

# Mouse Mutant Core Facility

The purpose of the IRB Barcelona Mouse Mutant Core Facility is to generate murine models of disease and development for researchers at IRB Barcelona and their collaborators. The Facility has been operating since January 2007 and is staffed by scientists with extensive experience in cell culture, embryo manipulation and molecular biology. Genetically modified mice play a vital role in basic 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, 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.

Early in 2008, the Mouse Mutant Core Facility moved into a refurbished, dedicated laboratory space of about 60 m<sup>2</sup>, containing a small self-contained tissue culture lab, office and bench space and equipment for carrying out molecular biology work. In addition, we have a dedicated microinjection lab within the SPF facility, which houses two independent microinjection stations, as well as other apparatus required for embryo manipulation and mouse surgery.

In the first year, after setting up the facility in 2007, we generated a number of transgenic founder lines. 2008 has seen the creation of the first of our gene-targeted lines.

During the year we have been working on standardised protocols for the production of gene-targeting vectors. This has been made possible by the recruitment of a molecular biologist, whose tasks are to develop technologies and to assist research groups in the production of targeting and transgenic vectors. In 2008, we hosted two students, one who came to spend the summer with us, and the other who worked with us for eight months as part of an undergraduate degree.

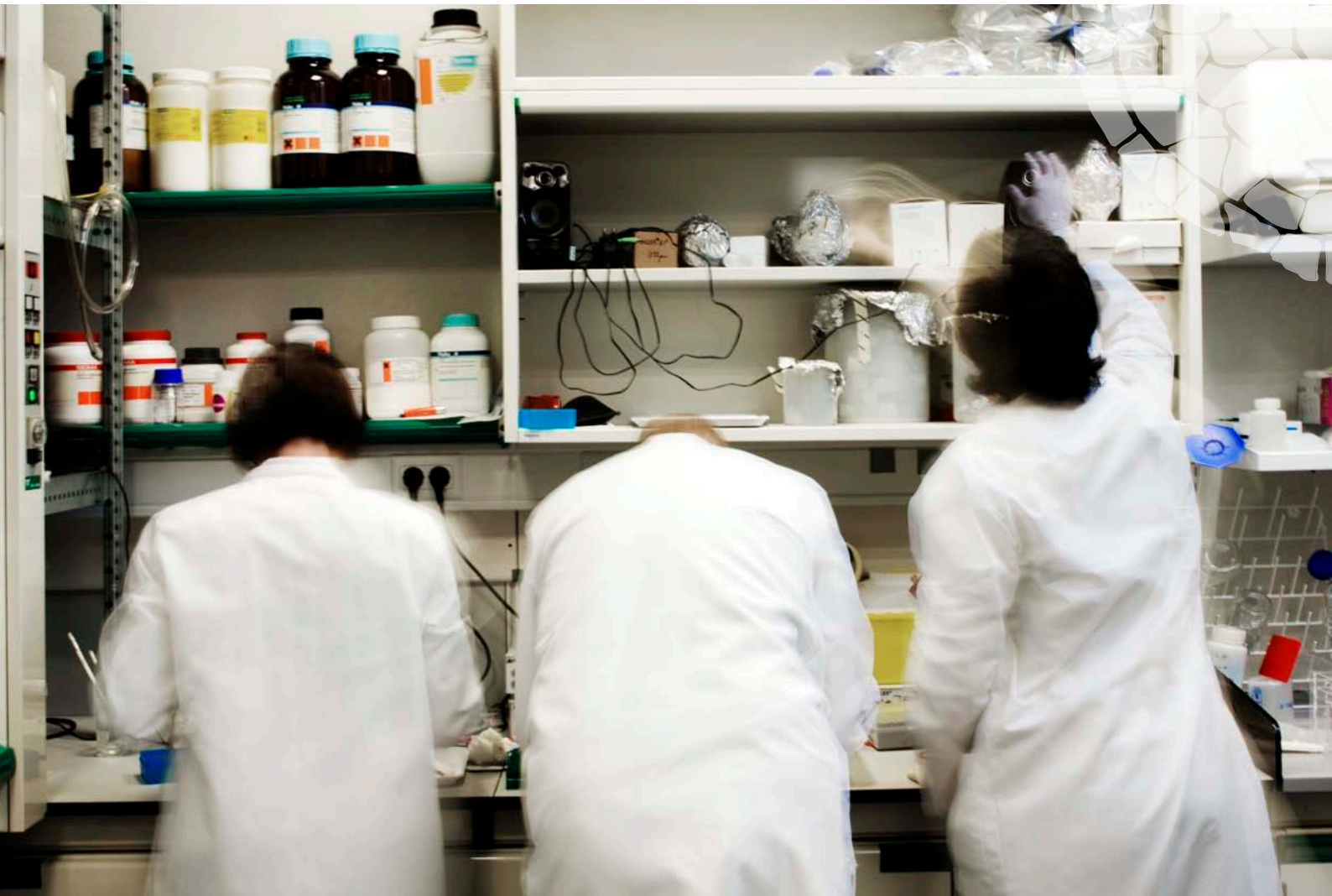
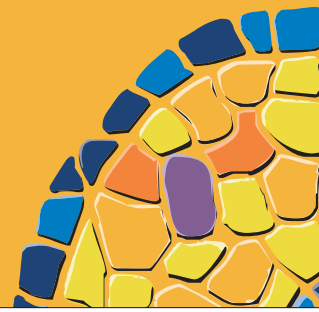
## Services for IRB Barcelona researchers

**Experimental design.** The Facility provides consultation on all aspects of the design of gene-targeting and transgenic DNA vectors. These designs usually begin by an examination of the gene structure, derived from data generated by the relevant

research group, or from databases (such as Ensemble or Vega) or a combination of both. We then propose an appropriate experimental strategy and a suitable cloning protocol. We also provide advice on screening strategies for transgenic and gene-targeted mice and cells.

**Vector construction.** DNA vector design and construction is important for the success of the transgenic or gene-targeting experiments. We have recently employed a full-time molecular biologist whose function is two-fold. The first aim is to design and generate a set of molecular and cellular tools and protocols in order to make the creation of recombinant DNA molecules and the screening for mutations both easier and faster. The second goal is to act as a consultant for those groups and researchers generating transgenic or targeting vectors.

**Generation of gene-targeted and transgenic mice.** In recent years, publically funded initiatives aimed at creating ready-made ES cell mutants, such as the European Conditional Mouse Mutagenesis Programme (EUCOMM) and the International Gene Trap Consortium (IGTC), have generated mutations in thousands of genes. We use these resources wherever possible, and in the last year we initiated the first of our gene-targeting projects using ready-made clones. The list of projects using these clones or vectors is rapidly increasing, and we expect to do many more in the coming year.



However, many types of genes and genetic modifications are not covered by the aforementioned consortiums, and these types of projects require the design and building of a gene/mutation-specific vector in collaboration with the research groups.

**Mouse ES cell culture.** The Facility has a dedicated tissue culture lab for the culture and manipulation of mouse ES cells and mouse embryonic fibroblast cells. We offer a complete gene-targeting service, from transfection of ES cells with gene-targeting vectors, drug selection of transfected cells, and the picking and expansion of drug-resistant clones, to the archiving of duplicate clones. After correctly targeted cell clones have been

identified, potential positives are expanded and further analysed before being microinjected into pre-implantation mouse blastocysts.

**Microinjection.** The Facility has two dedicated microinjection stations equipped with state-of-the-art micromanipulators. Two specialist technicians carry out microinjection and associated microsurgery techniques in addition to overseeing breeding strategies for lines generated or maintained by the Facility.