Salivary Gland Gene Expression Search Guide

The Salivary Gland Molecular Anatomy Project (SGMAP) provides a searchable gene expression database for mouse salivary gland development, healthy and irradiated human salivary glands, and differential gene expression in selected transgenic models.
Data for this gene expression database were generated using Agilent microarrays, bulk RNAseq, and single-cell RNAseq technologies.
The search term can be Gene Symbol, Gene Description or Gene Ontology Term as shown on the search page. If a single gene matches the search term, the individual expression page is displayed. If more genes match, a list of genes with mini expression patterns is presented. Note that mouse and human gene symbols may differ; therefore, if a gene does not show data across all technologies, it is likely that a synonym or equivalent gene symbol is required as input. On the top of the expression page, links to Entrez, Pubmed and GenBank are provided.

Page navigation:
On the expression page, microarray and LCM data are shown in the top panels.
The developmental time courses of SMG and SLGs (microarray data) and regions analyzed by laser capture microdissection (LCM) experiments are shown in the two explanatory images. Microarray data shows the temporal expression patterns of genes for submandibular (SMG) and sublingual (SLG) glands from embryonic day (E) 11.5 through adult, and spatial expression patterns are provided for selected developmental stages. The signal intensity range is around 10 to 500,000 arbitrary units. We recommend caution when the maximum signal in a pattern is below 100. The signal/noise ratio might be low. Data should always be confirmed by PCR. LCM patterns for SMG and SLG are also displayed. In addition, related Gene Ontology terms and pathways, if they exist, are displayed and linked to geneontology.org and kegg.jp respectively. Some genes do not have all three patterns due to experimental differences. Each gene symbol links to the expression pattern page. On the expression page, the “Similar Profile” link leads to a list of other genes that have similar expression patterns as generated by the Kmeans clustering method; gene names in red share more similar patterns than those in blue. Each name is linked to the expression page and the list of genes is provided at the bottom of the page. The list can be copied and pasted to other analysis computing applications. The link to MsigDB is provided and the list can be analyzed there. The Probe Pattern link leads to raw expression patterns of microarray probes of that gene. The Agilent platform has multiple probes for some genes and some probes work better than others, giving higher expression values. The probe expression pattern helps to evaluate the gene expression pattern.

The second row in the expression page includes bulk-RNAseq data from mouse and human salivary glands. These analyses show gene expression between the three major pairs of salivary glands (PG, SMG, and SLG) as well as male vs female in adult WT mice from Mukaibo *et al*. 2019 and Gao *et al*. 2019. RNA-sequencing data of CH3 female mice compares non-irradiated (non-IR) SMGs with both irradiated SMGs pre-treated with AAV2-GFP (IR-GFP) or AAV2-NRTN (IR-CERE) 10 days before IR and collected 300 days post-IR as described in Lombaert *et al*., *2020*. Expression data from selected mouse transgenics is also included, specifically from SLGs from Nkx2.3$^{+/-}$ vs Nkx2.3$^{-/-}$ mice (unpublished). Lastly, bulk RNAseq from healthy and irradiated human salivary glands obtained from head and neck cancer patients is shown separated by treatment and type of gland (SMG and PG only). All graphs show normalized expression values for the queried gene across treatments from each study.

The SGMAP was updated to include Single-cell RNAseq data from mouse SMG from embryonic (E12, E14, and E16) and postnatal (P1, P30, and adult) time points (Hauser *et al*., 2020). For embryonic samples, SMGs from up to 10 embryos were pooled and processed together, while postnatal samples were obtained from 2-6 SMGs. All mice from E12 to P30 are from ICR background. The P30 specimen contains 2 male SMG and 2 female SMG. The adult sample was obtained from a 10-month-old C3H female mouse. The expression for a queried gene will be shown in representative UMAP projections for each developmental stage and cluster annotations are shown after clicking in a specific UMAP projection.

The project was initiated by Matthew Hoffman, Kenneth Yamada and John Chiorini and funded by the Intramural Research Program of the NIDCR.
The expression profiles for developmental stages and epithelium compared to mesenchyme were generated by Matthew Hoffman, Ivan Rebustini, Vaishali Patel, and Sarah Knox.
The spatial gene expression data after LCM were generated by Kurt Musselmann, Khin Sone, Ian Bothwell, Sarah Johnson, and Kenneth Yamada.
Single-cell RNAseq was performed by Belinda Hauser, Marit Aure, and Alejandro Chibly, and bioinformatically analyzed by Alejandro Chibly.
Bulk-RNAseq of CH3 SMG mice samples from non-IR, IR-GFP and IR-CERE was performed by Vaishali Patel and bioinformatically analyzed by Daniel Martin.
Bulk-RNAseq from human samples was performed by Isabelle Lombaert and Vaishali Patel, and bioinformatically analyzed by Alejandro Chibly.
Additional bioinformatics and establishment of the web site were performed by Zheng Wei.

If you have questions or suggestions, please contact:
Matthew Hoffman for SMG and SLG developmental expression profiles.
Kenneth Yamada for LCM localization expression data.
Alejandro Chibly for scRNAseq and bulk-RNAseq expression data.
Zheng Wei for bioinformatics and web site.

Abbreviations:
E: Embryonic day
P: Postnatal day
Epith: Epithelium
Mesench: Mesenchyme
CL: Cleft
CB: Central bud
MD: Main duct
SD: Secondary duct
MB: Main bud
BMB: Basement membrane bud (peripheral bud)
IR: Irradiation
NRTN: Neurturin
PG: Parotid gland
SMG: Submandibular gland
SLG: Sublingual gland

Published studies:

Mukaibo, T., Gao, X., Yang, N.Y., Oei, M.S., Nakamoto, T., and Melvin, J.E. (2019). *Sexual dimorphisms in the transcriptomes of murine salivary glands*. FEBS Open Bio *9*, 947-958.

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Gao, X., Oei, M.S., Ovitt, C.E., Sincan, M., and Melvin, J.E. (2018). *Transcriptional profiling reveals gland-specific differential expression in the three major salivary glands of the adult mouse*. Physiol Genomics *50*, 263-271.
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Lombaert, I.M.A., Patel, V.N., Jones, C.E., Villier, D.C., Canada, A.E., Moore, M.R., Berenstein, E., Zheng, C., Goldsmith, C.M., Chorini, J.A.*, et al.* (2020). *CERE-120 Prevents Irradiation-Induced Hypofunction and Restores Immune Homeostasis in Porcine Salivary Glands*. Mol Ther Methods Clin Dev *18*, 839-855.
doi.org/10.1016/j.omtm.2020.07.016

Hauser, B.R., Aure, M.H., Kelly, M.C., Genomics, Computational Biology, C., Hoffman, M.P., and Chibly, A.M. (2020). *Generation of a Single-Cell RNAseq Atlas of Murine Salivary Gland Development*. iScience *23*, 101838.

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Unpublished data:

Chibly A., P.M., Gemma, M., Ghannam M., Andrade J., Denegre N., Simpson C., Goldstein D., Liu F., Lombaert I., and Matthew P. Hoffman. *Neurotrophin signaling is a central mechanism of salivary dysfunction after irradiation that disrupts myoepithelial differentiation*. Unpublished.