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About GUDMAP

The GenitoUrinary Development Molecular Anatomy Project (GUDMAP) is a consortium of laboratories working to provide the scientific and medical community with gene expression data, transgenic mice and tools to facilitate research.

GUDMAP data includes: Large-scale in-situ hybridisation screens, 3D OPT data, microarray gene expression data & next generation 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. GUDMAP data are **freely accessible** via **easy-to-use interfaces**.



In-Situ Data



A. Images. **B.** Expression mapped on anatomy ontology **C.** Probe details.

The high-resolution anatomy ontology (Little et al. **2007)**, used to annotated expression, has been developed by the GUDMAP consortium to describe in detail the subcompartments of the developing murine genitourinary tract

Microarray Data & Analysis



sion levels of probes across GUDMAP Heatmaps: r sample sets

GUDMAP microarray includes laser-captured & FACSisolated components of the GU system.

Analysed Genelists: Aronow Group has identified genes enriched in GU sub-compartments. There are >2,500 of these Genelists in GUDMAP.

Through the heatmap view they are integrated with the **ToppGene** analysis suite, giving the ability to perform onthe-fly analysis via ToppGene (CCHMC) (far-right, lower

http://toppgene.cchmc.org/

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

Harding SD et al. (2011). The GUDMAP database - an online resource for genitourinary research. Development. 138(13):2845-53 McMahon AP et al. (2008). GUDMAP: the genitourinary development molecular anatomy project. J. Am. Soc. Nephrology. 19(4):667-71 Little MH et al. (2007). A high-resolution anatomical ontology of the developing murine genitourinary tract. Gene Expr Patterns. 7(6):680-99. Ganghi D et al. (2013). Retinoid signaling in progenitors controls specification and regeneration of the urothelium. Dev. Cell. 26(5): 469-482.



A: Ptk2 expression in the urethra of the male (TS25; 17 dpc) B: Wnt4 RNA expression in the early nephro

- C: Ets1 RNA expression in components of the urogenital sinus and urorectal septu
- *C: Metanephros double-stained for Wt1 protein (orange) and Wnt4 RNA (blue)*
- E: OPT movie still of Cldn7 expression in genital tubercle of female *F:* Volume rendering heatmap image of Cldn7 expression in genital tubercle of female

www.gudmap.org

GUDMAP Genitourinary Development Molecular Anatomy Project

Database and website development: Harding, S.D., Haggarty, B., Roochun, Y., Baldock, R.A. (IGMM, University of Edinburgh). Editorial Office: Armstrong, J.F., Brennan, J., Lloyd-MacGilp, S., Davies, J.A. (University of Edinburgh). Current GUDMAP Consortium Members: Hoshizaki, D., (NIH), Aronow, B., Potter, S. (CCHMC, Cincinnati), Cohn, M.J. (HHMI, University of Florida), Keast, J. (University of Melbourne), Mendelsohn, C. (Columbia University), Georgas, K. and Little, M.H. (University of Queensland) & McMahon, A.P. (Keck School of Medicine, USC)

Summary 'gene-strips' provide an overview of expression data

Links out to in-situ data & images, disease/phenotype associations and



- 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



 Use BAC mediated mouse transgenesis to drive

• Goal to mark key cell populations, in order to isolate, trace and modulate gene activity.



High Resolution Mapping of LUT Innervation During Development (Keast)

3D Atlas and Deep Sequencing of Developing



Innervation of mouse urogenital organs is shown in A-C (dorsal at top). A: E14, Tuj1, red; tyrosine hydroxylase, green. B: E16, Hu, red; choline acetyltransferase, green. C: E16, PGP9.5, bladder and adjacent organs. D: part of whole mount of pelvic ganglion from adult mouse (nitric oxide synthase, red; tyrosine hydroxylase, green).

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Novel Mouse Strains for Visualising, Isolating & Genetically Modifying the Schematics, Tutorials & Tissue Summaries GU System (McMahon) GUDMAP holds an extensive archive of high-quality schematics diagrams that illustrate Anti Renin/Anti-CD31/DAPI Native nuc-Tag RFP-T 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. eGFP::CRE::ERT2 fusion proteins and RFP proteins within Renin/Anti-<mark>β-gal/DAPI</mark> 97-RFPT/+;Foxd1 GC/+;R26Rla in/Anti-RFPT/Anti-CD31/DAP specific cell types in the GU system. Akr1b7-Tag RFP-T: Strong signal in adrenal gland eGFPCreFRT2 fusion protein in epithelial cells of the ureter and bladde Dorsal Lateral Ventral and medullary vasculature in 15 5 dnc kidneys and ose association with Renin producing cells in the Idder. Ganghi D et al. (2013). Retinoid signaling in macula densa of the glomerulus enitors controls specification and regeneration of the urothelium. Dev. Cell. 26(5): 469-482. Above: 3 views of • Create novel strains that enable new research through specific cell Exon I FRI loxP E2 loxP E3 En2 SA IRES LacZ PA Hβ-act P Neo TS23 (15.5 dpc) GU marking by eGFP protein and modulation of gene activity through drug System inducible CRE recombinase + pDIRE (iCre and FlpO) Emphasis on cell populations in Lower Urinary Tract (LUT) *Right:* TS28 (adult) • Encourage nominations of candidate loci from community. ES cell clone annotated section obtained through KOMP(NIH) and EUCOMM Consortia. of the male bladder 2A 🗲 🗲 🗲 T2A: EGRGSLLTCGDVEENPGP • Mice made available through MMRC (JAX) & lower urinary P2A: ATNFSLLKQAGDVEENPGP tract Identifying Novel Urothelial Cell Types (Mendelsohn) Far-Right: TS23 (15.5 dpc) 3 cell types identified in urothelium based on metanephros marker expression. Integrative Analysis of GUDMAP Data Aim: Identify markers that label urothelial sub-Integrative analysis GUDMAP Genelist: P0_CapMes_Crym_20 populations. of GUDMAP gene GUDMAF signature data and its Important for identifying progenitors of analysis versus known urothelial cell types during development and functional/molecular progenitors giving rise to bladder cancers. Query to find all genetics and biology genelists that contain Six2 Microarray [0] · Tutorials [0] Use in situ hybridisation as a primary screen sue Summary Page [17] Example: Place Six2 ouse Strains [0] for novel urothelial cell markers identified in a developmental kidney e11.5 metaneph mesench from microarray and RNA-seq. kidney_e15.5_CapMes 1000 context-appropriate kidney P0 CapMes Crym 200 gene network to kidney_P3_CapMes_Crym_500 Cacl3 Microarray samples better understand its partners, mechanisms kidney single cell_e1115, MetanephMesench_Scamp_k3_200 and associated ToppGen Confirm with 2nd biological processes level analysis idney_e13.5_Podocyte_MafB_k4_200 velopingKidney_e15.5<mark>_Cap mesen</mark>chyme_emap-27738_k1_100 evelopingKidney_e15.5_Cap_mesenchyme_emap-27738_k4_200 using antibodies kidney_P0_CapMes_Crym_k3_200 impaired branching involv<mark>ed in u</mark>reteric bud morphogenesis kidney_P3_CapMes_Crym_k2_100 or transgenic ID Name Source P-value Term in Query Term in Gend nes. MP:0003036 vertebral transformation 1.435E-14 19 MP:0003446 renal hypoplasia Six2 defines and regulate<mark>s a mul</mark>tipotent self-renewing ... 7.907E-13 24 MP:0000459 abnormal presacral vertebrae morphol DNA-binding and regulation mechanisms of the SIX family MP:0003942 abnormal urinary system development 4.179E-12 19 Osr1 expression demarcates a multi-potent population of ...

IX2 and BMP4 mutations a<mark>ssociat</mark>e with anomalous kidney ...

The transcription factor Six2 activates expression of t ...

Deficiency in Six2 during prenatal development is assoc

Misexpression of Six2 is associated with heritable fron ... Notch2 activation in the empryonic kidney depletes neph ...

Six2 functions redundantly immediately downstream of Hoxa2





• Nominate strains: www.gudmap.org/MS_GeneNoms.html









Keck School of Medicine of US













MP:0002752 abnormal somatic nervous system morp

MP:0010981 abnormal branching involved in ureteric bud morphogenesis

1.022E-9 12 49

MP:0006032 abnormal ureteric bud morphology

MP:0004618 thoracic vertebral transformation

MP:0000527 abnormal kidney developmen

