Universitat Autònoma de Barcelona

2017/2018

# Molecular Biology

Code: 100858
ECTS Credits: 6

| Degree | Type | Year | Semester |
|---|---|---|---|
| 2500252 Biochemistry | OB | 2 | 2 |

## Contact

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## Use of languages

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

## Prerequisites

Part of the knowledge of the 1st and 2nd courses of the degree is needed to be able to follow the course. Some materials of the following courses are particularly needed : Biochemistry I, Biochemistry II, Chemistry and Engineering of Proteins, Basic and Advanced Instrumental Techniques, Cell Biology, Genetics and Microbiology.

## Objectives and Contextualisation

The students of the Biochemistry degree have previously acquired some descriptive knowledge of Molecular Biology. The Molecular Biology course will carry out a study in depth about the structure and function of nucleic acids. The subjects of the course are listed in the contents. The most important objective of the course is to get a good knowledge of the fundamentals and acquire the ability to assess the current state of scientific knowledge of the different subjects of Molecular Biology. For this reason, the experimental foundations on which the different subjects of Molecular Biology are based will be specifically addressed in this course. The foundations of genetic engineering will be also presented in this course, but they will be treated in detail in the course of Recombinant-DNA Technology (third year / second semester).

## Skills

- Collaborate with other work colleagues.
- Define the structure and function of proteins and describe the biochemical and molecular bases of their folding, intracellular traffic, post-translational modification and replacement.
- Identify molecular structure and explain the reactivity of the different biomolecules: carbohydrates, lipids, proteins and nucleic acids.
- Interpret experimental results and identify consistent and inconsistent elements.
- Read specialised texts both in English and ones own language.
- Stay abreast of new knowledge of the structure, organisation, expression, regulation and evolution of genes in living beings.
- Use ICT for communication, information searching, data processing and calculations.

## Learning outcomes

1. Collaborate with other work colleagues.

2. Compare the molecular mechanisms involved in the perpetuation, maintenance and generation of variability in genetic information.
3. Correctly describe the structural bases of the interaction between proteins and nucleic acids.
4. Describe the differential regulation of gene expression in prokaryotes and eukaryotes.
5. Describe the molecular mechanisms of the transmission of genetic information from nucleic acids to proteins.
6. Explain the structural and dynamic polymorphism of nucleic acids.
7. Explain the structural models of DNA folding in chromosomes.
8. Indicate the capacity of the different structural analysis techniques and decide which to apply in specific experimental situations.
9. Interpret experimental results and identify consistent and inconsistent elements.
10. Interpret findings from structural studies of proteins and nucleic acids.
11. Read specialised texts both in English and ones own language.
12. Use ICT for communication, information searching, data processing and calculations.

## Content

**Chapter 1. SECONDARY STRUCTURE OF DNA.** Introduction: Molecular Biology in the classical period and nowadays. Estructure of B DNA: the Watson and Crick model; structure of DNA in aqueous solutions. Denaturation and renaturation of DNA: effect of temperature and pH; stabilization by stacking of bases. Conformations of the ribose-phosphate backbone. Base pairs different from those proposed by Watson and Crick. X-ray crystallography and NMR studies of oligonucleotides: twist, tilt, roll and propellor twist angles; lateral displacement (slide) between base pairs. Structure of A and Z DNA . Structure poly(dA).poly(dT) sequences.

**Chapter 2.CIRCULAR DNA.** Circular DNA: discovery and initial interpretation of its properties. Topological properties of circular DNA: relationship between the number of topological links (L), the number of turns of the double helix (T) and the number of superhelical turns (W) in a circular DNA molecule; physical interpretation of L, T and W. Superhelical density of naturally occurring circular DNA. Intercalating agents: structural changes of DNA; effect on the rate of sedimentation and electrophoretic migration. Topoisomerases: structure and action mechanism of the type I and type II topoisomerases. Two-dimensional electrophoresis of circular DNA. Biological implications of the topological properties of DNA.

**Chapter 3. STRUCTURAL POLYMORPHISM OF DNA.** Structural basis of the flexibility of the double helix. DNA bending: intrinsic and induced by proteins. Biological implications of DNA bending. Double helices of DNA wit incorrectly paired bases and with two parallel chains. Structures induced by superhelical tension: bubbles; cruciform structures; B/Z transition; intramolecular triple-stranded DNA. Intermolecular structures: concatenated circular DNA and knots; D and R loops; Holliday junctions; triplex and quadruplex DNA; biotechnological applications of these structures. Artificial structures: properties and applications of the PNA. Nanotechnology based on DNA. Dynamics of DNA in solution.

**Chapter 4. PRIMARY STRUCTURE OF DNA.** Introduction: genetic and physical maps. DNA purification techniques. Kinetics of DNA reassociation: experimental design; physical chemistry of the reassociation; DNA complexity; biological implications; the importance of hybridization techniques in in Molecular Biology. Manipulation and analysis of intact chromosomal DNA molecules: electron microscopy; pulsed-field gel electrophoresis. Modification and restriction. Restriction enzymes: chemical basis of the recognition of specific sequences of DNA; restriction maps; applications in Genetic Engineering; restriction fragment length polymorphism and other methods of genetic diagnosis. CRISPR-Cas9 system: biological function; biotechnological applications.

**Chapter 5. DNA SEQUENCING.** Chemical method. Enzymatic method. Chemiluminiscent methods. Automated fluorescent methods. The human genome and other genomes: genomics. Biotechnological applications of DNA polymerases: improvement of enzymatic sequencing methods; preparation of cDNA; nick translation; polymerase chain reaction (PCR). New methods of DNA sequencing. Future perpectives on DNA sequencing and genetic diagnosis. Automated synthesis of oligonucleotides. Synthetic biology.

**Chapter 6. PACKAGING OF DNA.** Introduction: the biological problem of three-dimensional storage of the information contained in molecules having a linear structure. Packaging of DNA in viruses and bacteria.

Packaging of DNA in the chromatin of the cell nucleus: the nucleosome. Structure of DNA and histone proteins in the nucleosome core particle: chemical basis of nonspecific interaction between proteins and DNA. Higher-order chromatin structures: chromatin fibers; chromatin in the interphase nucleus; metaphase chromosomes.

**Chapter 7. REPLICATION and DNA METABOLISM**. Functional implications of the structure of DNA: semiconservative DNA replication. Molecular mechanism of prokaryotic DNA replication: initiation of the replication in sequences oriC; bidirectional replication; the replisome (helicase, RNA primase, DNA polymerase); single-stratded DNA binding proteins; DNA ligase; topoisomerases. DNA polymerases I and III: three-dimensional structure; polymerase and exonuclease activities; processivity. Replication of DNA in eukaryotes: cell cycle; sequences of replication origin and number of replisomes; proteins of the eukaryotic replisome.Nucleosome dynamics during chromatin replication. DNA repair. DNA recombination.

**Chapter 8. TRANSCRIPTION and RNA METABOLISM.** The central dogma of Molecular Biology. Messenger RNA. Transcription in prokaryotes: structure and function of the RNA polymerases; footprinting techniques for the characterization of promoters; dynamics of the association of RNA polymerase to the promoter; uncoiling of the DNA double helix in the initiation region; termination of RNA synthesis. Eukaryotic RNA polymerases and general transcription factors. Post-transcriptional mRNA processing: sequences of poly (A) at the 3' end and caps in 5 '; introns and exons; processing of the primary transcript; alternative splicing. RNA-dependent DNA and RNA synthesis: reverse transcriptase; telomerase; RNA replicase. Large-scale transcription studies.

**Chapter 9. TRANSLATION.** The genetic code. Transfer RNA. Aminoacyl-tRNA synthetases. The structure of ribosomes. Protein synthesis: initiation; elongation; termination. The post-translational modifications. Molecular mechanisms for protein sorting and degradation.

**Chapter 10. REGULATION OF GENE EXPRESSION.** General principles of the regulation of gene expression: positive and negative regulation, structure and function of regulatory proteins. Regulation of transcription in prokaryotes: the lac operon and other bacterial operons. Regulationof transcription in eukaryotes: implications of the structure of chromatin; enhancers; transcription activators; histone modifications and remodeling of chromatin; complex mediators. Regulation of gene activity by small non-coding RNA molecules.

## Methodology

**Theory.** The professor will explain much of the content of the course with the support of material that will be available to students in the Virtual Campus (VC). To be able to follow correctly the explanations, students should bring the VC material in class. The theory sessions address the conceptual parts of the course. Other parts of the course must be studied independently by students. The professor will indicate exactly which topics will have to be studied in this way and the material to be used.

**Problems.** The professor will propose 12 problems related with scientific research of specific topics of Molecular Biology. These problems will be indicated in the VC at the beginning of the semester. The group will be divided into 12 subgroups. Each of the subgroups will have to make the oral presentation of a specific problem and also will have to do a summary of another problem that will be exposed by another group. In this way each student will participate in the preparation and presentation in public of a specific problem, and in the writing of a summary of another problem. In addition, all students are required to study all the problems and listen carefully to the explanations corresponding to all the problems presented in the course. All students can participate actively in discussions about all the problems, and will be able to answer the questions that the professor can include in the exams about these problems.

**Tutorials.** In the sessions of tutoring in classroom, there will be guidance on the strategy to be followed in order to study the subjects of autonomous learning.

## Activities

| Title | Hours | ECTS | Learning outcomes |
|---|---|---|---|
| **Type: Directed** | | | |

| | | | |
|---|---|---|---|
| Lectures | 35 | 1.4 | 2, 3, 5, 4, 6, 7, 10, 9 |
| Problems/scientific works | 10 | 0.4 | 12, 1, 2, 3, 5, 4, 6, 7, 10, 9, 11 |
| **Type: Supervised** | | | |
| Tutorials in classroom | 4 | 0.16 | 2, 3, 5, 4, 6, 7, 10, 9 |
| **Type: Autonomous** | | | |
| Group activity: preparation of a seminar about a problem/scientific work | 6 | 0.24 | 12, 1, 2, 3, 5, 4, 6, 7, 10, 9, 11 |
| Grup activity: report of a problem/scientific work | 6 | 0.24 | 12, 1, 2, 3, 5, 4, 6, 7, 10, 9, 11 |
| Individual study | 67 | 2.68 | 12, 2, 3, 5, 4, 6, 7, 10, 9, 11 |
| Individual study of problems/scientific works | 15 | 0.6 | 2, 3, 5, 4, 6, 7, 10, 9, 11 |

## Evaluation

The evaluation is based on four elements:

(1) Oral presentation of a specific problem in class (group seminar): maximum 1 point (10%).

(2) Preparation of a report to a specific subject (group report): maximum 1 point (10%).

(3) Midterm exam: maximum 4 points (40%).

(4) Final exam: maximum 4 points (40%).

The day of the final exam (4), students can also do a reassessment exam to try to improve the score obtained in the midterm exam (3); the score obtained in this reassessment exam overrides the score obtained in the midterm exam (even if the score in the midterm exam was higher).

To pass the course the sum of the scores must be ≥ 5 points (maximum of 10 points).

Students who have completed evidence of learning with a weight less than 50% will be mark as "not evaluated".

The date for the review of the exams will be announced with a minimum of 2 days in advance.

## Evaluation activities

| Title | Weighting | Hours | ECTS | Learning outcomes |
|---|---|---|---|---|
| Assessment of problems/scientific works | 20% | 1 | 0.04 | 12, 1, 2, 3, 5, 4, 6, 7, 8, 10, 9, 11 |
| Final exam | 40% | 4 | 0.16 | 2, 3, 5, 4, 6, 7, 8, 10, 9, 11 |
| Midterm exam | 40% | 2 | 0.08 | 2, 3, 5, 4, 6, 7, 8, 10, 9, 11 |

## Bibliography

Lehninger: Principios de Bioquímica (2009, quinta edición). DL. Nelson y MM. Cox. Ediciones Omega.

Biochemistry (2011, fourth edition). D. Voet and JG. Voet. J. Wiley & Sons.

DNA Structure and Function (1994). RR. Sinden. Academic Press.

Understanding DNA: The Molecule and How it Works (1997, second edition). CR. Calladine and HR. Drew. Academic Press.

Biología Molecular del Gen (2005, quinta edición). JD. Watson et al. Editorial Médica Panamericana.

Molecular Biology of the Cell (2014, sixth edition). B. Alberts et al. Garland Science.

Molecular Biology: Structure and Dynamics of Genomes and Proteomes (2016). J. Zlatanova and KE. van Holde. Garland Science.

Original scientific articles that will be indicated at the VC.