The FaceBase Resource for Orofacial Clefting Research at The Jackson Laboratory

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Abstract

The JAX FaceBase Resource provides services and mice to the FaceBase consortium, as well as to the greater research community, to facilitate orofacial clefting research. The FaceBase Resource rederives, cryopreserves, provides genetic quality control, and distributes live mice from new and existing mouse models and tool strains relevant to clefting research. Genetically engineered, spontaneously occurring, and ENU-induced models are included.

- **65 strains are available for distribution. Since 2009, approximately 40 strains have been imported to the collection. Most strains are kept as breathing colonies and are readily available.**
- **The Resource is generating new inducible Cre driver lines specifically designed to support clefting research. Cre driver strains are the most popular component of the Repository, and in the past year two Cre strains accounted for 34% of mice distributed. In addition, we provide added value through extended characterization, with data posted publicly.**
- **JAX also has a complementary collection of mouse models of craniofacial dysmorphologies, discovered and characterized on site. These new models arose spontaneously as phenotypic deviants in breeding and research colonies at JAX, and from our ENU mutagenesis program. More are anticipated via newly developed strains resulting from participation in the NIH-wide Knockout Mouse Project (KOMP²). These new models are currently available at http://craniofacial.jax.org/.**
- **In addition to its presence on the FaceBase Hub, the Repository has a website at http://www.jax.org/facebase/. JAX provides quarterly downloads of updated and new strain information to the Hub.**

Why mouse repositories?

The laboratory mouse has played a key role in understanding the genetics underlying mammalian biology and human genetic disorders. The mouse is recognized as an ideal mammalian model organism for biomedical research because of its many anatomical and physiological similarities to human beings. Use of mice also offers significant advantages:

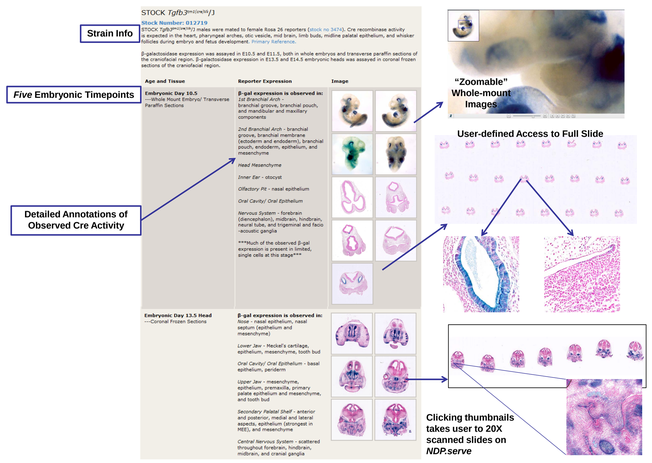
- **Mice require less space and food than larger mammals and have a short gestation period, short lifespan, and rapid development resulting in cost-savings and efficiency;**
- **The long period of research using mice has resulted in a wealth of background data, specialized panels for genetic analyses, technologies for manipulating the mouse genome, and a rich base of literature;**
- **The coding sequence of the mouse genome is 95% identical to the human genome, as shown when the mouse became the first non-human mammal sequenced in 2002.**

Ensuring the ongoing availability of these mouse strains preserves the investment made in creating and characterizing them and creates a global resource of enormous value. Centralized mouse repositories for distributing and archiving these resources provide critical access to and preservation of these strains, while ensuring greater quality control, genetic stability (background), fidelity (mutation), and optimal animal health status; and providing customer service and technical support for researchers using mice.

JAX Craniofacial Cre Characterization

Using the *lacZ*-based Cre reporter strain, B6.129S4-*Gt(ROSA)26Sor*^{tm1Sor}/J (JAX stock #003474), we perform a detailed analysis of craniofacial Cre activity at five embryonic timepoints, E10.5-to-E14.5. All craniofacial data are posted at cre.jax.org, the Cre Portal (www.creportal.org) and at the FaceBase Hub

Example *Tgfβ3-cre* Stock #012719:



JAX FaceBase Repository strain list

Genetically engineered strains

Strain Name	Stock #
129S-*Efnb1*^{tm1Sor}/J	7664
B6;129-*Cask*^{tm1Sud}/J	6382
B6;129-*Gabrb3*^{tm1Geh}/J	2711
B6;129-*Shh*^{tm2Amc}/J	4293
B6;129-*Tgfbr2*^{tm1Karl}/J	12603
B6;129S-*Jag1*^{tm2Grid}/J	10618
B6;129S-*Snai1*^{tm2Grid}/J	10686
B6;129S1-*Bambi*^{tm1Jian}/J	9389
B6;129S1-*Lfng*^{tm1Grid}/J	10619
B6;129S1-*Notch3*^{tm1Grid}/J	10547
B6;129S1-*Notch4*^{tm1Grid}/J	10544
B6;129S1-*Snai2*^{tm2Grid}/J	10722
B6;129S4-*Foxd1*$^{tm1(GFP/cre)Amc}$/J	12463
B6;129S7-*Acvr2a*^{tm1Zuk}/J	3277
B6;129S7-*Fst*^{tm1Zuk}/J	2788
B6;129S7-*Inhba*^{tm1Zuk}/J	2990
B6.129-*Ski*^{tm1Cco}/J	5709
B6.129-*Tgfb3*^{tm1Doe}/J	2619
B6.129P2(Cg)-*Dhcr7*^{tm1Gst}/J	7453
B6.129S-*Notch2*^{tm3Grid}/J	10525
B6.129S1-*Jag1*^{tm1Grid}/J	10616
B6.129S1-*Jag2*^{tm1Grid}/J	10546
B6.129S1-*Notch2*^{tm1Grid}/J	10620
B6.129S1-*Osr1*^{tm1Jian}/J	9387

Overbeek strains

Dr. Paul Overbeek (Baylor) donated nine mutant strains created by lentiviral insertion. He reports that his preliminary characterization indicates that these mutants exhibit cleft palate as homozygotes.

Strain Name	Stock #
FVB/N-*Bmp4*$^{Tn(sb\text{-}Tyr)1HCeb/Ove}$/J	17609
FVB/N-*Ckap5*$^{TgTn(sb\text{-}cHS4,Tyr)2320F\text{-}1Ove}$/J	17437
FVB/N-*Midn*$^{Tg(Tyr)2261EOve}$/J	17438
FVB/N-*Sdccag8*$^{Tn(sb\text{-}Tyr)2161B.CA1C2Ove}$/J	17598
FVB/N-*Skor2*$^{Tn(sb\text{-}Tyr)1799B.CA7BOve}$/J	17608
FVB/N-*Tapt1*$^{TgTn(sb\text{-}cHS4,Tyr)2508GOve}$/J	17436
FVB/NJ-*Ap2b1*$^{Tg(Tyr)427Ove}$/EtevJ	16870
STOCK *Shh*^{tm1Amc}/J	3318
STOCK *Tgfb2*^{tm1Doe}/J	3102
STOCK *Wnt9b*$^{tm1.2Amc}$/J	8469

Spontaneous mutations

Phenotypes of spontaneous mutants include defects in skull morphology, dentition, vision, and hearing as well as models of orofacial clefting. For many models, we identify the causative gene using high throughput sequencing technologies.

Strain Name	Stock #
B6.C3-*Gli3*$^{Xt\text{-}J}$/J	26
B6By.Cg-*Eh*/J	523
B6C3Fe *a/a-Papss2*^{bm} *Hps1*^{ep} *Hps6*^{ru}/J	278
B6CBACa *A*$^{w\text{-}J}$*/A-Sfn*^{Er}/J	515
C3HeB/FeJ x STX/Le-*Mc1r*$^{E\text{-}so}$ *Gli3*$^{Xt\text{-}J}$ *Zeb1*^{Tw}/J	1434
DC/LeJ	252

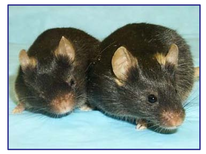
Cre tool strains

Strain Name	Stock #
B6;129S1-*Osr2*$^{tm2(cre)Jian}$/J	9388
B6.129P2(Cg)-*Foxg1*$^{tm1(cre)Skm}$/J	6084
B6.Cg-Tg(Nes-cre)1Kln/J	3771
B6.Cg-Tg(Prrx1-cre)1Cjt/J	5584
FVB-Tg(Col2a1-cre/ERT)KA3Smac/J	6774
STOCK Tg(KRT14-cre)1Amc/J	4782
STOCK Tg(KRT14-cre/ERT)20Efu/J	5107
STOCK Tg(Wnt1-cre)11Rth Tg(Wnt1-GAL4)11Rth/J	3829
STOCK *Tgfb3*$^{tm1(cre)Vk}$/J	12719

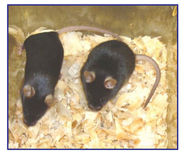
Spontaneous mutations

C57BL/6J-*sbse*/J
Stock #004246
The sbse (small body, short ear pinnae) homozygote on the left also shows the more domed skull typical of this phenotype (control littermate at right for comparison).

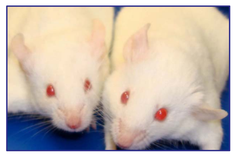
B6(NOD) *H2g7- Sostdc1*^{shk}/J
Stock # 005717
Mice homozygous for the sharkey (shk) mutation have supernumerary incisors which must be routinely trimmed, and provide a model for studying tooth development.



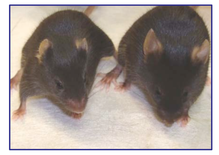
B6(AKR)-*Sofa*/J
Stock # 004235
The short face (Sofa) mutation affects skull shape characterized by a short nose, domed skull and wide set eyes. A Sofa heterozygote is shown on the left with a control littermate on the right.



C57BL/6J-*Arsb*^{m1J}/GrsrJ
Stock #005598
A mutant mouse (at right) has a skeletal phenotype consisting of a shortened snout, wide-set eyes, a thicker tail and digits and shortened limbs that become more noticeable with age.



BALB/cByJ-*Fgfr1*^{Eask}/GrsrJ
Stock #005412
Eask (ear askew) mutants, such as the one on the right above, have low-set ear pinnae. The phenotype shows a range of variability from very malformed to only slightly affected.



B6(CAST)-*Prkra*^{lear}/GrsrJ
Stock #008568
The little ears (lear) mutation causes mice to have a smaller overall body size and smaller ear pinnae. A homozygous mutant (at left) is pictured with a heterozygous littermate.

A/J-*frg*/J
Stock #3485
The recessive froggy (frg) mutation arose in a JAX research colony. The mutation affects body size and skull shape, and has varied penetrance. Some mutants have obviously shortened faces (above left), while others are less affected. All mutants can be determined by their wide set eyes.

KOMP Opportunities

The Knockout Mouse Project (KOMP) is a trans-NIH initiative to generate a public resource of mouse embryonic stem (ES) cells containing a null mutation in every gene in the mouse genome. The Jackson Laboratory is one of three centers converting the knockout embryonic stem cell libraries into mice, performing quality control (QC), phenotyping the mice, and cryopreserving germplasm.

JAX is expanding phenotyping capacity for use by the KOMP project, by faculty and by other groups at the Laboratory. The JAX KOMP² Phenotyping Center provides a ten-week long sequential assessment conducted on small cohorts of 8-18 week-old wildtype and mutant mice of both sexes, providing phenotyping modalities and time points in addition to those traditionally employed by our Repository.

As part of the KOMP Phenotyping, we will screen for craniofacial mutants. The information gathered will provide an opportunity to build new research programs around the availability of this resource.

Donate your unique strain to advance research

Contributing your model enables researchers across the globe to have greater access to tools for discovery, accelerating the pace of research.

Why donate a strain?

- Donating reduces your costs (maintaining strains, lab personnel, shipping and resources)
- Each donated strain is cryopreserved, protecting against accidental loss and genetic contamination.
- Each donated strain is rederived to a high health status and may be resupplied to donors (up to 3 breeder pairs as long as we have live mice available)
- Donating fulfills NIH obligations to share resources.

Acknowledgements

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www.jax.org/facebase/ **Contact: LeahRae.Donahue@jax.org or Steve.Murray@jax.org**