

# Ectopic Expression of Olfactory Receptors Surveyed in Fantom5 Libraries

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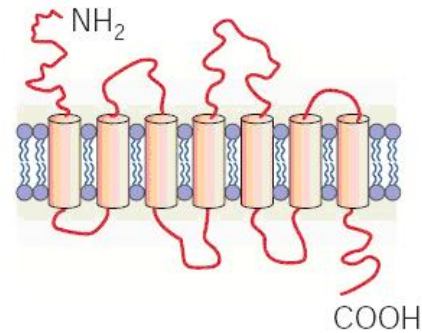
Functional Genomics Technology Team



# Overview of Olfaction and Olfactory Receptors

- ▶ Identified in early 90s by L. Buck and R. Axel (2004 Nobel Prize)

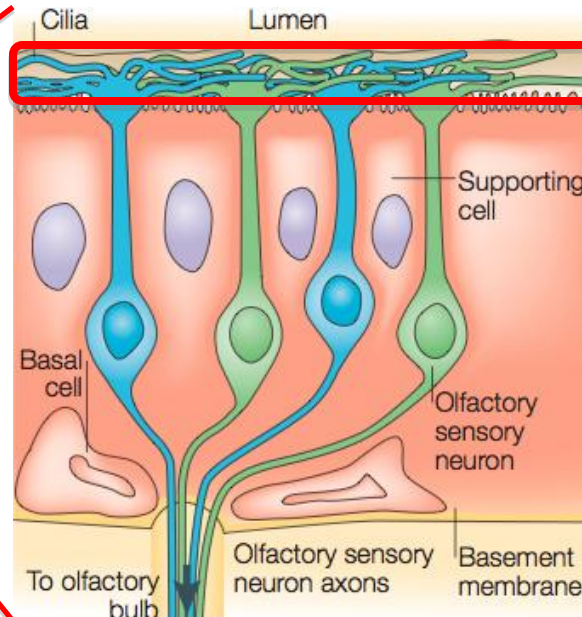
- ▶ ORs belong to GPCRs superfamily



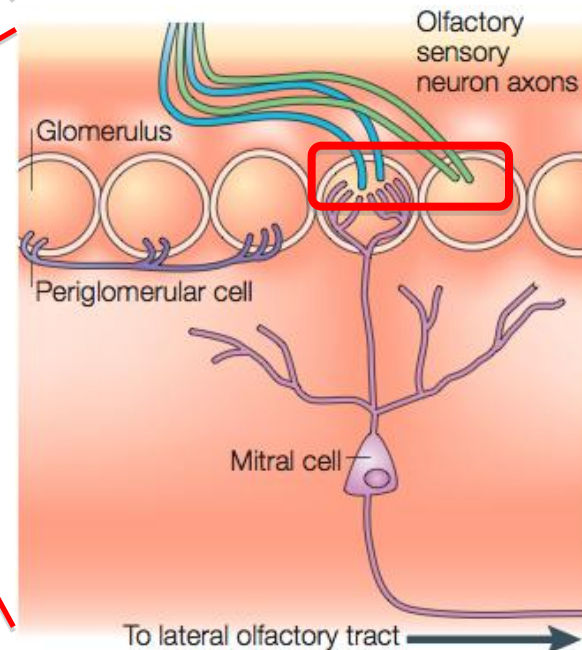
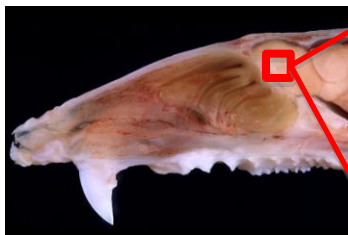
- ▶ Largest gene family in mammals (3-5% of all genes)

	OR genes	% pseudogenes	Functional
Mouse	~1400	20-25%	~1000
Human	~800	50%	~400

# Overview of Olfaction and Olfactory Receptors



A single OSN expresses a single OR gene from a single allele

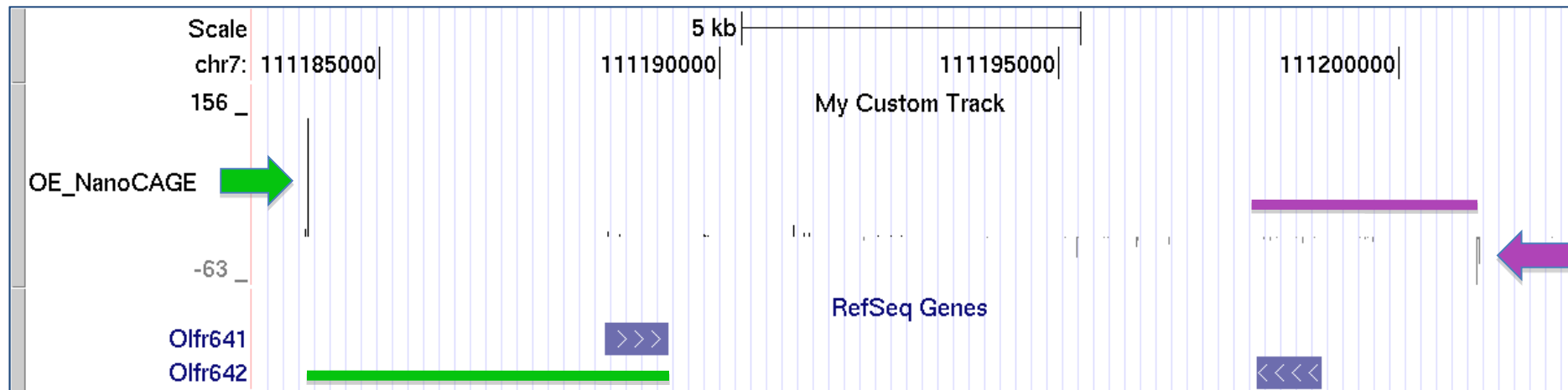


Axons of all OSNs expressing the same OR in the OE converge on the same glomeruli in the OB

# Ectopic Expression of Olfactory Receptors

- ▶ ORs have been detected in high number of human and mouse tissues: testis, germ cells, tongue, erythroid cells, prostate, placenta, brain, PNS, colon, fetal liver (GeneAtlas2 project)
  
- ▶ A clear biological function for ectopic ORs has been defined only in 3 cases:
  - ① Proliferation in human prostate cancer (hOR51E2)
  - ② Human and mouse sperm chemotaxis (hOR17-4, mOR23)
  - ③ Muscle regeneration, cell adhesion and migration (mOR23)

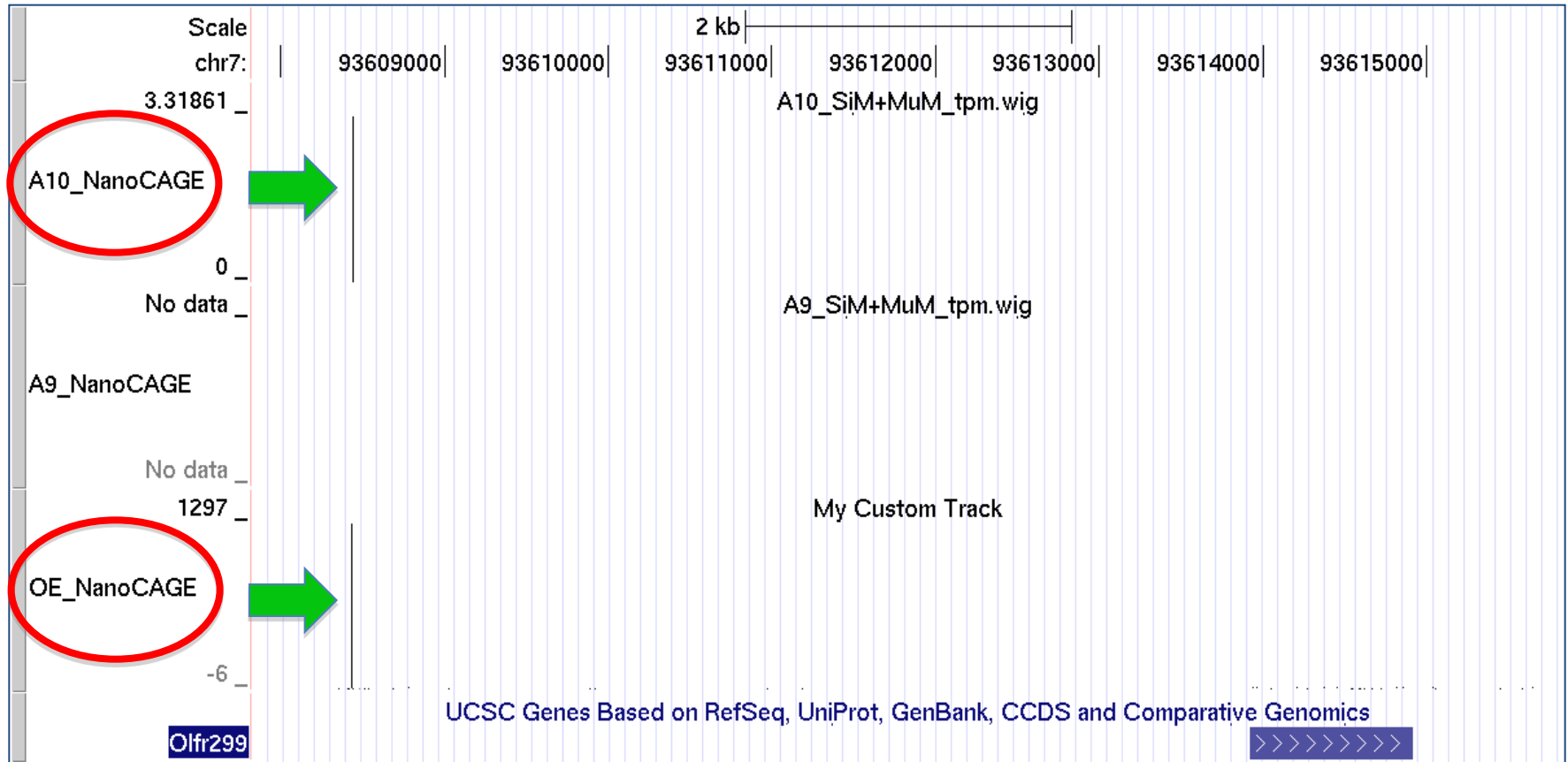
# NanoCAGE of mouse Olfactory Epithelium



- ▶ NanoCAGE analysis has revealed the map and architecture of ~90% of mouse ORs
- ▶ Identification of novel TFs involved in OR genes expression

# NanoCAGE of A9 and A10 dopaminergic neurons

- ▶ Several ORs expressed in A9 and A10 dopaminergic neurons



Promoters map of ~90% of mORs

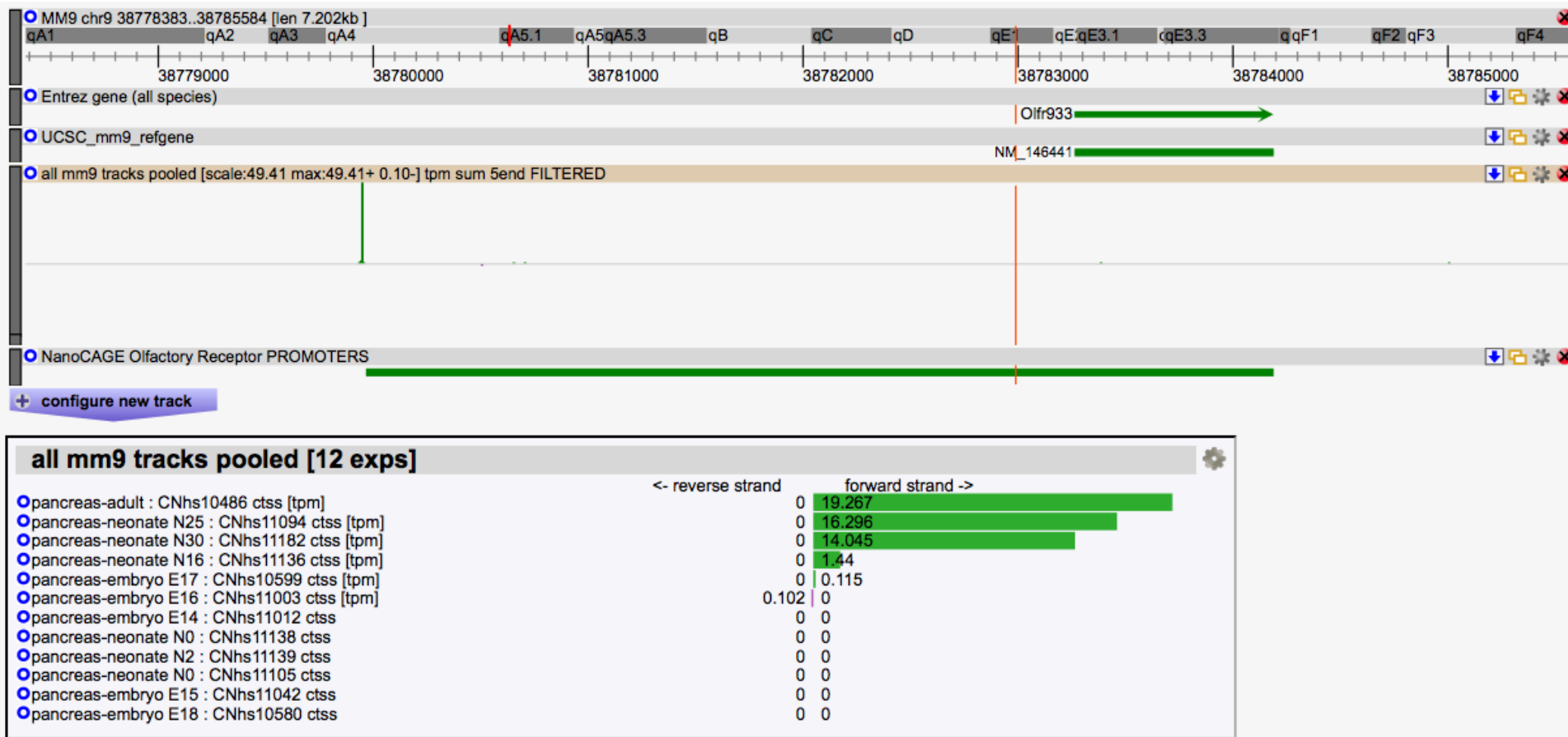


## Data mining from Fantom5 Mouse Libraries

[illegible]

# Ectopic Expression of OR Genes in Fantom5 Mouse Libraries

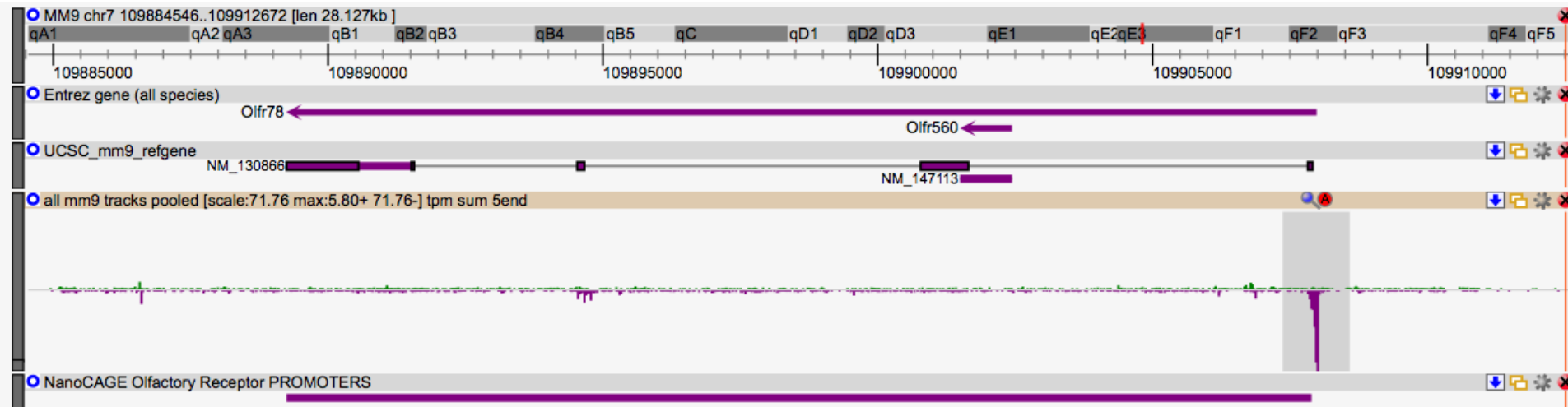
► Olfr933 is specifically expressed in Pancreas starting from N16 stage





# Ectopic Expression of OR Genes in Fantom5 Mouse Libraries

- ▶ Olfr78 has an alternative promoter preferentially used in Adrenal Gland libraries



+ configure new track

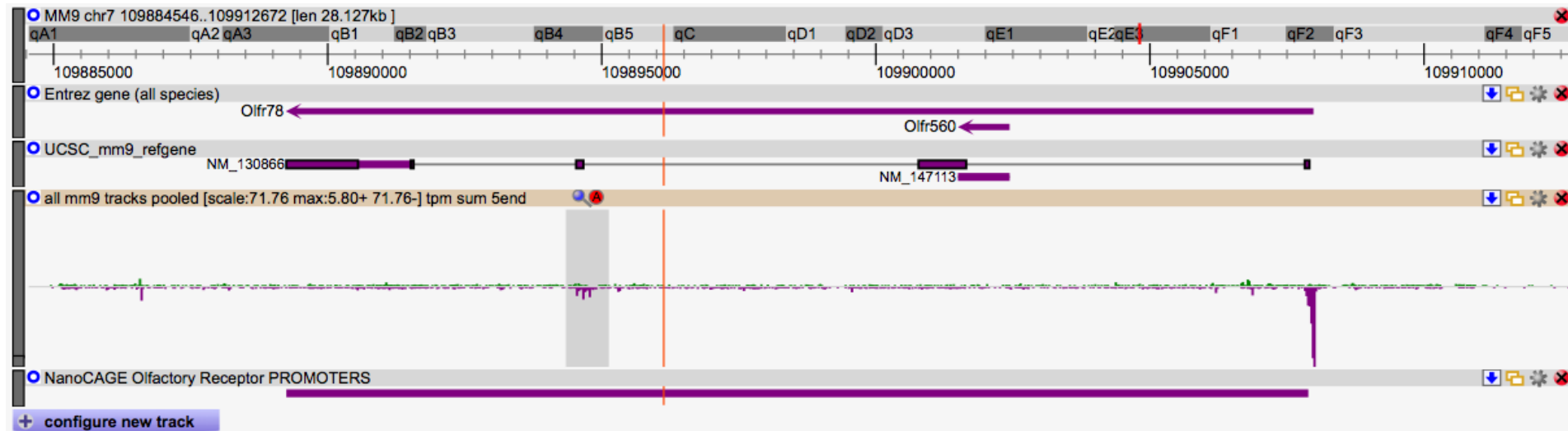
## all mm9 tracks pooled (109907365..109908554) 1.19kb [284 exps]



	<- reverse strand	forward strand ->
amnion-adult pregnant day 17.5 : CNhs1048... [tpm]	7.887	0
epididymis and seminiferous tubule-neonat... [tpm]	6.429	0.268
heart-neonate N16 : CNhs11209 ctss [tpm]	6.451	0
oviduct-adult pregnant day 1 : CNhs10500 ... [tpm]	5.195	0
tongue-adult : CNhs10499 ctss [tpm]	4.446	0
heart-neonate N20 : CNhs11127 ctss [tpm]	4.138	0
placenta-adult pregant day 17 : CNhs10464... [tpm]	3.934	0
heart-neonate N25 : CNhs11196 ctss [tpm]	3.434	0
uterus-adult pregnant day 18 : CNhs10497 ... [tpm]	3.32	0.107
heart-neonate N10 : CNhs11118 ctss [tpm]	3.174	0.069
Mouse E17.5 Internal control : CNhs11938 ... [tpm]	3.086	0
whole body-neonate N10 : CNhs10518 ctss [tpm]	3.038	0
heart-neonate N30 : CNhs11202 ctss [tpm]	2.843	0
heart-neonate N3 : CNhs11221 ctss [tpm]	2.802	0
lung-neonate N7 : CNhs11111 ctss [tpm]	2.801	0
stomach-neonate N30 : CNhs11134 ctss [tpm]	2.629	0

# Ectopic Expression of OR Genes in Fantom5 Mouse Libraries

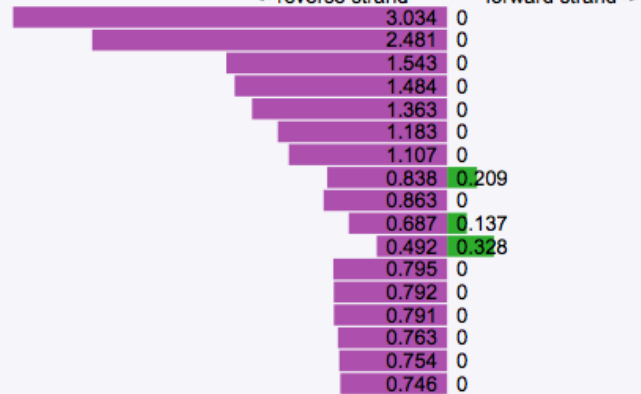
- Olfr78 has an alternative promoter preferentially used in Adrenal Gland libraries



## all mm9 tracks pooled (109894346..109895100) 755bp [284 expts]

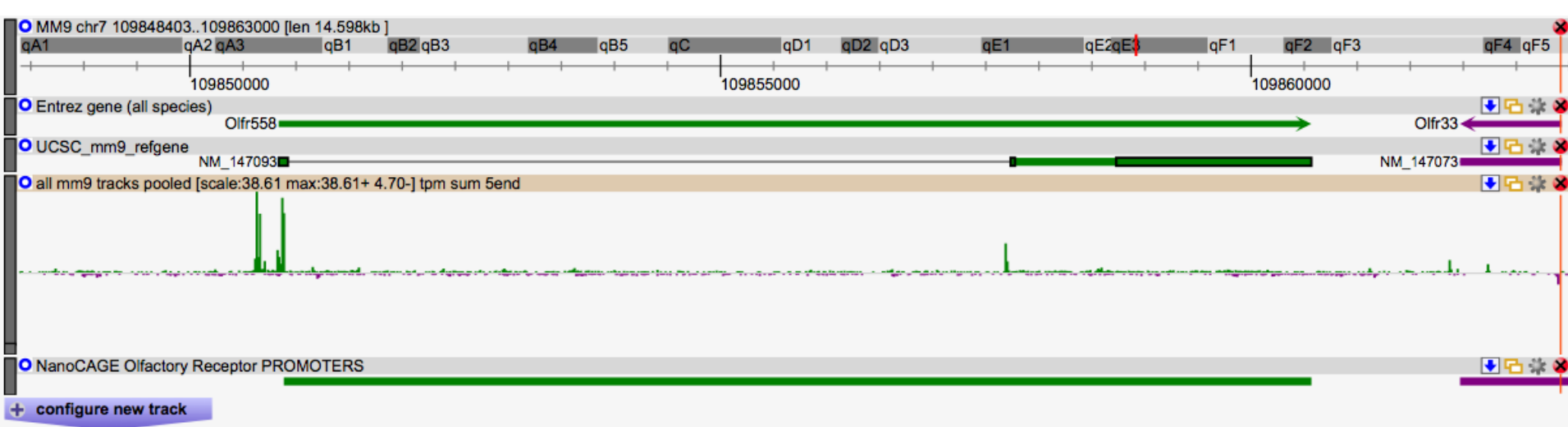
<- reverse strand forward strand ->

- adrenal gland-neonate N0 : CNhs11191 ctss [tpm]
- adrenal gland-embryo E18 : CNhs11026 ctss [tpm]
- Mouse E17.5 Internal control : CNhs11938 ... [tpm]
- adrenal gland-embryo E16 : CNhs11004 ctss [tpm]
- adrenal gland-embryo E14 : CNhs11038 ctss [tpm]
- Mouse E17.5 Internal control : CNhs11898 ... [tpm]
- cecum-adult : CNhs10467 ctss [tpm]
- adrenal gland-embryo E17 : CNhs11043 ctss [tpm]
- adrenal gland-adult : CNhs10508 ctss [tpm]
- pancreas-neonate N0 : CNhs11105 ctss [tpm]
- whole body-embryo E16 : CNhs10514 ctss [tpm]
- pituitary gland-embryo E15 : CNhs10592 ct... [tpm]
- prostate-adult : CNhs10470 ctss [tpm]
- stomach-neonate N7 : CNhs11210 ctss [tpm]
- stomach-neonate N30 : CNhs11134 ctss [tpm]
- stomach-embryo E15 : CNhs10603 ctss [tpm]
- Mouse E17.5 Internal control : CNhs11024 ... [tpm]



# Ectopic Expression of OR Genes in Fantom5 Mouse Libraries

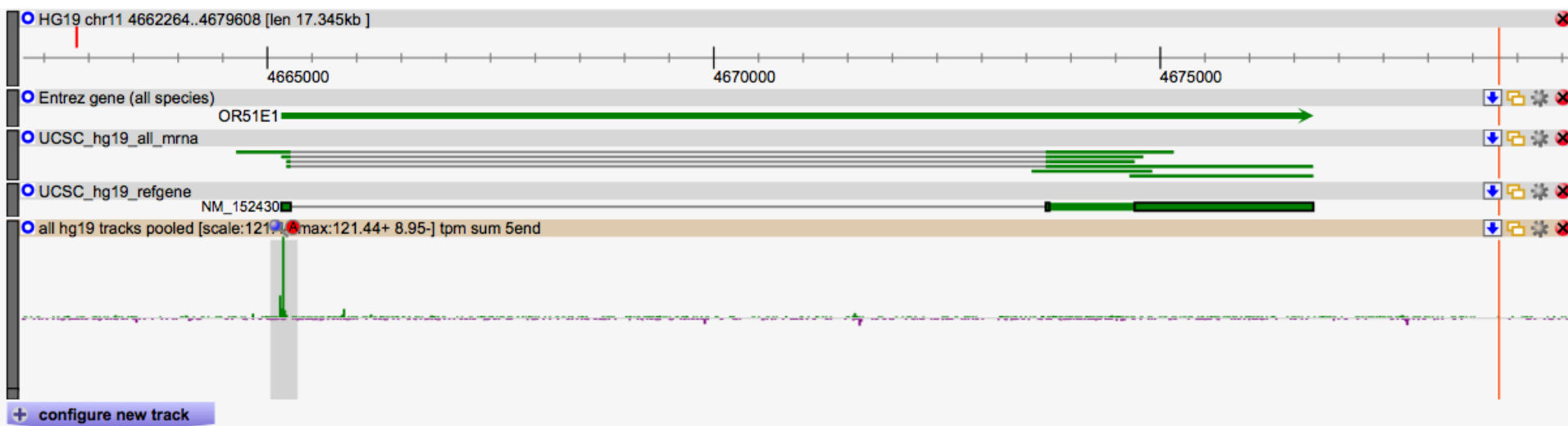
► Olfr558 is enriched in Heart (Neonate and Embryo) libraries



all mm9 tracks pooled [284 expts]			
		<- reverse strand	forward strand ->
heart-neonate N16 : CNhs11209 ctss [tpm]	0.25	7.051	
heart-neonate N10 : CNhs11118 ctss [tpm]	0.69	5.45	
bone (os femoris)-neonate N2 : CNhs11227 ... [tpm]	1.676	4.141	
whole body-neonate N10 : CNhs10518 ctss [tpm]	0.434	5.353	
heart-neonate N30 : CNhs11202 ctss [tpm]	0.374	5.313	
heart-neonate N20 : CNhs11127 ctss [tpm]	0.487	4.95	
bone (os femoris)-neonate N16 : CNhs11225... [tpm]	1.222	3.887	
heart-embryo E18 : CNhs11030 ctss [tpm]	0.593	4.154	
bone (os femoris)-neonate N20 : CNhs11195... [tpm]	2.1	2.471	
heart-neonate N25 : CNhs11196 ctss [tpm]	0.303	4.141	
whole body-neonate N6 : CNhs10515 ctss [tpm]	0.442	3.828	
heart-embryo E17 : CNhs11025 ctss [tpm]	0.618	3.582	
heart-neonate N0 : CNhs11213 ctss [tpm]	0.222	3.766	
Mouse E17.5 Internal control : CNhs11898 ... [tpm]	0.296	3.55	
forelimb-embryo E17 : CNhs10598 ctss [tpm]	0.425	3.4	
kidney-neonate N10 : CNhs11206 ctss [tpm]	0.699	3.066	
oviduct-adult pregnant day 1 : CNhs10500 ... [tpm]	0.38	3.294	

# Ectopic Expression of OR Genes in Fantom5 Mouse Libraries

► hOR51E1 (human ortholog of mouse Olfr558) is specifically expressed in carcinoma cells



all hg19 tracks pooled (4665035..4665321) 287bp [309 exps]				
			<- reverse strand	forward strand ->
small-cell gastrointestinal carcinoma cel... [tpm]	0	54.062		
lung adenocarcinoma cell line:A549 : CNhs... [tpm]	0	25.639		
prostate-adult : CNhs10628 ctss [tpm]	0	10.521		
gastrointestinal carcinoma cell line:ECC1... [tpm]	0	7.314		
placenta-adult : CNhs10627 ctss [tpm]	0	4.849		
breast-adult : CNhs11792 ctss [tpm]	0	4.33		
adipose tissue-adult : CNhs10615 ctss [tpm]	0	4.119		
uterus-adult : CNhs11676 ctss [tpm]	0	3.5		
heart-fetal : CNhs10653 ctss [tpm]	0.048	2.662		
tongue-fetal : CNhs11768 ctss [tpm]	0.176	2.46		
heart-adult : CNhs10621 ctss [tpm]	0.131	1.97		
kidney-adult : CNhs10622 ctss [tpm]	0	2.154		
small intestine-fetal : CNhs11773 ctss [tpm]	0	2.229		
left atrium-adult : CNhs11790 ctss [tpm]	0	1.762		
retina-adult : CNhs10636 ctss [tpm]	0	1.931		
kidney-fetal : CNhs10652 ctss [tpm]	0	1.573		
dura mater-adult : CNhs10648 ctss [tpm]	0.049	1.575		

# Ectopic Expression of OR Genes in Fantom5 Mouse Libraries...

► Future directions ◀

Data need to be improved and refined

## Bioinformatics:

- Analysis of tissue specificity

- Analysis of patterns of dynamic expression

- Analysis of architecture for alternative promoters in mouse

- Identification of human promoters and analysis of expression in human libraries

## Sequencing:

- Human Olfactory Epithelium

## Functional Validation:

- ORs with expression restricted to specific tissues / developmental stages

- ORs showing ubiquitous expression (editing?)

- De-orphanization of selected targets → Identification of endogenous ligands

## ◀ Acknowledgements ▶



🌸 Piero Carninci

🌸 Stefano Gustincich

🌸 Charles Plessy