



**INFRAFRONTIER**  
mouse disease models

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**INFRAFRONTIER-I3 / MOUSE PRODUCTION SERVICE**

**Application Form: FIRST CALL: March 2013, closing of call on March 31st**

<b>First name</b>	
<b>Family name</b>	
<b>Email</b>	
<b>Phone</b>	
<b>Fax</b>	
<b>Institution</b>	
<b>Address</b>	
<b>Town</b>	
<b>Postcode</b>	
<b>Country</b>	

**The following data is required by the EC for statistical purposes.  
Applications can only be considered if all data are provided.**

<b>Gender</b>	
<b>Birth year</b>	
<b>Nationality</b>	
<b>Researcher status (e.g. Prof, Postdoc)</b>	
<b>Scientific background</b>	

**Send your proposal to [info@infrafrontier.eu](mailto:info@infrafrontier.eu) by 31st March 2013**

## **Transnational Access (TA) Activity of the Infrafrontier-I3 project:**

### **Free of charge mouse production service**

- The EC FP7 funded Infrafrontier-I3 project (2013 – 2016) supports eligible customers with a **free of charge mouse production service** implemented as a Transnational Access activity providing a total of **30 access units**.
- The **access unit** is defined by the production of a minimum of two heterozygous mice carrying the targeted gene allele of choice from the corresponding validated gene-targeted ES cell clone(s).
- **Costs:** The access to the Infrafrontier-I3 resources allocated to this work package is free of charge. The free of charge access will also include the shipment cost of the produced live mice to the customer's facility (covering shipment cost of up to 800 Euros / shipment).
- **Eligibility:** Applications for the Infrafrontier-I3 TA can be submitted from customers based in eligible countries, namely:

**EU Member States:** Austria (AT), Belgium (BE), Bulgaria (BG), Cyprus (CY), Czech Republic (CZ), Denmark (DK), Estonia (EE), Finland (FI), France (FR), Germany (DE), Greece (GR), Hungary (HU), Ireland (IE), Italy (IT), Latvia (LV), Lithuania (LT), Luxembourg (LU), Malta (MT), Netherlands (NL), Poland (PO), Portugal (PT), Romania (RO), Slovakia (SK), Slovenia (SI), Spain (ES), Sweden (SE), United Kingdom (GB)

**Associated Countries:** Albania (AL), Croatia (HR), Iceland (IS), Israel (IL), Liechtenstein (LI), Macedonia (MK), Montenegro (ME), Norway (NO), Serbia (RS), Switzerland (CH), Turkey (TR)

- **Application:** Service requests for the first call of the Infrafrontier-I3 mouse production service can be made via this application form. **Applications for the Transnational Access activity must be accompanied by a short description of the project involving the resources being produced by the Infrafrontier-I3 mouse production service.** Applications may be submitted in response to a total of **3 calls** each providing 10 access units.
- **Selection procedure:** Service requests from eligible customers for free of charge access to the Infrafrontier-I3 mouse production capacities will be subject to a review procedure which will be initiated after calls for TA applications are closed. The review will be based on short descriptions of the projects involving the resources being generated by the TA service. Members of the Infrafrontier-I3 project and of the external Infrafrontier Evaluation Committee will assess service requests supported by the TA activity. In addition to scientific merit, the selection panel will try to ensure free access is granted to those users who have not previously benefited from this scheme. Only one access unit will be granted to a Principal Investigator per call. Applicants will be informed on the outcome of the evaluation within 6 weeks after the end of the call for which the TA application was submitted.
- **Acknowledgements:** Please do acknowledge any support under this scheme in all resulting publications with "Part of this work has been supported by Infrafrontier-I3 under the EU contract Grant Agreement Number 312325 of the EC FP7 Capacities Specific Programme"

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## Support offered

Infrafrontier-I3 will provide to eligible customers 30 free of charge access units for the generation of new mouse mutant lines from existing gene-targeted ES cell clones from either international consortia such as IKMC or from other sources. For each project a minimum of two independent ES cell clones will be requested to maximize the probability to obtain a germline-transmitting chimera. This follows recommendations given by the IKMC (<http://www.eummc.org/order.php>). All Infrafrontier-I3 mouse production centers will first validate the received ES cell clone(s). Confirmation of the quality of the ES cell clone(s) will increase the likelihood to eventually obtain germline-transmitting chimeric mice and the resulting heterozygous animals carrying the genetically-altered allele. However, for some genes it might be possible that no germline-transmitting (GLT) chimera will be obtained from the submitted and validated ES cell clone(s) (10% if 3 ES clones are injected). All requested mice will be produced in the SPF units of each participating node following FELASA health status recommendations. Mice will be shipped to the customer's animal facility from the production node by specialised couriers, according to standard mouse shipment procedures. The customer must have a valid licence to breed and analyse genetically modified mice. Heterozygous mice will be shipped within 8 to 12 months after the request has been approved by the Infrafrontier evaluation committee and the ES cell clone(s) have been received by the production centre. All mouse knockout models produced by the Infrafrontier-I3 TA will also be cryopreserved by the Infrafrontier production node. The frozen embryos or sperm will be deposited into the EMMA repository for subsequent use by the scientific community.

## Modality of access

- The **30 access units** will be extensively advertised by both Email lists and through the public Infrafrontier website ([www.infrafrontier.eu](http://www.infrafrontier.eu)) in a total of **3 calls each allocating a total of 10 access units**. Calls will be published in March 2013, September 2013 and March 2014.
- The conditions for free access are **1) the user must work in an institution of a EU Member State or Associated State, 2) the user must be selected by the external Infrafrontier Evaluation Committee and 3) the user must sign any related MTAs linked to specific ES cell lines and agree that the mice derived from them will be publicly distributed via EMMA using institutional MTAs of the successful applicants**. The TA applications will be scheduled in the request pipeline at the different participating Infrafrontier nodes.
- Service requests from eligible customers for 'free of charge' access to the resources will be subject to a **review procedure**. The review will be based on a short scientific project description and its expected relevance and impact in biology / biomedicine, including the expected role of the requested mouse resource in the proposed project.
- **The access to the Infrafrontier resources allocated to this work package will be free of charge**. The free of charge access will also include the shipment cost of the produced live mice to the customer's facility (covering shipment cost of up to 800 Euros / shipment)
- **The customer is responsible for providing and shipping the ES cell clone(s) to the indicated Infrafrontier production node**. The location of the production node will be communicated by the Project Office as soon as the application is approved by the Evaluation Committee.

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**Description of proposed project**

Please describe briefly the scientific reasons why you propose to generate a knockout mouse model from ES cell clones targeted for the indicated gene. This proposal will be the foundation for the evaluation of your project

Gene of interest	

Please, do not extend beyond the provide space (maximum space is 1 page)  
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## **Validation of ES cell clones at the Infrafrontier-I3 nodes**

All Infrafrontier-I3 partners providing the mouse production service will first validate the received ES cell clone(s). Confirmation of the quality of the ES cell clone(s) will increase the likelihood to eventually obtain germline-transmitting chimeric mice and the resulting heterozygous animals carrying the genetically-altered allele.

ES cell clone(s) will be expanded and the cells will be tested for the presence of known mouse pathogens, in particular for mycoplasmas. The ES cell clone(s) will be also karyotyped, aiming to at least 50% of euploidy ( $2n=40$  chromosomes) after counting a minimum of 30 chromosomal metaphases. Genomic DNA will be prepared and the presence of the inactivated gene allele, according to the expected genetic alteration, will be investigated by PCR and by Southern blot analysis. Suitable DNA probes for Southern blot analysis and the recommended primers will be provided by the customer according to the gene locus information and the expected genetic alteration. Only ES cell clones proved to be negative for known mouse pathogens, negative to mycoplasmas, with a level of euploidy  $> 50\%$  after counting a minimum of 30 chromosomal metaphase plates and with the expected genetically-altered allele will be further processed and microinjected to suitable mouse blastocysts. If none of the ES cell clone(s) provided can be validated by the production node, the project will be terminated. The customer will be provided with a dossier with detailed information of all activities and experiments undertaken along with recommendations for testing other ES cell clone(s) that might be available.

## **Infrafrontier-I3 partners providing the mouse production service**

- Biomedical Sciences Research Centre Alexander Fleming, Vari, Greece
- Agencia Estatal Consejo Superior de Investigaciones Cientificas (CSIC), National Centre for Biotechnology (CNB), Madrid, Spain
- University of Oulu, Biocenter Oulu (BCO), Oulu, Finland
- Institute of Molecular Genetics of the ASCR,v.v.i.(IMG, Czech Centre for Phenogenomics), Prague Czech Republic
- University of Veterinary Medicine Vienna - Biomodels Austria (VUW), Vienna, Austria

The infrastructure required for running the TA service is provided by five independent Infrafrontier nodes located in Vari-Athens (Greece), Madrid (Spain), Oulu (Finland), Prague (Czech Republic) and Vienna (Austria). All five nodes offer this service routinely to the researchers of their institutions and to external customers. They are equipped with up-to-date tools and have access to animal facilities where genetically modified animals are housed in specific units, their use is registered and reported to authorities and inspections are performed on a regular basis. They have proven capability to produce genetically-modified animals from embryonic stem (ES) cells. All five units have specialized personnel with the required expertise to produce genetically-modified animals using state-of-art technologies. All these five production units are associated with the corresponding archiving facilities at each centre. This allows the cryopreservation of all new mouse lines created by the Transnational Access service, thus allowing optimal integration of both production and archiving tasks and providing the new animal models to the requesting customer but also to the wider scientific community. The Infrafrontier-I3 TA activity is led by CSIC (Dr. Lluís Montoliu).

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