DEPARTMENT OF MEDICINE, SOLNA

K2F2186 Generating Genetically Modified Mice for Immunological Research, 1.5 credits (hec)

Att skapa genetiskt modifierade möss för immunologisk forskning, 1,5 högskolepoäng

Third-cycle level / Forskarnivå

Approval

This syllabus is approved by the The Committee for Doctoral Education on 2023-10-31, and is valid from Spring semester 2024.

Responsible department
Department of Medicine, Solna, Faculty of Medicine

Prerequisite courses, or equivalent

Swedish law and ethics on the protection of laboratory animals (theory).

Intended learning outcomes

Purpose

The purpose of this course is to enable the students to acquire an in-depth theoretical understanding of the technologies used for generating precise genetic modifications in mice. The course focuses on the classic gene targeting technique (homologous recombination in embryonic stem cells), CRISPR/Cas9 (non-homologous end joining and homology directed repair), and transgenesis by pronuclear injection in zygotes (e.g. TCR transgenes). Understanding these technologies will enable the students to design experiments to test hypotheses in vivo and generate new tools to ask complex immunological questions. These skills are becoming ever more important as science is getting more complex.

Intended learning outcomes

After taking the course the student should have acquired an in-depth knowledge of how to generate genetically modified mice. The students should be able to write a scientifically sound gene targeting project plan at the end of the course. The student should acquire enough practical and theoretical knowledge to allow them to independently generate genetically modified mice.

Specifically, the student should know how to design and make DNA constructs for classical gene targeting and for NEHJ and HDR using CRISPR/Cas9. The students should know how to design genotyping using e.g. Southern blotting and PCR, and finally how to use the modified mice in experiments. Furthermore, after the course the students should know how to critically analyze experiments presented in the scientific literature and judge their scientific quality.

Course content

1) Gene targeting and transgenesis in general.
-A short history of gene targeting, transgenesis and CRISPR/Cas9 in mice.
-When are these technologies suitable for immunological experiments?
-Overview of the work process.

2) Designing and making constructs for classical gene targeting, and for CRISPR/Cas9-based NHEJ and HDR.
-How to obtain the necessary information for designing a gene targeting construct.
-Different approaches to make DNA constructs for gene targeting and CRISPR/Cas9-based NHEJ and HDR.

3) Conditional gene targeting (Cre-lox system).

4) Common problems in gene targeting, transgenesis, and CRISPR/Cas9; and how to solve them.

5) How to use genetically modified mice in immunological research.
-Breeding strategies.
-Controls.

Forms of teaching and learning

Lectures will be the main form of teaching during the course. Workshops and a written examination are also critical elements of the course. For the examination, the students (in groups of 2-3) will design a gene modification project (both for classic gene targeting and with CRISPR/Cas) and present their research plan. The workshops and the take-home examination are compulsory. Absence from the workshops can be compensated by an individually written report in agreement with the course leader. Formative assessment during active participation in the workshop and summative assessment of the quality of the take-home examination in line with the intended learning outcomes of the course. Students will have a new examination opportunity within two months after the course is finished.

Language of instruction
The course is given in English.

Grading scale

Pass (G) /Fail (U)

Types of assessment

Compulsory components

The workshops and the take-home examination are compulsory.

Forms of assessment

Formative assessment during active participation in the workshop and summative assessment of the quality of the take-home examination in line with the intended learning outcomes of the course. Students will have a new examination opportunity within two months after the course is finished.

Course literature

Recommended literature:

Genome Editing in Mice Using CRISPR/Cas9 Technology
Curr Protoc Cell Biol. 2018 Dec;81(1). PMID: 30178917
https://pubmed.ncbi.nlm.nih.gov/30178917/

A mouse geneticist's practical guide to CRISPR applications.
Genetics. 2015 Jan;199(1):1-15. PMID: 25271304
https://pubmed.ncbi.nlm.nih.gov/25271304/

Transgenic Mouse Methods and Protocols
Methods in Molecular Biology Volume 693, 201.1 Editors: Marten H. Hofker, Jan van Deursen
ISBN: 978-1-60761-973-4
https://link.springer.com/book/10.1007/978-1-60761-974-1