Cre Portal (www.creports.org) Tutorial

This tutorial contains two parts: first, a step-by-step example that you can use to follow along on your computer; and second, a short set of questions (with answers) for you to test your skills.

Aims
1. Find your way to the Cre Portal and search for a cre transgene or knock-in that uses a particular driver/promoter or is known to have activity in a particular anatomical/tissue system.
2. Explore the contents of the Results Page returned and learn about customizing it for your use.
3. Explore detailed information about the cre activity of a specific cre transgene or knock-in and learn about customizing the view and linking to other data.
   - Cre construct information
   - Availability of mouse resources from repositories
   - Specifics of cre activity/specificity for a transgene in an anatomical location (here reproductive system)
   - Images
   - Publications involving this cre transgene/knock-in
   - Phenotypes observed when mice carrying this cre transgene/knock-in were mated to different gene knock-out heterozygotes
4. Return to the Cre Portal main page and view the data report for ‘all cre transgenes/knock-ins’.

Introduction
Cre is currently the most commonly used recombinase. It catalyzes site-specific recombination of DNA between loxP sites, thus making possible conditional mutagenesis, where specific genes can be knocked-out in particular tissues and at particular developmental time points. Other non-cre recombinases (such as Flp, Dre, phiC31, etc.) and various inducible forms of recombinases have been and are being developed. The Cre Portal contains curated data about all recombinase containing transgenes and knock-ins developed in mice to provide a comprehensive resource delineating known activity patterns and allowing users to find relevant mouse resources for their studies.

At present, researchers can search for “cre” data using the driver/promoter gene symbol or using an anatomical system in which the “cre” is expressed. In addition, data are available for all cre’s in a HTML viewable table, or as downloadable tab-delimited text.

Help with using the Cre Portal is available on the www.creports.org site. See the list of FAQs in the right-hand column or the ‘Help Documents’ tab in the bottom section of this page. You can also use the ‘Contact Us’ link in the navy blue navigation bar near the top of any of our web pages.

Worked examples:

1. Find the Cre Portal and search for a cre transgene or knock-in with a particular driver/promoter [or with cre activity in a particular anatomical/tissue system].
Type the URL: [http://creportal.org](http://creportal.org) into your web browser; OR go to the Mouse Genome Informatics (MGI) homepage ([http://www.informatics.jax.org](http://www.informatics.jax.org)) and select the Recombinase (cre) icon. The following illustrates the latter route: visiting the MGI homepage and selecting the icon.

**STEP 1:** Navigate to MGI  
[http://www.informatics.jax.org](http://www.informatics.jax.org)

**STEP 2:** Select the Recombinase (cre) icon.

**STEP 3:** Type in 'Pbsn' (probasin) driver/promotor and select it from the list that appears.

**STEP 4:** Select the 'Search' button.
2. Explore the contents of the Results Page returned from your search and learn about customizing it for your use.

This is the default Results Page from the search illustrated on the previous page. Now let’s explore the features of this page.

Recombinase Alleles - Tissue Summary

You searched for:
Driver equals Plan

Click column headings to sort table data.

<table>
<thead>
<tr>
<th>Driver View</th>
<th>Matrix Gene; Allele Name</th>
<th>Recombinase Activity Detected</th>
<th>Recombinase Activity Not Detected</th>
<th>Induced By</th>
<th>Find Mice</th>
<th>Refs</th>
<th>Allele Synonym</th>
</tr>
</thead>
<tbody>
<tr>
<td>Phan</td>
<td>Tg(Pbn-cre)4Phb</td>
<td>renal &amp; urinary system, reproductive system</td>
<td></td>
<td>tamoxifen</td>
<td>ACR29; C57BL/6J, B6-Cre58, B6-Cre59, FVB/Cre58</td>
<td>2</td>
<td>247</td>
</tr>
<tr>
<td>Phan</td>
<td>Pten-cre; flox/cre</td>
<td>renal &amp; urinary system, reproductive system</td>
<td></td>
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<td>247</td>
</tr>
<tr>
<td>Phan</td>
<td>Tg(Phan-cre)-20Fwan</td>
<td>renal &amp; urinary system, reproductive system</td>
<td></td>
<td>mouse-other</td>
<td>ACR29; C57BL/6J, B6-Cre58, B6-Cre59, Tg(Phan-cre)</td>
<td>1</td>
<td>27</td>
</tr>
<tr>
<td>Phan</td>
<td>Tg(Phan-cre)8113Ang</td>
<td>renal &amp; urinary system, reproductive system</td>
<td></td>
<td>mouse-other</td>
<td>ACR29; C57BL/6J, B6-Cre58, B6-Cre59, Tg(Phan-cre)</td>
<td>1</td>
<td>27</td>
</tr>
</tbody>
</table>

The columns of the table can be sorted (as indicated by the up/down arrows in the column headers) and reordered (by placing the cursor in any column header). For example, perhaps you want an alphabetic sort of the Drivers in your Results Page; or to sort by the number of references (an indicator of how widely this cre line is used); or to sort by the Find Mice column to bring all those cre lines that are in public repositories to the top of your Results Page.

Each line of the table provides basic information about the cre transgene or knock-in. Within a row of data, each of which represents a single cre line transgene or knock-in, there are a number of links and actions possible that lead to further data details (shown below). The link in the Allele Symbol column directs you to a page showing phenotypes reported in offspring of mice bearing this cre transgene and mice carrying floxed alleles of various genes. (See page 11 of this tutorial.)

If there are recombinase activity data for any allele using a driver that is a mouse gene, a grid icon will appear in the Matrix View column for all alleles that use that mouse driver gene. The icon links to a matrix which allows you to compare endogenous wild-type gene expression with reported recombinase activity data.

available mice Links to all referen
3. Explore detailed information about the cre activity of a specific cre transgene or knock-in and learn about customizing the view.

On the Tg(Pbsn-cre)4Prb Transgene Detail page (shown on page 9), in the Recombinase activity section, click on one of the colored cells for reproductive system. In the pop-up that launches, click on View All Result Details and Images.

Below is the cre specificity detail page for Tg(Pbsn-cre)4Prb in the Reproductive System. Many rows of the Recombinase Activity table have been omitted to save space in this tutorial document. We will explore each sections of this page (delineated by the blue title column at left).
A. Allele Information. This section contains essentials about the cre transgene itself; its correct nomenclature (symbol and name), the driver involved, other synonyms that have been used in publications, a molecular description of what the transgene is carrying (in this case, the cre recombinase gene under the control of a composite promoter derived from the rat Pbsn gene) and a ‘Find mice’ IMSR summary indicating whether mice or cell lines carrying this transgene are available from public repositories.

B. Tissue Information. This section lists all other cre transgenes and knock-ins that have reported activity in the Reproductive System. Each symbol is a link to the cre specificity page for that transgene or knock-in for the Reproductive System. The …(more) indicates there are others and clicking on (more) will bring back the entire list.
Now we will look at some of the links and actions on this page....
Step 1. Click on the ‘1 line available’ in the Find Mice (IMSR) section of the Allele Information. This brings you to the IMSR Summary page (below).

Step 2. Click on the ‘more’ in the Tissue Information section to see all of the other cre transgenes and knock-ins known to express in the Reproductive System. Clicking on any of the symbols will bring you to their comparable Recombinase Activity Detail page.

Step 3. Enlarge an image by dragging at its corners and move to a convenient viewing place on the page. (see screenshot on page 8).

Below, Result of Step 1. View of IMSR (International Mouse Strain Resource) results and access to a Tg(Pbsn-cre)4Prb bearing strain.
Below, Result of Step 2. List of all other cre transgenes and knock-ins that show activity in the Reproductive System (there are 100 listed here). Each symbol is a link to the respective Reproductive System cre details for that transgene or knock-in. Note the (less) at the end of the list, which will collapse the list back to its original few.

Below, Result of Step 3. The enlarged image was made by dragging the image corners. If you click an image, the image legend and attribution pops up to the right of the image. Multiple images may be enlarged and moved as you work. Note the ‘Reset Images’ Button (arrow) that can be used to bring all images enlarged or moved back to their original size and placement on this page.
Finally, we learn about **phenotypes observed** when mice carrying a particular cre transgene/knock-in are mated to mice carrying different genes with loxP sites (genes that will be knocked-out when exposed to cre recombinase).

Phenotype data can be accessed either:

1. By clicking on the **phenotype data** link in the cre search summary page (see page 5 of the tutorial).  
2. By clicking on the **transgene or knock-in symbol** on the Recombinase Detail page (starting at page 5 of the tutorial).
This is the Transgene detail page for Tg(Pbsn-cre)4Prb, which contains the phenotype data. Like the Recombinase Activity page for the Reproductive System, the information at the top of the page is basic information on nomenclature, the description of the molecular construct and includes links to IMSR to obtain mice carrying this transgene. There is also a section summarizing recombinase activity with links to the Recombinase Activity pages as we have reviewed previously. Two phenotype sections on this page, labeled (A) Phenotypes and (B) Genotypes are described below.
A. The Phenotypes Section provides a high-level look at the kinds of systems affected in mice carrying this transgene in conjunction with other genes (the genotype). This section displays a matrix of ‘Affected systems’ (left column) by Genotype (row), where each abbreviation along the top of the matrix represents a unique genotype. As in other examples, there is a toggle (◮) that expands the table to more detailed data. Left, a copy of the table from the Phenotype Page (page 10) with the toggle circled. Below, the expansion of the reproductive system terms attributed to various genotypes.

B. Genotypes. Each genotype includes its allelic composition and genetic background. The third conditional genotype described, cn3, includes the Tg(Pbsn-cre)4Prb transgene and Rfwd2 targeted alleles on a congenic B6N background. Click on the cn3 button to open a new window containing phenotypic details reported in the mice (shown at left).
4. Return to the Cre Portal main page & view the data report for ‘all cre transgenes/knock-ins’

Find the Cre Portal main page using http://www.creportal.org. Locate the “Retrieve All Alleles Section” and choose either the MGI Recombinase Alleles Report (an html page view format) or the Tab-delimited version if you wish to copy the file into Excel or some other analysis program.

Step 1. Locate the file link of interest.

Step 2. Follow the link. Here a few lines of the html web page version are shown.
Self Directed Tasks

1. Using the Cre Portal, find cre carrying transgenes or knock-ins that are driven by AMH. How many are there? Which one do you think has been used most experimentally? Are any mice available with these cre transgenes from public repositories? If so, from where? For the AMH driven cre transgenes, what tissues are listed as “not detected” for cre recombinase activity? What ages were assayed?

(explanation note: You will note that the search is case-in-sensitive. In your results you will see AMH and Amh cre alleles. This is because nomenclature follows that of the species where the gene originated. AMH is the human gene (all capital letters); Amh is the mouse gene (first letter only capitalized).

2. For Plekha5^Tg(AMH-cre)1Flor, what tissues were reported with staining ‘Present’ (indicating cre activity) at postnatal day 35?

What reporter gene was used in the assays for Plekha5^Tg(AMH-cre)1Flor and Tg(Amh-cre)8815Reb?

3. For Plekha5^Tg(AMH-cre)1Flor, when mated to other targeted mutations, what other classes of phenotypes are observed in addition to “reproductive” related?

Answers (These are likely to change due to database updates, etc.)

1. From www.creportal.org, select the driver Amh in the ‘search for alleles by promoter/driver specificity’ and then click ‘GO’.

There are 6 cre transgenes with an Amh driver. Two are driven by the human AMH promoter, the other 4 by the mouse Amh promoter. These symbols follow species’ nomenclature convention. You can also learn this by reading the molecular description in the transgene detail pages.

Because there are 107 references for Plekha5^Tg(AMH-cre)1Flor, this allele is likely to have been used most frequently.

Yes, 2 of these cre transgenes are available from public repositories. Plekha5^Tg(AMH-cre)1Flor is available from the EMMA repository (EM) in Europe as frozen embryos. Tg(Amh-cre)8815Reb is available from the Jackson Laboratory repository (JAX) as sperm.

On the summary page, for the Plekha5^Tg(AMH-cre)1Flor transgene, in the Recombinase Activity Not Detected column, the data indicate recombinase (cre) activity is not detected in the anatomical class “embryo-other”. Following this link to this ‘anatomical class’ one sees that cre activity was not detected at embryonic day 12.5 and 13.5.

2. For Plekha5^Tg(AMH-cre)1Flor at day 35, staining was found in ovary antral follicle, ovary secondary follicle and ovary stratum granulosum.

The reporter gene for cre transgene Plekha5^Tg(AMH-cre)1Flor was lacZ; for cre transgene Tg(Amh-cre)8815Reb, the reporter gene was hemagglutinin.

3. Through the “phenotype data” link for Plekha5^Tg(AMH-cre)1Flor, you can see that there are cellular, endocrine/exocrine gland, homeostasis/metabolism, and immune system phenotypes observed.
We welcome your feedback in improving this resource. Contact us through the “Contact Us” link in the navy blue navigation bar at the far right; or email mgi-help@jax.org