
- Cooper, G.M. y R.E. Hausman (2003). The Cell: A Molecular Approach. 3rd ed. Sinauer Associates Inc.
- Gilbert, S.F. (2005) Biología del Desarrollo. 7ª ed. Editorial Médica Panamericana.
- Karp, G. (2010). Cell and Molecular Biology. 6ª ed., Wiley.

ADDENDUM COVID-19

This addendum will only be activated if the health situation requires so and with the prior agreement of the Governing Council

Contenidos y Volumen de trabajo

Sin cambios.

Metodología

El punto de inicio dado el número de estudiantes y las aulas disponibles es de plena presencialidad en las actividades. Sin embargo, si la evolución de la situación derivada de la COVID-19 obliga a una reducción de la presencialidad, se tomarán las siguientes medidas:

1) Las actividades presenciales en aula se sustituirían en función de las herramientas tecnológicas disponibles en el aula en el momento de desarrollo del curso, por las siguientes metodologías:

-Videoconferencia síncrona

-Videos de presentaciones en mmedia.uv.es

-Presentaciones Powerpoint locutadas en Aula Virtual

-Presentaciones Powerpoint con apuntes extendidos en Aula Virtual

-Propuestas de actividades de resolución de Cuestionarios de Aula Virtual y entrega de tareas y cuestiones por Aula Virtual

2) Las actividades presenciales de prácticas de laboratorio, se sustituirían por las siguientes metodologías:

- prácticas de laboratorio simuladas mediante videoconferencia

- Presentaciones Powerpoint locutadas en Aula Virtual

- Trabajo con datos experimentales suministrados

- Discusiones en foros asíncronos en Aula Virtual

3) Para tutorías y dudas se utilizarían las siguientes metodologías:

-Chats síncronos en Aula Virtual

-Foros asíncronos en Aula Virtual

-Comunicación directa profesor-estudiante a través del correo institucional

Evaluación

En caso de que los exámenes no pudieran ser presenciales, se realizarían ‘on line’ en Aula Virtual mediante las herramientas disponibles.

Los detalles concretos de la adaptación a las situaciones que se pudieran producir se supervisarán por la CAT y se comunicaran a los estudiantes a través de Aula Virtual.