Teaching guide

IDENTIFICATION DETAILS

Degree:	Biomedicine
Scope	Biology and Genetics
Faculty/School:	Experimental Sciences
Course:	GENETICALLY MODIFIED ORGANISMS
Type:	Compulsory
ECTS credits:	4,50
Year:	4
Code:	2165
Teaching period:	Seventh semester
Subject:	Biomedical Research Tools
Module:	Experimental Methodology in Biomedicine
Teaching type:	Classroom-based
Language:	Spanish
Total number of student study hours:	112,50

SUBJECT DESCRIPTION

The course of Genetically Modified Organisms, taught in the seventh semester of the Degree in Biomedicine, focuses on the study of the various strategies for the generation of genetically modified animal organisms, for the generation of in vivo models and their possible applications to various biological problems.

The technologies developed in the last 30 years, approximately, to modify in a more or less targeted manner the genome of various animal organisms have made it possible to make enormous progress in the generation of physiological models with which to answer questions of a diverse biological nature. Thanks to techniques such as Gene Targeting, microinjection of foreign DNA or, more recently, Genome Editing technologies (CRISPR/Cas 9, among others), it is possible to ascertain the biological function of a gene in a context closer to reality than the use of cell cultures and other in vitro tools. The generation of Knock-Out, Knock-In, Transgenic models... makes it

possible to study complex diseases such as cancer (polygenic, multifactorial).

GOAL

The objective of the course Genetically Modified Organisms is to provide students with knowledge related to techniques for manipulating the genome of animal organisms (although focused on the mouse as an animal laboratory model par excellence) applied to the resolution of various problems such as the generation of products of interest, organisms with desired properties, studies of the role of genes in the body's vital processes, etc.

The specific aims of the subject are:

To know the genetic manipulation technologies to be used in invertebrate animal models such as Drosophila melanogaster to generate gains or losses in gene function in a germline context or in a conditioned development and/or tissue context.

Know the genetic manipulation technologies to be used in lower vertebrate animal models such as Dario Rerio to generate gains or losses in gene function in a germline context or in a conditioned development and/or tissue context.

Know the genetic manipulation technologies to be used in invertebrate animal models such as Mus musculus to generate gains or losses of gene function in a germline context or in a conditioned development and/or tissue context.

Once the various genetic manipulation strategies are known, be able to critically consider (advantages and disadvantages) the possible animal models to be used to answer questions about the functionality of one or more genes in a diverse biological process.

PRIOR KNOWLEDGE

The student who takes the course of Genetically Modified Organisms and wishes to obtain optimal use of it, must have basic knowledge of Cell Biology, Animal and Human Physiology, Molecular Genetics and Genetic Engineering.

COURSE SYLLABUS

Topic 1. Introduction to the generation of genetically modified animal organisms: Introduction. Work method. A brief history of genetic modification in animals.
Theme 2. Introduction to M.musculus: The mouse as a model par excellence: biology, strains... Maintenance and care: SPF animals. Mouse sampling and histopathological analysis. Mouse embryonic development. Obtaining

mouse embryonic stem cells (ES cells). ES cell propagation and maintenance. ES cell electroporation and colony screening for the identification of homologous recombination events (PCR, Southern Blot).
Theme 3. Transgenic mouse models: Introduction. Generation of transgenesis vectors (Plasmids, YACs, BACs...). Nuclear transfer. Conventional and conditional models (tissue-specific, time-specific).
Topic 4. Mouse models generated by homologous recombination (I) -Classic models: Introduction to homologous recombination. Generation of substitution vectors. Generation of insertion vectors. Blastocyst microinjection and morule aggregation. Conventional Knock Out (KO) and Knock In (KI) models.
Topic 5. Mouse models generated by homologous recombination (II) -Conditional models: Cre-loxP and FLP-FRT inducible systems. Conditional KO and KI models (tissue-specific, time-specific).
Topic 6: Mouse and siRNA models-Examples of the use of siRNA technology in the mouse.
Topic 7: Latest technologies applied to the generation of mouse models (Zinc-Finger Nucleases, TALeNS, Crisp/Cas9...).

EDUCATION ACTIVITIES

The classes in the subject of Genetically Modified Organisms will make use of various methodologies in order to achieve the proposed objectives. The face-to-face hours will be divided between the master classes given by the teacher of the subject and the discussion of scientific articles read and worked on by the students during the time of non-face-to-face activity. In more detail, the various teaching activities will consist of: -Face-to-face work: 1) Master classes taught by the teacher. 2) Critical discussion of scientific literature focused on the generation and use of murine models in the context of biomedicine. The articles will be proposed by the teacher. In principle, two articles will be analyzed, although this will depend on the precise scheduling of the course. Through seminars, each student will be asked to summarize in writing and discuss in class part of some of the articles depending on the number of models used in each article. 3) Resolution of practical cases where the student must be able to reasonably propose murine models to answer biological questions posed by the teacher. The student will not only critically discuss their own proposal, but they must also discuss those made by other classmates. More specifically, the student (or two students together depending on the number of them enrolled in each group) will solve in writing one of the exercises proposed by the teacher. On the other hand, you should comment on the proposals for an exercise carried out by one of your classmates. 4) Personalized student attention to review the contents explained in class, answer questions or discuss specific topics in order for the student to achieve the objectives pursued by the module. 5) Carrying out evaluation tests. -Autonomous work: 1) Study of the theoretical contents. 2) Use of complementary materials designed in the virtual network spaces of the different subjects. 3) Personal readings of the proposed scientific literature. 4) Resolution of practical assumptions. 5) Preparation of the

questions to be raised and discussed in the tutorials.
The teachers of the subject do not authorize the publication by the student of the material provided by the teachers of the subject in the virtual classroom, or by any other means.

DISTRIBUTION OF WORK TIME

TEACHER-LED TRAINING ACTIVITIES	INDIVIDUAL WORK
45 Horas	67,50 Horas

LEARNING RESULTS

Know how to define and know how to apply genetic engineering techniques to the study of gene expression and function in different systems, as well as the manipulation and modulation of such expression.

To know the different methods for the generation of genetically modified animal organisms as the foundations of animal experimentation and their relevance for the study in the different areas of Biomedicine.

SPECIFIC LEARNING RESULTS

To be able to design a gene strategy to achieve a gain of function at a locus or several loci of an animal organism, either by increasing the expression of the corresponding gene or by the presence of an activating point mutation in the corresponding protein product.

To be able to design a gene strategy to achieve a loss of function at one locus or several loci of an animal organism, either due to loss of expression of the corresponding gene or due to the presence of an inactivating point mutation in the corresponding protein product.

Be able to vary the genetic strategies studied depending on the need to manifest the introduced mutation either in the germline (classic models) or in a context dependent on tissue or time of development (conditional models) .

Critically propose (with their advantages and disadvantages) different genetically modified animal models for the study of gene functionalities in both physiological and pathological contexts.

Interpret correctly and with a critical sense the gene modification strategies and the corresponding animal models presented in the scientific literature that are used during the development of the seminars.

LEARNING APPRAISAL SYSTEM

The evaluation system distributes the final grade of the subject into two sections, an important part of which is the evaluation of master classes. In addition, it will be necessary to add up the evaluation obtained in the preparation and discussion of scientific articles.
In more detail, the ratings will be distributed as follows:
1. The criteria set out here will apply both to the ordinary and to the extraordinary call, plus any other extra call that the student has requested and that was granted, unless otherwise specified.
2. 70% of the final grade will correspond to the evaluation of the theoretical content of the subject. This section will evaluate learning outcomes RA1, 2, 3 and 4.
3. 20% of this final grade will correspond to the evaluation of the completion of the practical work; that is, the resolution and discussion of the practical cases proposed by the teacher. The format for resolution and discussion of cases will be indicated by the teacher in due course. This section will evaluate learning outcomes RA1, 2, 3, 4 and 5.
4. The remaining 10% of the final grade will include the evaluation of the seminars; that is, the reading and discussion of the scientific literature proposed by the teacher. The format of the abstract and the conditions for its delivery will be indicated by the teacher in due course. This section will evaluate learning outcomes RA4 and 5.
5. In order to pass the course, it will be necessary to obtain a minimum grade of 5 in each of the previous sections. If one of the sections is passed in the ordinary call but not the others, for the extraordinary call, the passing grade will be saved and the student must only pass the part (s) of the pending subject (s).
6. Any written evaluation will take into account spelling correction and, for this purpose, the criteria applied in the EvAU of the Community of Madrid in recent years will be applied. Namely: 1) Each error in the spelling will subtract 0.25 points from the final grade of the exercise and the errors in the accents 0.15 points, up to a maximum of 4 points in both cases. 2) The same repeated fault will be taken into account only once. 3) The repetition of misspellings may even lead to the qualification of suspense. 4) Abbreviations, syntactic errors, grammatical errors will be penalized...

IMPORTANT NOTES:

1) Students in second or subsequent enrollment may take advantage of an alternative evaluation system in which the 20% corresponding to the evaluation of the practical work and the 10% corresponding to the evaluation of the seminars will be replaced by the completion of individually tutored exercises and which will be equivalent to 30% of the final grade (and in which it will also be necessary to obtain a grade of 5). Students interested in taking advantage of this evaluation system should contact the subject teacher.
2) Plagiarism, as well as the use of illegitimate means in evaluation tests, will be sanctioned in accordance with the provisions of the Evaluation Regulations and the University's Coexistence Regulations.

ETHICAL AND RESPONSIBLE USE OF ARTIFICIAL INTELLIGENCE

1.- The use of any Artificial Intelligence (AI) system or service shall be determined by the lecturer, and may only be used in the manner and under the conditions indicated by them. In all cases, its use must comply with the following principles:
a) The use of AI systems or services must be accompanied by critical reflection on the part of the student regarding their impact and/or limitations in the development of the assigned task or project.
b) The selection of AI systems or services must be justified, explaining their advantages over other tools or methods of obtaining information. The chosen model and the version of AI used must be described in as much detail as possible.
c) The student must appropriately cite the use of AI systems or services, specifying the parts of the work where they were used and describing the creative process followed. The use of citation formats and usage examples may be consulted on the Library website(https://www.ufv.es/gestion-de-la-informacion_biblioteca/).
d) The results obtained through AI systems or services must always be verified. As the author, the student is responsible for their work and for the legitimacy of the sources used.
2.- In all cases, the use of AI systems or services must always respect the principles of responsible and ethical use upheld by the university, as outlined in the Guide for the Responsible Use of Artificial Intelligence in Studies at UFV. Additionally, the lecturer may request other types of individual commitments from the student when deemed necessary.
3.- Without prejudice to the above, in cases of doubt regarding the ethical and responsible use of any AI system or service, the lecturer may require an oral presentation of any assignment or partial submission. This oral evaluation shall take precedence over any other form of assessment outlined in the Teaching Guide. In this oral defense, the student must demonstrate knowledge of the subject, justify their decisions, and explain the development of their work.

BIBLIOGRAPHY AND OTHER RESOURCES

Basic

I.J. Jackson and C.M. Abbot (eds.) Mouse Genetics and Transgenetics Oxford University Press

Fernando J. Benavides and Jean-Louis Guénet Manual of Laboratory Rodent Genetics: Basic Principles and Applications. Editorial de la Universidad de Alcala and Spanish Society for Laboratory Animal Sciences

Additional

AA.VV. Miscellaneous scientific articles