

Genetic engineering in model organisms: technology and application in basic and medical research

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Date:	June every two years
Location:	LUMC, Leiden
Duration:	5 days (including 2 days int. workshop on Innovative Mouse Models)

The ability to modify genes at the level of the germ line by transgenesis and gene targeting has been crucial for our understanding of gene function and has yielded many highly valuable models for human diseases.

This course will deal with the basic principles underlying the generation of transgenic, knock-out (KO) and knock-in (KI, i.e., gene-modified rather than gene-inactivated) mice.

Transgenesis, when combined with the recently developed technology of whole-animal cellular and molecular imaging (e.g., bioluminescence, MRI, multiphoton imaging), allows direct visual access to complex biological processes in their native environment, thus providing better insight into mammalian biology than ever before.

KO and KI mice were traditionally made through Embryonic stem cell (ESC) technology. ESC derivation, *in vitro* genetic modification and use in the generation of chimeric mice represent another main theme of the course.

Most recently, the spectacular advances in CRISPR/Cas9-assisted gene modification have found wide application in mouse genetics. CRISPR/Cas9-technology strongly facilitates gene targeting in ESCs, but can also directly be used in zygotes, evading the ESC route. Both applications will be presented, as well as the application of CRISPR/Cas9 technology in non-germ-line gene modification.

The course will consist of lectures covering technology and applications of genetic engineering in basic and medical research. Practical demonstrations will show crucial steps in the generation of transgenic, KO and KI mice, and principles of *in vivo* imaging.

The first three days of the course will prepare participants for the 2-day international workshop on Innovative Mouse Models (IMM) immediately following the course. Keynote lectures from leading laboratories and presentations from selected abstracts will discuss the latest developments on advanced genome modification protocols and its applications in fundamental biology and biomedical research. **Course participants will participate in 'meet-the-expert' sessions.**

This introductory course is aimed at PhD students with little or no experience in the field of transgenesis and *in vivo* imaging, but is also of interest to those already working with animal models but wishing to expand their knowledge of the above technologies for applications in their own research.

Content:

- Conventional transgenesis including mouse genetics
- Gene targeting / replacement and conditional gene targeting, inducible gene expression
- CRISPR/Cas9-assisted gene modification
- Construct design including promoters and other regulators of gene transcription
- In vivo* imaging
- Embryonic stem cell derivation via 2i culture
- Dedifferentiation via iPSCs
- Presentations on applications in cardiovascular disorders, cancer, immunology etc.

PhD students from outside the MGC institutions are charged a € 500 enrolment fee.