UNIVERSIDAD PABLO DE OLAVIDE SEVILLA

PROGRAMME

Year 2017-2018

1.SUBJECT DESCRIPTION

Degree:	**Biotechnology**
Subject:	**Molecular Genetics**
Module:	**Biochemistry and Molecular Biology**
Departament:	**Molecular Biology and Biochemical Engineering**
Academic Year:	**2017-2018**
Semester:	**Second semester**
Credits:	**4,5 ECTS**
Course:	**2º**
Type:	**Basic**
Lenguge:	**English**

Teaching Model:	**B1**
a. Basic teaching (EB):	**60%**
b. Practical teaching (EPD):	**40%**

PROGRAMME
Year 2017-2018

2. PROFESSORS

2.1. Coordinator Rafael Rodríguez Daga

2.2. Profesors	
Name:	**Rafael Rodríguez Daga**
School:	**Experimental Sciences**
Departament:	**Molecular Biology and Biochemical Engine**
Area:	**Genetics**
Category:	**Associated professor**
Tutorial clases:	**Thursdays 13-15h**
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3. TRAINING PLAN

3.1. Goals

The subject of Molecular Genetics has several main objectives that will be addressed in two blocks. In the first block, students must first know the molecular mechanisms of eukaryotic transcription and translation; second, the regulatory mechanisms of both processes, including the mechanisms of epigenetic regulation of gene expression, analysis in vivo and global or differential expression analysis using microarrays, third, understand the molecular mechanisms of mRNA processing and maturation and the quality control mechanisms for both proteins and mRNAs; Fourth, understand the processes of replication, recombination and DNA repair.

In a second block of the course students will be introduced to the study of cellular processes such as control of eukaryotic cell proliferation. This block is designed so students know the molecular basis of eukaryotic cell proliferation, including the basic machinery of cell cycle control, the various regulatory mechanisms, the different cell cycle control transitions and checkpoints . Finally, students should know the implication of the checkpoints in human diseases such as cancer and their importance as targets of antiproliferative drugs.

3.2. Contribution of Molecular Genetics to Biotechnolgy global training plan

Molecular Genetics is a basic matter and is framed in the training module comprising Biochemistry and Molecular Biology.

Within this module Molecular Genetics provides the basics of regulation of eukaryotic gene expression and cell cycle control. The goal is to train students in the use and understanding at the molecular level of genetic pathways that control these processes in order to eventualy apply this knowledge to the development of biotechnological strategies to cure or alleviate human diseases such as cancer.

3.3. Recommendations and previous requirements

Essential prerequisites: Basic knowledge of General Genetics, Genetic Analysis and Genetic Engineering.

Desirable prerequisites: Management of scientific literature databases.

4. COMPETENCES

1.Know and understand biological processes at the molecular level.

2.Use adequated expressions and specific terminology and nomenclature.

3.Acquire instrumental management and work habits in a laboratory.

4.Acquire the ability to design, analysis, and interpretation of experiments andscientific results.

5.Know and apply the tools, techniques and experimental protocols.

6.Perform cultures of microorganisms.

7.Apply preparation techniques, staining and observing biological samples.

8.Design, analyze and interpret the results of experiments aimed at the disruption ofgene function in its most common variants.

9.Interpret the phenotypes associated to lack of function key regulators of differentcheckpoints of the cell cycle.

10.Apply techniques for analyzing DNA content as flow cytometry, and interpret theresults.

11.Analyze and interpret different strategies of regulation of gene expression.

12.Acquire abilities in solving problems.

13.Acquire habits of discussion on scientific problems.

14.Establish a working hypothesis from experimental data.

15.Develop the capabilities of search and selection of specific scientific information inbibliographic databases.

16.Acquire habits of reading, writing and presentation of scientific results.

5. CONTENT

TOPICS

Introduction. Objectives and knowledge to learn. The information flow in the cell. Central Dogma of Molecular Biology.

Item 1. Transcription.

RNA polymerases, transcription factors, formation of the initiation complex, transcription cycle. Promoter TATA box, site of transcription initiation. Regulatory elements: silencers, enhancers. Insulators. Locus control regions (LCRs). Binding regions to nuclear matrix (MARs). RNA modifications: processing introns, alternative splicing. 5 'capping, trimming (rRNA, tRNA) and polyadenylation. mRNA quality control.

Item 2. Regulation of transcription.

Chromatin modifications. CG island methylation, Methylation-Acetylation - Deacetylation of histones. Incorporation of histone variants. Compaction of chromatin: euchromatin and heterochromatin. Frome gene silencing to protein in vivo.

RNA interference. Differential expression (tumor cells) and analysis of gene expression by microarrays.

Item 3. Translation.

Translation. Ribosomes, tRNAs, genetic code. Codon-Anticodon. Codon usage. Initiation elongation and termination of translation. Polysomes. Coupling transcription and translation.

Item 4. Translational regulation mechanisms.

Ternary complex, Regulation of translation mediated by uORFs (GCN4), Regulation of translation by hairpin (ferritin, IRE). Cap-independent translation (IRES). Protein quality control.

Item 5. DNA Replication, recombination and repair.

Replication. Replicons. DNA polymerases. Replication forks. Telomeres and telomerase. The mutation at the molecular level. DNA repair and mutation. Mutagens

agents. Homologous and non-homologous recombination. Transposition

Item 6. Molecular basis of eukaryotic cell proliferation.

The cell cycle and its control points. Mechanisms of cell cycle regulation by cyclin-CDK complexes. Cell cycle regulation by phosphorylation. Regulation of CDK activity by CKIs. CKIs: types and mechanisms of action. Monitoring checkpoints mechanisms. The DNA damage and the mitotic checkpoints: molecular mechanisms.

PRACTICAL TEACHING TOPICS.

The subject Molecular Genetics has two scheduled practices, organized in five separate sessions. During the practice, two different model organisms, the fission yeast *S. pombe,* one of eukaryotic organisms in which cell cycle control mechanisms is better known, and *C. elegans*, a small nematode that has emerged in recent years as an excellent model organism for studying numerous biological problems such as aging, or nervous system development and function. *C elegans* allows the use of iRNA technique to transiently control gene expression of target genes in a ease and effective way.

PRACTISE I. Gene silencing by RNA interference (RNAi) in *Caenorhabditis elegans*. Production of transient mutants.

Summary

The interference RNA technique (iRNA) allows temporary and selective inactivation of a gene transcript by expression of an antisense RNA. This technique is used in many organisms, but is particularly effective and easily accomplished in *C. elegans*.

In the practise we will inactivate by iRNA genes involved in coordination of movement, body symmetry and genes responsible for the formation of dauer, a stage of resistance of this worm. This practice will be also implemented by using RNAi in thermosensitive mutant of genes required for dauer formation. The goal will be to infer the genetic pathway which determine the decision of entering in the dauer lifestyle during early development of *C. elegans.* ruta genética que determina la decisión del modo de vida *daue*r durante el desarrollo de *C. elegans*.

PRACTISE II. Analysis of conditional mutants in genes that control cell cycle in the fission yeast *S. po*mbe.

Summary

The objective of this practice is to introduce students to the mechanisms of cell cycle regulation. We will analyse a collection of thermosensitive mutants in genes governing different transitions during cell cycle progression. Through analysis of these mutants we will design gene pathways that explain the observed phenotypes and discuss the consequences of the deregulation of the mechanisms of cell proliferation control.

6. METHODOLOGY & RESOURCES

METHODOLOGY

In the course of Molecular Genetics a mixed teaching method is used. This method is, based on lectures, practical, problem solving and class discussion of the results and completion and presentation of scientific works.

The use of the web through the WebCT tool is not used as a teaching method in itself, but as an interface between students and the teacher to share contents and teaching materials, as well as a permanent method of communication that, sometimes it is even in real time.

The classes are held in the classroom during about 55 minutes. The first 5 minutes of each class are used, if necessary, to discuss planning issues, as well as for resolving possible doubts of the previous class.

The practical classes are conducted in the labs and begin with a brief explanation of the purpose of the practice or the session and for planning.

In the course not only individual work and reasoning is stimulated but also group organization and planning, which is, how most businesses and research centers work.
During the course several series of problems are provided. They will be resolved by students, and discussed in class. This work aims to promote knowledge through study, analysis and problem solving. While is not the final goal, problem solving also fosters teamwork. Exposure and defense of the solutions of the problems in the class promotes individual reflection.
In addition to the series of problems, they professor may deliver series of additional problems (which have no score) if during the course the profesor deems it necessary.
In the course of Molecular Genetics, a scientific review work has to be delivered at the end of the course. Scientific work aimed at stimulating the literature search, the selection of scientific articles and research topics that are more relevant today. It also allows the exposure of students to different experimental methodologies to be understood and interpreted. Some of the best works will be discused in class.
Students have the opportunity to make individual or group tutoring, so all the learning process will be acompained with the constant support of the teacher.

RESOURCES

Students have a number of resources to acquire the desired competencies.
These are:

1.Classrooms for delivery of lectures, seminars, conferences, etc.

The classrooms are equipped with a projector and direct access to internet via WiFi. Generally the classes are well equipped, with sufficient light and ventilation in addition to heating and air conditioning operating normally.

2.Laboratory Practices

The labs have adequate instruments. The number of students in practice is limited to 20.

3.Library

The library at the University, besides being a place for reading and studying is a place of coexistence for many students and is where they gather for teamwork in many cases.

7. EVALUATION

The subject of Molecular Genetics will be evaluated continuously and the final grade will be the sum of the final exam and the notes of the various activities (practices I and II, the two sets of problems, and a written work). The scores for each section are:

Rating summary:

Problems (2 x 0.5 points) 1 point

Written work 1 point

Evaluation practise I 1 point

Evaluation practise II 1 point

Midterm Exam 2 points

Final Exam 4 points

The approval is achieved with 5 points.

Midterm Exam. This test will consist of the resolution of problems similar to the type of problems that are resolved in the problems series. This exam may be done along with evaluation of practices I and II.

The final exam first call. It will consist of solving several similar problems plus several questions. In some of these questions the use of certain terms, or keywords, will be positively evaluated.

The final exam, second call. This test will be the same type as in the first call and all notes of the continuous evaluation will be kept.

8. RECOMMENDED LITERATURE

Manuals and information related to the central dogma of molecular biology and cell cycle control:

1.Lewin B. Genes VII. Marbán, cop. 2003.

2.Klug W.S. Cummings, M.R. y Spencer C.A. 2006 "Conceptos de Genética". PrenticeHall 2006.

3.Genética. Un enfoque conceptual. 2ª Edicion. Pierce.

4.Griffiths y col. "Genética" Mc Graw Hill 2000

5.The Cell Cycle: Principles of Control. David O. Morgan. Oxford University Press2007.

Scientific articles (supplementary material suggested)

1.Transcription in eukaryotes Cap. Libro (inglés) TRANSCRIPTION OFEUKARYOTIC PROTEIN-CODING GENES Tong Ihn Lee and Richard A. Young 2000

2.Regulated Unproductive Splicing and Translation (RUST). Brenner ComputationalBiology Research Group. http://compbio.berkeley.edu/people/ed/rust

3.Nonsense-mediated mRNA decay: terminating erroneous gene expresión. K. E Bakerand R. Parke. Current Opinion in Cell Biology 2004, 16:293–299

4.Epigenetics: A Landscape Takes Shape

A. D. Goldberg,1 C. D. Allis,1, and E. Bernstein. 2007. Cell 128, 635-638

5.Chromatin Modifications and Their Function. T. Kouzarides. 2007 Cell 128, 693–705.2007

6.Beyond the Sequence: Cellular Organization of Genome Function T. Misteli. 2007.Cell 128, 787–800.

7.The Dynamics of Chromatin Remodeling at Promoters. J. Mellor. 2005. MolecularCell, Vol. 19, 147–157.

8.From Silencing to Gene Expression: Real-Time Analysis in Single Cells. Janicki etal. 2004. Cell, Vol. 116, 683–698.

9.Structure,function and evolution of CpG island promoters. F.Antequera. (2003) Cell.Mol. Life Sci. 60 1647–1658.

10.Cell cycle kinases as therapeutic targets for cancer (2009). Lapenna S, Giordano A.. Nat

Rev Drug Discov. (7):547-66.

11.Whole chromosome instability and cancer: a complex relationship (2008). Ricke RM, van Ree JH, van Deursen JM. Trends Genet. (9):457-66

12.Boveri revisited: chromosomal instability, aneuploidy and tumorigenesis (2009). Holland AJ, Cleveland DW. Nat Rev Mol Cell Biol. (7):478-87.

11.p65cdc18 plays a major role controlling the initiation of DNA replication in fission yeast (1995). Nishitani H, Nurse P. Cell. 83(3):397-405.

13.Cell cycle regulation of DNA replication (2007). Sclafani RA, Holzen TM. Annu Rev Genet. 41:237-80.