Transcriptome Atlases of the Craniofacial Sutures

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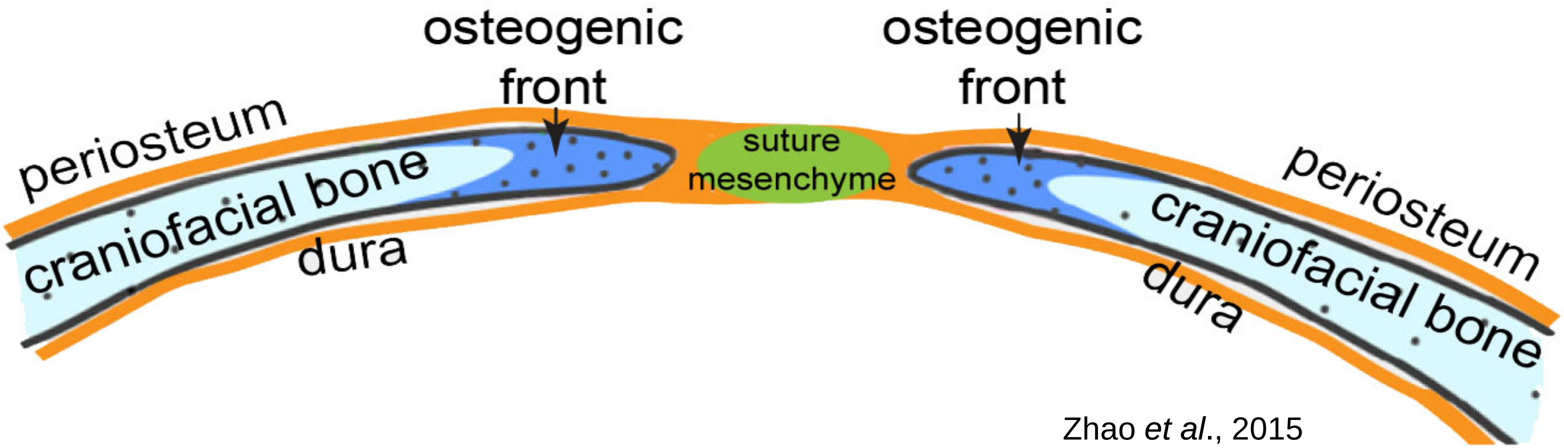
NIH/NIDCR 5U01 DE024448

Mount Sinai

Suture Development

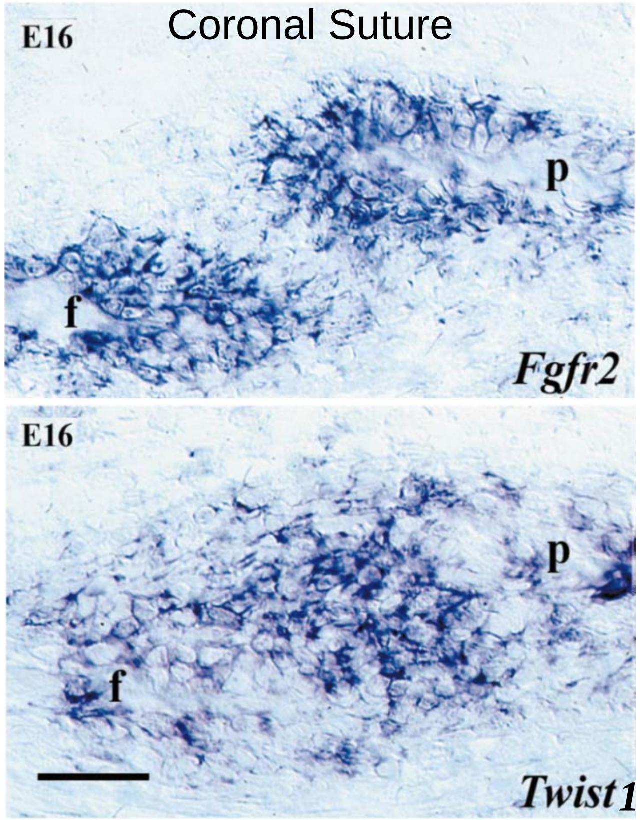


Zhao *et al*., 2015

- **Osteogenic fronts** - proliferation and differentiation of preosteoblasts

- **Suture mesenchyme** - separates osteogenic fronts; a niche for osteoblast stem cells

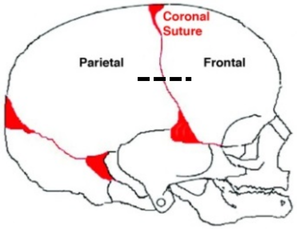
Differential Gene Expression Underlies Suture Development and Disease



Johnson *et al.*, 2000

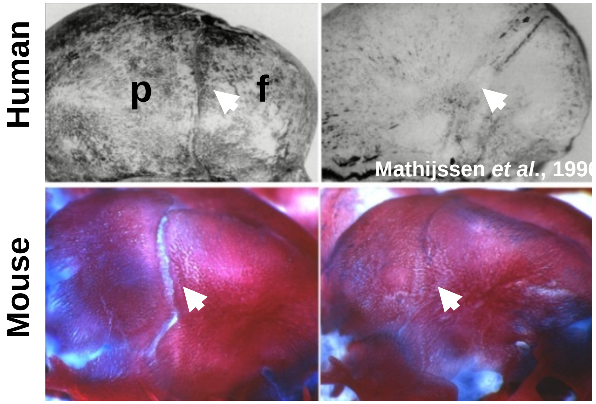
Apert syndrome

Fgfr2$^{+/S252W}$



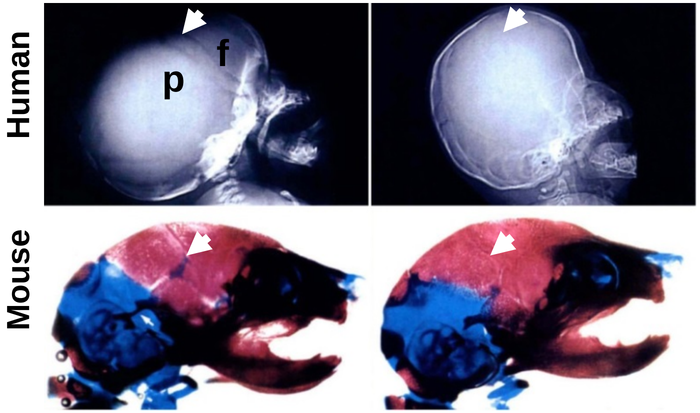
Saethre-Chotzen syndrome

Twist1$^{+/-}$



Mathijssen *et al.*, 199

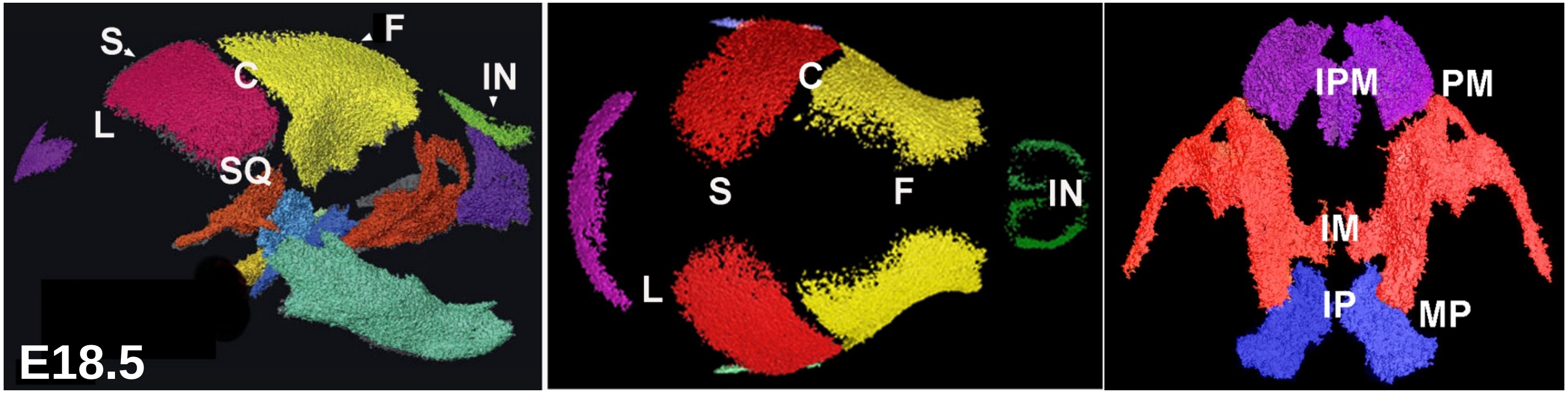
Holmes *et al.*, 2009



El Ghouzzi *et al.*, 1997

Comprehensive expression profiling needed to understand suture biology

Eleven Major Craniofacial Sutures

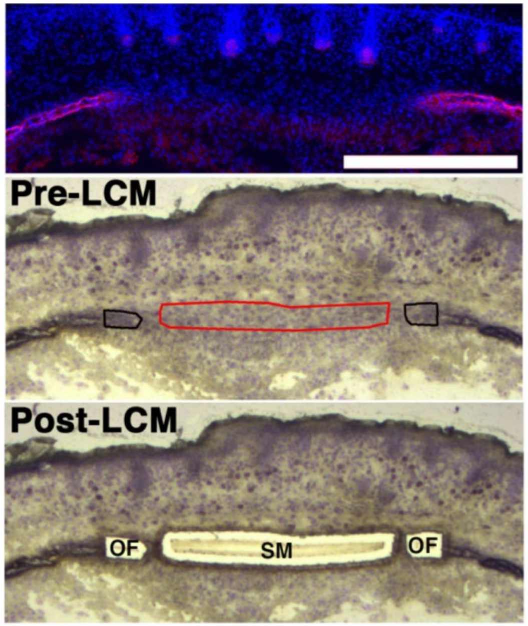

[redacted]

Chris Percival

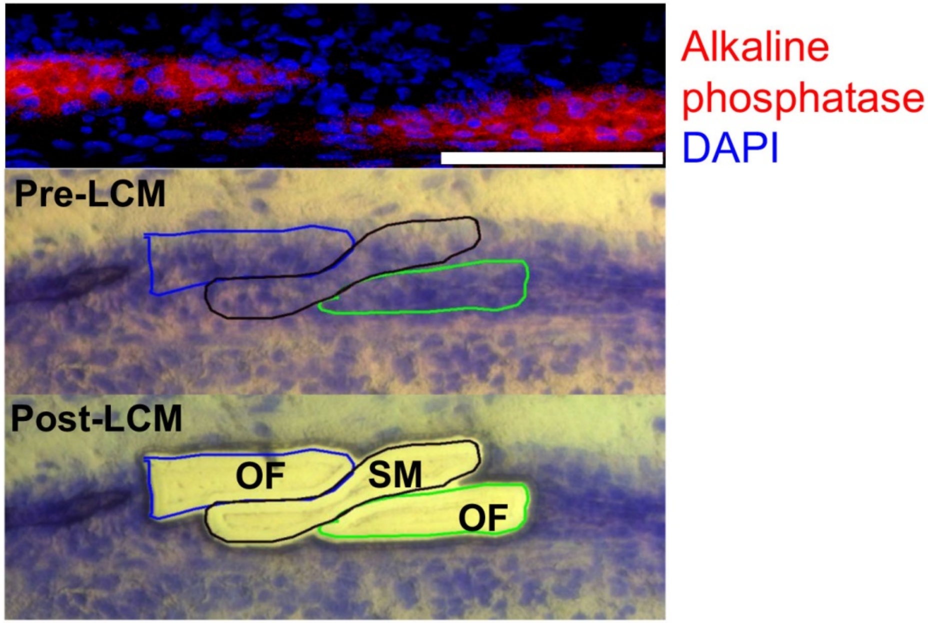
Suture	Location	Lineage	Bone Pair Homology	Structure
Frontal (F)	Cranial	Neural crest	Homologous	End-to-end
Sagittal (S)	Cranial	Mixed	Homologous	End-to-end
Coronal (C)	Cranial	Mixed	Non-homologous	Overlapping
Lambdoid (L)	Cranial	Mesoderm	Non-homologous	Overlapping
Squamoparietal (SQ)	Cranial	Mixed	Non-homologous	Overlapping
Internasal (IN)	Facial	Neural crest	Homologous	End-to-end (broad)
Interpremaxillary (IPM)	Facial	Neural crest	Homologous	End-to-end (broad)
Intermaxillary (IM)	Facial	Neural crest	Homologous	End-to-end
Interpalatine (IP)	Facial	Neural crest	Homologous	End-to-end
Premaxillary/maxillary (PM)	Facial	Neural crest	Non-homologous	End-to-end
Maxillary/palatine (MP)	Facial	Neural crest	Non-homologous	Overlapping

Laser Capture Microdissection of Suture Subregions

End to End, Homologous
E18.5 Frontal Suture

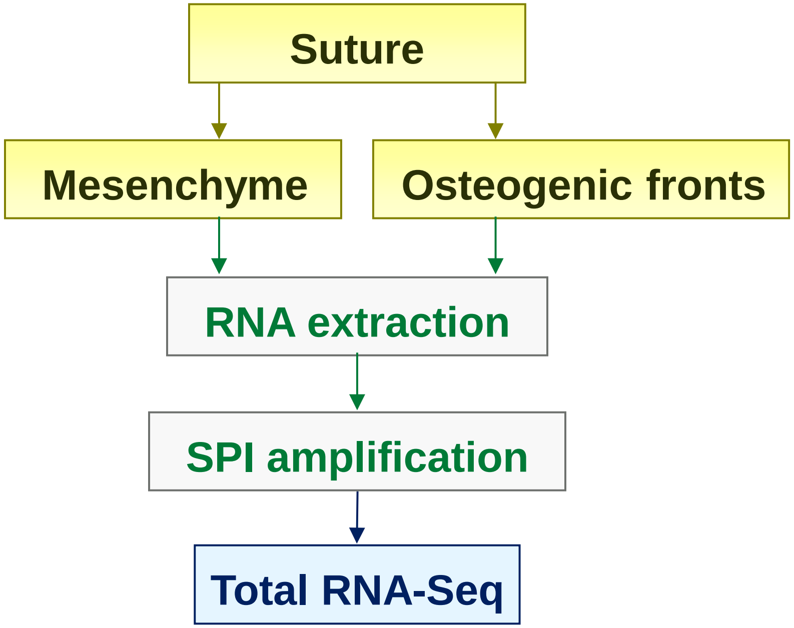


Overlapping, Non-Homologous
E18.5 Coronal Suture



Suture mesenchyme (SM) & osteogenic front (OF) subregions

Data Generation for Each Suture



Suture

Mesenchyme

Osteogenic fronts

RNA extraction

SPI amplification

Total RNA-Seq

→ LCM

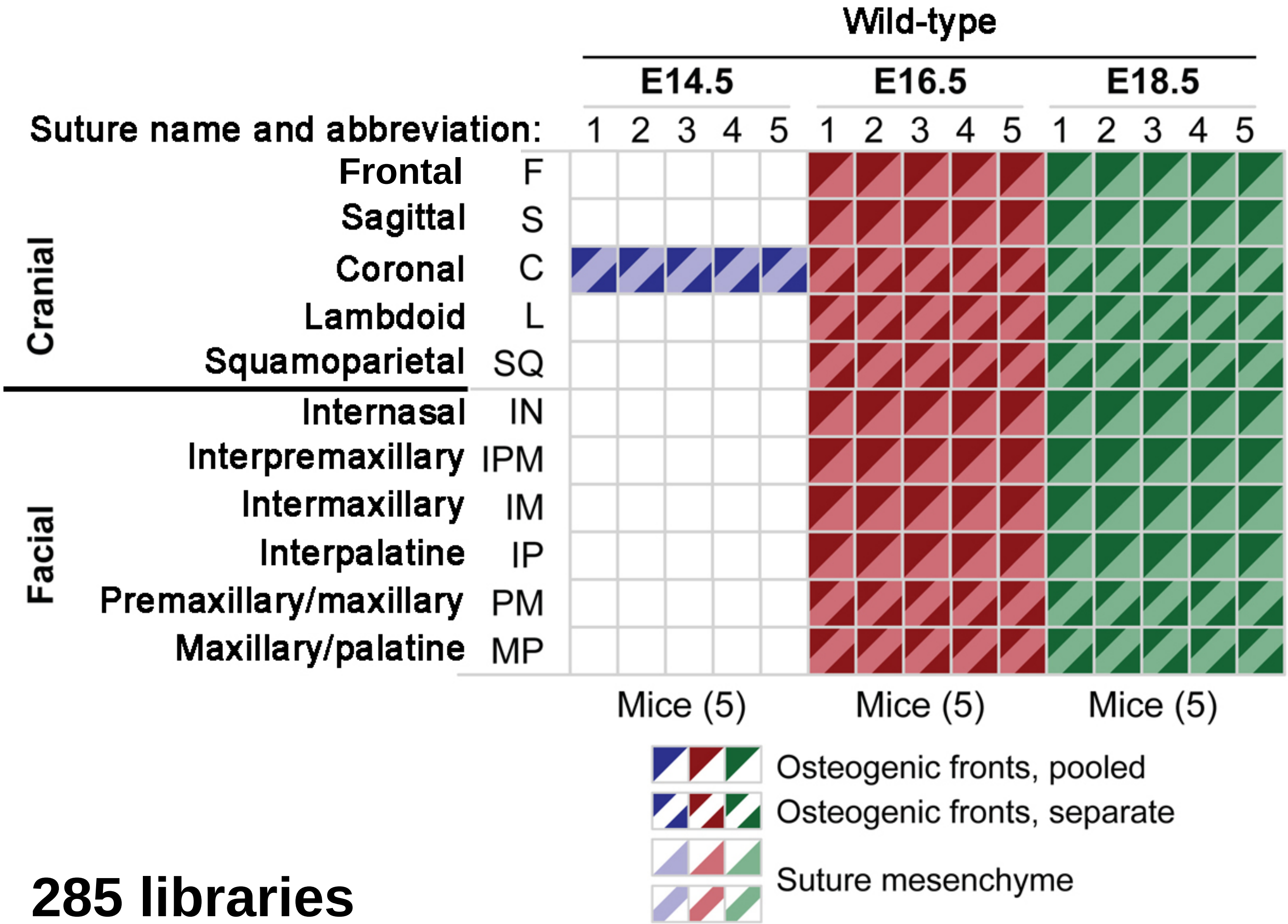
→ 5 replicates (mice)

→ 1-10 ng

→ rRNAs suppressed

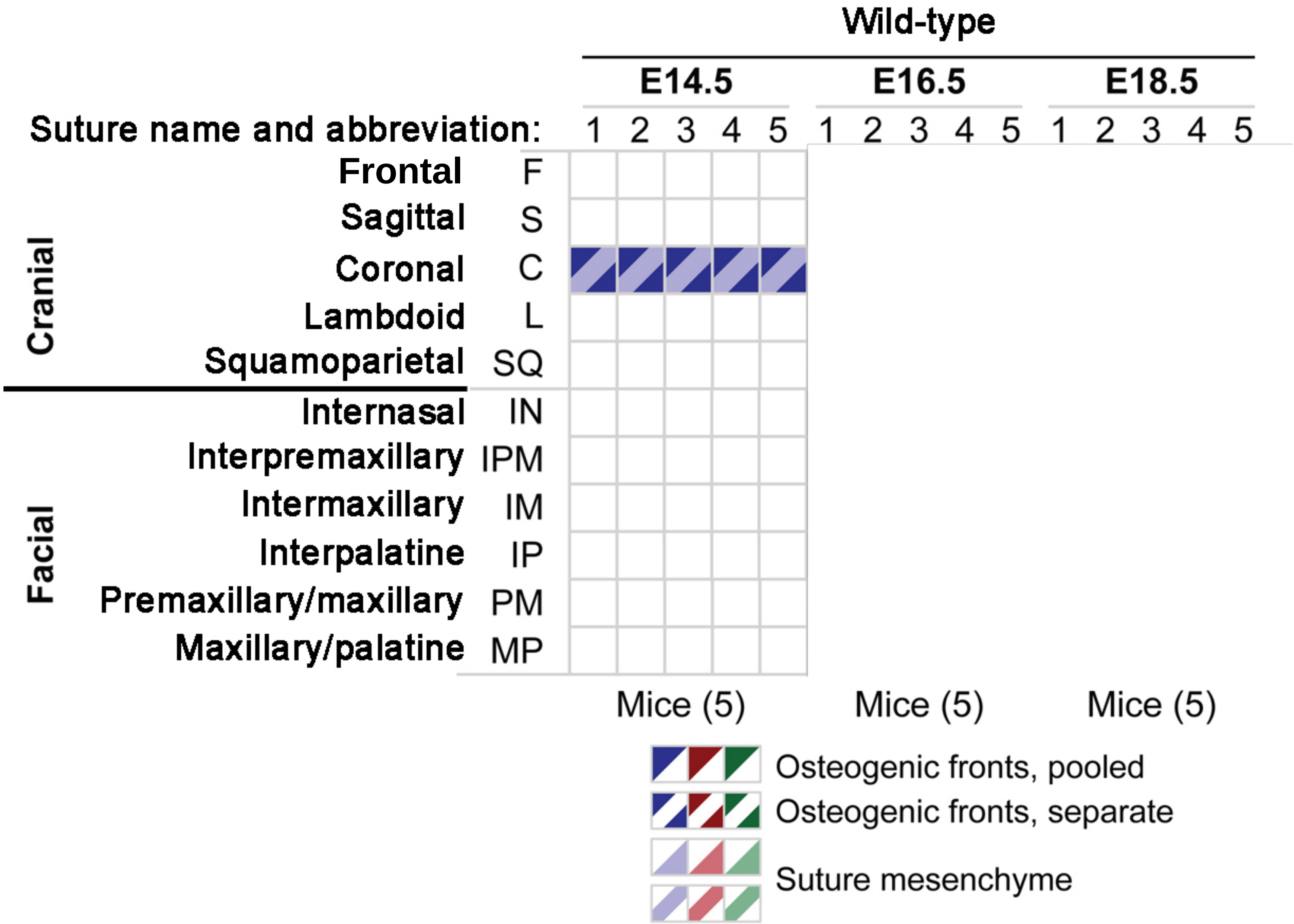
- Illumina HiSeq 2500
- Paired-end 100 nt reads (capture alternate splicing)
- Depth: ~40M read pairs (comprehensive gene detection)

WT Suture RNA-Seq Libraries



285 libraries

WT Suture RNA-Seq Libraries



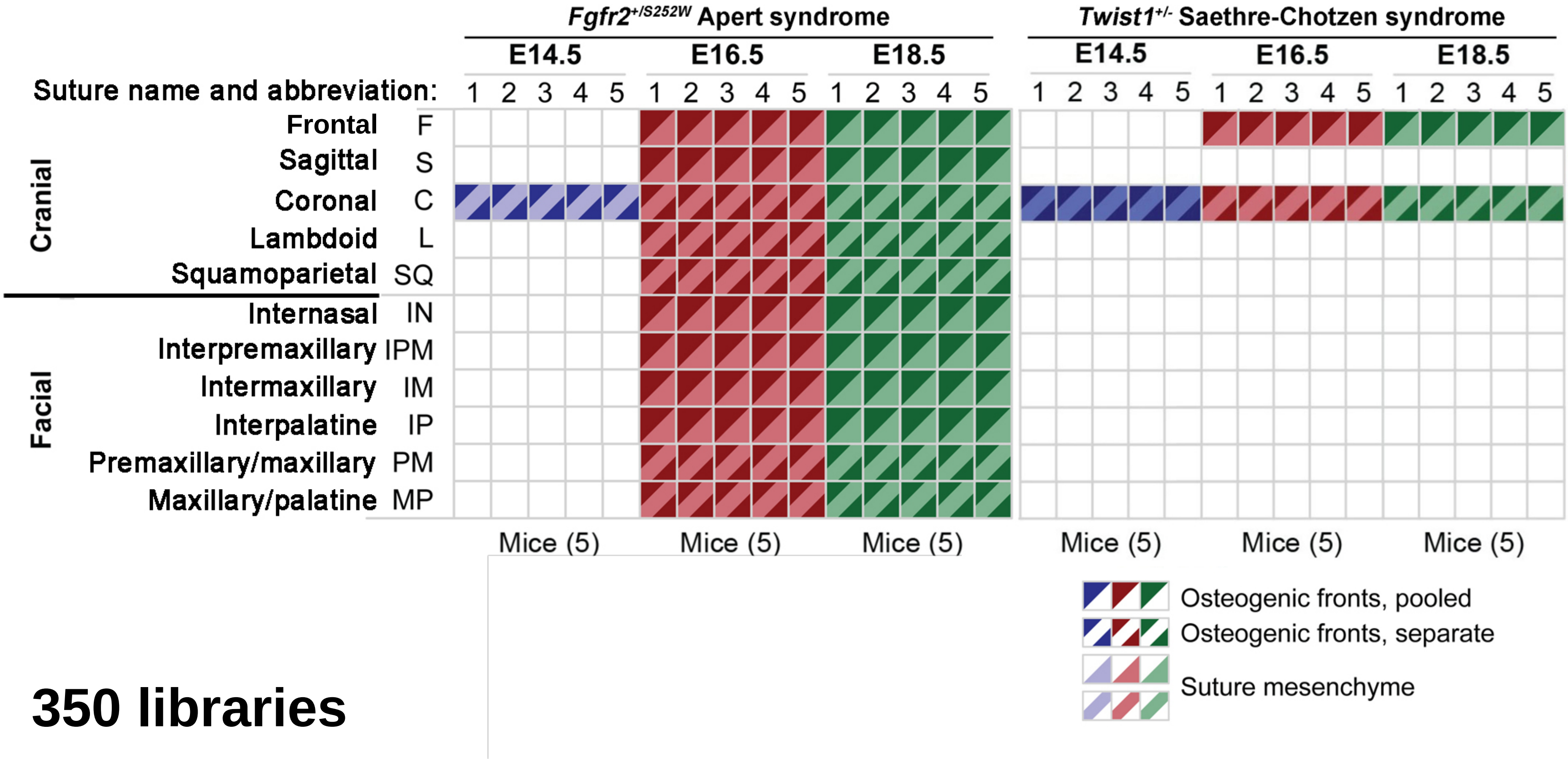
			Wild-type														
			E14.5					E16.5					E18.5				
	Suture name and abbreviation:		1	2	3	4	5	1	2	3	4	5	1	2	3	4	5
Cranial	Frontal	F															
	Sagittal	S															
	Coronal	C	▨	▨	▨	▨	▨										
	Lambdoid	L															
	Squamoparietal	SQ															
Facial	Internasal	IN															
	Interpremaxillary	IPM															
	Intermaxillary	IM															
	Interpalatine	IP															
	Premaxillary/maxillary	PM															
	Maxillary/palatine	MP															
			Mice (5)					Mice (5)					Mice (5)				

Osteogenic fronts, pooled

Osteogenic fronts, separate

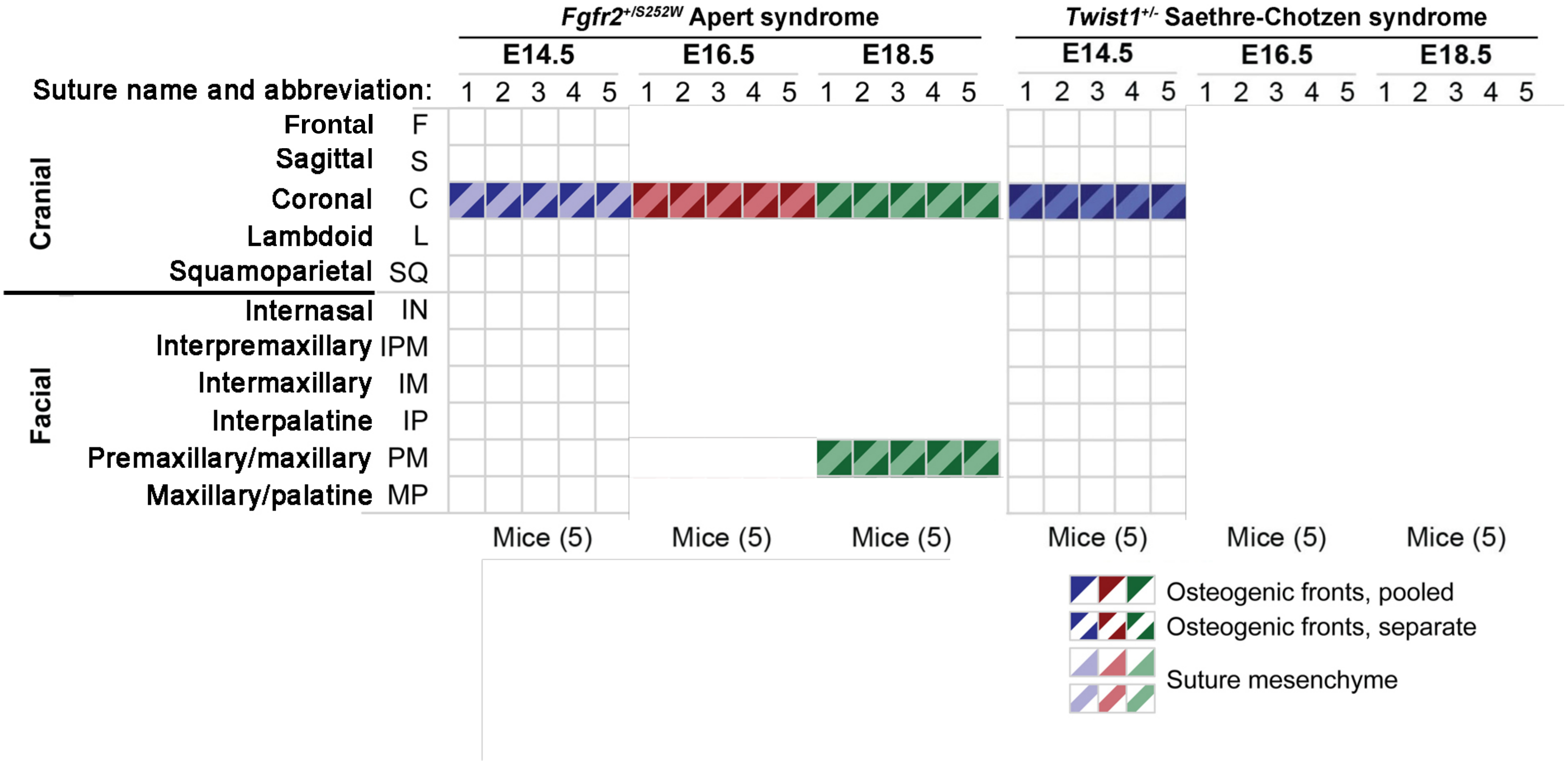
Suture mesenchyme

Fgfr2$^{+/S252W}$ and *Twist1*$^{+/-}$ Suture RNA-Seq Libraries



350 libraries

Fgfr2$^{+/S252W}$ and *Twist1*$^{+/-}$ Suture RNA-Seq Libraries



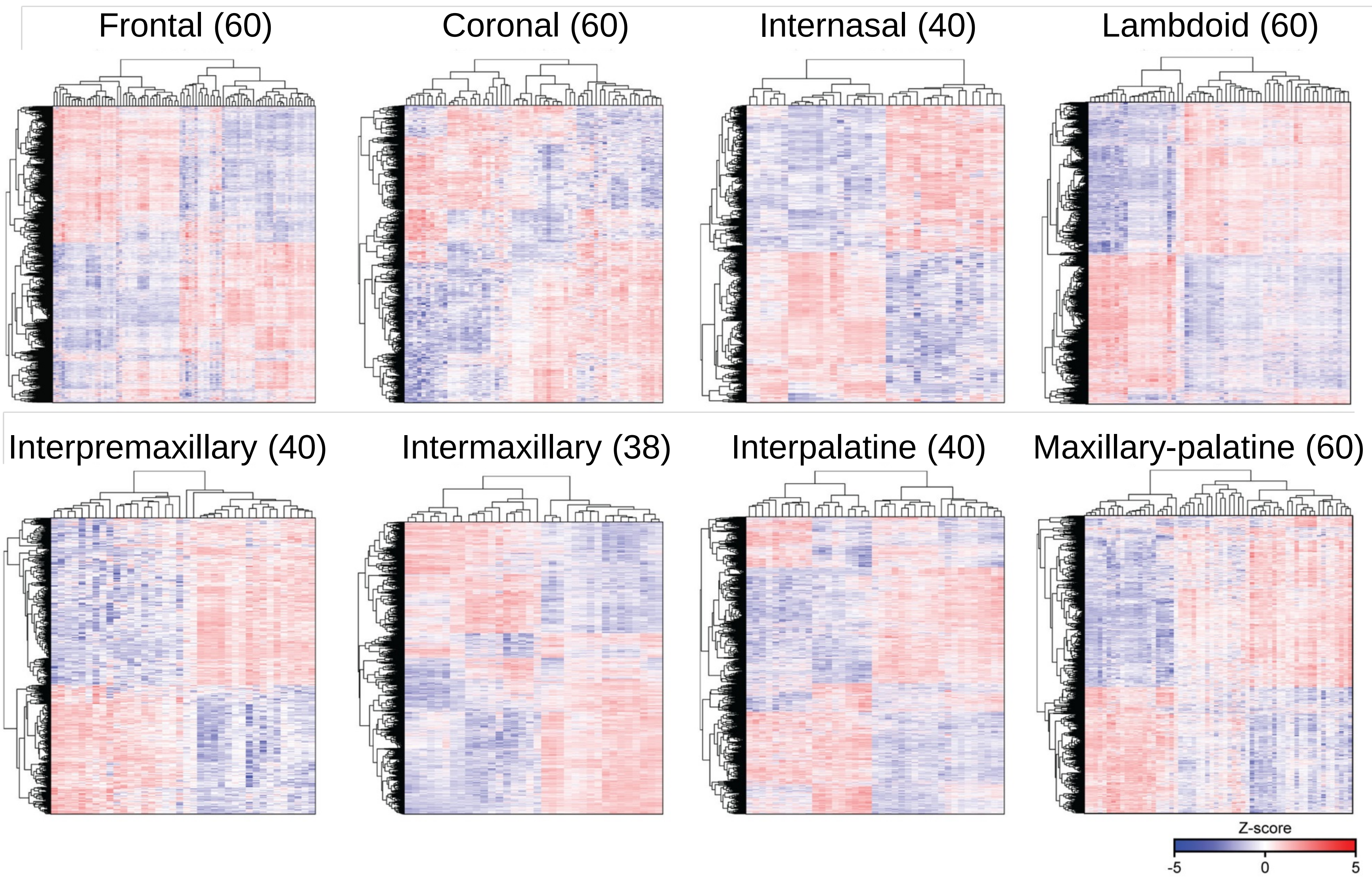
		Fgfr2$^{+/S252W}$ Apert syndrome															*Twist1*$^{+/-}$ Saethre-Chotzen syndrome														
		E14.5					E16.5					E18.5					E14.5					E16.5					E18.5				
	Suture name and abbreviation:	1	2	3	4	5	1	2	3	4	5	1	2	3	4	5	1	2	3	4	5	1	2	3	4	5	1	2	3	4	5
Cranial	Frontal F																														
	Sagittal S																														
	Coronal C	▨	▨	▨	▨	▨	▨	▨	▨	▨	▨	▨	▨	▨	▨	▨	▨	▨	▨	▨	▨										
	Lambdoid L																														
	Squamoparietal SQ																														
Facial	Internasal IN																														
	Interpremaxillary IPM																														
	Intermaxillary IM																														
	Interpalatine IP																														
	Premaxillary/maxillary PM											▨	▨	▨	▨	▨															
	Maxillary/palatine MP																														
		Mice (5)					Mice (5)					Mice (5)					Mice (5)					Mice (5)					Mice (5)				

▨ ▨ ▨ Osteogenic fronts, pooled

▨ ▨ ▨ Osteogenic fronts, separate

▨ ▨ ▨ Suture mesenchyme

FaceBase Bulk RNA-Seq Datasets



Frontal (60)

Coronal (60)

Internasal (40)

Lambdoid (60)

Interpremaxillary (40)

Intermaxillary (38)

Interpalatine (40)

Maxillary-palatine (60)

>7,000 differentially expressed genes across suture subregions, ages, & genotypes

FaceBase Bulk RNA-Seq Datasets

- 500 suture subregions have been microdissected from the 11 sutures
- 398 RNA-Seq libraries deposited in FaceBase
- 100 RNA-Seq libraries currently being synthesized from sagittal (40) & squamoparietal (60) sutures
- 45 RNA samples isolated for RNA-Seq library synthesis from premaxillary-maxillary sutures (WT, *Fgfr2*$^{+/S252W}$)

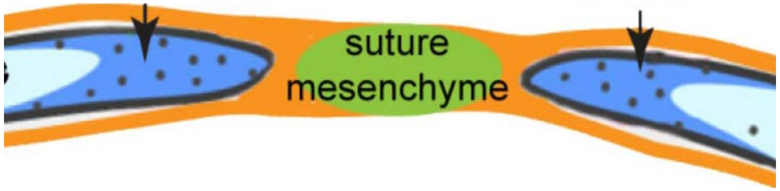
TOTAL OF 543

Remaining Bulk RNA-Seq Libraries (no-cost extension period)

- Premaxillary-maxillary: *Fgfr2*$^{+/S252W}$; 15 libraries

- Coronal:
  - E14.5 WT and *Twist1*$^{+/-}$; 30 libraries
  - E14.5, E16.5, E18.5 *Fgfr2*$^{+/S252W}$; 45 libraries

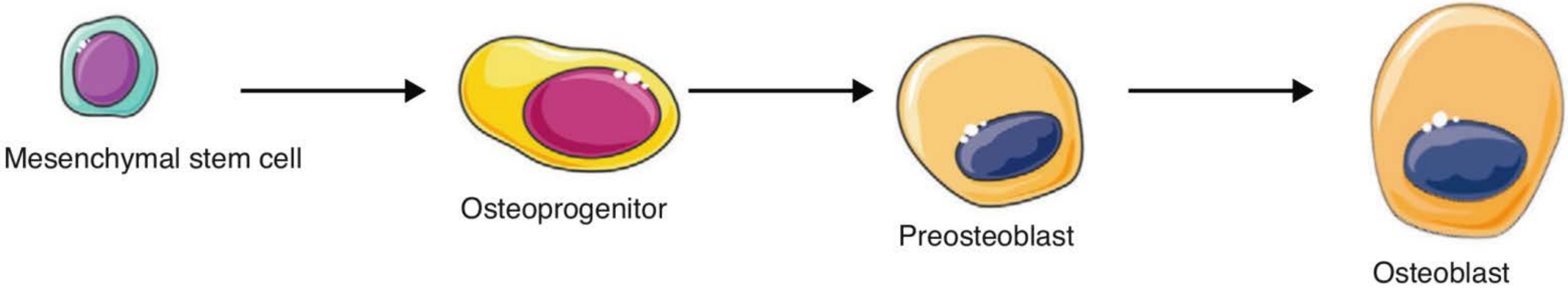
Single-cell Analysis of Suture Cell Populations



osteogenic front

osteogenic front

Zhao *et al*., 2015



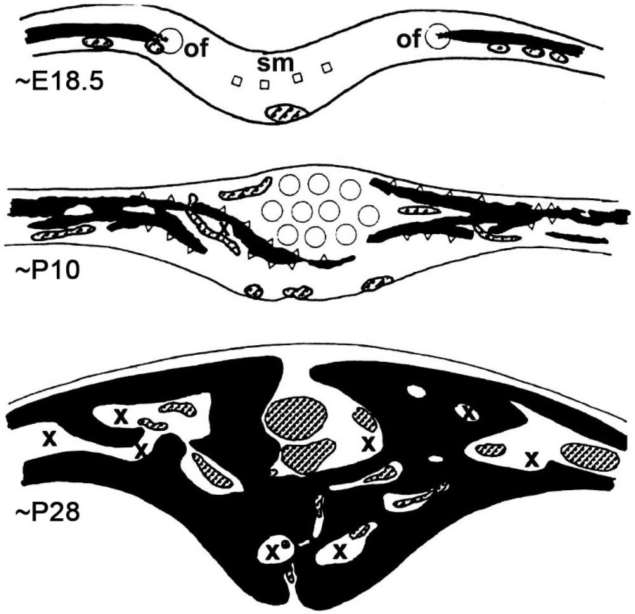
Arboleya *et al.,* 2013

Single-cell Sequencing of 4 WT Sutures at 3 Ages

WT Sutures:

- Coronal
- Frontal
- Lambdoid
- Sagittal

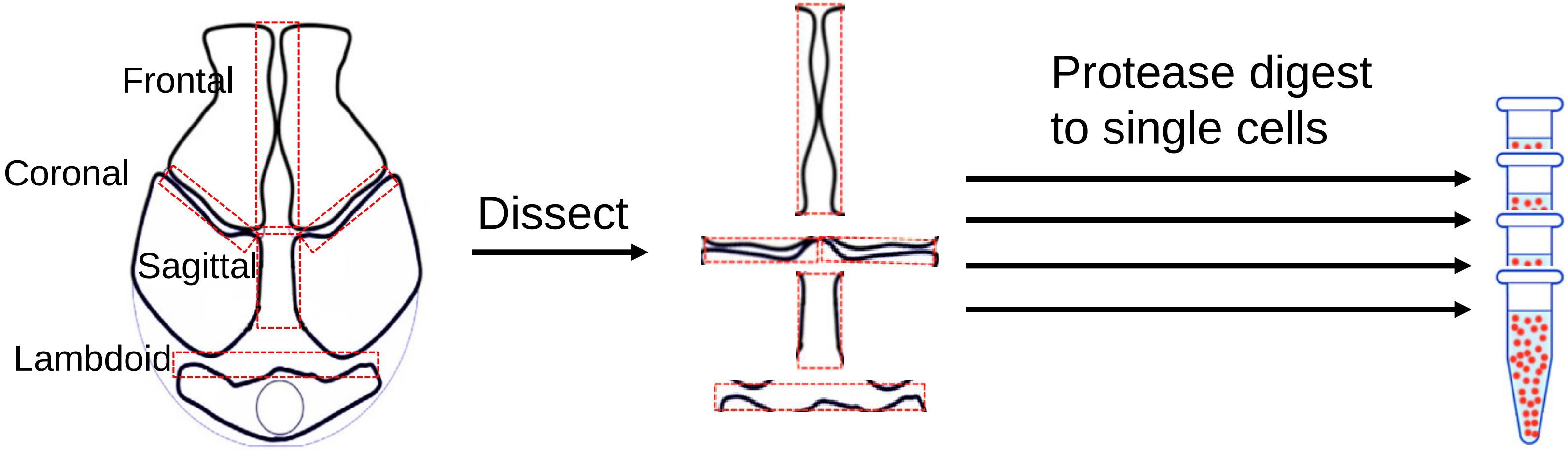
- **E18.5:** embryonic skull growth, suture formation
- **P10:** postnatal skull growth, posterior frontal suture fusion, stem cell niche
- **P28:** skull and suture maintenance



Sagittal Suture

Adapted from Zimmerman, *et al*., 1988

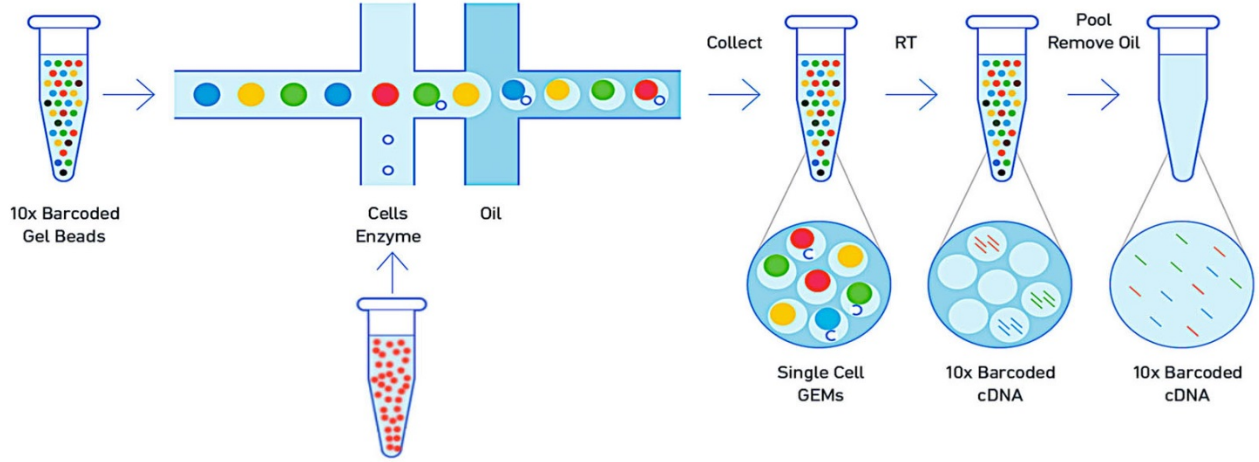
10X Genomics Chromium Single-cell RNA-Seq



Dissect

Protease digest to single cells

Chromium microfluidics cell tagging → Library synthesis

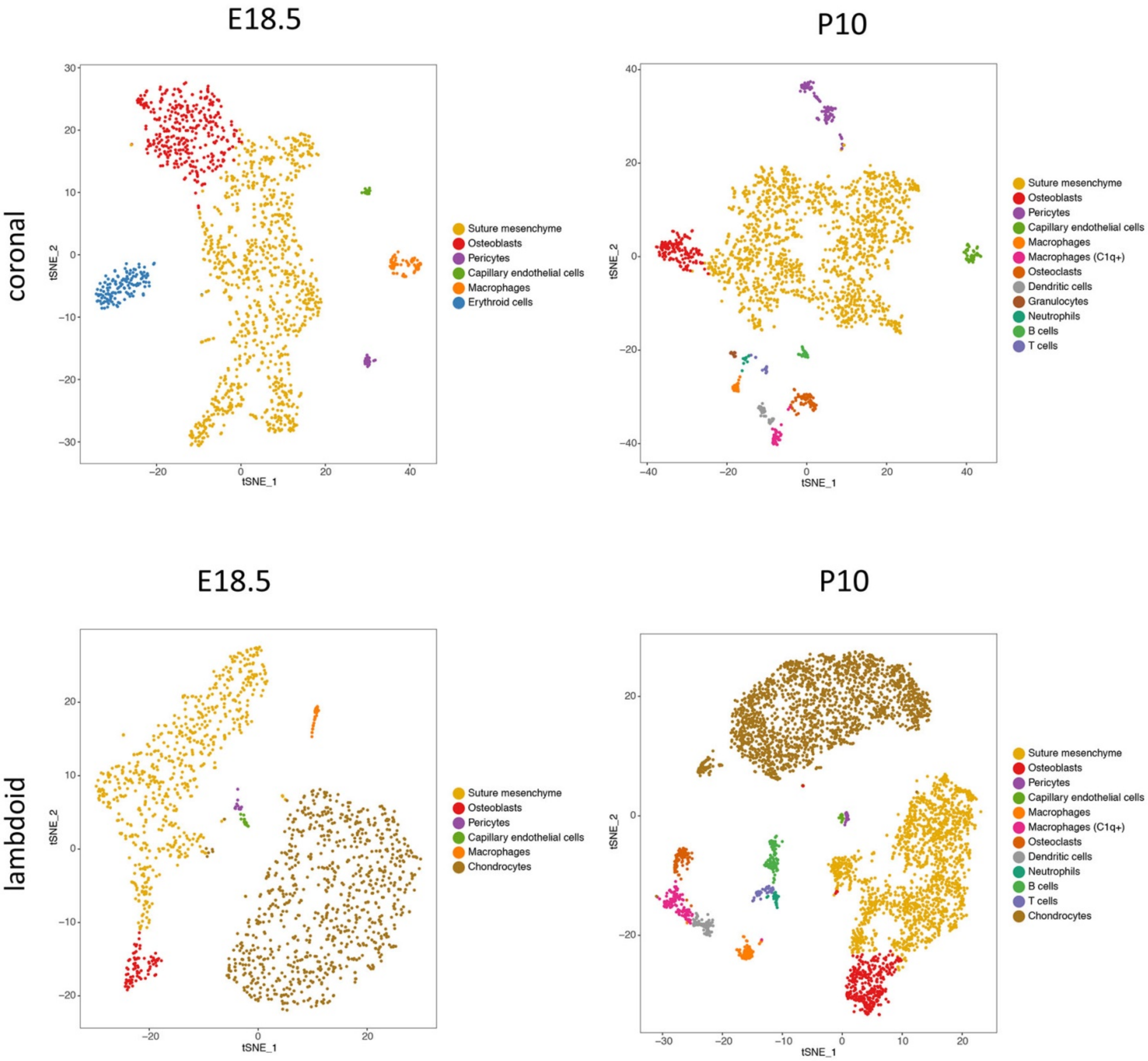


FaceBase Single-cell RNA-Seq Datasets

Mouse Genotype	Stage (E)	Suture Name	Cell Counts	Reads per cell
WT	E.18.5	Coronal	1594	229,500
WT	E.18.5	Lambdoid	1602	262,512
WT	E.18.5	Frontal	939	218,382
WT	E.18.5	Sagittal	3,052	66,213
WT	P10	Coronal	2026	81,632
WT	P10	Lambdoid	4657	79,290

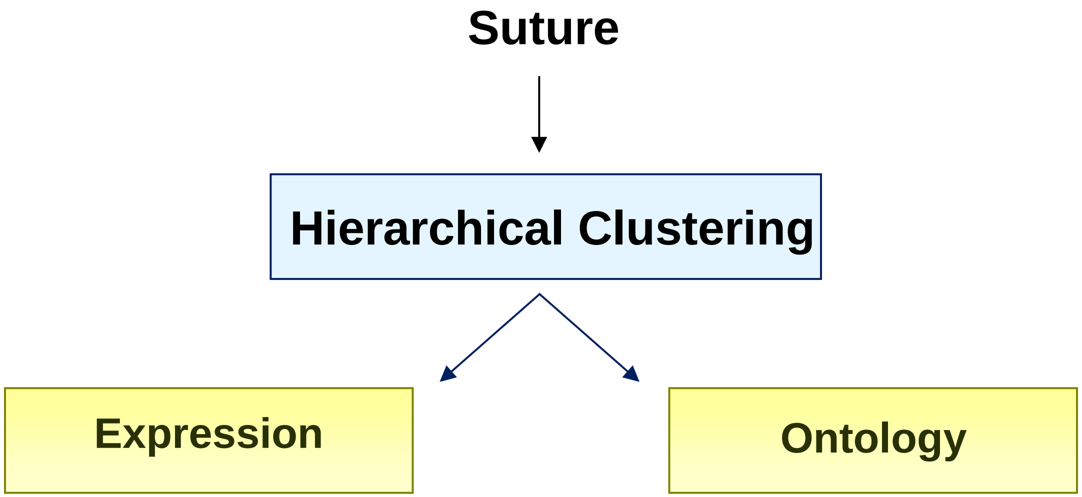
Remaining P10 and P28 sutures to be completed during the no-cost extension period

scRNA-Seq Data Analysis



Use Case #1: Differential Gene Expression within Suture Subregions

- What genes are differentially expressed between suture mesenchyme and osteogenic front subregions?
- How does gene expression change within a subregion during development?
- What gene ontology terms are enriched for a given suture subregion?



Suture

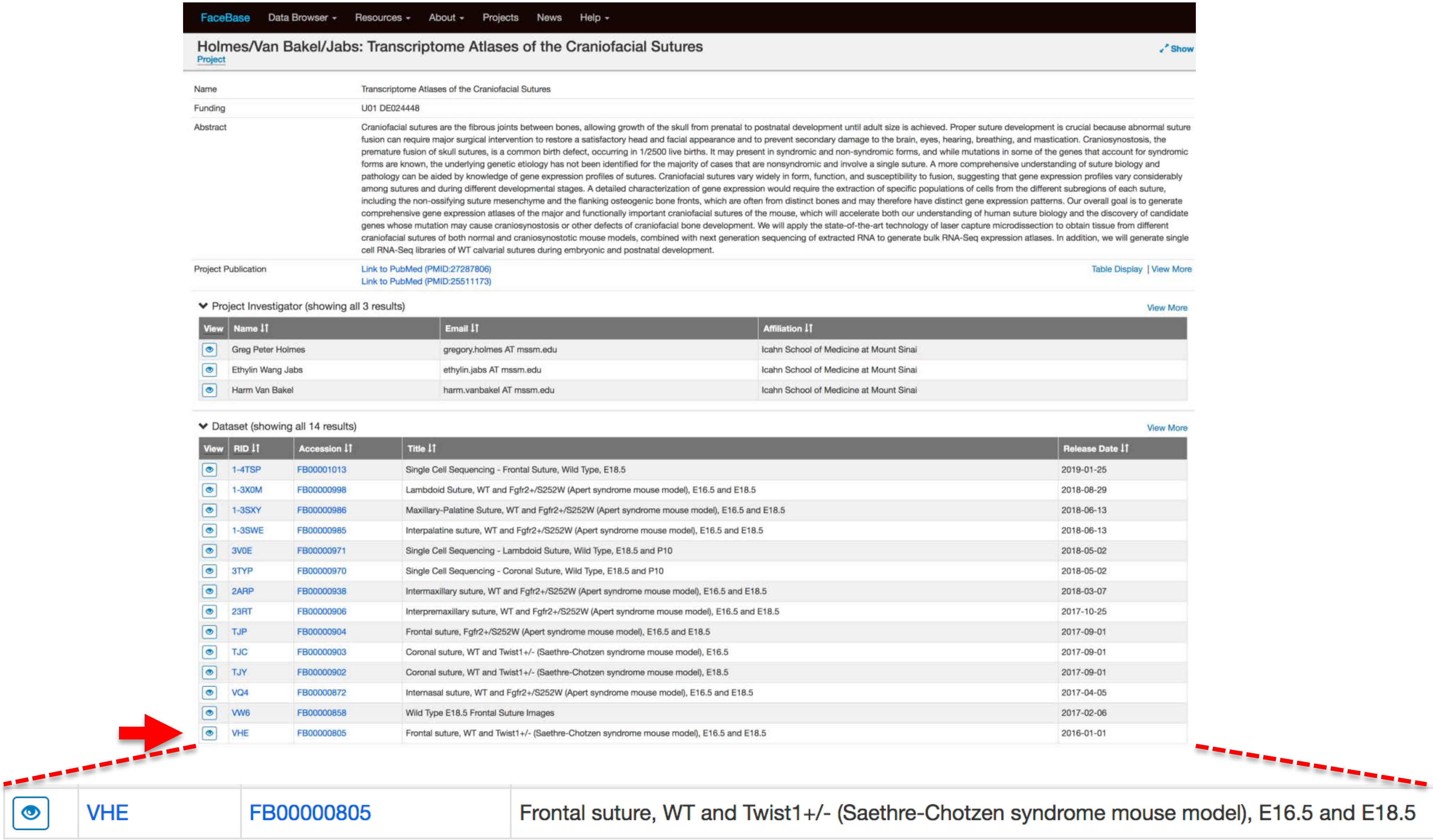
Hierarchical Clustering

Expression

Ontology

Use Case #1: Differential Gene Expression within the Frontal Suture

https://www.facebase.org/chaise/record/#1/isa:project/RID=1WW8



Holmes/Van Bakel/Jabs: Transcriptome Atlases of the Craniofacial Sutures

Project

Name	Transcriptome Atlases of the Craniofacial Sutures
Funding	U01 DE024448
Abstract	Craniofacial sutures are the fibrous joints between bones, allowing growth of the skull from prenatal to postnatal development until adult size is achieved. Proper suture development is crucial because abnormal suture fusion can require major surgical intervention to restore a satisfactory head and facial appearance and to prevent secondary damage to the brain, eyes, hearing, breathing, and mastication. Craniosynostosis, the premature fusion of skull sutures, is a common birth defect, occurring in 1/2500 live births. It may present in syndromic and non-syndromic forms, and while mutations in some of the genes that account for syndromic forms are known, the underlying genetic etiology has not been identified for the majority of cases that are nonsyndromic and involve a single suture. A more comprehensive understanding of suture biology and pathology can be aided by knowledge of gene expression profiles of sutures. Craniofacial sutures vary widely in form, function, and susceptibility to fusion, suggesting that gene expression profiles vary considerably among sutures and during different developmental stages. A detailed characterization of gene expression would require the extraction of specific populations of cells from the different subregions of each suture, including the non-ossifying suture mesenchyme and the flanking osteogenic bone fronts, which are often from distinct bones and may therefore have distinct gene expression patterns. Our overall goal is to generate comprehensive gene expression atlases of the major and functionally important craniofacial sutures of the mouse, which will accelerate both our understanding of human suture biology and the discovery of candidate genes whose mutation may cause craniosynostosis or other defects of craniofacial bone development. We will apply the state-of-the-art technology of laser capture microdissection to obtain tissue from different craniofacial sutures of both normal and craniosynostotic mouse models, combined with next generation sequencing of extracted RNA to generate bulk RNA-Seq expression atlases. In addition, we will generate single cell RNA-Seq libraries of WT calvarial sutures during embryonic and postnatal development.
Project Publication	Link to PubMed (PMID:27287806) Link to PubMed (PMID:25511173)

Table Display | View More

Project Investigator (showing all 3 results)

View More

View	Name	Email	Affiliation
👁	Greg Peter Holmes	gregory.holmes AT mssm.edu	Icahn School of Medicine at Mount Sinai
👁	Ethylin Wang Jabs	ethylin.jabs AT mssm.edu	Icahn School of Medicine at Mount Sinai
👁	Harm Van Bakel	harm.vanbakel AT mssm.edu	Icahn School of Medicine at Mount Sinai

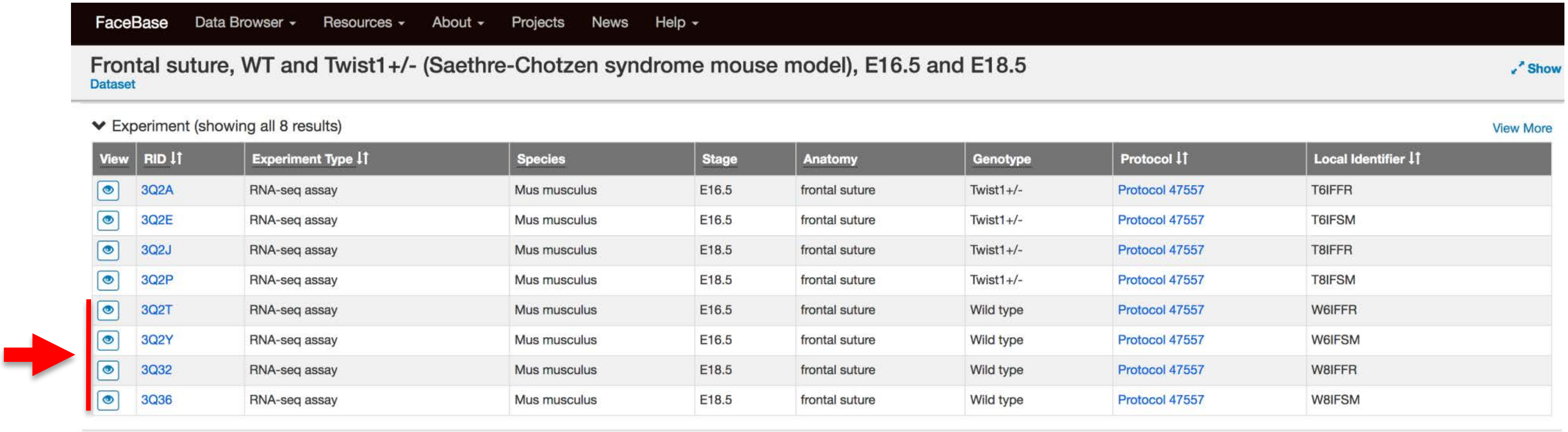
Dataset (showing all 14 results)

View More

View	RID	Accession	Title	Release Date
👁	1-4TSP	FB00001013	Single Cell Sequencing - Frontal Suture, Wild Type, E18.5	2019-01-25
👁	1-3X0M	FB00000998	Lambdoid Suture, WT and Fgfr2+/S252W (Apert syndrome mouse model), E16.5 and E18.5	2018-08-29
👁	1-3SXY	FB00000986	Maxillary-Palatine Suture, WT and Fgfr2+/S252W (Apert syndrome mouse model), E16.5 and E18.5	2018-06-13
👁	1-3SWE	FB00000985	Interpalatine suture, WT and Fgfr2+/S252W (Apert syndrome mouse model), E16.5 and E18.5	2018-06-13
👁	3V0E	FB00000971	Single Cell Sequencing - Lambdoid Suture, Wild Type, E18.5 and P10	2018-05-02
👁	3TYP	FB00000970	Single Cell Sequencing - Coronal Suture, Wild Type, E18.5 and P10	2018-05-02
👁	2ARP	FB00000938	Intermaxillary suture, WT and Fgfr2+/S252W (Apert syndrome mouse model), E16.5 and E18.5	2018-03-07
👁	23RT	FB00000906	Interpremaxillary suture, WT and Fgfr2+/S252W (Apert syndrome mouse model), E16.5 and E18.5	2017-10-25
👁	TJP	FB00000904	Frontal suture, Fgfr2+/S252W (Apert syndrome mouse model), E16.5 and E18.5	2017-09-01
👁	TJC	FB00000903	Coronal suture, WT and Twist1+/- (Saethre-Chotzen syndrome mouse model), E16.5	2017-09-01
👁	TJY	FB00000902	Coronal suture, WT and Twist1+/- (Saethre-Chotzen syndrome mouse model), E18.5	2017-09-01
👁	VQ4	FB00000872	Internasal suture, WT and Fgfr2+/S252W (Apert syndrome mouse model), E16.5 and E18.5	2017-04-05
👁	VW6	FB00000858	Wild Type E18.5 Frontal Suture Images	2017-02-06
👁	VHE	FB00000805	Frontal suture, WT and Twist1+/- (Saethre-Chotzen syndrome mouse model), E16.5 and E18.5	2016-01-01

👁	VHE	FB00000805	Frontal suture, WT and Twist1+/- (Saethre-Chotzen syndrome mouse model), E16.5 and E18.5

Use Case #1: Differential Gene Expression within the Frontal Suture



Frontal suture, WT and Twist1+/- (Saethre-Chotzen syndrome mouse model), E16.5 and E18.5

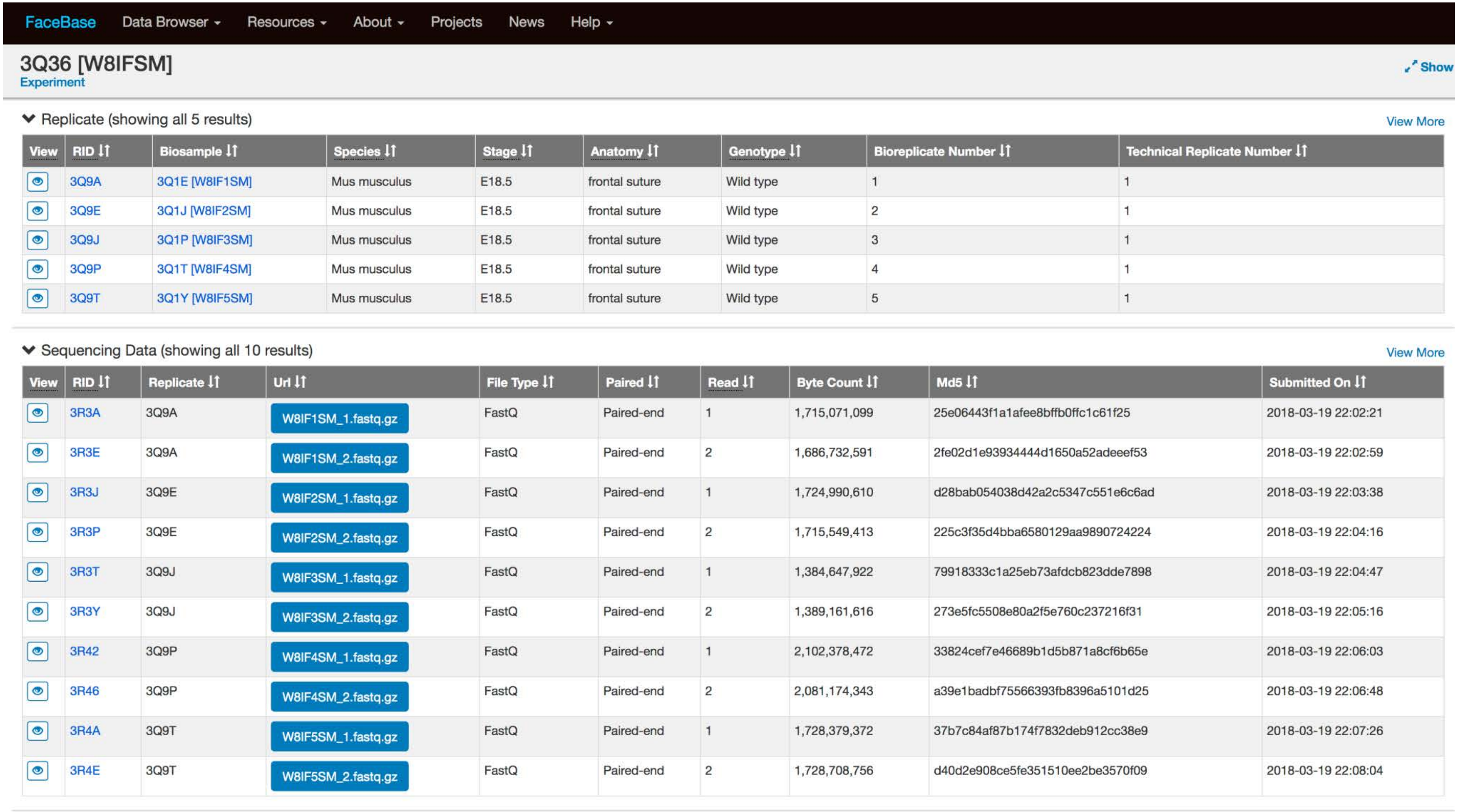
Dataset

Experiment (showing all 8 results)

View	RID	Experiment Type	Species	Stage	Anatomy	Genotype	Protocol	Local Identifier
👁	3Q2A	RNA-seq assay	Mus musculus	E16.5	frontal suture	Twist1+/-	Protocol 47557	T6IFFR
👁	3Q2E	RNA-seq assay	Mus musculus	E16.5	frontal suture	Twist1+/-	Protocol 47557	T6IFSM
👁	3Q2J	RNA-seq assay	Mus musculus	E18.5	frontal suture	Twist1+/-	Protocol 47557	T8IFFR
👁	3Q2P	RNA-seq assay	Mus musculus	E18.5	frontal suture	Twist1+/-	Protocol 47557	T8IFSM
👁	3Q2T	RNA-seq assay	Mus musculus	E16.5	frontal suture	Wild type	Protocol 47557	W6IFFR
👁	3Q2Y	RNA-seq assay	Mus musculus	E16.5	frontal suture	Wild type	Protocol 47557	W6IFSM
👁	3Q32	RNA-seq assay	Mus musculus	E18.5	frontal suture	Wild type	Protocol 47557	W8IFFR
👁	3Q36	RNA-seq assay	Mus musculus	E18.5	frontal suture	Wild type	Protocol 47557	W8IFSM

-download WT frontal suture files

Use Case #1: Differential Gene Expression within the Frontal Suture



3Q36 [W8IFSM]
Experiment

Replicate (showing all 5 results)

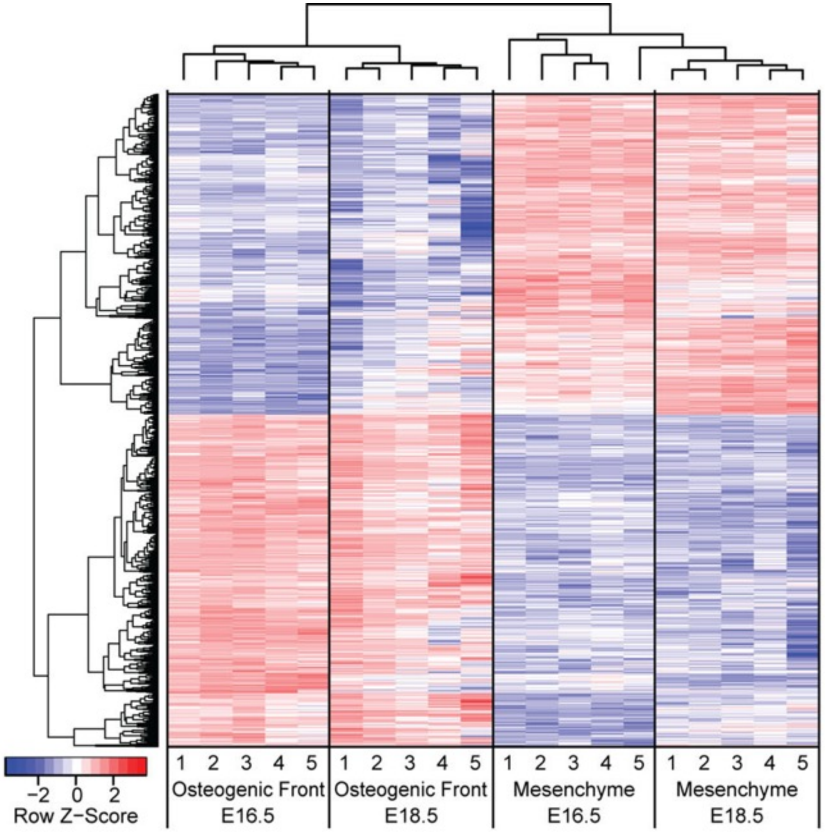
View	RID	Biosample	Species	Stage	Anatomy	Genotype	Bioreplicate Number	Technical Replicate Number
👁	3Q9A	3Q1E [W8IF1SM]	Mus musculus	E18.5	frontal suture	Wild type	1	1
👁	3Q9E	3Q1J [W8IF2SM]	Mus musculus	E18.5	frontal suture	Wild type	2	1
👁	3Q9J	3Q1P [W8IF3SM]	Mus musculus	E18.5	frontal suture	Wild type	3	1
👁	3Q9P	3Q1T [W8IF4SM]	Mus musculus	E18.5	frontal suture	Wild type	4	1
👁	3Q9T	3Q1Y [W8IF5SM]	Mus musculus	E18.5	frontal suture	Wild type	5	1

Sequencing Data (showing all 10 results)

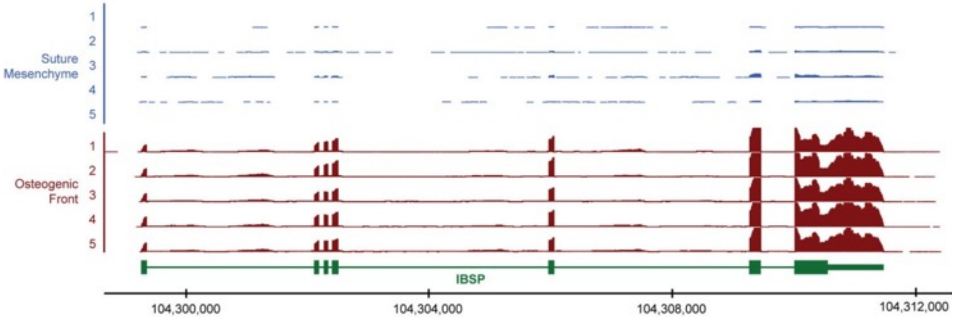
View	RID	Replicate	Url	File Type	Paired	Read	Byte Count	Md5	Submitted On
👁	3R3A	3Q9A	W8IF1SM_1.fastq.gz	FastQ	Paired-end	1	1,715,071,099	25e06443f1a1afee8bffb0ffc1c61f25	2018-03-19 22:02:21
👁	3R3E	3Q9A	W8IF1SM_2.fastq.gz	FastQ	Paired-end	2	1,686,732,591	2fe02d1e93934444d1650a52adeeef53	2018-03-19 22:02:59
👁	3R3J	3Q9E	W8IF2SM_1.fastq.gz	FastQ	Paired-end	1	1,724,990,610	d28bab054038d42a2c5347c551e6c6ad	2018-03-19 22:03:38
👁	3R3P	3Q9E	W8IF2SM_2.fastq.gz	FastQ	Paired-end	2	1,715,549,413	225c3f35d4bba6580129aa9890724224	2018-03-19 22:04:16
👁	3R3T	3Q9J	W8IF3SM_1.fastq.gz	FastQ	Paired-end	1	1,384,647,922	79918333c1a25eb73afdcb823dde7898	2018-03-19 22:04:47
👁	3R3Y	3Q9J	W8IF3SM_2.fastq.gz	FastQ	Paired-end	2	1,389,161,616	273e5fc5508e80a2f5e760c237216f31	2018-03-19 22:05:16
👁	3R42	3Q9P	W8IF4SM_1.fastq.gz	FastQ	Paired-end	1	2,102,378,472	33824cef7e46689b1d5b871a8cf6b65e	2018-03-19 22:06:03
👁	3R46	3Q9P	W8IF4SM_2.fastq.gz	FastQ	Paired-end	2	2,081,174,343	a39e1badbf75566393fb8396a5101d25	2018-03-19 22:06:48
👁	3R4A	3Q9T	W8IF5SM_1.fastq.gz	FastQ	Paired-end	1	1,728,379,372	37b7c84af87b174f7832deb912cc38e9	2018-03-19 22:07:26
👁	3R4E	3Q9T	W8IF5SM_2.fastq.gz	FastQ	Paired-end	2	1,728,708,756	d40d2e908ce5fe351510ee2be3570f09	2018-03-19 22:08:04

Use Case #1: Differential Gene Expression within the Frontal Suture

Hierarchical Clustering (1,272 genes)



Browser track: *Integrin-binding sialoprotein*

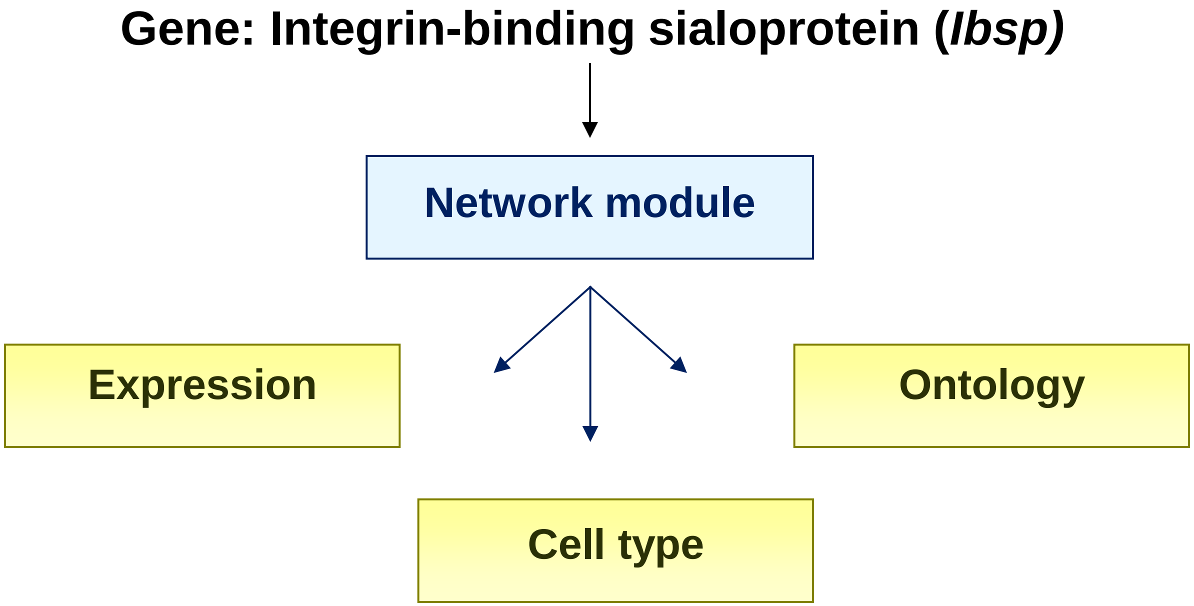


Gene Ontology: Osteogenic Fronts

Description	# Genes	P-value
skeletal system development	27	5.93E-07
biomineral formation	11	1.55E-06
bone development	17	2.03E-06
ossification	16	2.62E-06
sterol metabolic process	12	2.13E-04
regulation of ossification	10	4.33E-04
cholesterol metabolic process	11	5.00E-04
sterol biosynthetic process	8	5.27E-04
cholesterol biosynthetic process	7	1.26E-03
regulation of epithelial cell proliferation	10	1.15E-03
regulation of cell proliferation	29	1.62E-03

Use Case #2: Query Gene Network

- Where is my gene of interest expressed in a suture?
- How does its expression change during development?
- In what cell types is it expressed?
- With what other genes is it co-expressed?
- What gene ontology terms are enriched for its co-expression module?



Gene: Integrin-binding sialoprotein (*Ibsp*)

Network module

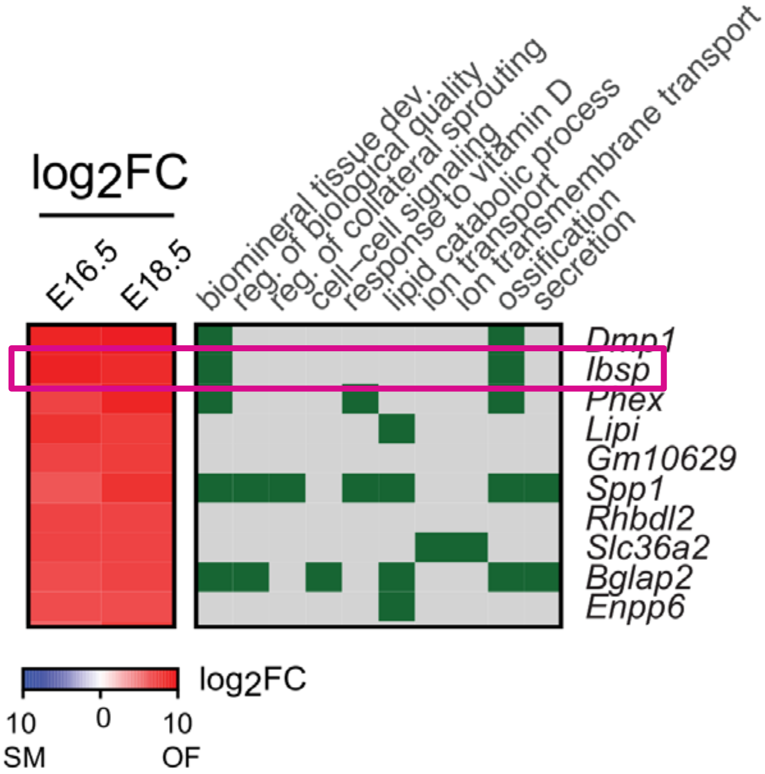
Expression

Ontology

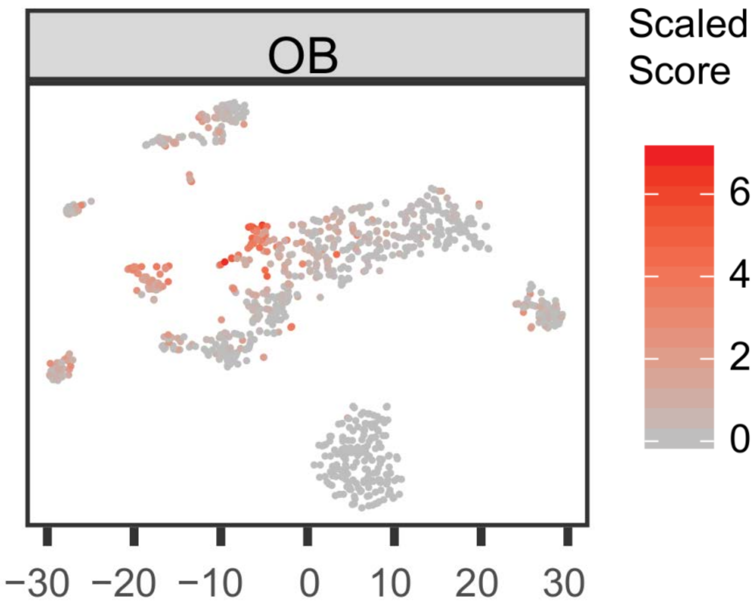
Cell type

Use Case #2: Query Gene Network

Osteogenic front of frontal suture from bulk RNA-Seq

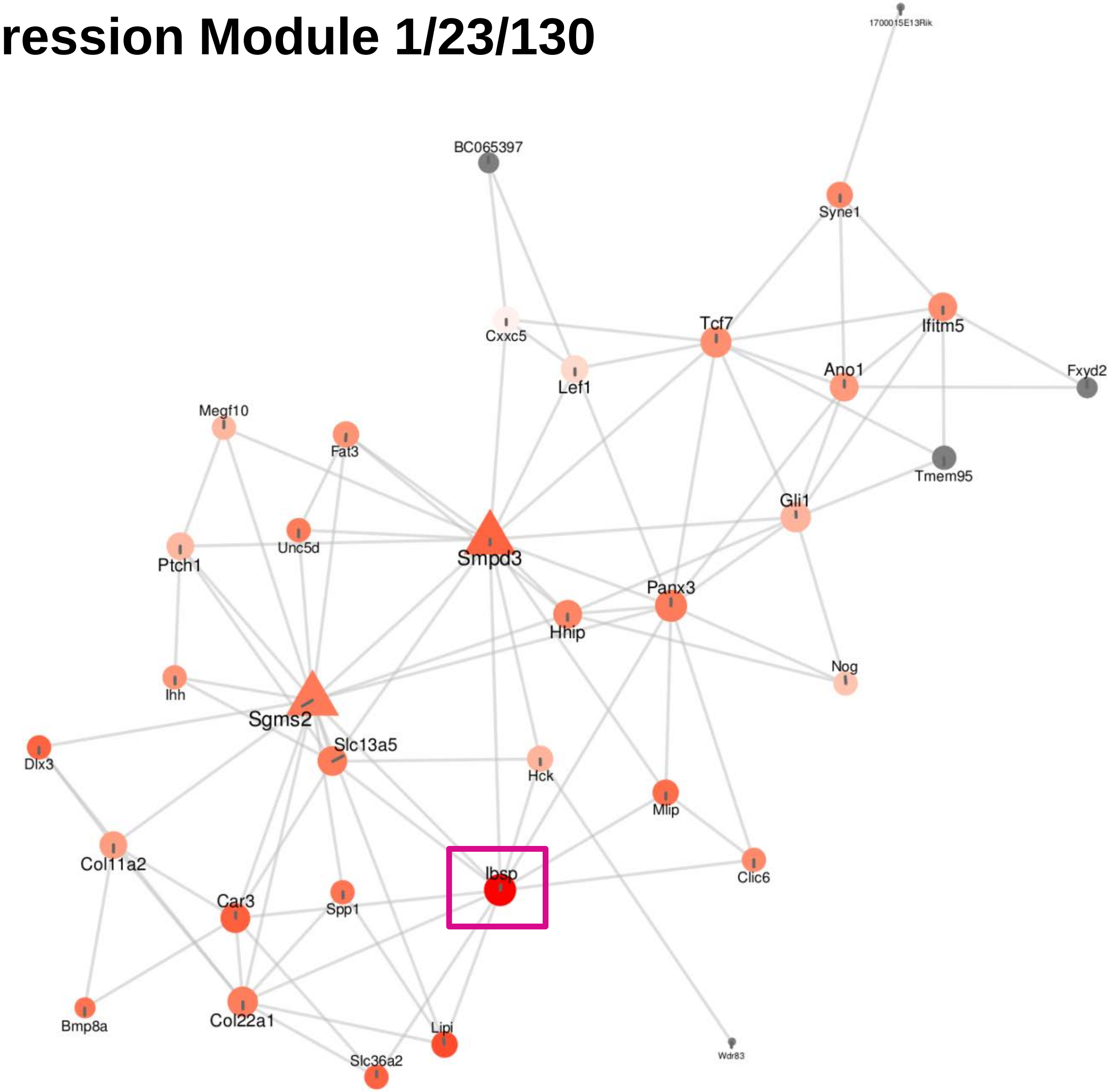


Osteoblast population of frontal suture from single-cell RNA-Seq



Use Case #2: Query Gene Network

Co-Expression Module 1/23/130



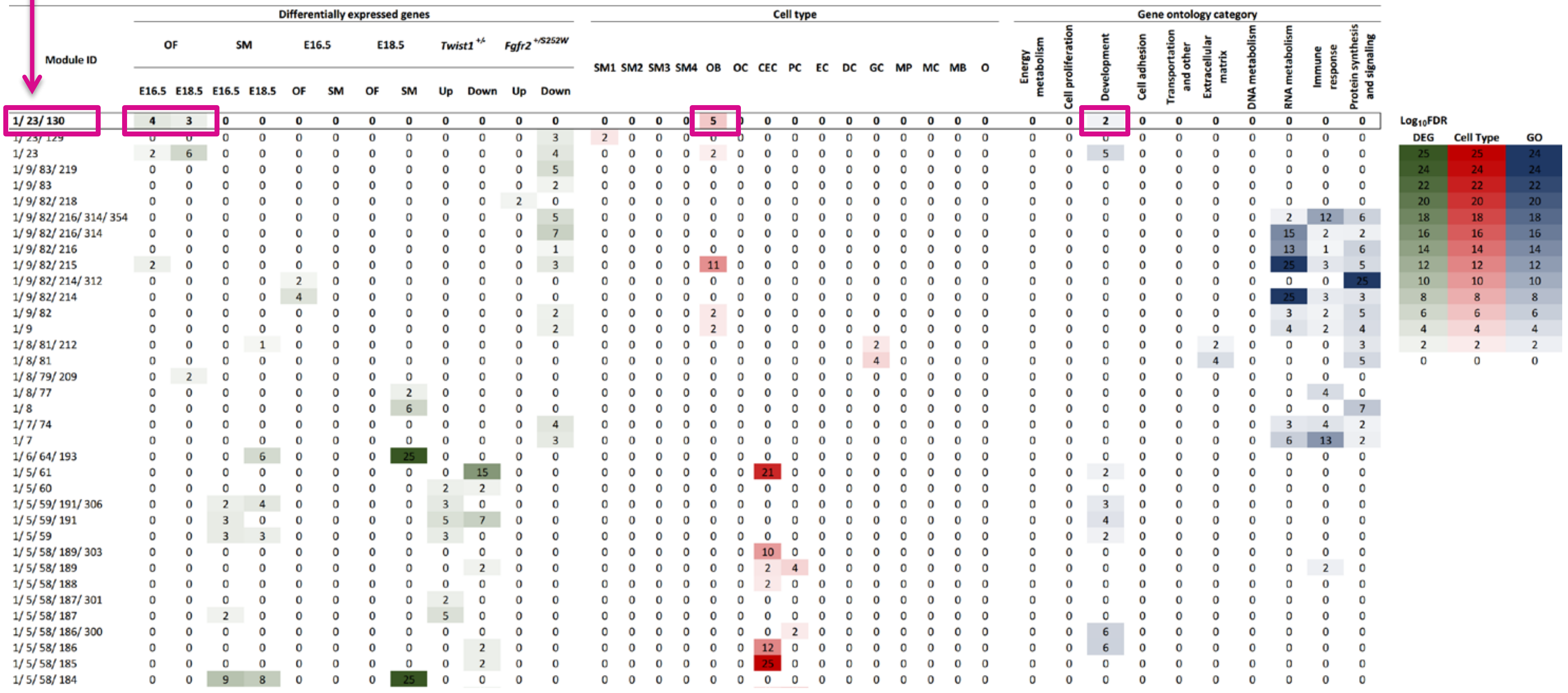
Use Case #2: Query Gene Network

Network module
(35 genes)

DEG of bulk subregions, ages, and genotypes

Single cell types

Gene ontology categories



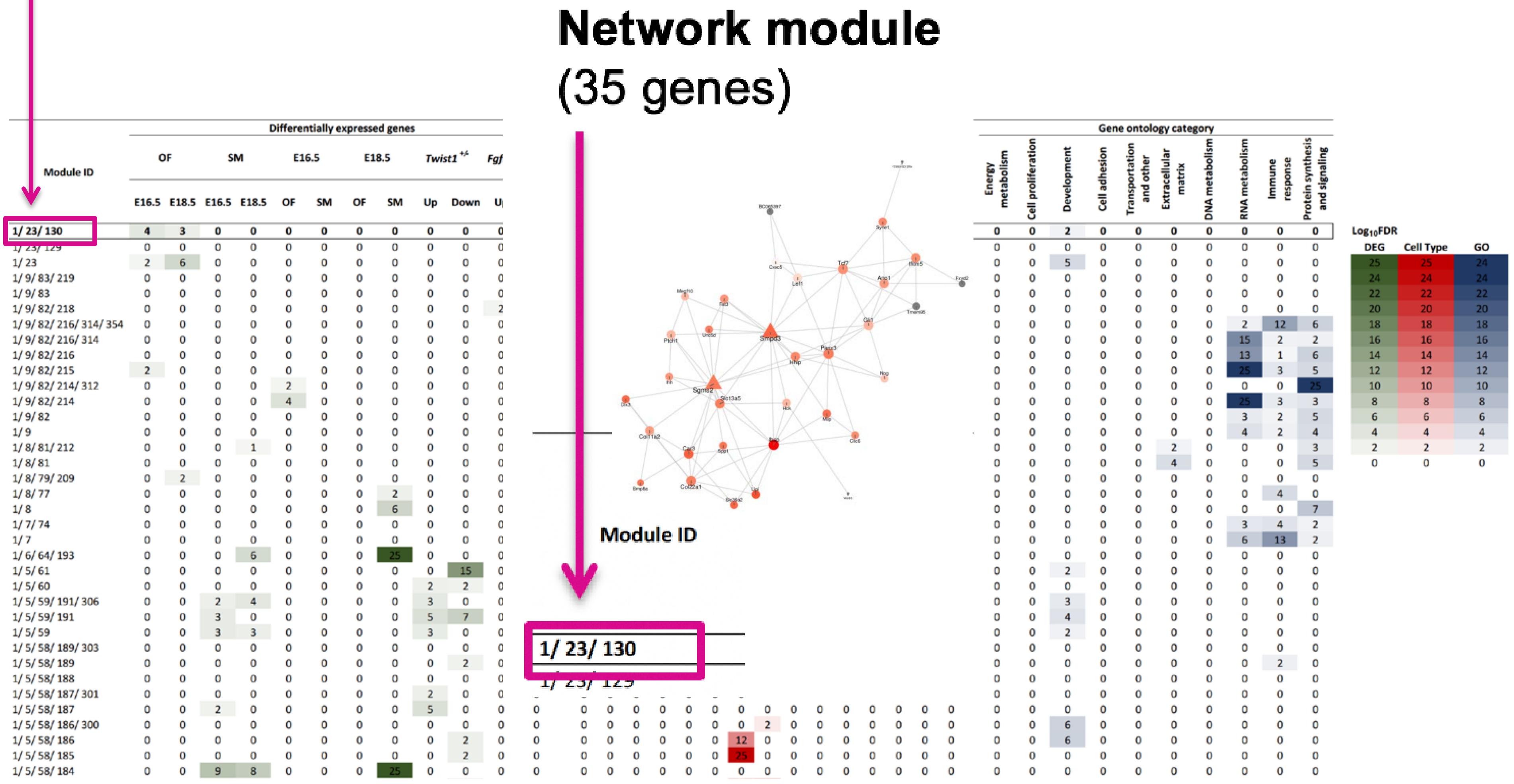
Module ID	Differentially expressed genes												Cell type															Gene ontology category									
	OF		SM		E16.5		E18.5		*Twist1* $^{+/-}$		*Fgfr2* $^{+/S252W}$																										
	E16.5	E18.5	E16.5	E18.5	OF	SM	OF	SM	Up	Down	Up	Down	SM1	SM2	SM3	SM4	OB	OC	CEC	PC	EC	DC	GC	MP	MC	MB	O	Energy metabolism	Cell proliferation	Development	Cell adhesion	Transportation and other	Extracellular matrix	DNA metabolism	RNA metabolism	Immune response	Protein synthesis and signaling
1/ 23/ 130	**4**	**3**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**5**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**2**	**0**	**0**	**0**	**0**	**0**	**0**	**0**
1/ 23/ 129	0	0	0	0	0	0	0	0	0	0	0	3	2	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
1/ 23	2	6	0	0	0	0	0	0	0	0	0	4	0	0	0	0	2	0	0	0	0	0	0	0	0	0	0	0	0	5	0	0	0	0	0	0	0
1/ 9/ 83/ 219	0	0	0	0	0	0	0	0	0	0	0	5	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
1/ 9/ 83	0	0	0	0	0	0	0	0	0	0	0	2	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
1/ 9/ 82/ 218	0	0	0	0	0	0	0	0	0	0	2	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
1/ 9/ 82/ 216/ 314/ 354	0	0	0	0	0	0	0	0	0	0	0	5	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	2	12	6
1/ 9/ 82/ 216/ 314	0	0	0	0	0	0	0	0	0	0	0	7	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	15	2	2
1/ 9/ 82/ 216	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	13	1	6
1/ 9/ 82/ 215	2	0	0	0	0	0	0	0	0	0	0	3	0	0	0	0	11	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	25	3	5
1/ 9/ 82/ 214/ 312	0	0	0	0	2	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	25
1/ 9/ 82/ 214	0	0	0	0	4	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	25	3	3
1/ 9/ 82	0	0	0	0	0	0	0	0	0	0	0	2	0	0	0	0	2	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	3	2	5
1/ 9	0	0	0	0	0	0	0	0	0	0	0	2	0	0	0	0	2	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	4	2	4
1/ 8/ 81/ 212	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	2	0	0	0	0	0	0	0	0	0	2	0	0	0	3
1/ 8/ 81	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	4	0	0	0	0	0	0	0	0	0	4	0	0	0	5
1/ 8/ 79/ 209	0	2	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
1/ 8/ 77	0	0	0	0	0	0	0	2	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	4	0
1/ 8	0	0	0	0	0	0	0	6	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	7
1/ 7/ 74	0	0	0	0	0	0	0	0	0	0	0	4	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	3	4	2
1/ 7	0	0	0	0	0	0	0	0	0	0	0	3	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	6	13	2
1/ 6/ 64/ 193	0	0	0	6	0	0	0	25	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
1/ 5/ 61	0	0	0	0	0	0	0	0	0	15	0	0	0	0	0	0	0	0	21	0	0	0	0	0	0	0	0	0	0	2	0	0	0	0	0	0	0
1/ 5/ 60	0	0	0	0	0	0	0	0	2	2	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
1/ 5/ 59/ 191/ 306	0	0	2	4	0	0	0	0	3	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	3	0	0	0	0	0	0	0
1/ 5/ 59/ 191	0	0	3	0	0	0	0	0	5	7	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	4	0	0	0	0	0	0	0
1/ 5/ 59	0	0	3	3	0	0	0	0	3	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	2	0	0	0	0	0	0	0
1/ 5/ 58/ 189/ 303	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	10	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
1/ 5/ 58/ 189	0	0	0	0	0	0	0	0	0	2	0	0	0	0	0	0	0	0	2	4	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	2	0
1/ 5/ 58/ 188	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	2	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
1/ 5/ 58/ 187/ 301	0	0	0	0	0	0	0	0	2	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
1/ 5/ 58/ 187	0	0	2	0	0	0	0	0	5	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
1/ 5/ 58/ 186/ 300	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	2	0	0	0	0	0	0	0	0	0	6	0	0	0	0	0	0	0
1/ 5/ 58/ 186	0	0	0	0	0	0	0	0	0	2	0	0	0	0	0	0	0	0	12	0	0	0	0	0	0	0	0	0	0	6	0	0	0	0	0	0	0
1/ 5/ 58/ 185	0	0	0	0	0	0	0	0	0	2	0	0	0	0	0	0	0	0	25	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
1/ 5/ 58/ 184	0	0	9	8	0	0	0	25	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0

Log$_{10}$FDR

DEG	Cell Type	GO
25	25	24
24	24	24
22	22	22
20	20	20
18	18	18
16	16	16
14	14	14
12	12	12
10	10	10
8	8	8
6	6	6
4	4	4
2	2	2
0	0	0

Use Case #2: Query Gene Network

Network module
(35 genes)



Network module
(35 genes)

Module ID	Differentially expressed genes										
	OF		SM		E16.5		E18.5		*Twist1* $^{+/-}$		*Fgf*
	E16.5	E18.5	E16.5	E18.5	OF	SM	OF	SM	Up	Down	U
1/ 23/ 130	**4**	**3**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**
1/ 23/ 129	0	0	0	0	0	0	0	0	0	0	0
1/ 23	2	6	0	0	0	0	0	0	0	0	0
1/ 9/ 83/ 219	0	0	0	0	0	0	0	0	0	0	0
1/ 9/ 83	0	0	0	0	0	0	0	0	0	0	0
1/ 9/ 82/ 218	0	0	0	0	0	0	0	0	0	0	2
1/ 9/ 82/ 216/ 314/ 354	0	0	0	0	0	0	0	0	0	0	0
1/ 9/ 82/ 216/ 314	0	0	0	0	0	0	0	0	0	0	0
1/ 9/ 82/ 216	0	0	0	0	0	0	0	0	0	0	0
1/ 9/ 82/ 215	2	0	0	0	0	0	0	0	0	0	0
1/ 9/ 82/ 214/ 312	0	0	0	0	2	0	0	0	0	0	0
1/ 9/ 82/ 214	0	0	0	0	4	0	0	0	0	0	0
1/ 9/ 82	0	0	0	0	0	0	0	0	0	0	0
1/ 9	0	0	0	0	0	0	0	0	0	0	0
1/ 8/ 81/ 212	0	0	0	1	0	0	0	0	0	0	0
1/ 8/ 81	0	0	0	0	0	0	0	0	0	0	0
1/ 8/ 79/ 209	0	2	0	0	0	0	0	0	0	0	0
1/ 8/ 77	0	0	0	0	0	0	0	2	0	0	0
1/ 8	0	0	0	0	0	0	0	6	0	0	0
1/ 7/ 74	0	0	0	0	0	0	0	0	0	0	0
1/ 7	0	0	0	0	0	0	0	0	0	0	0
1/ 6/ 64/ 193	0	0	0	6	0	0	0	25	0	0	0
1/ 5/ 61	0	0	0	0	0	0	0	0	0	15	0
1/ 5/ 60	0	0	0	0	0	0	0	0	2	2	0
1/ 5/ 59/ 191/ 306	0	0	2	4	0	0	0	0	3	0	0
1/ 5/ 59/ 191	0	0	3	0	0	0	0	0	5	7	0
1/ 5/ 59	0	0	3	3	0	0	0	0	3	0	0
1/ 5/ 58/ 189/ 303	0	0	0	0	0	0	0	0	0	0	0
1/ 5/ 58/ 189	0	0	0	0	0	0	0	0	0	2	0
1/ 5/ 58/ 188	0	0	0	0	0	0	0	0	0	0	0
1/ 5/ 58/ 187/ 301	0	0	0	0	0	0	0	0	2	0	0
1/ 5/ 58/ 187	0	0	2	0	0	0	0	0	5	0	0
1/ 5/ 58/ 186/ 300	0	0	0	0	0	0	0	0	0	0	0
1/ 5/ 58/ 186	0	0	0	0	0	0	0	0	0	2	0
1/ 5/ 58/ 185	0	0	0	0	0	0	0	0	0	2	0
1/ 5/ 58/ 184	0	0	9	8	0	0	0	25	0	0	0

Module ID																
1/ 5/ 58/ 187	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
1/ 5/ 58/ 186/ 300	0	0	0	0	0	0	0	0	2	0	0	0	0	0	0	0
1/ 5/ 58/ 186	0	0	0	0	0	0	0	12	0	0	0	0	0	0	0	0
1/ 5/ 58/ 185	0	0	0	0	0	0	0	25	0	0	0	0	0	0	0	0
1/ 5/ 58/ 184	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0

Module ID	Gene ontology category									
	Energy metabolism	Cell proliferation	Development	Cell adhesion	Transportation and other	Extracellular matrix	DNA metabolism	RNA metabolism	Immune response	Protein synthesis and signaling
1/ 23/ 130	**0**	**0**	**2**	**0**	**0**	**0**	**0**	**0**	**0**	**0**
1/ 23/ 129	0	0	0	0	0	0	0	0	0	0
1/ 23	0	0	5	0	0	0	0	0	0	0
1/ 9/ 83/ 219	0	0	0	0	0	0	0	0	0	0
1/ 9/ 83	0	0	0	0	0	0	0	0	0	0
1/ 9/ 82/ 218	0	0	0	0	0	0	0	0	0	0
1/ 9/ 82/ 216/ 314/ 354	0	0	0	0	0	0	0	2	12	6
1/ 9/ 82/ 216/ 314	0	0	0	0	0	0	0	15	2	2
1/ 9/ 82/ 216	0	0	0	0	0	0	0	13	1	6
1/ 9/ 82/ 215	0	0	0	0	0	0	0	25	3	5
1/ 9/ 82/ 214/ 312	0	0	0	0	0	0	0	0	0	25
1/ 9/ 82/ 214	0	0	0	0	0	0	0	25	3	3
1/ 9/ 82	0	0	0	0	0	0	0	3	2	5
1/ 9	0	0	0	0	0	0	0	4	2	4
1/ 8/ 81/ 212	0	0	0	0	0	2	0	0	0	3
1/ 8/ 81	0	0	0	0	0	4	0	0	0	5
1/ 8/ 79/ 209	0	0	0	0	0	0	0	0	0	0
1/ 8/ 77	0	0	0	0	0	0	0	0	4	0
1/ 8	0	0	0	0	0	0	0	0	0	7
1/ 7/ 74	0	0	0	0	0	0	0	3	4	2
1/ 7	0	0	0	0	0	0	0	6	13	2
1/ 6/ 64/ 193	0	0	0	0	0	0	0	0	0	0
1/ 5/ 61	0	0	2	0	0	0	0	0	0	0
1/ 5/ 60	0	0	0	0	0	0	0	0	0	0
1/ 5/ 59/ 191/ 306	0	0	3	0	0	0	0	0	0	0
1/ 5/ 59/ 191	0	0	4	0	0	0	0	0	0	0
1/ 5/ 59	0	0	2	0	0	0	0	0	0	0
1/ 5/ 58/ 189/ 303	0	0	0	0	0	0	0	0	0	0
1/ 5/ 58/ 189	0	0	0	0	0	0	0	0	2	0
1/ 5/ 58/ 188	0	0	0	0	0	0	0	0	0	0
1/ 5/ 58/ 187/ 301	0	0	0	0	0	0	0	0	0	0
1/ 5/ 58/ 187	0	0	0	0	0	0	0	0	0	0
1/ 5/ 58/ 186/ 300	0	0	6	0	0	0	0	0	0	0
1/ 5/ 58/ 186	0	0	6	0	0	0	0	0	0	0
1/ 5/ 58/ 185	0	0	0	0	0	0	0	0	0	0
1/ 5/ 58/ 184	0	0	0	0	0	0	0	0	0	0

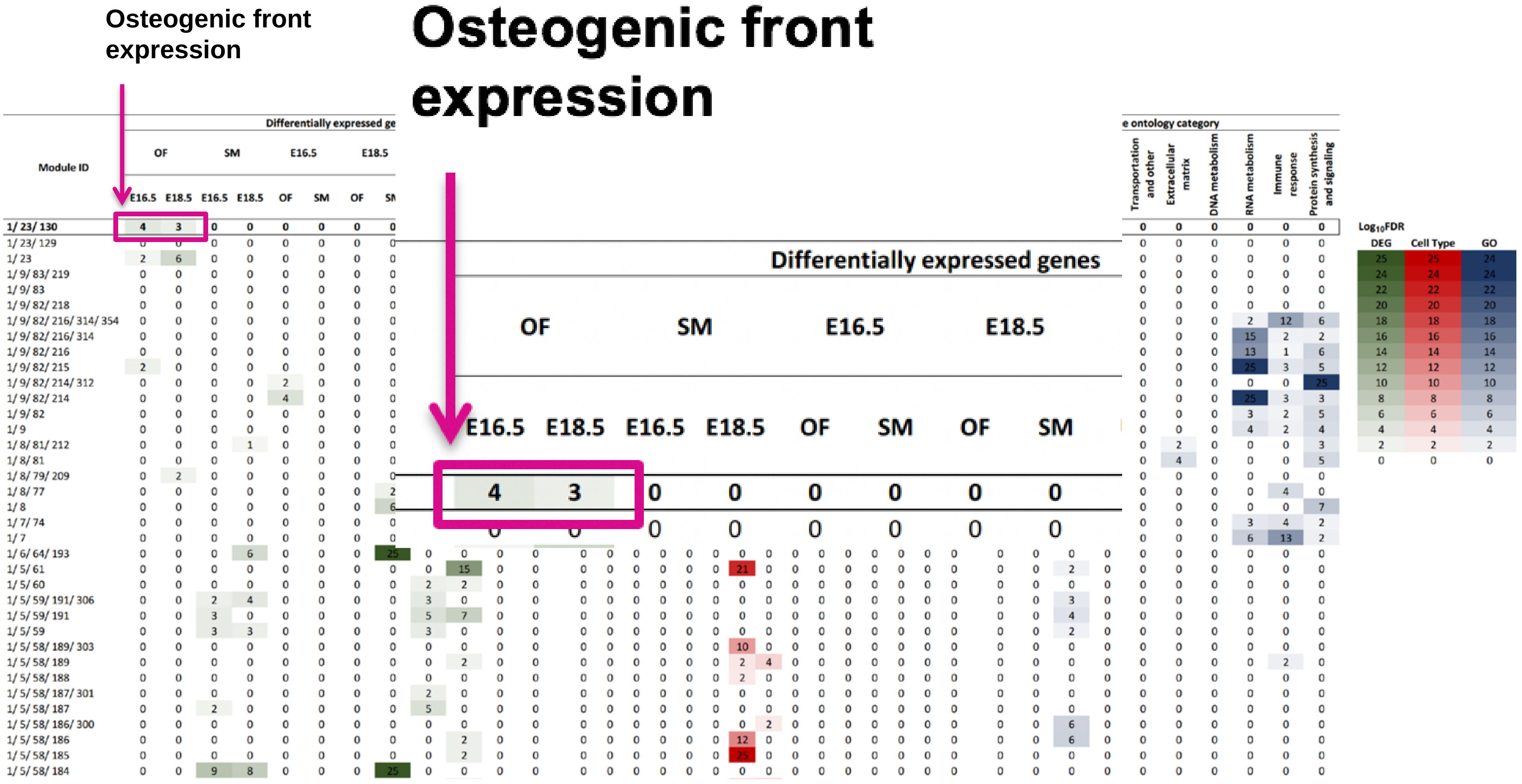
$Log_{10}FDR$		
DEG	Cell Type	GO
25	25	24
24	24	24
22	22	22
20	20	20
18	18	18
16	16	16
14	14	14
12	12	12
10	10	10
8	8	8
6	6	6
4	4	4
2	2	2
0	0	0

Module ID

1/ 23/ 130

Use Case #2: Query Gene Network

Osteogenic front expression



Osteogenic front expression

Differentially expressed genes							
OF		SM		E16.5		E18.5	
E16.5	E18.5	E16.5	E18.5	OF	SM	OF	SM
4	3	0	0	0	0	0	0
0	0	0	0	0	0	0	0

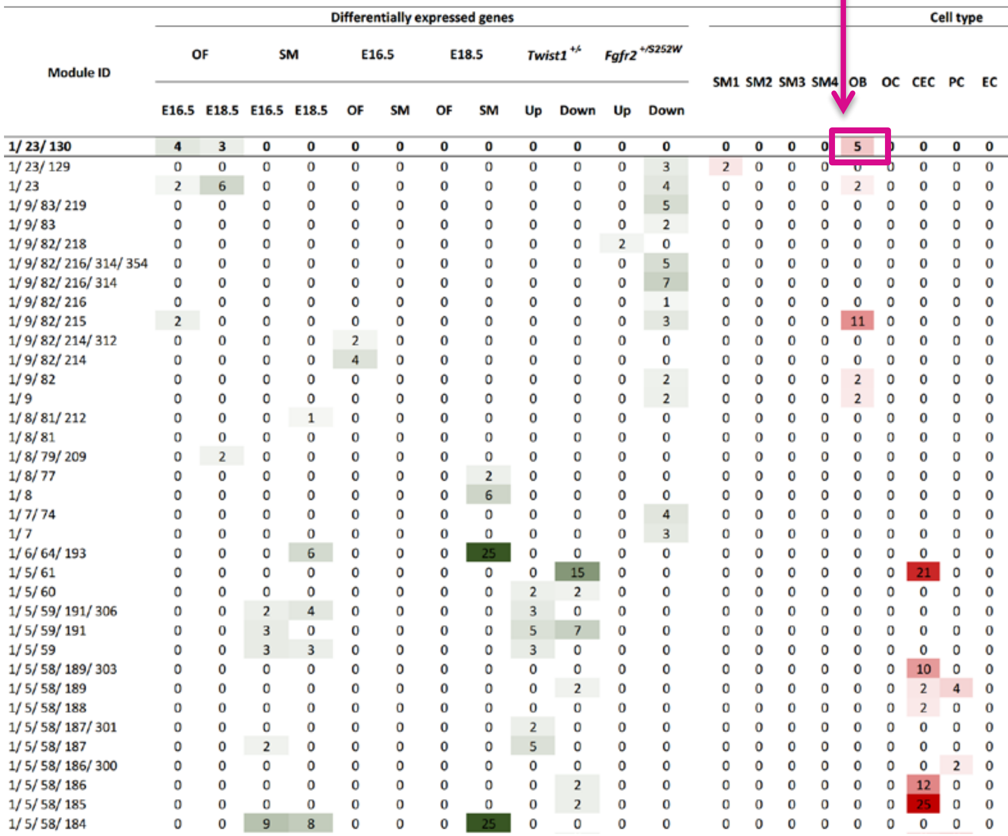
Module ID	Differentially expressed ge																																e ontology category					
	OF		SM		E16.5		E18.5																														
	E16.5	E18.5	E16.5	E18.5	OF	SM	OF	SM																									Transportation and other	Extracellular matrix	DNA metabolism	RNA metabolism	Immune response	Protein synthesis and signaling
1/ 23/ 130	4	3	0	0	0	0	0	0																								0	0	0	0	0	0
1/ 23/ 129	0	0	0	0	0	0	0	0																								0	0	0	0	0	0
1/ 23	2	6	0	0	0	0	0	0																								0	0	0	0	0	0
1/ 9/ 83/ 219	0	0	0	0	0	0	0	0																								0	0	0	0	0	0
1/ 9/ 83	0	0	0	0	0	0	0	0																								0	0	0	0	0	0
1/ 9/ 82/ 218	0	0	0	0	0	0	0	0																								0	0	0	0	0	0
1/ 9/ 82/ 216/ 314/ 354	0	0	0	0	0	0	0	0																								0	0	0	2	12	6
1/ 9/ 82/ 216/ 314	0	0	0	0	0	0	0	0																								0	0	0	15	2	2
1/ 9/ 82/ 216	0	0	0	0	0	0	0	0																								0	0	0	13	1	6
1/ 9/ 82/ 215	2	0	0	0	0	0	0	0																								0	0	0	25	3	5
1/ 9/ 82/ 214/ 312	0	0	0	0	2	0	0	0																								0	0	0	0	0	25
1/ 9/ 82/ 214	0	0	0	0	4	0	0	0																								0	0	0	25	3	3
1/ 9/ 82	0	0	0	0	0	0	0	0																								0	0	0	3	2	5
1/ 9	0	0	0	0	0	0	0	0																								0	0	0	4	2	4
1/ 8/ 81/ 212	0	0	0	1	0	0	0	0																								0	2	0	0	0	3
1/ 8/ 81	0	0	0	0	0	0	0	0																								0	4	0	0	0	5
1/ 8/ 79/ 209	0	2	0	0	0	0	0	0																								0	0	0	0	0	0
1/ 8/ 77	0	0	0	0	0	0	0	2																								0	0	0	0	4	0
1/ 8	0	0	0	0	0	0	0	6																								0	0	0	0	0	7
1/ 7/ 74	0	0	0	0	0	0	0	0																								0	0	0	3	4	2
1/ 7	0	0	0	0	0	0	0	0																								0	0	0	6	13	2
1/ 6/ 64/ 193	0	0	0	6	0	0	0	25	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
1/ 5/ 61	0	0	0	0	0	0	0	0	0	15	0	0	0	0	0	0	0	0	21	0	0	0	0	0	0	0	0	0	0	2	0	0	0	0	0	0	0
1/ 5/ 60	0	0	0	0	0	0	0	0	2	2	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
1/ 5/ 59/ 191/ 306	0	0	2	4	0	0	0	0	3	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	3	0	0	0	0	0	0	0
1/ 5/ 59/ 191	0	0	3	0	0	0	0	0	5	7	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	4	0	0	0	0	0	0	0
1/ 5/ 59	0	0	3	3	0	0	0	0	3	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	2	0	0	0	0	0	0	0
1/ 5/ 58/ 189/ 303	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	10	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
1/ 5/ 58/ 189	0	0	0	0	0	0	0	0	0	2	0	0	0	0	0	0	0	0	2	4	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	2	0
1/ 5/ 58/ 188	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	2	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
1/ 5/ 58/ 187/ 301	0	0	0	0	0	0	0	0	2	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
1/ 5/ 58/ 187	0	0	2	0	0	0	0	0	5	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
1/ 5/ 58/ 186/ 300	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	2	0	0	0	0	0	0	0	0	0	6	0	0	0	0	0	0	0
1/ 5/ 58/ 186	0	0	0	0	0	0	0	0	0	2	0	0	0	0	0	0	0	0	12	0	0	0	0	0	0	0	0	0	0	6	0	0	0	0	0	0	0
1/ 5/ 58/ 185	0	0	0	0	0	0	0	0	0	2	0	0	0	0	0	0	0	0	25	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
1/ 5/ 58/ 184	0	0	9	8	0	0	0	25	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0

$Log_{10}FDR$

DEG	Cell Type	GO
25	25	24
24	24	24
22	22	22
20	20	20
18	18	18
16	16	16
14	14	14
12	12	12
10	10	10
8	8	8
6	6	6
4	4	4
2	2	2
0	0	0

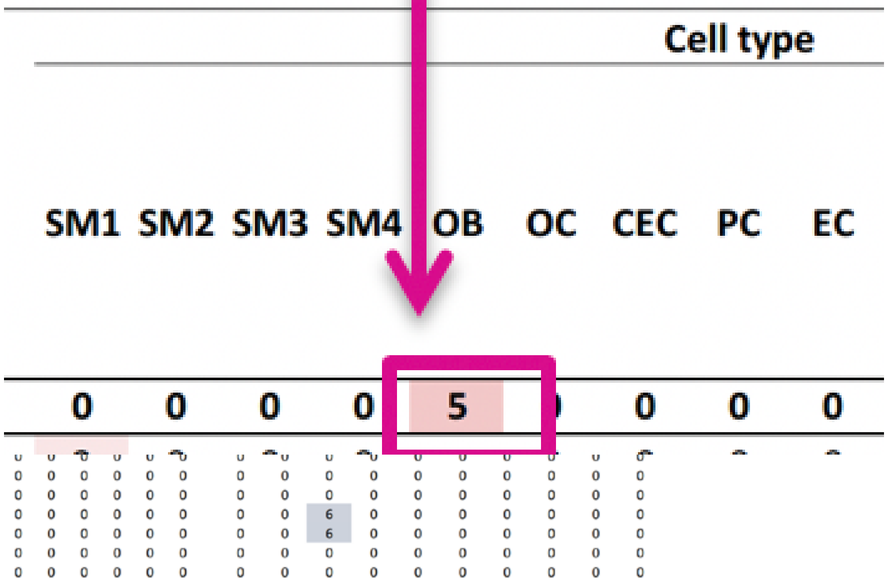
Use Case #2: Query Gene Network

Osteoblast
cells



Module ID	Differentially expressed genes: OF E16.5	OF E18.5	SM E16.5	SM E18.5	E16.5 OF	E16.5 SM	E18.5 OF	E18.5 SM	*Twist1* $^{+/-}$ Up	*Twist1* $^{+/-}$ Down	*Fgfr2* $^{+/S252W}$ Up	*Fgfr2* $^{+/S252W}$ Down	Cell type: SM1	SM2	SM3	SM4	OB	OC	CEC	PC	EC
1/ 23/ 130	**4**	**3**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**5**	**0**	**0**	**0**	**0**
1/ 23/ 129	0	0	0	0	0	0	0	0	0	0	0	3	2	0	0	0	0	0	0	0	0
1/ 23	2	6	0	0	0	0	0	0	0	0	0	4	0	0	0	0	2	0	0	0	0
1/ 9/ 83/ 219	0	0	0	0	0	0	0	0	0	0	0	5	0	0	0	0	0	0	0	0	0
1/ 9/ 83	0	0	0	0	0	0	0	0	0	0	0	2	0	0	0	0	0	0	0	0	0
1/ 9/ 82/ 218	0	0	0	0	0	0	0	0	0	0	2	0	0	0	0	0	0	0	0	0	0
1/ 9/ 82/ 216/ 314/ 354	0	0	0	0	0	0	0	0	0	0	0	5	0	0	0	0	0	0	0	0	0
1/ 9/ 82/ 216/ 314	0	0	0	0	0	0	0	0	0	0	0	7	0	0	0	0	0	0	0	0	0
1/ 9/ 82/ 216	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0
1/ 9/ 82/ 215	2	0	0	0	0	0	0	0	0	0	0	3	0	0	0	0	11	0	0	0	0
1/ 9/ 82/ 214/ 312	0	0	0	0	2	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
1/ 9/ 82/ 214	0	0	0	0	4	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
1/ 9/ 82	0	0	0	0	0	0	0	0	0	0	0	2	0	0	0	0	2	0	0	0	0
1/ 9	0	0	0	0	0	0	0	0	0	0	0	2	0	0	0	0	2	0	0	0	0
1/ 8/ 81/ 212	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
1/ 8/ 81	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
1/ 8/ 79/ 209	0	2	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
1/ 8/ 77	0	0	0	0	0	0	0	2	0	0	0	0	0	0	0	0	0	0	0	0	0
1/ 8	0	0	0	0	0	0	0	6	0	0	0	0	0	0	0	0	0	0	0	0	0
1/ 7/ 74	0	0	0	0	0	0	0	0	0	0	0	4	0	0	0	0	0	0	0	0	0
1/ 7	0	0	0	0	0	0	0	0	0	0	0	3	0	0	0	0	0	0	0	0	0
1/ 6/ 64/ 193	0	0	0	6	0	0	0	25	0	0	0	0	0	0	0	0	0	0	0	0	0
1/ 5/ 61	0	0	0	0	0	0	0	0	0	15	0	0	0	0	0	0	0	0	21	0	0
1/ 5/ 60	0	0	0	0	0	0	0	0	2	2	0	0	0	0	0	0	0	0	0	0	0
1/ 5/ 59/ 191/ 306	0	0	2	4	0	0	0	0	3	0	0	0	0	0	0	0	0	0	0	0	0
1/ 5/ 59/ 191	0	0	3	0	0	0	0	0	5	7	0	0	0	0	0	0	0	0	0	0	0
1/ 5/ 59	0	0	3	3	0	0	0	0	3	0	0	0	0	0	0	0	0	0	0	0	0
1/ 5/ 58/ 189/ 303	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	10	0	0
1/ 5/ 58/ 189	0	0	0	0	0	0	0	0	0	2	0	0	0	0	0	0	0	0	2	4	0
1/ 5/ 58/ 188	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	2	0	0
1/ 5/ 58/ 187/ 301	0	0	0	0	0	0	0	0	2	0	0	0	0	0	0	0	0	0	0	0	0
1/ 5/ 58/ 187	0	0	2	0	0	0	0	0	5	0	0	0	0	0	0	0	0	0	0	0	0
1/ 5/ 58/ 186/ 300	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	2	0
1/ 5/ 58/ 186	0	0	0	0	0	0	0	0	0	2	0	0	0	0	0	0	0	0	12	0	0
1/ 5/ 58/ 185	0	0	0	0	0	0	0	0	0	2	0	0	0	0	0	0	0	0	25	0	0
1/ 5/ 58/ 184	0	0	9	8	0	0	0	25	0	0	0	0	0	0	0	0	0	0	0	0	0

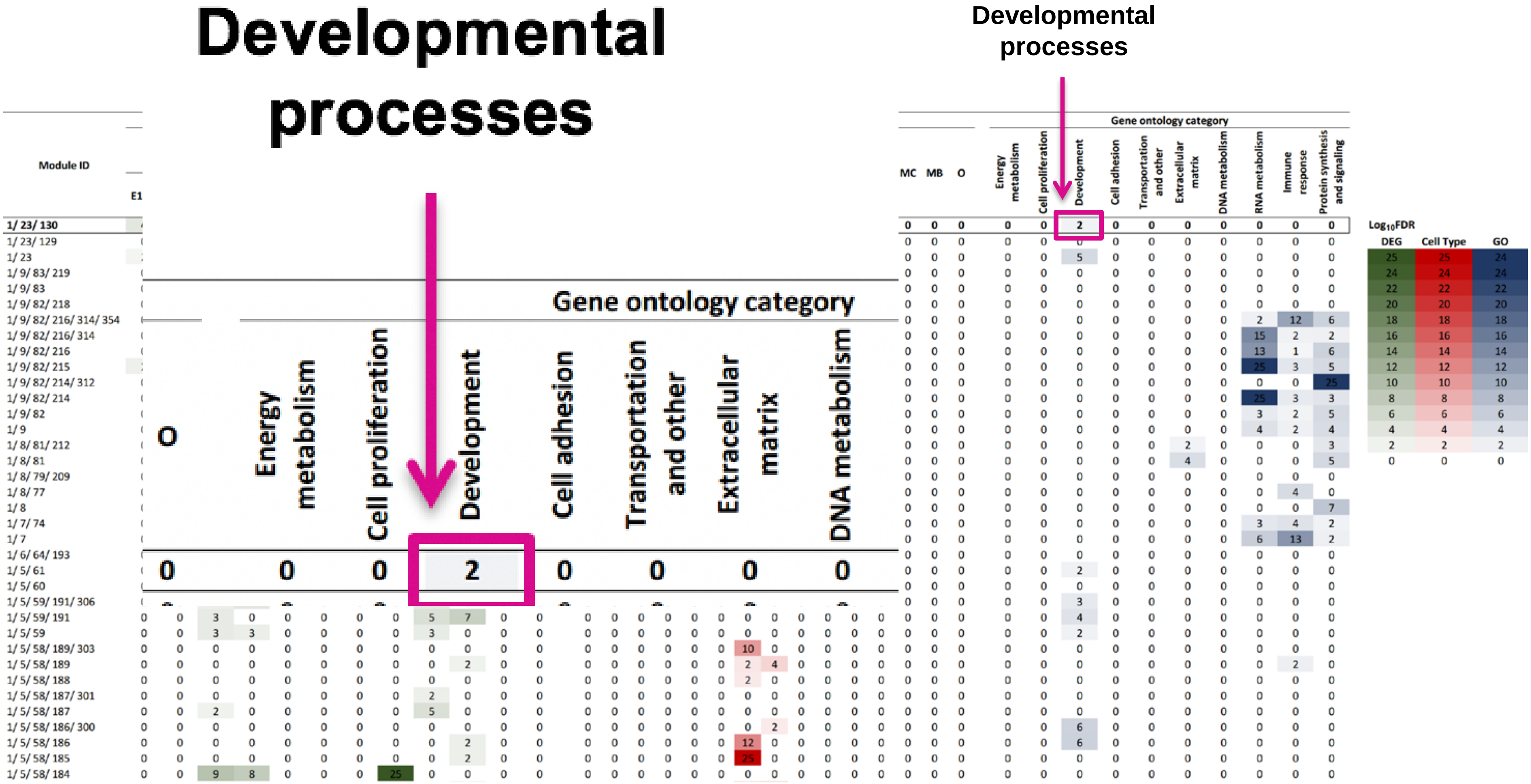
Osteoblast
cells



Cell type: SM1	SM2	SM3	SM4	OB	OC	CEC	PC	EC
0	0	0	0	5	0	0	0	0

0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
0	0	0	0	0	0	0	0	0	6	0	0	0	0	0	0	0
0	0	0	0	0	0	0	0	0	6	0	0	0	0	0	0	0
0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0

Use Case #2: Query Gene Network



Developmental processes

O	Energy metabolism	Cell proliferation	Development	Cell adhesion	Transportation and other	Extracellular matrix	DNA metabolism
0	0	0	2	0	0	0	0

Developmental processes

Module ID	MC	MB	O	Energy metabolism	Cell proliferation	Development	Cell adhesion	Transportation and other	Extracellular matrix	DNA metabolism	RNA metabolism	Immune response	Protein synthesis and signaling
1/ 23/ 130	**0**	**0**	**0**	**0**	**0**	**2**	**0**	**0**	**0**	**0**	**0**	**0**	**0**
1/ 23/ 129	0	0	0	0	0	0	0	0	0	0	0	0	0
1/ 23	0	0	0	0	0	5	0	0	0	0	0	0	0
1/ 9/ 83/ 219	0	0	0	0	0	0	0	0	0	0	0	0	0
1/ 9/ 83	0	0	0	0	0	0	0	0	0	0	0	0	0
1/ 9/ 82/ 218	0	0	0	0	0	0	0	0	0	0	0	0	0
1/ 9/ 82/ 216/ 314/ 354	0	0	0	0	0	0	0	0	0	0	2	12	6
1/ 9/ 82/ 216/ 314	0	0	0	0	0	0	0	0	0	0	15	2	2
1/ 9/ 82/ 216	0	0	0	0	0	0	0	0	0	0	13	1	6
1/ 9/ 82/ 215	0	0	0	0	0	0	0	0	0	0	25	3	5
1/ 9/ 82/ 214/ 312	0	0	0	0	0	0	0	0	0	0	0	0	25
1/ 9/ 82/ 214	0	0	0	0	0	0	0	0	0	0	25	3	3
1/ 9/ 82	0	0	0	0	0	0	0	0	0	0	3	2	5
1/ 9	0	0	0	0	0	0	0	0	0	0	4	2	4
1/ 8/ 81/ 212	0	0	0	0	0	0	0	0	2	0	0	0	3
1/ 8/ 81	0	0	0	0	0	0	0	0	4	0	0	0	5
1/ 8/ 79/ 209	0	0	0	0	0	0	0	0	0	0	0	0	0
1/ 8/ 77	0	0	0	0	0	0	0	0	0	0	0	4	0
1/ 8	0	0	0	0	0	0	0	0	0	0	0	0	7
1/ 7/ 74	0	0	0	0	0	0	0	0	0	0	3	4	2
1/ 7	0	0	0	0	0	0	0	0	0	0	6	13	2
1/ 6/ 64/ 193	0	0	0	0	0	0	0	0	0	0	0	0	0
1/ 5/ 61	0	0	0	0	0	2	0	0	0	0	0	0	0
1/ 5/ 60	0	0	0	0	0	0	0	0	0	0	0	0	0
1/ 5/ 59/ 191/ 306	0	0	0	0	0	3	0	0	0	0	0	0	0
1/ 5/ 59/ 191	0	0	0	0	0	4	0	0	0	0	0	0	0
1/ 5/ 59	0	0	0	0	0	2	0	0	0	0	0	0	0
1/ 5/ 58/ 189/ 303	0	0	0	0	0	0	0	0	0	0	0	0	0
1/ 5/ 58/ 189	0	0	0	0	0	0	0	0	0	0	0	2	0
1/ 5/ 58/ 188	0	0	0	0	0	0	0	0	0	0	0	0	0
1/ 5/ 58/ 187/ 301	0	0	0	0	0	0	0	0	0	0	0	0	0
1/ 5/ 58/ 187	0	0	0	0	0	0	0	0	0	0	0	0	0
1/ 5/ 58/ 186/ 300	0	0	0	0	0	6	0	0	0	0	0	0	0
1/ 5/ 58/ 186	0	0	0	0	0	6	0	0	0	0	0	0	0
1/ 5/ 58/ 185	0	0	0	0	0	0	0	0	0	0	0	0	0
1/ 5/ 58/ 184	0	0	0	0	0	0	0	0	0	0	0	0	0

Use Cases: Relevant FaceBase Projects

- Marazita: *Human Genomics Analysis Interface for FaceBase 2* - genes identified in human genomics data, e.g., associated with SNPs

- Maas/Liao: *Rapid Identification and Validation of Human Craniofacial Development Genes* - genes associated with craniofacial defects

- Selleri/Wysocka: *Epigenetic landscapes and regulatory divergence of human craniofacial traits* - genes associated with species-specific neural crest enhancers

- Visel: *Genomic and Transgenic Resources for Craniofacial Enhancer Studies -* genes associated with craniofacial enhancers

- Fisher/Harris: *Anatomical atlas and transgenic toolkit for late skull formation in zebrafish* - specific genes affecting zebrafish craniofacial development

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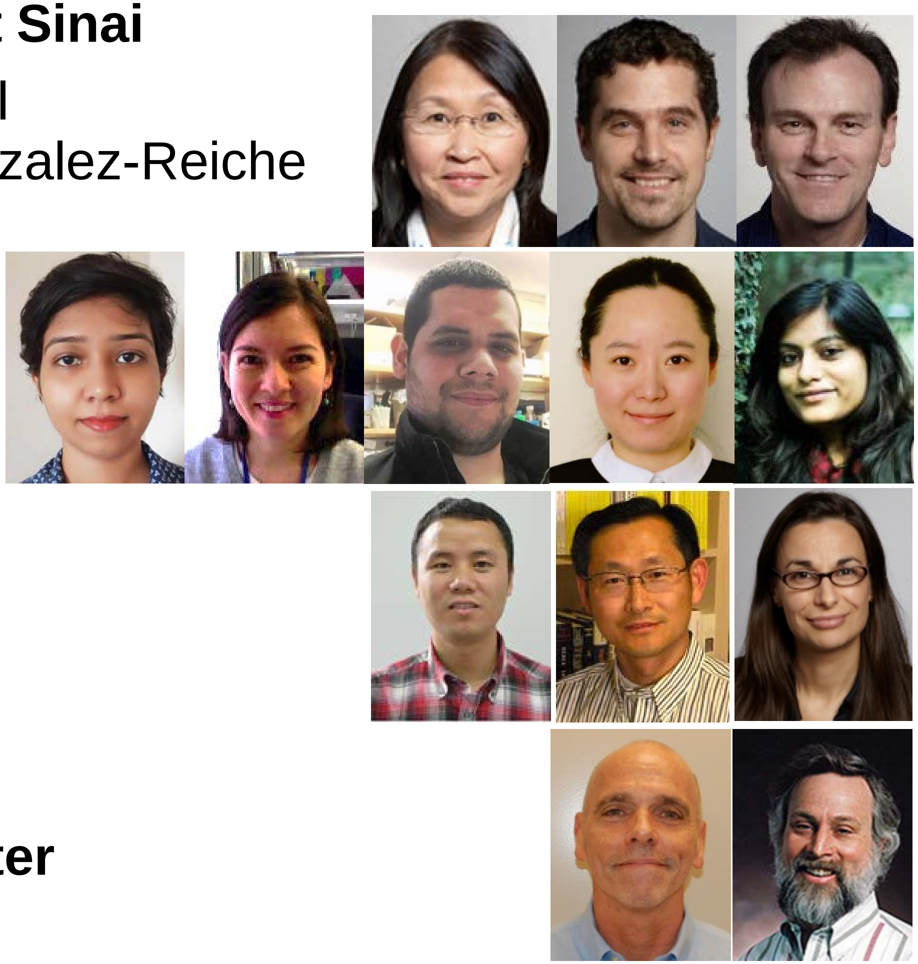

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NIH National Institute of Dental and Craniofacial Research

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