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Although thousands of mouse models have been generated, finding relevant data and knowledge about these models is complicated by a general lack of compliance in the published literature with nomenclature and annotation standards for genes, alleles, mouse strains, and cancer types. The Mouse Models of Human Cancer database (MMHCdb; http://tumor.informatics.jax.org) is an expertly curated knowledgebase of cancer phenotypes reported for diverse types of mouse models of human cancer such as inbred mouse strains, genetically engineered mouse models (GEMMs), Patient Derived Xenografts (PDXs), and mouse genetic diversity panels (e.g., the Collaborative Cross). MMHCdb includes data on more than 60,000 mouse models for over 1200 tumor classifications curated from more than 25,000 peer-reviewed publications.

A primary goal of MMHCdb is **to highlight the impact of genetic background on the incidence and presentation of different tumor types in mice.** The same allele on different backgrounds can result in very different cancer characteristics and, therefore, impact the appropriateness of a model for a specific research application. In MMHCdb, users can review the impact of genetic background on the frequency of spontaneous tumors for inbred mouse strains using an interactive table generated from different published and unpublished data sources. In addition, color-coded tabular summaries of individual papers are available that allow researchers to quickly assess how genetic background affects cancer phenotypes in the mouse models reported in a specific publication.

MMHCdb is supported by NCI R01 CA089713

The impact of genetic background on cancer phenotypes of mouse models of human cancer

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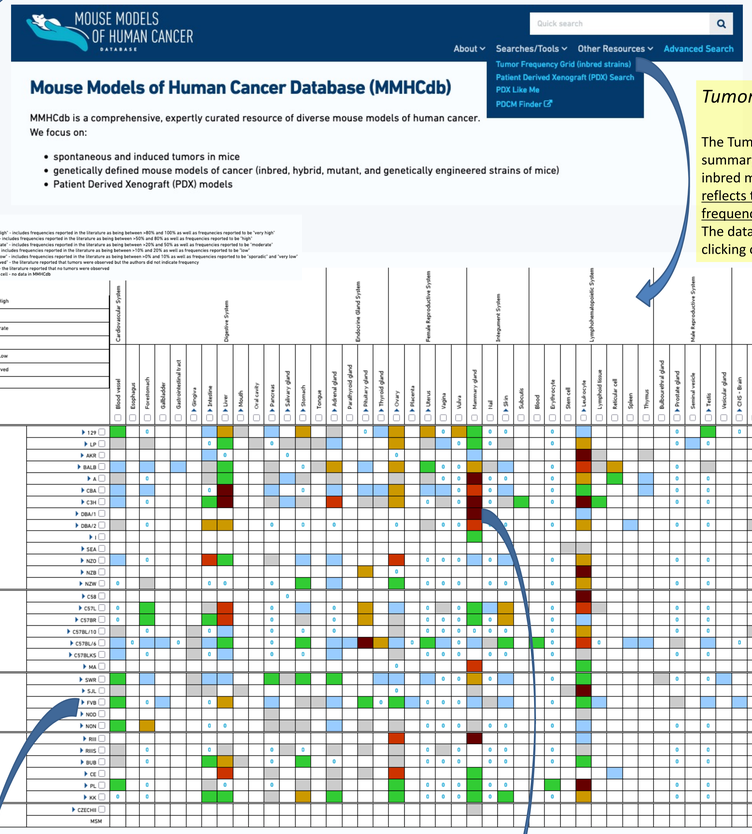
MOUSE MODELS OF HUMAN CANCER DATABASE

Mouse Models of Human Cancer Database
https://tumor.informatics.jax.org

MMHCdb contains information on over 60,000 mouse models in 8,725 strains of mice from more than 25,000 papers published in peer-reviewed journals.



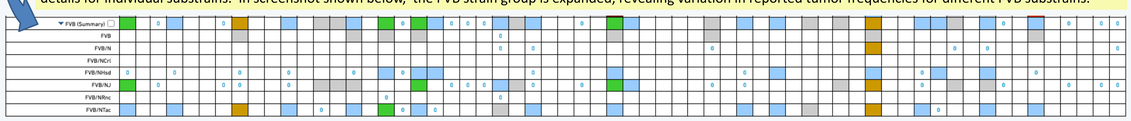
Tumor Frequency Grid

The Tumor Frequency Grid is an interactive graphical summary of the characteristic cancers observed in over 700 inbred mouse strains. The color of the cells in the grid reflects the information in published reports of the frequency of spontaneous tumors in various organ systems. The data supporting the frequency estimation is available by clicking on a shaded cell in the grid.

A mouse click on a cell in the grid opens a table of the frequency of spontaneous tumors for the selected inbred strain group/organ system with links to a summary of the source(s) of the tumor frequency information and to additional information about the strains.

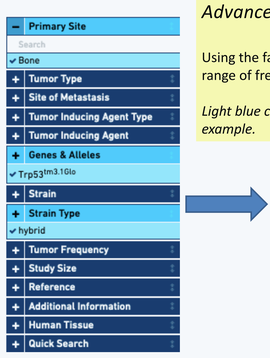
Tumor Name	Organ Affected	Treatment Type *Agents*	Strain Name *Strain Types*	Tumor Frequency Range F	M	Mixed	Un.	Metastasizes To	Images	Tumor Summary
Mammary gland adenocarcinoma	Mammary gland	None (spontaneous)	DBA/1J *inbred*	61 - 90	0					Summary
Mammary gland adenocarcinoma	Mammary gland	None (spontaneous)	DBA/1LacJ *inbred*	observed						Summary
Mammary gland tumor	Mammary gland	None (spontaneous)	DBA/1J *inbred*	33 - 80			high			Summary
Mammary gland tumor	Mammary gland	None (spontaneous)	DBA/1LacY *inbred*	61.5						Summary
Mammary gland tumor	Mammary gland	None (spontaneous)	DBA/1 *inbred*	61.5			observed - 75			Summary

The tumor frequency information in each row of the Tumor Frequency Grid is a summary of data across different substrains. Selecting a strain name expands the grid to reveal details for individual substrains. In screenshot shown below, the FVB strain group is expanded, revealing variation in reported tumor frequencies for different FVB substrains.



The *Trp53* $^{tm3.1Glo}$ allele is a targeted mutation in the Trp53 gene that corresponds to the R175H hot-spot mutation in human tumors (Liu et al. 2000).

This *Trp53* $^{tm3.1Glo}$ allele on different genetic backgrounds of mice strongly influences the "tissue type of the tumor produced and the number of tumors formed in a single mouse" (Chan et al, 2020)



Advanced Search (faceted search) and Search Results Summary

Using the faceted search option for MMHCdb, the Trp53 $^{tm3.1Glo}$ allele is selected for bone tumors in hybrid strains. The results summary shows the range of frequencies for osteosarcomas across hybrid mouse strains carrying the allele of interest.

Light blue color shows facets used for the search. The dark blue color indicates facets available for expanding or refining searches not used in this example.

Model Name	Tumor Inducing Agent(s)	Strain	Frequency Range	Additional Information	Model Details
Bone osteosarcoma		(SWR/J x C57BL/6JF1-*Trp53*$^{tm3.1Glo}$/+ hybrid targeted mutation (knock-in))	20	1 Reference: Chan CS, Life Sci Alliance (2021)	
Bone osteosarcoma		(A/J x C57BL/6JF1-*Trp53*$^{tm3.1Glo}$/+ hybrid targeted mutation (knock-in))	17	1 Reference: Chan CS, Life Sci Alliance (2021)	
Bone osteosarcoma		(NOD/ShiLtJ x C57BL/6JF1-*Trp53*$^{tm3.1Glo}$/+ hybrid targeted mutation (knock-in))	16	1 Reference: Chan CS, Life Sci Alliance (2021)	
Bone osteosarcoma		(BALB/cByJ x C57BL/6JF1-*Trp53*$^{tm3.1Glo}$/+ hybrid targeted mutation (knock-in))	11	1 Reference: Chan CS, Life Sci Alliance (2021)	
Bone osteosarcoma		(C3H/HeJ x C57BL/6JF1-*Trp53*$^{tm3.1Glo}$/+ hybrid targeted mutation (knock-in))	8	1 Reference: Chan CS, Life Sci Alliance (2021)	
Bone osteosarcoma		(129S1/SvImJ x C57BL/6JF1-*Trp53*$^{tm3.1Glo}$/+ hybrid targeted mutation (knock-in))	6	1 Reference: Chan CS, Life Sci Alliance (2021)	
Bone osteosarcoma		(DBA/1J x C57BL/6JF1-*Trp53*$^{tm3.1Glo}$/+ hybrid targeted mutation (knock-in))	4	1 Reference: Chan CS, Life Sci Alliance (2021)	

Reference Summary

Chan CS, Life Sci Alliance 2021 Mar;4(3):

Title	Genetic and stochastic influences upon tumor formation and tumor types in Li-Fraumeni mouse models.
Authors	Chan CS; Sun Y; Ke H; Zhao Y; Belete M; Zhang C; Feng Z; Levine AJ; Hu W
Journal	Life Sci Alliance
Volume	4
Issue	3
Year	2021
Pages	
Abstract	p53 is the most frequently mutated gene in human cancers. Li-Fraumeni syndrome patients inheriting heterozygous p53 mutations often have a much-increased risk to develop cancer(s) at early ages. Recent studies suggest that some individuals inherited p53 mutations do not have the early onset or high frequency of cancers. These observations suggest that other genetic, environmental, immunological, epigenetic, or stochastic factors modify the penetrance of the cancerous mutant Tp53 phenotype. To test this possibility, this study explored dominant genetic modifiers of Tp53 mutations in heterozygous mice with different genetic backgrounds. Both genetic and stochastic effects upon tumor formation were observed in these mice. The genetic background of mice carrying Tp53 mutations has a strong influence upon the tissue type of the tumor produced and the number of tumors formed in a single mouse. The onset age of a tumor is correlated with the tissue type of that tumor, although identical tumor tissue types can occur at very different ages. These observations help to explain the great diversity of cancers in different Li-Fraumeni patients over lifetimes.
Links	J:305009 – MGI References 33376133 – National Library of Medicine/PubMed

Reference Summary

Selecting the reference from the search summary brings you to the reference summary page with the publication abstract and links to Mouse Genome Informatics (MGI) and to PubMed.

For papers with information on the impact of genetic background, a visual summary of the paper is presented showing the types of tumors discussed in the paper and their frequencies across strains/cancer models.

Visual Summary

Genotype	Genetic Background	Adipose tissue tumor	Blood vessel hemangioma	Bone osteosarcoma	Leukocyte lesion	Mesodermal cell/mesoblast sarcoma	(Unspecified organ) adenocarcinoma	(Unspecified organ) carcinoma	(Unspecified organ) tumor	(Unspecified organ) tumor - malignant
		Untreated	Untreated	Untreated	Untreated	Untreated	Untreated	Untreated	Untreated	Untreated
Trp53 $^{tm3.1Glo}$/+	(129S1/SvImJ x C57BL/6)F1	2	2	6	10	0	2	2	2 - 38	
	(A/J x C57BL/6)F1	20	0	17	10	7	3	0	3 - 69	87
	(BALB/cByJ x C57BL/6)F1	0	2	11	4	4	13	6	15 - 80	
	(C3H/HeJ x C57BL/6)F1	0	0	8	23	4	4	0	0 - 70	
	(DBA/1J x C57BL/6)F1	4	4	4	21	0	7	0	4 - 47	
	(NOD/ShiLtJ x C57BL/6)F1	0	3	16	24	8	3	1	1 - 65	69
	(SWR/J x C57BL/6)F1	0	1	20	30	4	11	8	4 - 96	

The Visual Summary shows that the frequency of specific tumor types reported by Chan et al. (2020) varied with genetic background. Additional observations of animals by gross anatomy and histopathology yielded presence of different types of cancerous events and tumors of unspecified origin that also varied by genetic background of the hybrid animals.

References

Liu G, McDonnell TJ, Montes de Oca Luna R, Kapoor M, Mims B, El-Naggar AK, Lozano G. High metastatic potential in mice inheriting a targeted p53 missense mutation. Proc Natl Acad Sci U S A. 2000 Apr 11;97(8):4174-9. doi: 10.1073/pnas.97.8.4174. PMID: 10760284; PMCID: PMC18187.

Chan CS, Sun Y, Ke H, Zhao Y, Belete M, Zhang C, Feng Z, Levine AJ, Hu W. Genetic and stochastic influences upon tumor formation and tumor types in Li-Fraumeni mouse models. Life Sci Alliance. 2020 Dec 29;4(3):e202000952. doi: 10.26508/lsa.202000952. PMID: 33376133; PMCID: PMC7772779.