Introduction
The ability to manipulate the mouse genome and to generate specific gene knockout and transgenic models has led to an explosion of mouse models of disease. It is important to be aware that the background strain of the mouse model can have a substantial effect on the observed phenotype.

Materials and methods
GenoMouse by Elchrom Scientific is a service that characterizes mouse background strains. Panels of tetranucleotide repeat polymorphisms have been generated to distinguish between common strains, and custom panels can be designed upon request. Panels consist of 96 markers spaced evenly across the 19 mouse autosomes.

The markers are amplified by PCR, using primers to unique regions flanking the repeats. The PCR products are electrophoresed using the patented, high-resolution Elchrom hydrogels.

Customers are provided with hard copies of the electrophoretic data, a report and expert recommendations on the steps to take to advance their projects.

Examples
1. EGF receptor knockout

<table>
<thead>
<tr>
<th>Strain</th>
<th>Survival time</th>
</tr>
</thead>
<tbody>
<tr>
<td>CF-1</td>
<td>peri-implantation</td>
</tr>
<tr>
<td>129/Sv</td>
<td>mid-gestation</td>
</tr>
<tr>
<td>129/Sv x C57BL/6</td>
<td>birth</td>
</tr>
<tr>
<td>129 x B6 x MF-1</td>
<td>day 20</td>
</tr>
<tr>
<td>CD-1</td>
<td>three weeks</td>
</tr>
</tbody>
</table>


2. APP transgenics

C57BL6/SJL mice were created to overexpress a fragment of the human amyloid precursor protein, believed to play a role in the development of Alzheimer’s disease.

The phenotype was highly dependent on background strain:
- FVB had neurological abnormalities, cortical glialosis and premature death
- C57BL/6 showed reduced birefractance and premature death
- DBA/2 experienced premature death
- 129 exhibited enhanced survival
- CAST/Ei had no premature deaths
- B6xFVB had cortical glialosis and died prematurely
- D2xFVB died prematurely

(Karen Hoos Aske Group at U. Minnesota)

3. Pde6b(rd1) mutations

2 mutations: nonsense mutation and retroviral insertion
Caus es degradation of rods in retina
Recessive
Result in impaired vision or blindness
Animals impaired in spatial skills, visual memory tasks
Affects strains C3H, SJL, FVB and others

Factors influencing strain choice
- Desirable physiological parameters
- 129 have robust ES cells for generating knockouts
- FVB have large progenitors for transgenic production
- Known strain characteristics
- C57BL/6 prefer alcohol, DBA/2 are alcohol-adverse
- Many 129s perform poorly on behavioral tests
- Availability of strain
- Follow on previously published studies
- 14% of all strain-specific studies are on C57BL/6
- C57BL/6 may be suboptimal for many studies
- Appropriate control strain (not always obvious)
- NOD non-obese diabetes
- Identified modifier loci
- Reproductive characteristics
- Fecundity
- Maternal care
- Serendipity

Ideally, choose at least two distantly related strains

Strain resources
- Michael Feingold’s Inbred Strains of Mice and Rats
  [http://www.informatics.jax.org/external/feingold/search_form.cgi](http://www.informatics.jax.org/external/feingold/search_form.cgi)
- Institute for Laboratory Animal Research strain list
  [http://dels.nas.edu/ilar_n/ilarhome/models.shtml](http://dels.nas.edu/ilar_n/ilarhome/models.shtml)
- International Mouse Strain Resource:
  [www.imsr.org](http://www.imsr.org)

Recommendations
Specific mutations in mice provide powerful systems for experimental analysis. The genetic background strain of mice contributes significantly to the observed phenotype, due to modifier loci and interacting genes at sites distinct from the targeted mutation.

The effects of background strain may not be possible to predict in advance.

A comprehensive analysis of a mutation should involve phenotyping and characterization in two or more distantly-related inbred strains.

Multiple inbred strains offer more predictive power than outbred strains, higher reproducibility, and less background noise.

Be aware that substrains can diverge significantly.

Background strain effects on mouse phenotype
Michele A. Gilson, Anatoli Tassis and Daniela Lang
Elchrom Scientific AG

Fig. 1. Different inbred strains of mice. Determining the appropriate strain or strains for a particular study can be difficult. An empirical approach is often needed.

Fig. 2. Mouse chromosomes. The positions of microsatellite markers on chromosomes one are indicated by the colored circles.

Fig. 3. Microsatellite polymorphisms between C57BL/6 and 129 mouse strains. Shown are four of the six markers from chromosomes one.

For further information
Please contact mgilson@elchrom.com, or visit our websites www.elchrom.com and www.mouseoftruth.com.

About Elchrom Scientific
Founded in 1989 as a spin-off from ETH Zurich
In the first time focus on contract research
40 patents
15 employees, most with scientific background
Start of commercialisation of precast gels and equipment in
2005 launch of GenoMouse service
2006 launch of all-in-one electrophoresis apparatus

Mission:
Resolution – Reproducibility - Reliability