

**COURSE DATA****Data Subject**

Code	43462
Name	Fundamental basis in gene expression
Cycle	Master's degree
ECTS Credits	3.0
Academic year	2022 - 2023

Study (s)

Degree	Center	Acad. year	Period
2210 - M.D. in Research in Molecular, Cellular and Genetics Biology	Faculty of Biological Sciences	1	First term

Subject-matter

Degree	Subject-matter	Character
2210 - M.D. in Research in Molecular, Cellular and Genetics Biology	7 - Fundamental basis in gene expression	Optional

Coordination

Name	Department
PARICIO ORTIZ, NURIA	194 - Genetics

SUMMARY

To know how gene expression is regulated is an essential aspect to understand how prokaryotic and simple eukaryotic organisms operate as well as how higher eukaryotes develop under normal and pathological conditions. "Bases in gene expression" is an optional subject within the Master in Research in Molecular and Cellular Biology and Genetics. The course is designed to provide specific training and updates on gene regulation in prokaryotes and eukaryotes. In prokaryotes, particular emphasis will be placed in transcriptional regulation and function of operons, but also in different regulatory mechanisms described at the level of translation. Although it was initially thought that bacterial mechanisms of gene regulation based on the operon model could be conserved in eukaryotes, the discovery of pre-mRNAs processing and the existence of chromatin in these organisms revealed that they have developed specific regulatory systems. Therefore we will explain eukaryotic transcriptional (chromatin level, transcription factors and RNA-based mechanisms) and posttranscriptional (alternative splicing, RNA editing) control systems, the integration of gene regulation with the physiology of the organism (control regulators) as well as biomedical implications of abnormal gene regulation. During the course we will also present several experimental approaches for determining at what level and how gene expression regulation is occurring.



PREVIOUS KNOWLEDGE

Relationship to other subjects of the same degree

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

Other requirements

None.

OUTCOMES

2210 - M.D. in Research in Molecular, Cellular and Genetics Biology

- Students should apply acquired knowledge to solve problems in unfamiliar contexts within their field of study, including multidisciplinary scenarios.
- Students should be able to integrate knowledge and address the complexity of making informed judgments based on incomplete or limited information, including reflections on the social and ethical responsibilities associated with the application of their knowledge and judgments.
- Students should communicate conclusions and underlying knowledge clearly and unambiguously to both specialized and non-specialized audiences.
- Students should demonstrate self-directed learning skills for continued academic growth.
- Be able to make quick and effective decisions in professional or research practice.
- Students should possess and understand foundational knowledge that enables original thinking and research in the field.
- Be able to access to information tools in other areas of knowledge and use them properly.
- To be able to assess the need to complete the scientific, historical, language, informatics, literature, ethics, social and human background in general, attending conferences, courses or doing complementary activities, self-assessing the contribution of these activities towards a comprehensive development.

LEARNING OUTCOMES

Gene expression is a process that is described in several subjects in the degree taught at the Faculty of Biological Sciences. However, the regulation of this process is one of the fundamentals in biology and related disciplines, but it is explained a superficial way. Therefore, the overall objective of this course is to fill this formative gap and describe in detail the different regulatory mechanisms of gene expression in both prokaryotes and eukaryotes. As a result, we intend to extend the knowledge acquired on gene expression with the following goals:



- To know the different methodologies that allow the study of gene expression.
- To differentiate the various levels of control and the main regulatory mechanisms used by prokaryotes and eukaryotes.
- To get a reasonably deep knowledge of the different molecular mechanisms controlling gene expression in prokaryotes and eukaryotes.
- To know common regulatory mechanisms specific to the main living taxa.
- To develop the ability to critically assess the various methodological and conceptual issues included in the program.
- To become familiar with the current literature and be able to discriminate between the essential and the accessory concepts.
- To exercise the ability to synthesize scientific information.
- To learn how to coordinate different techniques to solve specific problems.
- To determine the importance of the alterations in gene expression in disease states.
- To understand the relevance of gene expression regulation in biotechnological applications.
- To understand the importance of certain types of regulation in the pattern of inheritance of some characters
- To understand the importance of gene expression regulation during development.
- Development of analytical skills and the use of logic for understanding complex phenomena.
- Acquisition of a clear understanding of the importance of experimental model organisms.

DESCRIPTION OF CONTENTS

1. Gene Expression in prokaryotes

The process of transcription in prokaryotes. RNA polymerase. Structure of the promoter. Transcription initiation. Transcription terminators: intrinsic terminators and the Rho factor.

2. Gene expression regulation in prokaryotes

Alternative sigma factors and their organization in cascades. Operons: operon structure. Inducible and repressible operons. Positive and negative control of operons. Examples of operons: the lac operon and the trp operon. The mechanism of attenuation. Antitermination. Transcriptional regulation: ribosomal switches. antisense RNAs.

**3. Gene expression in eukaryotes**

Tissue specific expression of proteins and messenger RNAs. Levels of gene regulation. Special cases of regulation by DNA loss, amplification and reorganization. Transcription in eukaryotes. Promoters. General transcription factors, TAFs and pre-initiation complex. The RNA polymerases: the CTD domain of RNA polymerase II. RNAs modifications: capping, polyadenylation, splicing, coupling of transcription and processing, transport and translation.

4. Control of transcription in eukaryotes (I): chromatin structure

Higher levels of chromatin and nuclear organization. DNase hypersensitive sites. Modification of bases: CG island methylation. Histone modifications: the histone code hypothesis. Histone variants. Chromatin remodeling complexes. Long-term gene silencing: parental imprinting and dosage compensation.

5. Control of transcription in eukaryotes (II): cis-regulatory elements

Regulatory sequences within or adjacent to the promoter: the regulatory promoter. Enhancers, silencers and insulators. Mechanisms of action. Modular construction of gene regulatory regions: integration into complex expression patterns.

6. Control of transcription in eukaryotes (III): regulatory transcription factors

Structure of transcription factors: modularity. DNA-binding domains: a systematic classification. Transcription activation mechanisms: TFIID, TFIIB, mediator complex, co-activators. Selectivity of the TFs. Classification of transcription factors based on function and activation mode. Regulation of regulatory TFs: seven general mechanisms. Visual summary and web resources. CRISPRa and CRISPRi.

7. Transcriptome diversification: Alternative splicing of pre-mRNAs and RNA editing

General mechanism for alternative splicing (AS). Main families of AS regulatory proteins: RNA-binding domains. The role of RNA structure in AS. Kinetic coupling of the AS and epigenetic regulation. Regulation of AS in response to signals. Splicing in trans. The EJC complex: functions. Nonsense-mediated decay (NMD). Alternative polyadenylation. RNA editing. Edition by insertion/deletion: trypanosome mitochondria. Edition by substitution. mRNA stability: SMD and ARE sequences. Regulation of stability and translation. Location of RNAs.

8. RNA-based mechanisms of gene regulation in eukaryotes

The RNAi mechanism. miRNAs biogenesis. Regulation of miRNAs. Effector complexes of silencing. Mechanisms of repression. Nuclear functions of miRNAs. miRNAs as hormones and biomarkers. The end of the life of microRNAs. endo siRNAs: biogenesis and transcriptional silencing. The nascent transcript model in *S. pombe*. Transposon silencing by piRNAs. Transcriptional gene activation. Long ncRNAs. lncRNAs as transcription gene regulators. The case of "smORFs." Biogenesis of circRNAs,



modulators, and functions. snoRNAs.

WORKLOAD

ACTIVITY	Hours	% To be attended
Theory classes	29,00	100
Other activities	1,00	100
Preparation of evaluation activities	30,00	0
Preparing lectures	15,00	0
TOTAL	75,00	

TEACHING METHODOLOGY

The teaching methodology used in this course is based on learning theory known as constructivism. In brief, this theory is based on the idea that learning occurs when students construct new knowledge from reflection on the information supplied to it. Therefore, the role of the teacher in this course will be to promote intellectually active learning by the student, including student's reflection about the concepts and principles developed by the professor or studied independently.

The course is divided into several weekly sessions of two hours. In each session the teacher will present the contents of the course items. Furthermore, these presentations will serve as theoretical basis for the explanation and discussion of a scientific article, containing primary information (experiments) or a review, selected by the teacher. This discussion will be led by the teacher, who will explain the contents of the article, but it should also involve the students to establish a small debate.

EVALUATION

At the end of the course, an exam about the contents of the items will take place. The theoretical exam will constitute 80% of the final mark. In addition, several scientific articles related with the course contents will be discussed. In those sessions, the reasons that led the researchers to perform the work, the results obtained, the experimental approach followed and the conclusions reached will be explained. Each student must respond to questionnaires on articles discussed during the course. The rating of these questionnaires will constitute 20% of the final mark.

To pass the course will be necessary to achieve a score of at least 5 points on a total of 10. The final mark will be obtained by adding the mark of the theoretical examination and the questionnaires about scientific articles. A minimum mark at any section is not required to pass the course.



REFERENCES

Basic

- Alberts B., Johnson A., Lewis J., Raff M., Roberts K. y Walter P. (2014). Molecular Biology of the Cell, 6th edition. Garland science Editions.
- Dale J.W. y Park S.F. (2010). Molecular Genetics of Bacteria, 5th edition. John Wiley & Sons.
- Barresi M. y Gilbert S.F. (2019). Developmental Biology, 12th edition. Sinauer Associates Inc. Publishers.
- Hartwell, L., Goldberg, M. L. y Fischer, J. (2018). Genetics: from genes to genomes, 6th edition. McGraw-Hill.
- Hughes T.R. (2011). A Handbook of Transcription Factors. Elsevier.
- Krebs J.E., Goldstein E.S. y Kilpatrick S. T. (2017). Lewins Genes XII. Jones & Barlett Publishers.
- Latchman D. (2015). Gene control. Garland Science.
- Lodish H., Berk A., Kaiser, C.A., Krieger M., Scott M.P., Bretscher A., Ploegh H., Martin K.C., Yaffe M. y Amon A. (2021). Molecular Cell Biology, 9th edition. Macmillan Learning.
- Turner B. M. (2008). Chromatin and Gene Regulation: Mechanisms in Epigenetics. John Wiley & Sons.
- Watson J.D., Baker T.A., Bell S.P., Gann A., Levine M. y Losick R. (2014). Molecular Biology of the Gene, 7th edition. Pearson Education, Inc.
- Pierce B. A. (2020). Genetics: A conceptual approach, 7th edition (3ª edición traducida al castellano). Mcmillan Learning.
- Elliott D. y Ladomery M. (2016). Molecular Biology of RNA. Oxford University Press.
- Carlberg C. y Molnár F. (2020). Mechanisms of Gene Regulation: How Science Works. Elsevier.
- Kolodny G. M. (2018). Eukaryotic Gene Regulation: Volume I and II. CRC Press.
- Pascual L. y Silva F. (2018). Principios básicos de genética. 1ª edición. Editorial Síntesis.

Additional

- En cada tema se proporcionará bibliografía específica, principalmente artículos de investigación o de revisión, que servirá para que los estudiantes puedan profundizar en algunos de los aspectos tratados. Dada su naturaleza, estos artículos se irán actualizando cada año.