

Mouse Mutant Core Facility

The purpose of the Mouse Mutant Core Facility is to generate murine models of disease and development for researchers at IRB Barcelona and their collaborators. The Facility was initiated in January 2007 and consists of three members of staff, with an additional member joining in March 2008.



The transgenic mouse plays a vital role in fundamental and applied biomedical research. The study of normal and abnormal gene expression, of regulatory elements and of gene mutations relevant for human disease are examples of applications of genetically modified animal models in experimental research. A wide range of modifications can now be made to the mouse genome, including the introduction of simple exogenous transgene DNA, targeted deletions and insertions, the introduction of conditional sequences, point mutations and other modifications. These mutations are produced using a variety of techniques, most of which involve the manipulation of pre-implantation stage embryos or mouse embryonic stem (ES) cells.

The period from January 2007 to December 2007 has been the first full operational year of the Mouse Mutant Core Facility. During this time, we have grown from 2 to 3 members of staff, with the recruitment of an additional microinjection specialist. This has enabled us to produce over 40 transgenic founder lines during the year. Part of the future service will include the design and cloning of gene targeting vectors. Therefore, we have begun to develop and implement the various molecular techniques required for this aspect of the service. Very recently we have moved into a new fully equipped laboratory space dedicated to the molecular and cellular facets of our work.

Services for IRB Barcelona researchers

The Mouse Mutant Core Facility aims to offer a full and comprehensive range of services for the production of genetically modified mice, including:

Experimental design

We provide consultation on all aspects of design for transgenic and gene targeting projects, such as the design and construction of recombinant vectors, screening for mutations and analysis of mutant mice.

Construction of gene targeting vectors

An eventual aim of the facility will be to offer the construction of various types of recombinant DNA vectors for genome modification. These will include gene knock-out vectors, conditional gene knock-out vectors, modified bacterial artificial chromosomes (BACs), point mutation vectors, knock-in vectors and

other types of vectors. Most modifications will be carried out using the techniques of 'recombineering'. The recruitment of a full-time molecular biologist will enable us to fully implement this aspect of the service in the coming year.

Mouse embryonic stem cell culture

The Facility has a dedicated tissue culture laboratory used exclusively for the culture of mouse ES cells and related cell lines. We offer a complete gene targeting service, from transfection of stem cells with gene targeting vectors, selection and picking of drug resistant clones to archiving of clones and preparation of DNA from duplicate plates and expansion of targeted clones prior to microinjection. In addition, the facility offers karyotyping of clones and derivation of novel ES lines as required.

Microinjection

The Facility has two experienced microinjection specialists, who have the skills required to inject plasmid and BAC-based vectors into single-cell embryos, or modified ES cells into blastocysts. These modified pre-implantation embryos are then placed back into the reproductive tract of recipient mice and allowed to develop to term.

The technologies for creating mutant mice are continually being refined and advanced, and it is the aim of the Facility to keep abreast of these developments, and incorporate them into our methodologies where appropriate.