

Cre Module

You want to design an experiment where you study the effects of removing **cadherin 2** (*Cdh2*) from mouse *stomach glandular epithelium*, but NOT the respiratory system.

To do this requires use of a cre-lox strategy, where you have (1) a mouse with a targeted conditional allele of *Cdh2*, with loxP recombinase recognition sites used to flank some portion of the *Cdh2* gene, and (2) a mouse carrying a cre transgene with recombinase activity detected in the stomach glandular epithelium along with no activity in the respiratory system.


8. Of the following, which allele of *Cdh2* would be most appropriate?
- a) *Cdh2*^{Gt(OST49160)Lex} (MGI:3525642)
 - b) *Cdh2*^{tm1Glr} (MGI:3522469)
 - c) *Cdh2*^{tm1Hyn} (MGI:1861181)
 - d) *Cdh2*^{tm1e(EUCOMM)Wtsi} (MGI:4433958)
 - e) None of the above


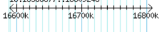
Type “Cdh2” into the **Quick Search** and navigate to the Gene Detail page for cadherin 2. There, scroll to the **Alleles and phenotypes** row which indicates “All alleles (5)”. Click the hyperlink to view on the **Phenotypes, Alleles and Disease Models Summary** page. Use the **Category** column to determine the Generation Method and Allele Attributes.

To do tissue-specific gene manipulation requires a *conditional ready* targeted allele. Introduction of the recombinase recognition sites in the absence of recombinase co-expression is expected to have no functional impact, and the gene product should be expressed at normal levels, with normal function.

The *Cdh2^{tm1Glr}* allele has the **Category** of “**Targeted (Conditional ready, no functional change)**”. Click on the **Allele Symbol** to go to the Allele Detail page, which has more specific and detailed information about the allele generation and/or characterization, along with a reference in the **Mutation Details** row.

9. Which exon(s) of the *Cdh2* gene are flanked by loxP (floxed) in *Cdh2^{tm1Glr}*?
- a) The entire gene
 - b) Exon 1 and upstream transcriptional regulatory sequences
 - c) Exon 3
 - d) Exons 4&5
 - e) It is not specified

On the **Allele Detail** page, click the triangle toggle () next to **Mutation details** in the **Mutation description** row. The text there describes flanking of exon 1.

	Cdh2	Gene Detail
Symbol Name ID	Cdh2 cadherin 2 MGI:88355	
Synonyms	Ncad, N-cadherin	
Feature Type	protein coding gene	
Genetic Map	Chromosome 18 10.10 cM Detailed Genetic Map ± 1 cM Mapping data(14)	
Sequence Map	Chr18:16588877-16809246 bp, - strand From VEGA annotation of GRCh38 Get FASTA 220375 bp + 0 kb flank VEGA Genome Browser Ensembl Genome Browser UCSC Browser NCBI Map Viewer	 MGI Gene Features P01_095955_Cdh2 +1 * - - - - - protein coding gene P01_192032_310000_P1981k unclassified gene P01_2442732_3430011C15 unclassified gene P01_3795289_0m15d unclassified gene Mouse Genome Browser
Vertebrate homology	HomoloGene:20424 Vertebrate Homology Class 1 human; 1 mouse; 1 rat; 1 chimpanzee; 1 rhesus macaque; 1 dog; 1 chicken; 1 zebrafish Protein SuperFamily: cadherin Gene Tree: Cd2b	
Human homologs	Human Homolog CDH2, cadherin 2, type 1, N-cadherin (neuronal) NCBI Gene ID 1000 refSeqProt AC NX.P19022 Human Synonyms CD325, CDHN, Cdw325, NCAD Human Chr (location) 18q11.2; chr18:27950966-28177481 (-) GRCh38	
Allèles et phenotypes	All alleles(5) : Gene trapped(L1 Targeted(d)) Incidental mutations (data from Mutagenex , APE) A spontaneous mutation of this gene results in death by E10. Mutant embryos exhibit several developmental abnormalities such as growth retardation, an enlarged heart, distended pericardial sacs, abnormal heart tube, wavy neural tube, irregular somite shape, and abnormal embryo turning.	
Gene Ontology	All GO classifications: (57 annotations)	

Symbol

Cdh2

Name

cadherin 2

ID

MGI:88355

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Allele Symbol	Gene Allele Name	Chr	Synonyms	Category	Abnormal Phenotypes Reported in these Systems	Human Disease Models
Cdh2 ^{000154160.0}	cadherin 2, gene trap	18	Cdh2 ^{000154160.0}	Gene trapped	cardiovascular, homeostasis, mortality/aging, muscle, nervous system	
Cdh2 ^{000154160.0}	cadherin 2, targeted mutation 1, Cleon 1, Rapidie	18	N-cad ^{fl}	Targeted (Conditional ready, No functional change)	cardiovascular, cellular, mortality/aging, muscle, nervous system	
Cdh2 ^{000154160.0}	cadherin 2, targeted mutation 1, Richard Hayes	18	Cdh2 ⁻ , N-cadherin ⁻	Targeted (Null/knockout)	cardiovascular, embryogenesis, growth/size, mortality/aging, muscle, nervous system	
Cdh2 ^{000154160.0}	cadherin 2, targeted mutation 1a, Wellcome Trust Sanger Institute			Targeted (Conditional ready, Null/knockout, Reporter)		
Cdh2 ^{000154160.0}	cadherin 2, targeted mutation 1a, Wellcome Trust Sanger Institute	18		Targeted (Null/knockout, Reporter)		

10. How many cre alleles have recombinase activity results annotated to “stomach glandular epithelium”?

- a) none
 → b) 6
 c) 61
 d) 122
 e) It is impossible to tell

To search for recombinase alleles, use the **Recombinase** tab along the top, or click on the “**Recombinases (cre)**” button on MGI’s home page.

In the **Access Data** section, begin typing “*stomach glandular epithelium*” in the box beneath “**Recombinase activity in:**” and select the term when it appears. Structures in black text have at least one recombinase activity annotation, while structures in grey text do not have any activity annotations.

Six rows, corresponding to six transgenes will be returned after running the query.

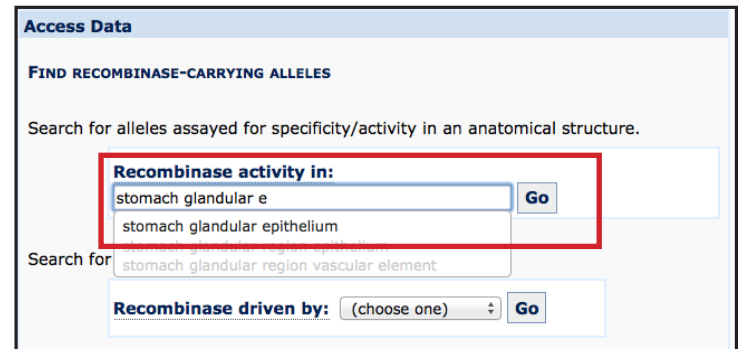
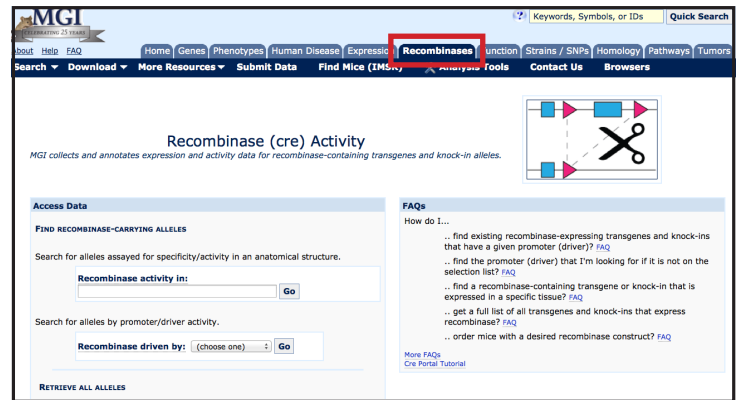
11. Of the following, which transgene is the best match for recombinase activity “**detected in: alimentary system**” (which contains *stomach glandular epithelium*) and also has recombinase activity known to be “**not detected in: respiratory system**”?

- a) *Tg(Atp4b-cre)1Jig* (MGI:3040892)
 b) *Mnx1^{tm4(cre)Tmj}* (MGI:2447793)
 c) *Tg(Chst4-cre)1Hkwa* (MGI:3842784)
 d) Any/all of the above
 e) None of the above

The query from question 10 will return all transgenes that have a recombinase activity result reported in *stomach glandular epithelium* (whether examined and detected, or examined and not detected).

Alimentary system is bolded to indicate that this system contains the structure “*stomach glandular epithelium*” which was originally searched. It is additionally underlined with a solid line in the image on the right. In each case here, the transgene satisfies the “**detected in: alimentary system**” requirement.

Examining both columns for respiratory system (underlined with a dashed line on the right) shows three alleles (*Tg(Chst4-cre)1Hkwa*, *Mnx1^{tm4(cre)Tmj}*, and *Tg(Sftpa1-cre)1Xya*) where recombinase activity was detected in some structure of the respiratory system, two transgenes (*Tg(Atp4b-cre)3Xya* and *Tg(Cyp1a1-cre)1Dwi*) with no information reported on recombinase activity in the respiratory system, with only one (*Tg(Atp4b-cre)1Jig*) where respiratory system is reported, and classed as not detected.



Driver	Allele Symbol Gene: Allele Name	Recombinase Activity Detected	Recombinase Activity Not Detected	Allele Synonym	Inducible	Find Mice (MSR)	Refs
Atp4b	<i>Tg(Atp4b-cre)1Jig</i> transgene insertion 1, Jeffrey I Gordon	alimentary system	hemolymphoid system, liver and biliary system, renal and urinary system, respiratory system	HKCre			4
Atp4b	<i>Tg(Atp4b-cre)3Xya</i> transgene insertion 3, Xue Yang	alimentary system		Atp4b-Cre			1
Chst4	<i>Tg(Chst4-cre)1Hkwa</i> transgene insertion 1, Hiroto Kawashima	alimentary system , cardiovascular system, hemolymphoid system, liver and biliary system, nervous system, reproductive system, respiratory system	renal and urinary system	Gli3Acad5T-2-Cre			3
Cyp1a1	<i>Tg(Cyp1a1-cre)1Dwi</i> transgene insertion 1, Douglas J Winton	alimentary system , cardiovascular system, liver and biliary system, renal and urinary system		Alb-cre, AlbCre, Cre ^{OP4A1}	Yes		52
Mnx1	<i>Mnx1^{tm4(cre)Tmj}</i> mouse strain and paracrine homeobox 1; targeted mutation 4, Thomas H Jessell	alimentary system , cardiovascular system, embryo-other, endocrine system, hemolymphoid system, integumental system, limbs, muscle, nervous system, renal and urinary system, reproductive system, respiratory system, sensory organs	adipose tissue, branchial arches, extraembryonic component, head, liver and biliary system, mesenchyme, skeletal system, tail	Hb9 ^{Cre} , Hb9 ^{Cre} , Hb9-Cre, Hb9 ^{Cre} /Hb9 ^{Cre}		2	34
Sftpa1	<i>Tg(Sftpa1-cre)1Xya</i> transgene insertion 1, Xue Yang	alimentary system , cardiovascular system, embryo-other, nervous system, respiratory system		SP-A-Cre			4

Recombinase Activity Detected	Recombinase Activity Not Detected
<u>alimentary system</u>	hemolymphoid system, liver and biliary system, renal and urinary system, <u>respiratory system</u>
<u>alimentary system</u>	
<u>alimentary system</u> , cardiovascular system, hemolymphoid system, liver and biliary system, nervous system, reproductive system, <u>respiratory system</u>	renal and urinary system
<u>alimentary system</u> , cardiovascular system, liver and biliary system, renal and urinary system	
<u>alimentary system</u> , cardiovascular system, embryo-other, endocrine system, hemolymphoid system, integumental system, limbs, muscle, nervous system, renal and urinary system, reproductive system, <u>respiratory system</u> , sensory organs	adipose tissue, branchial arches, extraembryonic component, head, liver and biliary system, mesenchyme, skeletal system, tail
<u>alimentary system</u> , cardiovascular system, embryo-other, nervous system, <u>respiratory system</u>	

