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GUDMAP

Genitourinary Development Molecular Anatomy Project

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About GUDMAP

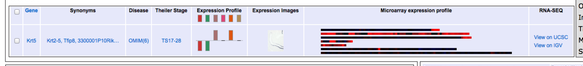
The **GenitoUrinary Development Molecular Anatomy Project (GUDMAP)** is an open access online resource developed by a consortium of laboratories working to provide the scientific and medical community with gene expression data, transgenic mice and tools to facilitate research and teaching.

GUDMAP data includes: **Large-scale in-situ hybridisation screens**, **3D OPT data, microarray gene expression data & sequencing data** of the developing mouse genitourinary (GU) system. Expression data are annotated using a **high-resolution ontology** specific to the developing murine GU system.

Initially, GUDMAP focused on the murine GU system. More recently, GUDMAP has extended its focus to two new projects: **Nociceptive GUDMAP (nGUDMAP) and Human GUDMAP (hGUDMAP)**. nGUDMAP focuses on nociceptors and associated cell types in pain processing of the murine urinary tract and pelvic region. hGUDMAP extends the gene expression data to include Human studies in bladder, urethra and kidney.

GUDMAP Data

Summary '*gene-strip*' (below) provides an overview of expression data available for a gene. Links out to in-situ data & images, disease/phenotype associations and microarray expression data.

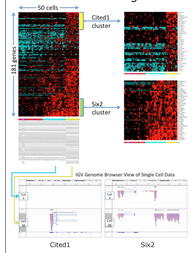


Database Statistics 15-Jun-2015

Assay Type	Entries	Genes
All In Situ Hybridisation (ISH):	10766	3692
Wholemount ISH (WISH):	7352	2896
Section ISH (SISH):	3414	1437
OPT ISH:	64	32
Immunohistochemistry (IHC):	103	31
Transgenic Reporters:	72	35
Microarray:	461	-
Sequencing:	240	-

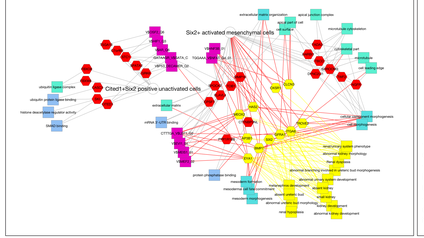
Gene Expresssion Profile Analyses of GUDMAP Data (Aronow, Potter)

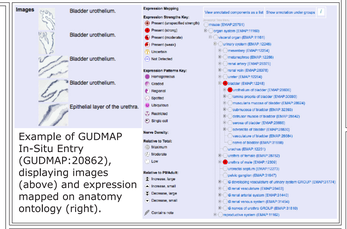
GUDMAP Sequencing: an atlas for dissecting kidney and genitourinary development



Left: Single cell gene expression profile analyses (E11.5 metanephric mesenchyme) via FluidigmC1.

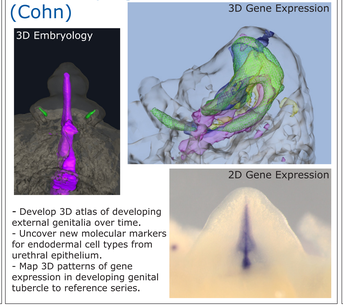
Bottom: Topcluster-based gene network analysis of genes tightly co-regulated with Six2 and Cited1 in single cells from E11.5/E12.5 metanephric mesenchyme. Genes known to play a role in nephrogenesis are highlighted in yellow and connected via yellow edges to other significant biological processes. Genes in the signature that are not known to be critical for nephrogenesis are coloured red and connected via gray edges to significant processes, components, or cis elements. Thus, in this manner, genes such as Shroom3, Twf2, and Ctnnbp2nl can be initially implicated to be participating in processes necessary for mesenchymal nephrogenesis.





Example of GUDMAP In-Situ Entry (GUDMAP:20862), displaying images (above) and expression mapped on anatomy ontology (right).

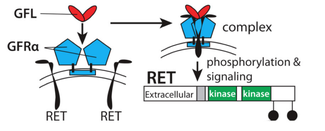
3D Atlas and Deep Sequencing of Developing Penis and Urethra (Cohn)

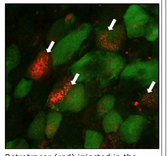


- Develop 3D atlas of developing external genitalia over time.
- Uncover new molecular markers for endodermal cell types from urethral epithelium.
- Map 3D patterns of gene expression in developing genital tubercle to reference series.

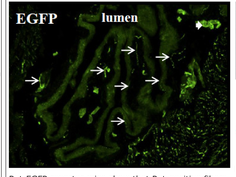
Expression Profiles of Ret-positive DRG Neurons (Jain)

- GDNF family ligands signal through RET receptor tyrosine kinase.
- Major roles in neuronal survival and sensation.

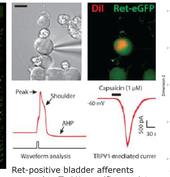




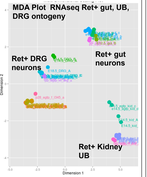
Retrotracer (red) injected in the bladder labels Ret+ (green) sensory neurons in the DRG (arrows)



Ret-EGFP reporter mice show that Ret-positive fibers (green) innervate adult mouse bladder (arrows)



Ret-positive bladder afferents respond to TrpV1 specific agonist capsaicin



Identifying Novel Urothelial Cell Types and Genes that Label them (Mendelsohn)

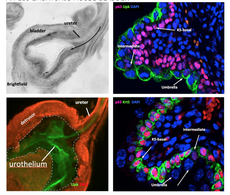
At present we can only identify 3 cell types in the urothelium based on marker expression. A number of important questions need to be addressed, including the identity of progenitors that give rise to these urothelial cell types during development, and the identity of progenitors that give rise to the different types of bladder cancers.

Identifying markers that label distinct urothelial sub-populations will be important for reaching these goals.

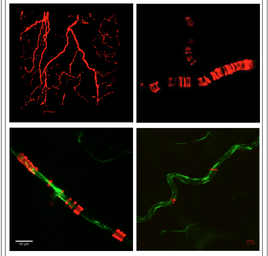
Three populations known at present:

K5-BASAL:	(KRT5+ P63+	UPK-)
INTERMEDIATE:	(KRT5- P63+	UPK+)
SUPERFICIAL:	(KRT5- P63-	UPK+)

AN E18 EMBRYONIC MOUSE BLADDER



Nociceptive Ion Channels in Bladder (Ahern)



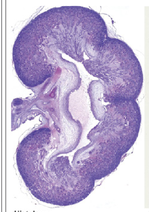
Top left: TRPV1-Cre/Tomato labels ~95% of bladder nociceptive nerves.

Top right: TRPV1-Cre/Tomato labels vascular smooth muscle in a subset of bladder arterioles.

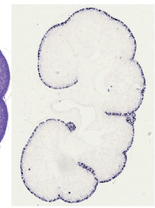
Bottom left: TRPV1-Tomato labels vascular smooth muscle in a third-order arteriole (25-40 μm).

Bottom right: TRPV1-Tomato labels vascular smooth muscle in a second-order arteriole (50-65 μm).

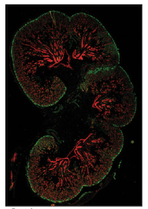
Comparing Mouse and Human Kidney Development (McMahon)



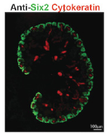
-Histology
16 week Human Kidney stained with: Hematoxylin & Eosin.

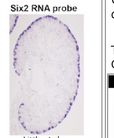


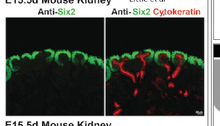
-RNA
15 week 2 day Human Kidney probed with: Six2 RNA probe.

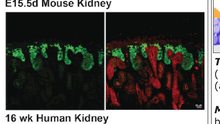


-Protein
Immunohistochemistry on 16 wk Human Kidney: Anti-Six2 and Cytokeratin antibodies.

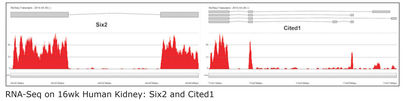






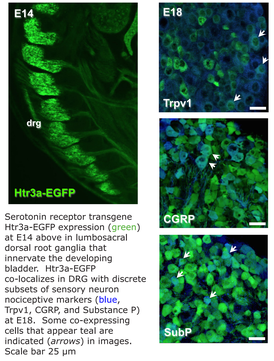


-Gene Expression and Regulation
ChIp-Seq and RNA-Seq on Human Kidney: 9-11wk, 13-14wk, 16-17wk



RNA-Seq on 16wk Human Kidney: Six2 and Cited1

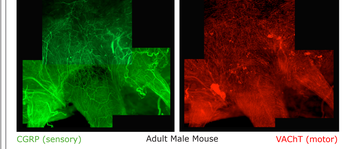
Mapping Serotonin Receptors in LUT Innervation (Southard-Smith)



Serotonin receptor transgene Htr3a-EGFP expression (green) at E14 above in lumbosacral dorsal root ganglia that innervate the developing bladder. Htr3a-EGFP co-localizes in DRG with discrete subsets of sensory neuron nociceptive markers (blue, Trpv1, CGRP, and Substance P) at E18. Some co-expressing cells that appear teal are indicated (*arrows*) in images. Scale bar 25 μm

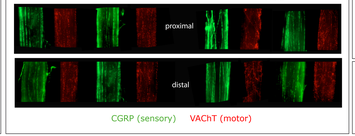
Comparing Innervation of Trigone/ Ureter/Urethral regions of LUT (Keast)

Whole-mount preparations of ureter-trigone-urethra junction



CGRP (sensory) Adult Male Mouse VAChT (motor)

Whole-mount preparations of ureter



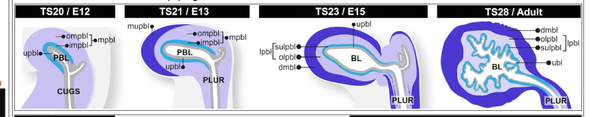
CGRP (sensory) VAChT (motor)

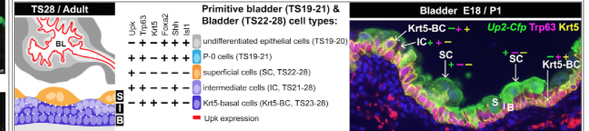
Schematics, Tutorials & Tissue Summaries

GUDMAP holds an extensive archive of high-quality schematics diagrams that illustrate differing views of the developing mouse GU system

www.gudmap.org/Schematics/index.php

These help supplement **tutorials** describing GU organogenesis (Matt Kaufman) and enrich the GUDMAP Tissue Summary pages.

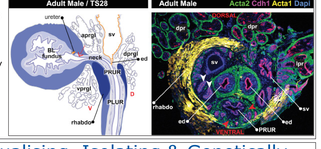




Top: Annotated sections of the bladder at TS20 (12 dpc), TS21 (13 dpc), TS23 (15 dpc) and TS28 (adult).

Middle: TS28 (adult) annotated section of the bladder with corresponding immunohistochemistry section.

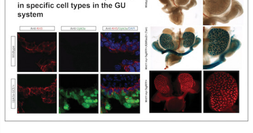
Right: TS28 (adult) annotated section of the male prostate with corresponding immunohistochemistry section.



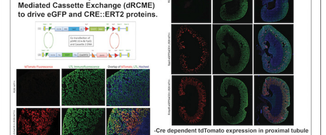
Novel Mouse Strains for Visualising, Isolating & Genetically Modifying the GU System (McMahon)

Goals:
- To mark key cell populations in order to isolate, trace and modulate gene activity through drug inducible CRE recombinase.
- Encourage nominations of candidate loci from scientific community.
- Mice made available through the MMRRC (Jackson Labs).
- Nominate strains: **www.gudmap.org/MS_GeneNoms.html**

Part I: Use BAC mediated mouse transgenesis to drive eGFP and RFPT::Cre::ERT2 fusion proteins in specific cell types in the GU system



Part II: Obtain ES Cell clones through KOMP(NIH) and EUCOMM Consortia, create new alleles by dual Recombinase Mediated Cassette Exchange (dRCME) to drive eGFP and CRE::ERT2 proteins.



-Cre dependent tdTomato expression in proximal tubule cells in the kidney following tamoxifen injection in the adult 3 times prior to collection: d1, d3, d5 collected d7.

References

All past contributors to GUDMAP can be found at **www.gudmap.org/About/Projects/**

Georgas KM et al. (2015). An illustrated anatomical ontolgy of the developing mouse lower urogenital tract. Development. 142(10):1893-908.
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