

**EUROPEAN COURSE ON PATHOLOGY & EMBRYOLOGY
OF GENETICALLY ENGINEERED MICE**

Organized by The D.E.S.V. of Veterinary Pathology

In partnership with:

The French Society of Veterinary Pathology

Veterinary School of Nantes (France)

May 9 – 13, 2005



Eumorphia

Phenotype screens for mice Developing an integrated platform

The collage features the following logos and institutions:

- GBF (German Research Community for Biotechnology)
- GENOSCOPE (Genome Sequencing Platform)
- ICRF (International Centre for Reproductive Health)
- MRC HUMAN GENETICS UNIT EDINBURGH
- EMBL (European Molecular Biology Laboratory)
- cnio (Centro Nacional de Investigaciones Oncológicas)
- KAROLINSKA INSTITUTET (Institutionen för Cell- och Molekylärbiologi)
- CNRS (Centre National de la Recherche Scientifique)
- EMBL (RESEARCH, SERVICES, NEWS)
- IGBMC (Institut de Génétique et de Biologie Moléculaire et Cellulaire)
- ANIMAGE (Association Nationale pour l'Imagerie Médicale)
- MRC (Medical Research Council HARWELL)
- UKVAV (UK Veterinary and Veterinary Associates)
- MRC (Medical Research Council FUNCTIONAL GENETICS UNIT)
- INSTITUT PASTEUR
- The Wellcome Trust Sanger Institute
- UNIVERSITÉ DE GENÈVE
- UNIL (UNIVERSITÉ DE LAUSANNE)

On the right, a map of Europe is shown with red stars indicating the locations of the participating institutions across various countries including Spain, France, Germany, Italy, and the UK.

EUMORPHIA - the consortium

- MRC Mammalian Genetics Unit, UK
- IGBMC, Strasbourg, France
- MRC Human Genetics Unit, UK
- MRC Functional Genetics, UK
- ANIMAGE, Lyon, France
- CNG/CNRS Paris, France
- GSF, Munich, Germany
- GBF, Braunschweig, Germany
- NKI, Amsterdam, Netherlands
- EMBL Monterotondo, Italy
- CNR-IBC, Monterotondo, Italy
- Karolinska, Stockholm, Sweden
- UNIL-IBA, Lausanne, Switzerland
- UNIGE, Geneva, Switzerland
- Sanger Institute, Hinxton, UK
- CNIO, Madrid, Spain
- Univ. Manchester, UK

18 centres across Europe



EUMORPHIA

European
Union Mouse
Genetics
Research for
Public Health
And
Industrial
Applications

Phenotyping

Mutagenesis

Informatics

Archiving

Networking and
Training



EUMORPHIA

Phenotyping

**European
Union Mouse
Genetics
Research for
Public Health
And
Industrial
Applications**

- **Working groups to develop and standardise primary and secondary phenotyping protocols for all body systems**
- **To develop them in collaboration with other centres throughout the world and in consultation with clinicians, human geneticists, physiologists and informaticians**

Phenotyping - Workpackages

- **Standardisation - animal handling**

European Mouse Phenotyping
Resource for Standardised Screens -
EMPreSS

- **Clinical Chemistry/Haematology**

- **Renal systems**

- **Central, peripheral nervous system,
muscle**

- **Behaviour and cognition**

- **Imaging**

- **Necropsy, pathology, histology**

- **Cardiovascular**

- **Hormonal/metabolic**

- **Allergy and infection**

- **Sensory systems**

- **Pulmonary**

- **Cancer**

- **Bone, Cartilage**

- **Expression analysis**

What is EMPReSS?

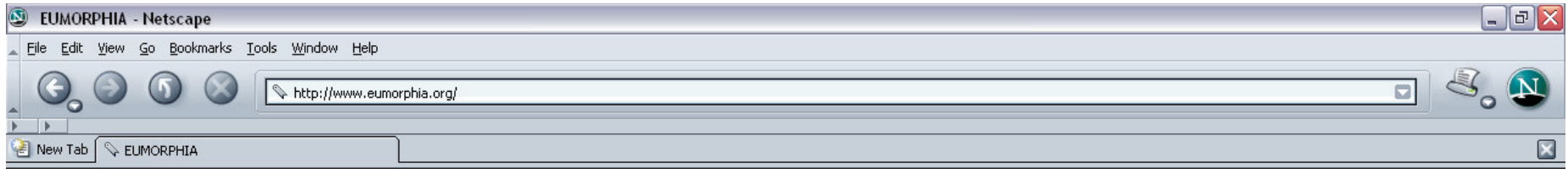
- European Mouse Phenotyping Resource for Standardised Screens
- The EMPReSS provides a platform for the systematic and standardised primary characterisation of mouse mutant models
- It is a comprehensive database of validated SOPs for systematic screens and tests that allows us to describe the phenotype of a mouse

www.eumorphia.org



Importance of standardisation

- Better reproducibility of test outcome
- Better comparability of test outcome
- Sharing of phenome results
- Reduction in the number of mice used in research



Understanding Human Disease Through Mouse Genetics

Unit, Harwell

Home Description Work Packages Jobs Partners Meetings Contact Training Courses Software Links

EUMORPHIA Summer School / Lecture Course

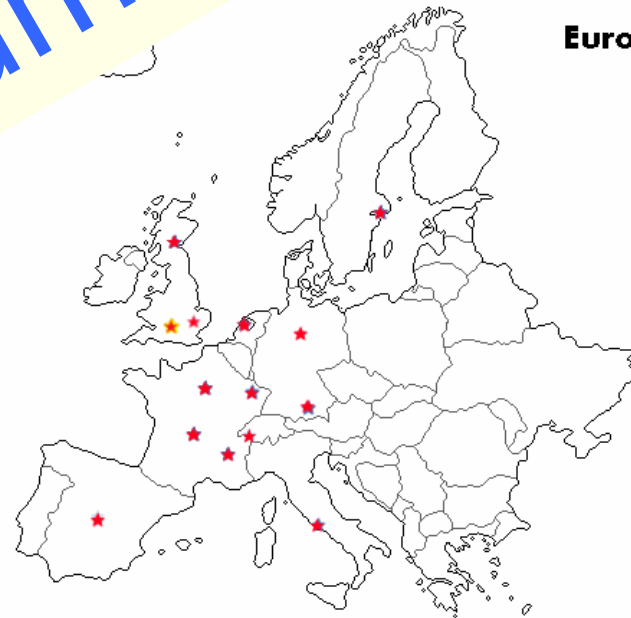
Mouse Models for

EUMORPHIA is an integrated research programme involving the development of mouse models for human disease through the use of genetics and informatics leading to improved characterisation of mouse models for human disease.

Our Partners

Please mouse over a site in Europe to

MRC Mammalian Genetics Unit, Harwell & MRC
Functional Genomics Unit, Oxford




Europe

EMPreSS Browser - Netscape

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http://www.eumorphia.org/EMPreSS/servlet/EMPreSS.Frameset

New Tab EMPReSS Browser



- EMPreSS
 - Clinical chemistry and haematology
 - Hormonal and Metabolic Systems
 - Cardiovascular
 - Allergy and Infectious diseases
 - Sensory Systems
 - Central/Peripheral Nervous and Skeletal M
 - Behaviour and cognition
 - Cancer Phenotyping
 - Bone, Cartilage, Arthritis, Osteoporosis
 - Gene Expression
 - Necropsy Exam, Pathology, Histology

Please Select a Document Type Query Term: >>

EUMORPHIA is proud to present its first online version of the European Mouse Phenotyping Resource of Standardised Screens(EMPreSS).

Individual standard operating procedures (SOPs) for phenotyping a mouse are available on this site. Together these form a platform for the systematic and standardised primary screening of mouse mutant models.

EMPreSS has been developed in the EUMORPHIA project with funding from the European Commission. It is the first time that these phenotyping tests have been integrated together to form a comprehensive validated platform for first line phenotyping of the mouse. Eumorphia is currently engaged in developing more specialised secondary and tertiary tests designed to more fully characterise a phenotype.

The SOPs are grouped and integrated according to research area, e.g. sensory systems or cancer, with links to supporting annexes or related protocols within other areas of EMPReSS. The site is searchable.

The SOPs are categorised according to the experience required and the amount of specialised equipment. The primary tests are divided into:

- **Primary first line** for those tests that are simple to apply and require little specialist equipment
- **Primary extended** which give further information on the phenotype, but require more specialised skills or equipment.

[FAQ](#)

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How does it work?

- The SOPs are categorised according to the experience required and the amount of specialised equipment.
- The primary tests are divided into:
 - **Primary first line** for those tests that are simple to apply and require little specialist equipment
 - **Primary extended** which give further information on the phenotype, but require more specialised skills or equipment.

EMPReSS to date

- WP groups established March 2003
- All relevant WPs have contributed
- A total of 107 SOPs, both primary and primary extended, have been submitted and accepted by the EMPReSS along with annexes

Format for the SOPs


- **Purpose:** Main objectives and the basic principles underlying the protocol
- **Scope:** Who the procedure is intended for
- **Safety Requirements:** Details of the necessary precautions to be taken when carrying out the procedure.
- **Associated Documents:** Lists the SOPs within the EMPReSS, which are specifically associated with the protocol, including those that are referred to within the procedure.
- **Notes:** Any important additional factors that must be taken into account *before* carrying out this procedure.
- **Quality Control:** Any methods/means of calibrating equipment used for experimentation and how often it is undertaken. Details on how to validate the quality of a particular assay may also be contained within this section.
- **Equipment:** Any one-off purchases of equipment required for the procedure.
- **Supplies:** Any consumables that will be required for the procedure, including any solutions.
- **Procedure:** A step-by-step, detailed description of how the procedure must be carried out.
- **Data Records and Reports:** A list of any data or literature available that supports the SOP.
- **History Review:** Details of any other versions of the SOP that have since been modified.
- **Emergency Procedures:** Actions that must be taken in the event of an emergency situation during the procedure.

EMPreSS Browser - Netscape

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http://www.eumorphia.org/EMPreSS/servlet/EMPreSS.Frameset

New Tab EMPreSS Browser



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 - Sensory Systems
 - Central/Peripheral Nervous and Skeletal M
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 - Open Field
 - Appendix: Open Field
 - Modified SHIRPA**
 - Appendix: Modified SHIRPA
 - Grip Strength
 - Y-maze
 - Appendix: Y-maze
 - Acoustic startle and pre pulse inhibition
 - Appendix: Acoustic startle and pre puls
 - Tail Flick
 - Appendix: Tail Flick
 - Tail suspension
 - Appendix: Tail suspension
 - Swim ability test
 - Appendix: Swim ability score
 - Cancer Phenotyping
 - Bone, Cartilage, Arthritis, Osteoporosis
 - Gene Expression
 - Necropsy Exam, Pathology, Histology

Please Select a Document Type Query Term: >>


 Standard Operating Procedure	Title: Modified SHIRPA Doc. Number: 10_002 Rev No: 0 Date Issued: 01/06/04 Status: 3 Validation: ★★ Type: 1F
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1 Purpose

1.1 Use modified SHIRPA for a simple first-line phenotyping screen.

2 Scope

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Review of the SOPs

- Once the SOPs have been written they are reviewed by a number of routes. The status of review indicated by status levels at the top of each SOP.

Status levels:

1. Initial development, discussion and review within expert working groups leading to a SOP
2. Review by the EMPReSS resource team
3. Review and sign off of SOP by a EUMORPHIA scientist outside the working group

Validation of the SOPs

The SOPs are then subjected to evaluation by one or a number of the partners. The validation levels are given at the top of each SOP



Validation by testing on selected inbred mouse strains and/or selected mutants at one EUMORPHIA laboratory



Validation by testing on selected inbred mouse strains and/or selected mutants at two EUMORPHIA laboratories




Full comparison of results of testing on selected inbred mouse strains and/or selected mutants at more than two EUMORPHIA laboratories

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1 Purpose

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Status Levels - Netscape

Status Levels

1. Initial development, discussion and review within expert working groups leading to a SOP
2. Review by the EMPReSS resource team
3. Review and sign off of SOP by a Eumorphia scientist outside the working group

Please Select a Document Type [v] [v] Query Term: [] >>

Title: **Modified SHIRPA**

Doc. Number: 10_002	Date Issued: 01/06/04
Rev No: 0	Type: 1F
Status: 3	
Validation: ★★	

- EM
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Validation Levels - Netscape

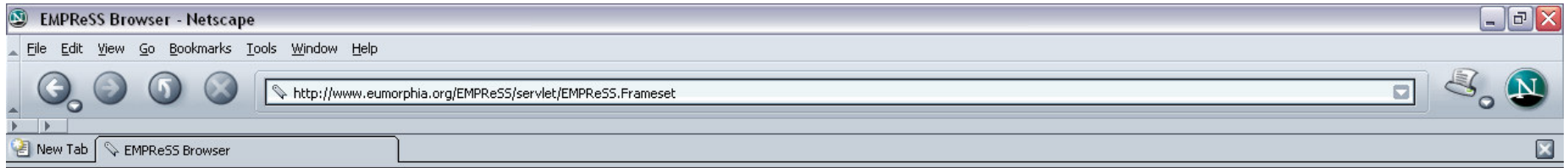
Validation Levels

★	Validation by testing on selected inbred mouse strains and/or selected mutants at one EUMORPHIA laboratory
★★	Validation by testing on selected inbred mouse strains and/or selected mutants at two EUMORPHIA laboratories
★★★	Full comparison of results of testing on selected inbred mouse strains and/or selected mutants at more than two EUMORPHIA laboratories

1.1 Use modified SHIRPA for a simple first-line phenotyping screen.

2 [Scope](#)

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Status Levels - Netscape

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Scope - Netscape

Scope

Who the procedure is intended for, and who must be approached for any queries or deviances relating to the protocol.

Validation Levels - Netscape

Validation Levels

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1.1 Use modified SHIRPA for a simple first-line phenotyping screen.

2 [Scope](#)

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All Documents All Sections Query Term: blood >>

80 hits returned from query, contained in 37 documents retrieved in 473 ms

Document Name	Number of hits	
Cancer Phenotyping		
The macroscopic description of a tumor process	1	View Hits
Annex 1: Staining with Harrison's fixative	1	View Hits
Bone, Cartilage, Arthritis, Osteoporosis		
Ionic fraction of Ca ²⁺ in whole blood	4	View Hits
Micro-CT Imaging	1	View Hits
Gene Expression		
Annex 2: <i>In situ</i> hybridisation: Working with RNA	1	View Hits
Necropsy Exam, Pathology, Histology		
First line phenotyping necropsy	2	View Hits
Tissue fixation by perfusion	1	View Hits
<i>In situ</i> detection of cell death	1	View Hits
Clinical chemistry and haematology		
Differential blood count	3	View Hits
Blood Collection by retro-orbital puncture	4	View Hits
Blood collection by intra-cardiac puncture	3	View Hits
Blood sample handling - Biochemistry	2	View Hits
Blood sample handling - Haematology	4	View Hits
Blood sample handling - Coagulation	2	View Hits
Clinical chemistry parameters	4	View Hits
Haematology tests	5	View Hits
Coagulation tests	2	View Hits
Annex 1: Reagents for blood biochemistry on AU400	1	View Hits
Hormonal and Metabolic Systems		
Appendix 2: Simplified Intra-Peritoneal Glucose Tolerance Test (I.P.G.T.T)	1	View Hits
Appendix 1: Simplified Intra-Peritoneal Glucose Tolerance Test (I.P.G.T.T)	1	View Hits
Simplified Intra-Peritoneal Glucose Tolerance Test (I.P.G.T.T)	2	View Hits

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 Standard Operating Procedure	Title: Micro-CT Imaging	
	Doc. Number: 12_002 Rev No: 0 Status: 3 Validation: ★	Date Issued: 01/06/04 Type: 1F

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1 Purpose

1.1 Construct and analyse micro-CT images in immobilised mice. Micro-CT images can be used in many diagnostic applications including imaging and quantitative analysis of bones and joints in osteoarthritis, rheumatoid arthritis, and osteoporosis; quantification of tumor volume and growth; and documentation of blood vessel distribution and integrity.

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 Standard Operating Procedure	Title: Micro-CT Imaging	
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1 Purpose










1.1 Construct and analyse micro-CT images in immobilised mice. Micro-CT images can be used in many diagnostic applications including imaging and quantitative analysis of bones and joints in osteoarthritis, rheumatoid arthritis, and osteoporosis; quantification of tumor volume and growth; and documentation of blood vessel distribution and integrity.

2 Scope

2.1 Individuals who are trained and competent in using the VAMP Micro-CT machine and in handling laboratory animals must follow this procedure.


2.2 Any queries, comments or suggestions, either relating to this SOP in general


8.26 x 11.69 in 1 of 2


SOP Title	Completed		Shared with	Validation in Progress	Validation completed
	Primary	Primary Extended			
Modified Shirpa	✓		WP 9 & 10		✓ 
Elevated platform and reaching response	✓				✓ 
Acoustic Startle and PPI	✓		WP 9 & 10		✓ 
Swim Ability	✓		WP 9 & 10		✓ 
Acoustic Brainstem Response		✓		✓	
Optokinetic Response Test (OKR)		✓			✓ 
Fundus and Angiography		✓			✓ 
Using and Indirect Ophthalmoscope		✓			✓ 
Using a Slit Lamp		✓			✓ 

Sensory SOPs

Validation Levels

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EUMORPHIA

**European
Union Mouse
Genetics
Research for
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Industrial
Applications**

Phenotyping

Mutagenesis

Informatics

**Networking and
Training**

EMPReSS Database

- SOPs engineered for XML format
- Links between SOPs and baseline phenotype data, assisting validation, EMPReSS evaluation and SOP development
- EMPReSS will allow systematic integration of the **ASSAY** with phenotype ontologies

EUMORPHIA

Phenotype Ontologies

Informatics

An ontology is an explicit formal specification of the terms in a domain (*concepts*) and the relationships (*attributes*) amongst them

- We need to develop systematic and comprehensive systems to describing phenotypes - phenotype ontologies
- Phenotype ontologies will be central to the development and mining of comprehensive animal phenotype databases
- Integration with SOPs - the assay is central to the development of ontologies

Developing ontologies - the centrality of the assay

CONCEPT {has_attribute} ATTRIBUTE {characterised_by} ASSAY {has_value} VALUE

e.g.

Eye {has_attribute} Colour {characterised_by} Visual Inspection {has_value} Brown

or

Mouse {has_attribute} Body Position {characterised_by} SHIRPA {has_value} Flat

All phenotypes are the result of
an assay

Building EMPReSS as an international resource

- Examine with our partners EMPReSS as a model to develop an international repository for SOPs and baseline data
- Discussions with developers, managers and users of other related resources worldwide to determine ways to link the resources and build upon EMPReSS

Summary

- EMPReSS allows standardisation of primary mouse screening platforms across Europe ensuring reproducibility and comparability of functional genomics research
- Baseline phenome data provided through validation and SOP development will underpin mouse genetics studies
- Enhances efforts towards the refinement and reduction of animal use

Please look at EMPReSS

www.eumorphia.org

And send us your comments

