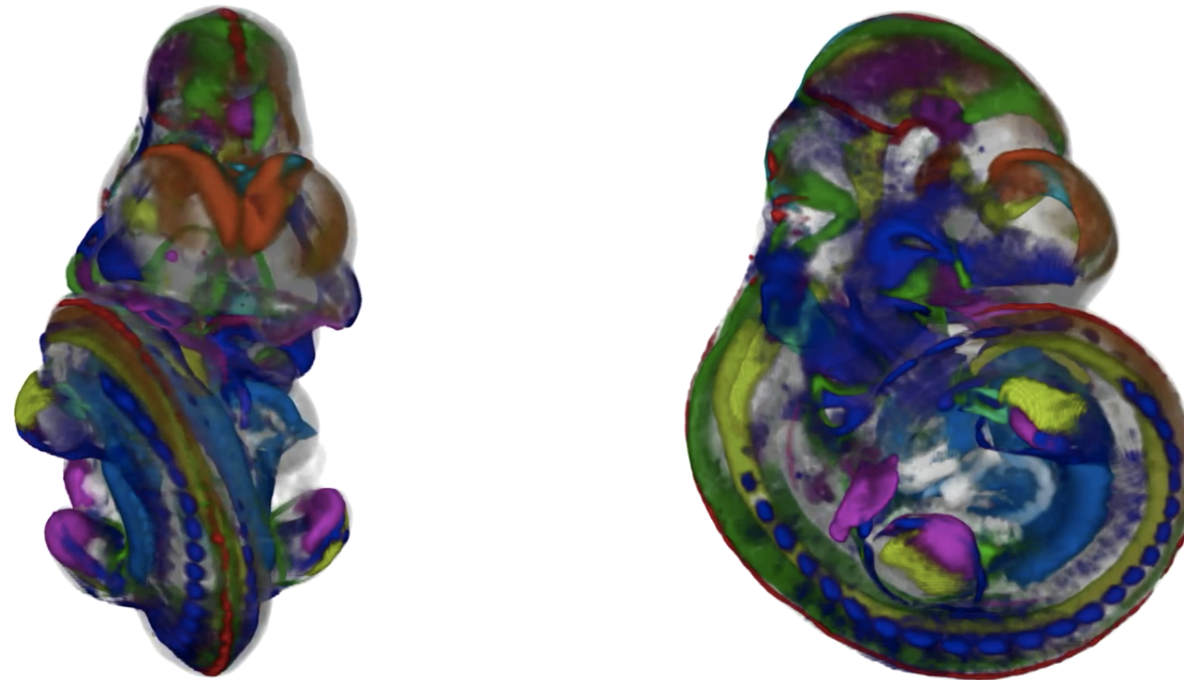


New Dimensions to eMouseAtlas



Chris Armit

Senior Editor

EMAGE Database

MRC Human Genetics Unit @ IGMM @ UoE

emouseatlas
www.emouseatlas.org

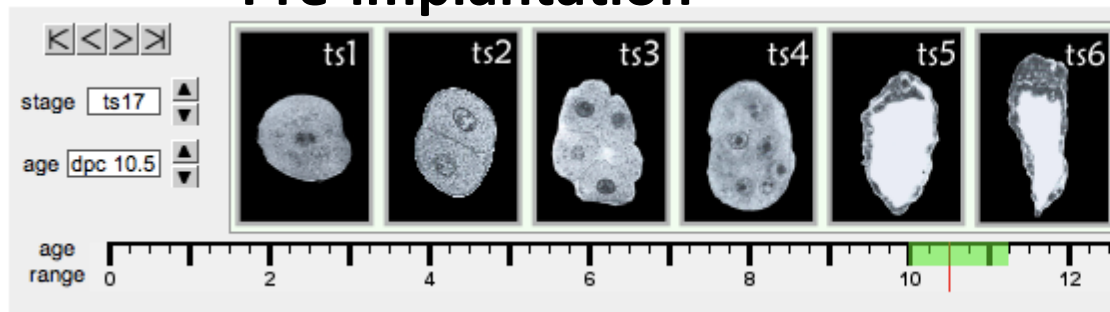


- **a non-profit freely available online resource that allows researchers to visualise mouse development and explore the genetic regulation of mouse development**
- **models of post-implantation mouse embryo development are used as a spatial framework for mouse embryo data**

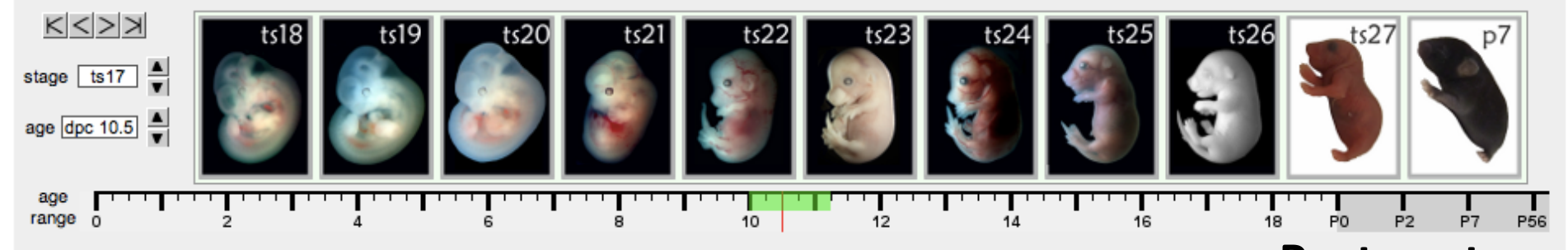
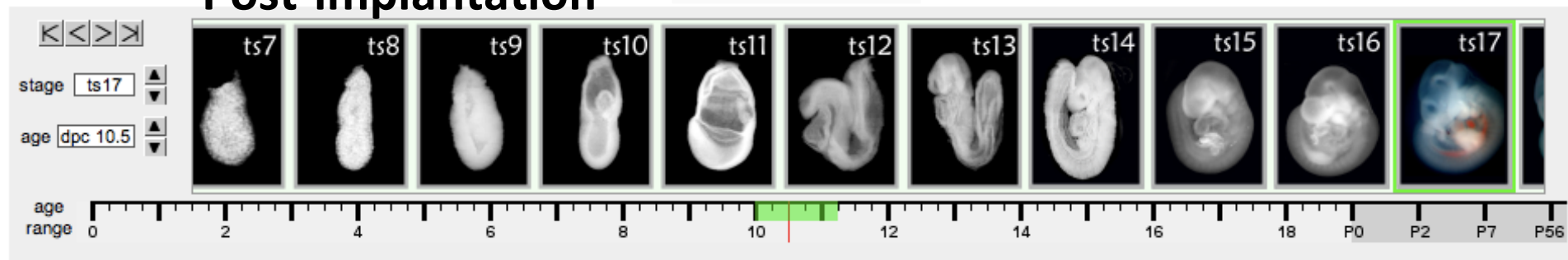


Theiler Staging

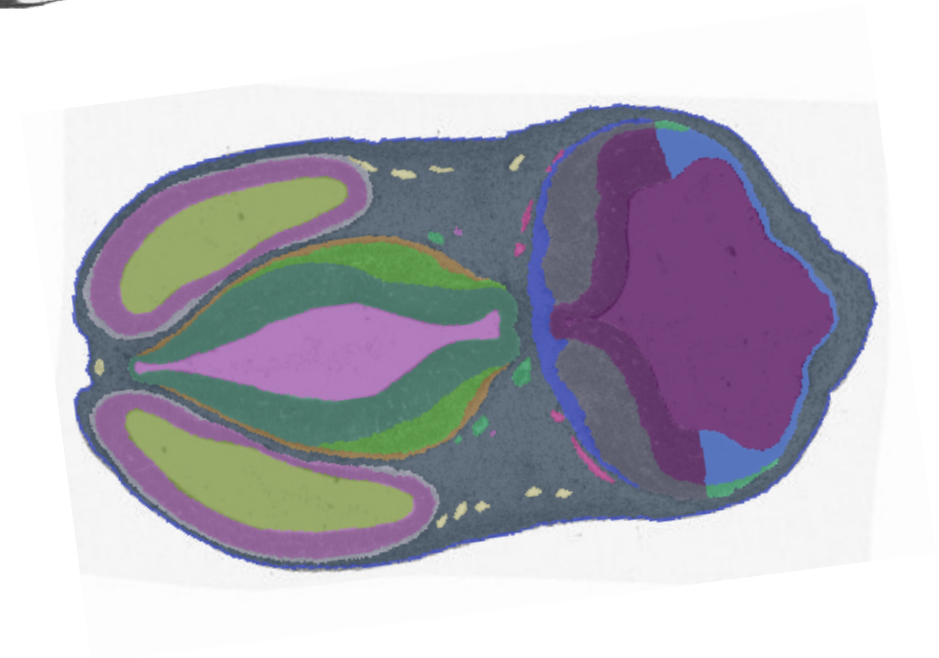
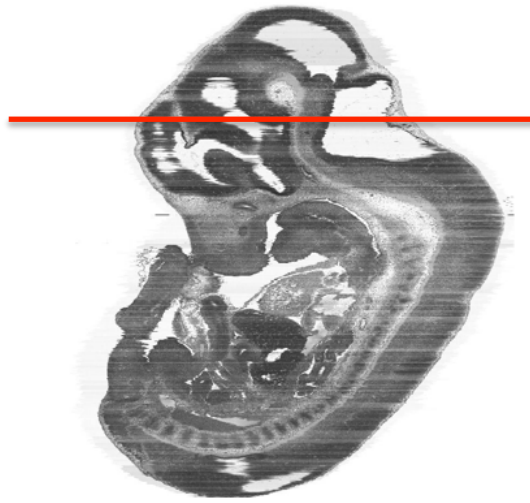
Pre-implantation



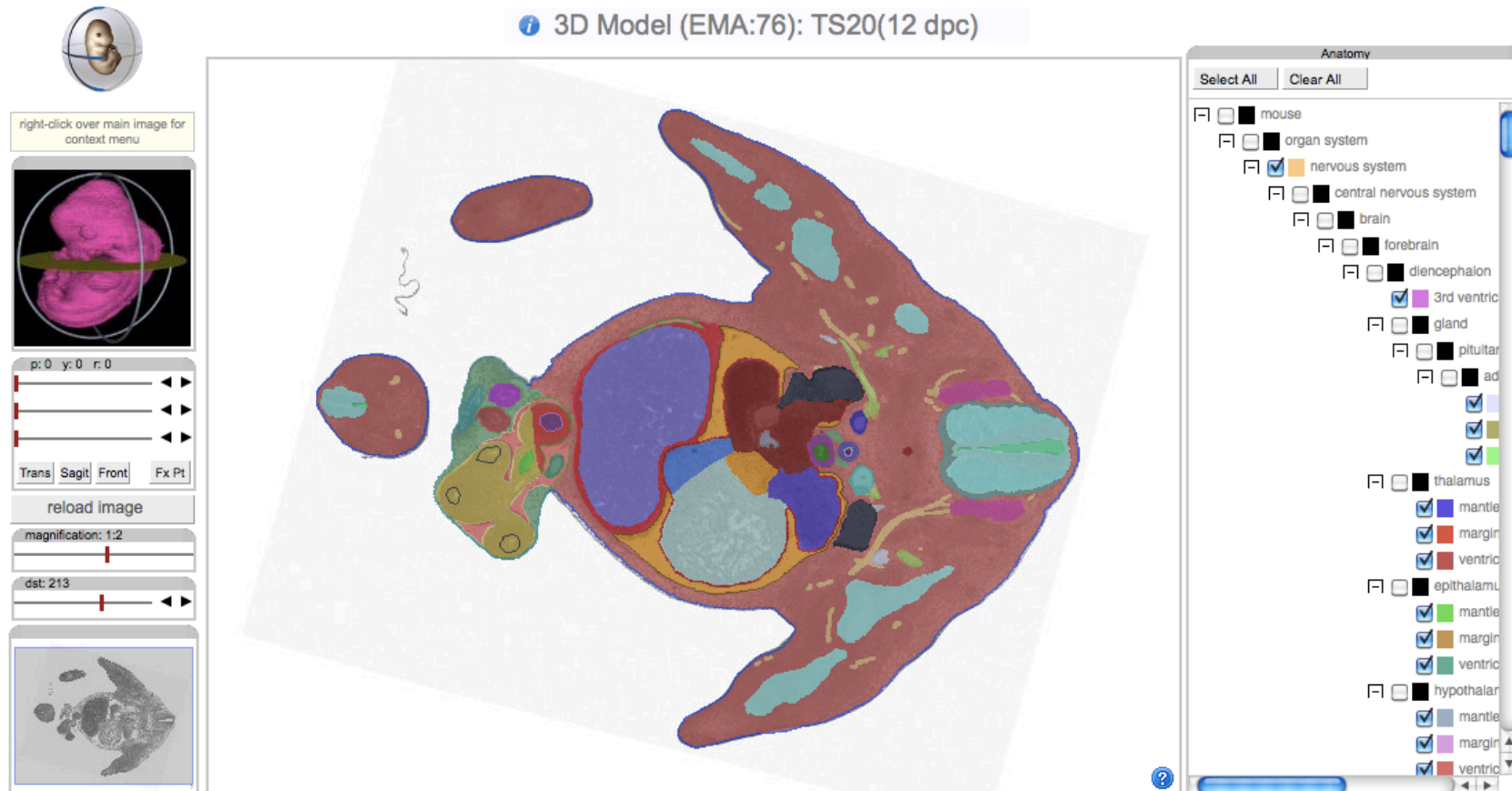
Post-implantation



Post-partum



- **Delineated anatomy represented as colour domains**

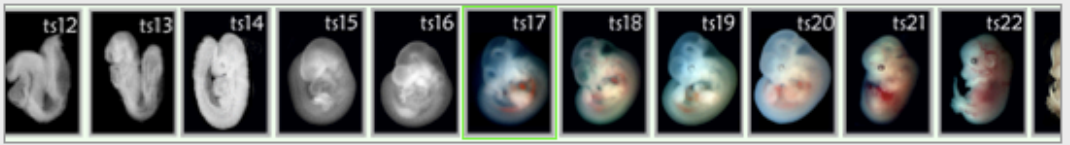


- Delineated anatomy visualised using interactive IIP3D viewer

Stage Selection ?

stage:

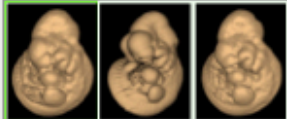
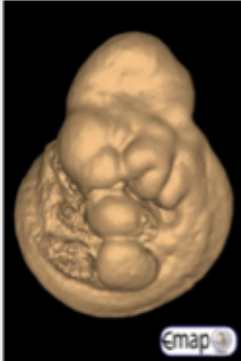
age:



age range: 0 2 4 6 8 10 12 14 16 18 P0 P2 P7 P56

TS17 Model Selection ?

EMA:49



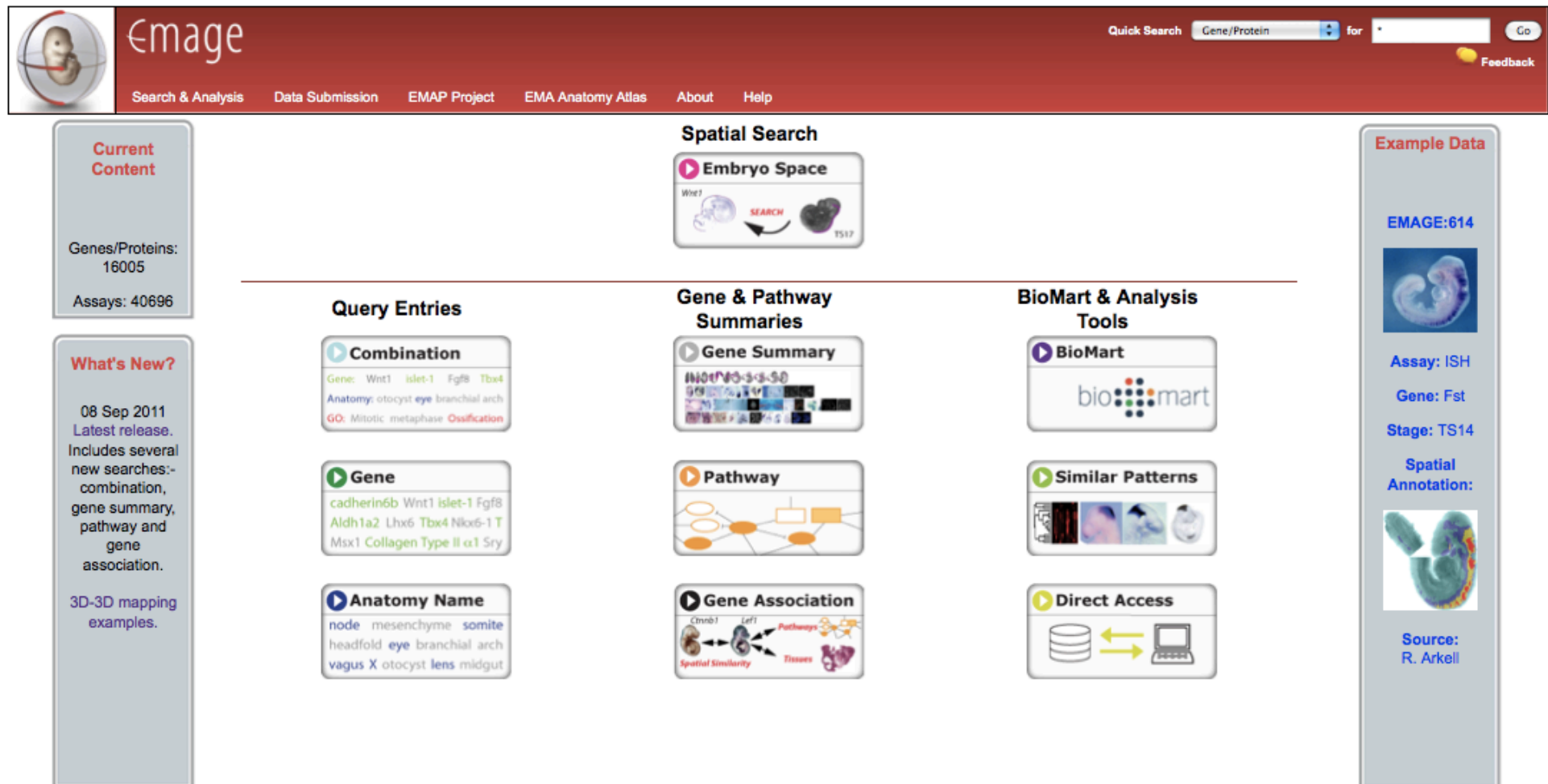
Available Data ?

- A** [High Resolution Sections](#)
- [3D Reconstruction](#)
- [Movies](#)
- [Litter Variation](#)


Special Systems

- [Anatomy](#)
- [Theiler Stage](#)
- [Interactive Anatomy Browser](#)
- [Download](#)

- EMAGE Gene Expression Database

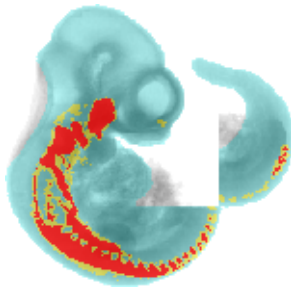


The screenshot shows the EMAGE website interface. At the top, there is a navigation bar with the EMAGE logo, a search bar, and links for Search & Analysis, Data Submission, EMAP Project, EMA Anatomy Atlas, About, and Help. The main content area is divided into several sections:

- Current Content:** Genes/Proteins: 16005, Assays: 40696.
- What's New?:** 08 Sep 2011 Latest release. Includes several new searches: combination, gene summary, pathway and gene association. 3D-3D mapping examples.
- Spatial Search:** Embryo Space. Includes a search interface with a 'SEARCH' button and a 'Feedback' button.
- Query Entries:**
 - Combination:** Gene: Wnt1, islet-1, Fgf8, Tbx4. Anatomy: otocyst, eye, branchial arch. GO: Mitotic metaphase, Ossification.
 - Gene:** cadherin6b, Wnt1, islet-1, Fgf8, Aldh1a2, Lhx6, Tbx4, Nkx6-1, T, Msx1, Collagen Type II alpha 1, Sry.
 - Anatomy Name:** node, mesenchyme, somite, headfold, eye, branchial arch, vagus X, otocyst, lens, midgut.
- Gene & Pathway Summaries:**
 - Gene Summary:** INO1P3-3-3-50.
 - Pathway:** A diagram showing a network of genes and their interactions.
 - Gene Association:** A diagram showing gene associations with spatial similarity and tissues.
- BioMart & Analysis Tools:**
 - BioMart:** bio::mart logo.
 - Similar Patterns:** A diagram showing similar patterns in gene expression.
 - Direct Access:** A diagram showing direct access to data.
- Example Data:** EMAGE:614. Assay: ISH. Gene: Fst. Stage: TS14. Spatial Annotation: . Source: R. Arkell.

- **EMAGE Gene Expression Database**

- *spatial annotation*
- *text (ontology) annotation*
- *ancillary information (MISFISHIE-compliant)*



EMAGE:672

Sox10 SRY-box containing gene 10 ([MGI:98358](#))
TS17 (9.5 dpc)
in situ hybridisation

Structure	Level	Pattern	Notes
otocyst	■ strong	regional	Expression detected in otic vesicle.
dorsal root ganglion	■ strong	regional	Expression in the trunk is observed at the level of the anterior halves of the somites (ventrally migrating neural crest) before and during the formation of dorsal root ganglia condensations and the sympathetic ganglia.
acoustic viii ganglion	■ strong	not applicable	Expression is described as being in the acoustic ganglion.
trigeminal v ganglion	■ strong	not applicable	Expression is described as being in the trigeminal ganglion
glossopharyngeal ix ganglion	■ strong	not applicable	Expression is described as being in the superior ganglion ie. proximal IX or glossopharyngeal ganglion.
vagus x ganglion	■ strong	not applicable	Expression is described as being in the jugular ganglion ie. proximal/superior X or vagus ganglion.
facial vii ganglion	■ strong	not applicable	Expression is described as being in the geniculate ie. distal VII (facial) ganglion.
nasal epithelium	■ moderate	regional	Expression detected in olfactory placode.

- **EMAGE Gene Expression Database**

Query Entries

▶ Combination

Gene: Wnt1 islet-1 Fgf8 Tbx4
 Anatomy: otocyst eye branchial arch
 GO: Mitotic metaphase Ossification

▶ Gene

cadherin6b Wnt1 islet-1 Fgf8
 Aldh1a2 Lhx6 Tbx4 Nkx6-1 T
 Msx1 Collagen Type II α 1 Sry

▶ Anatomy Name

node mesenchyme somite
 headfold eye branchial arch
 vagus X otocyst lens midgut

Gene & Pathway Summaries


▶ Gene Summary



▶ Pathway



▶ Gene Association



Ctnnb1 Lef1 Pathways Tissues
 Spatial Similarity

BioMart & Analysis Tools

▶ BioMart




▶ Similar Patterns



▶ Direct Access



- EMAGE Gene Expression Database



Emage

Quick Search for

Search & Analysis Data Submission EMAP Project EMA Anatomy Atlas About Help

Export results:- csv format










Select All On This Page | Deselect All On This Page

Column Selection

Display 20 entries per page

Page 1 of 1

Flexible Scroll

Select	Gene/Protein	Data Image	Find Similar	Theiler Stage	Stage Given	ID	Specimen Type	Data Source
?	(1)	(3)	(1)	(3)	(3)	(3)	(2)	(1)
<input type="checkbox"/>	Fzd8			16	10.5dpc	EMAGE:3727 view entry	section	Emage 
<input type="checkbox"/>	Fzd8	 +3 MORE IMAGES		17	10.5 dpc	EMAGE:6125 view entry	opt	Emage 
<input type="checkbox"/>	Fzd8	 +3 MORE IMAGES		15	9.5 dpc	EMAGE:6124 view entry	opt	Emage 




- EMAGE Gene Expression Database



Export results:- csv format

Select All On This Page | Deselect All On This Page

Page 1 of 1

Select	Gene/Protein	Data Image
<input type="checkbox"/>	Fzd8 (1)	
<input type="checkbox"/>	Fzd8	 + 3 MORE IMAGES
<input type="checkbox"/>	Fzd8	 + 3 MORE IMAGES

EMAGE:3727

Fzd8 frizzled homolog 8 (Drosophila) (MGI:108460)
TS16 (10.5 dpc)
in situ hybridisation

Data Images

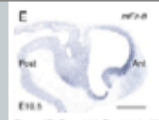


Figure 1E. Copyright: Reprinted with permission from Elsevier from [doi:10.1016/S0925-4773(01)00040-2] Mach Dev 103: 167-72, Kim AG, Lowenstein DR, Pleasure SJ. Ret receptors and their inhibitors are expressed in gradients in the developing telenocephalon. Copyright 2001.

Expression pattern clarity: ★★★

Find spatially similar expression patterns [Open](#)

Notes

Note: Parasagittal section. Post, posterior; Ant, anterior. Scale bar, 0.5mm.

Detection Reagent

Type: in situ hybridisation probe
 Identifier: MGI:2675380
 Entity Detected: Fzd8, frizzled homolog 8 (Drosophila) (MGI:108460)
 Notes: The Fzd8 probe used in this study by Kim et al., 2001 [PMID:11335128] was obtained from J. Nathans, Johns Hopkins University and is of undefined sequence.
 Chemistry: RNA
 Strand: antisense
 Label: digoxigenin

Specimen

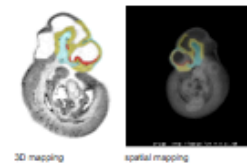
Organism: mouse
 Strain: CD-1
 Age: 10.5 dpc
 Thelcer Stage: TS16
 Mutations: none (wild-type)
 Preparation: section

Expression Pattern Description

Text Annotation:

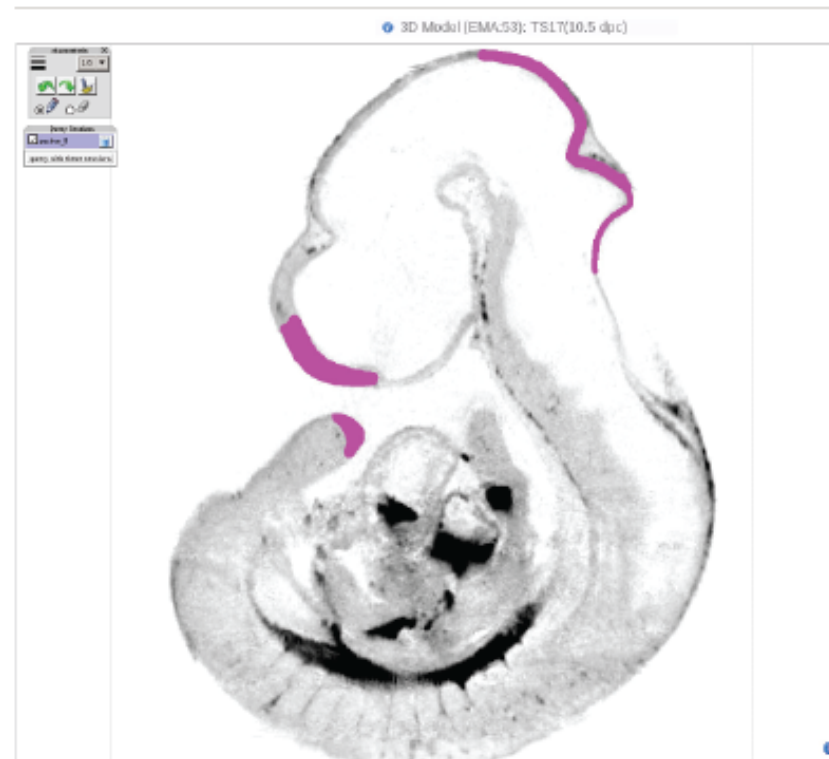
Structure	Level	Pattern	Notes
telenocephalon	detected	regional	Expression is in an anterior domain.

Spatial Annotation:



- **EMAGE Gene Expression Database**

Spatial Search




- **Using the Paint Tool is one method of generating a spatial query**

- EMAGE Gene Expression Database

emage Quick Search for

[Search & Analysis](#) [Data Submission](#) [EMAP Project](#) [EMA Anatomy Atlas](#) [About](#) [Help](#)

Query: genes - detected - query pattern - ts17 to ts17





















 [download query region as wlz file](#)

Export results:- csv format

Select All On This Page | Deselect All On This Page

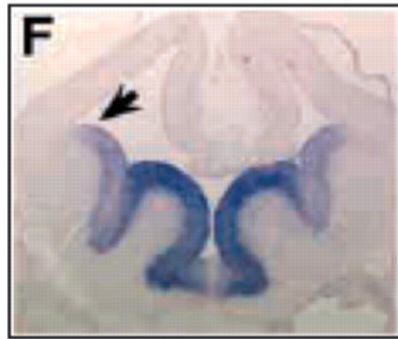
Page 1 of 111 Go to page:

Add/Remove Columns Display entries per page Flexible Scroll

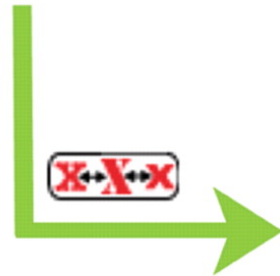
Select	Gene/Protein (991)	Data Image (1109)	Region (1109)	Find Similar (1)	Theller Stage (1)	Stage Given (12)	Similarity to query region (248)	Structures (173) <input type="checkbox"/> show all <input type="checkbox"/> show less	ID (1109)	Pattern Clarity (3)	Data Source (4)
<input type="checkbox"/>	Etv5				TS17	10.5 dpc	0.340	Go to annotation details <input type="checkbox"/> show all ■ hindbrain ■ midbrain ■ lens pit	EMAGE:2830 view entry	★★★	
<input type="checkbox"/>	Pax5				TS17	10.5 dpc	0.305	Go to annotation details ■ midbrain	EMAGE:3372 view entry	★★	
<input type="checkbox"/>	Smarca1				TS17	10.5 dpc	0.301	-	EMAGE:3083 view entry	★	
<input type="checkbox"/>	Nfib				TS17	10.5 dpc	0.300	Go to annotation details ■ hindbrain ■ telencephalon ■ midbrain	EMAGE:3188 view entry	★★★	
<input type="checkbox"/>	Tcf7l2				TS17	10.5 dpc	0.296	-	EMAGE:3049 view entry	★★★	

- Spatial queries return a ranked list based on local spatial similarity


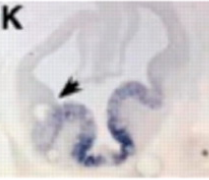

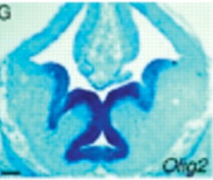
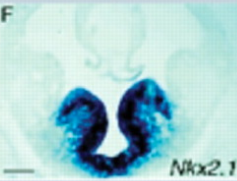
Example of a 'Find Similar Pattern' 3D search.



QUERY PATTERN



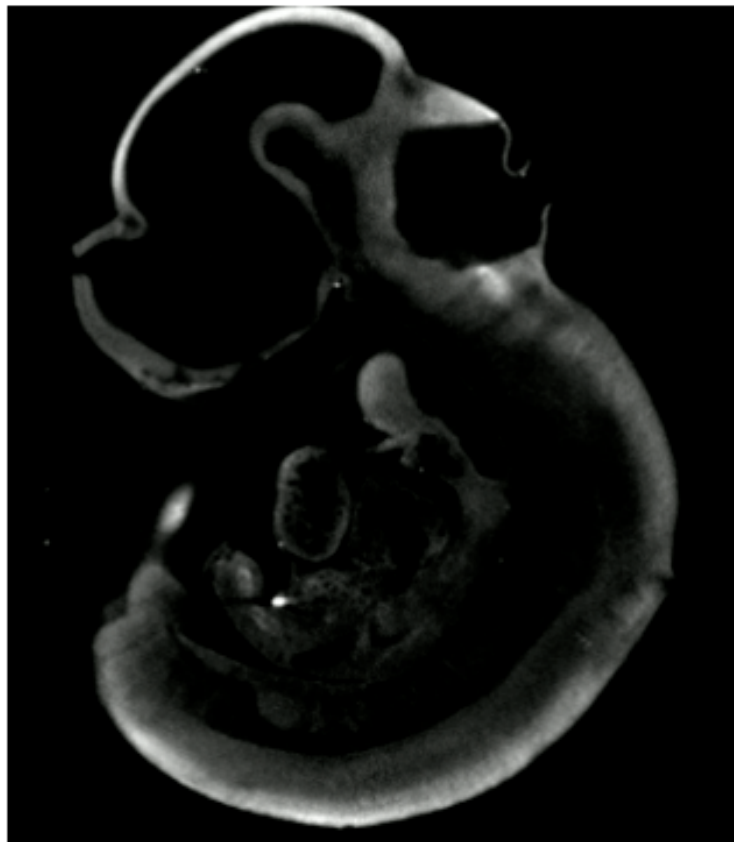
RESULT:
SPATIALLY
SIMILAR
PATTERNS

Gene/Protein ? (20)	Data Image ? (23)	Similarity to query region ? (14)
Olig2		1.000
Gsx1		0.033
Gsx2		0.031
Olig2		0.030
Nkx2-1		0.026

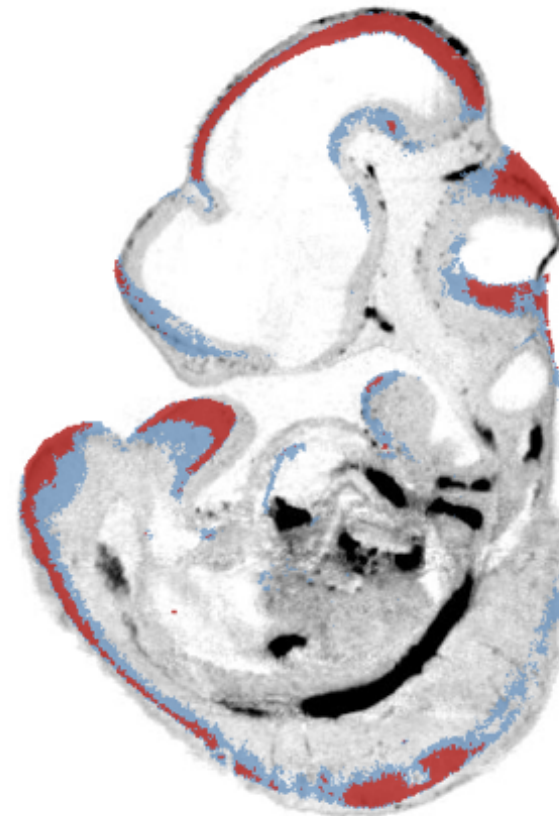


Optical Projection Tomography (OPT)

- collaboration with Dr Paula Murphy (Trinity College Dublin)
- 3D mapping of *in situ* hybridisation gene expression patterns



Fzd10
Theiler stage (TS) 17

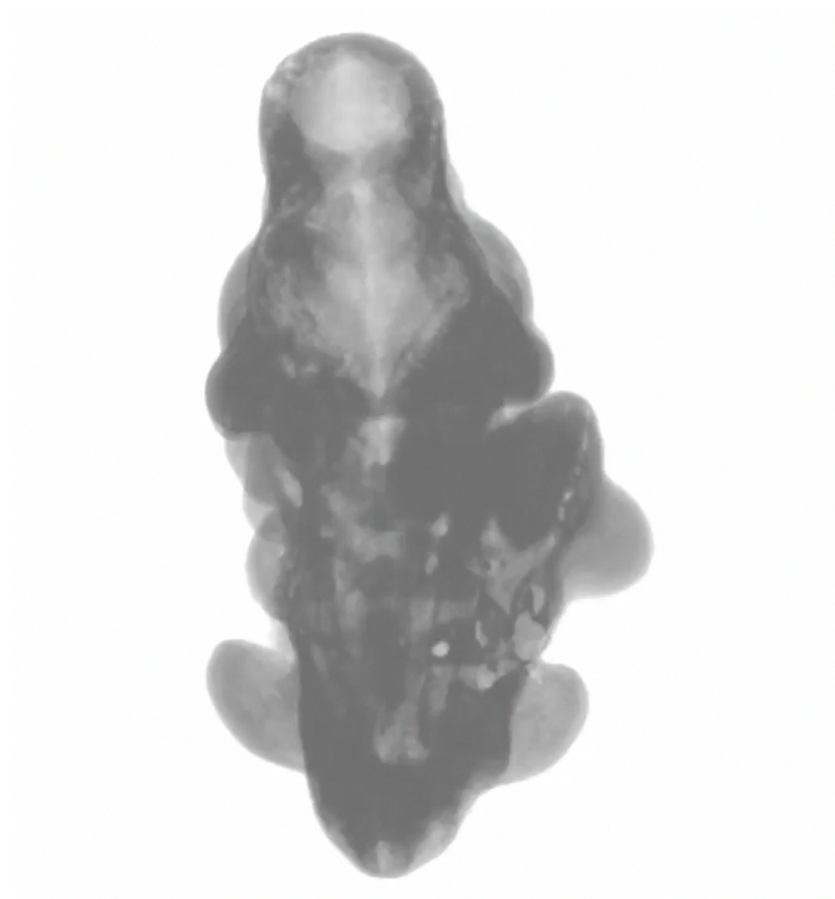


Map of Fzd10
eMouseAtlas TS17 model

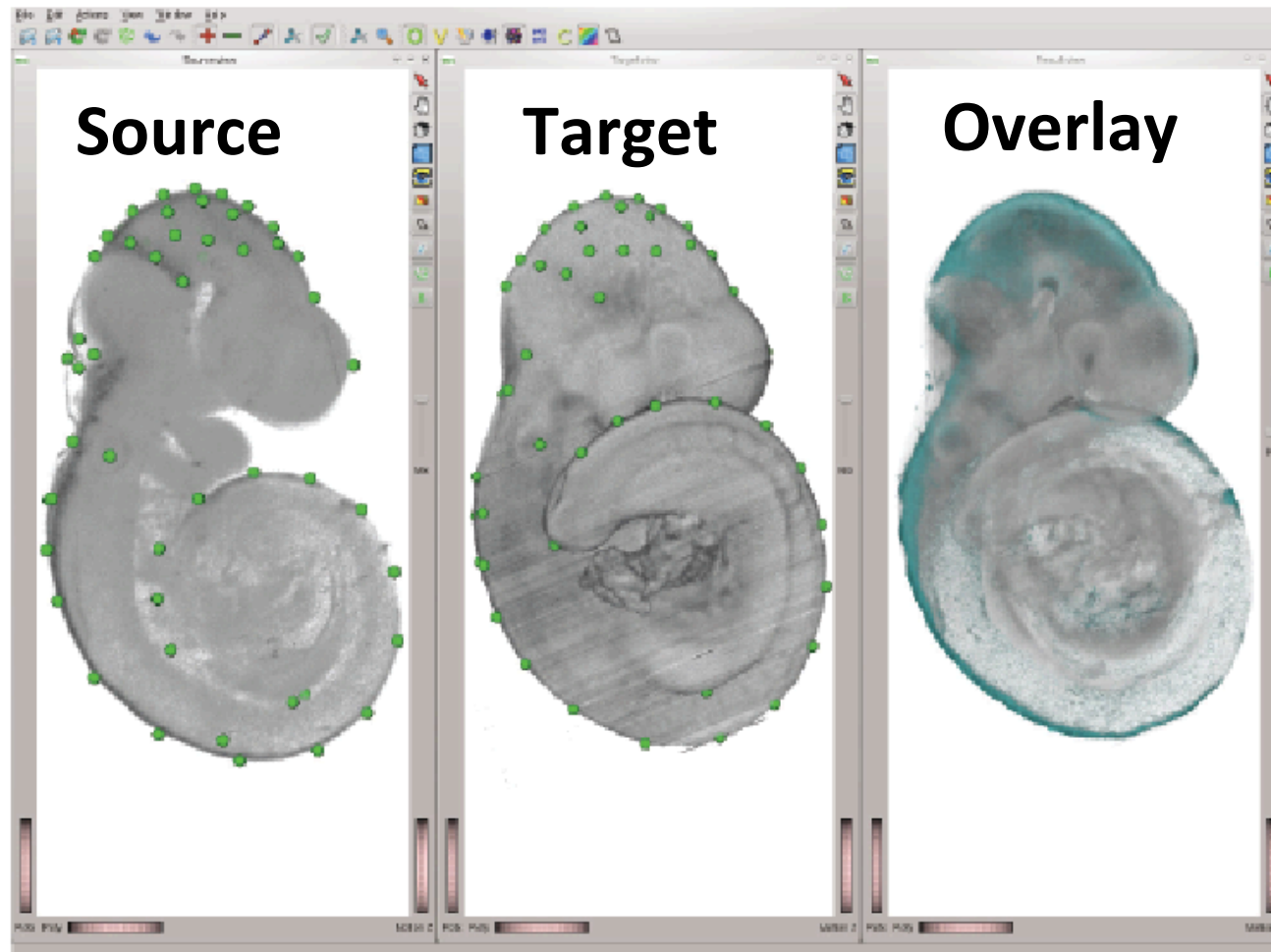


Optical Projection Tomography (OPT)

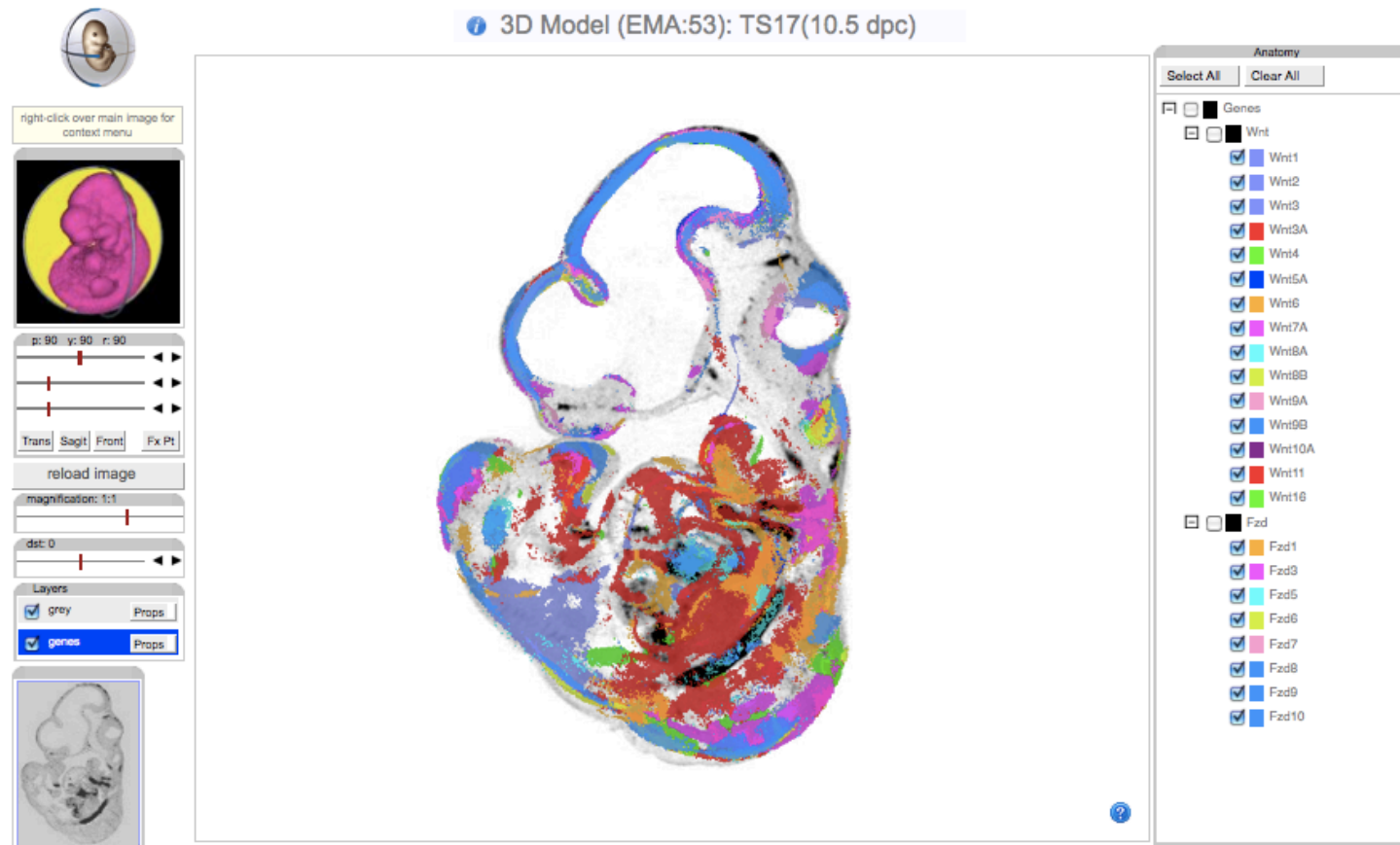
- collaboration with Dr Paula Murphy (Trinity College Dublin)
- 3D mapping of *in situ* hybridisation gene expression patterns



CDT and WlzWarp



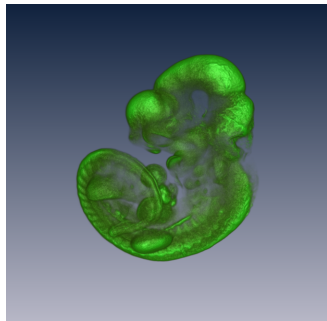
- 3D-to-3D mapping using WlzWarp
- Landmarks are added to Source and Target Objects



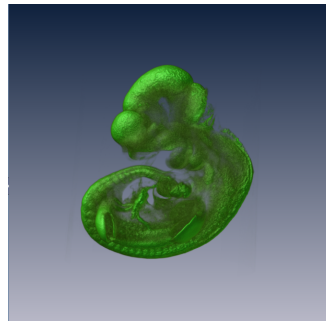
- Maps of *in situ* hybridisation OPT gene expression patterns visualised using IIP3D viewer



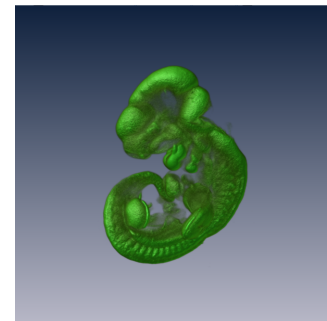
TS17 model



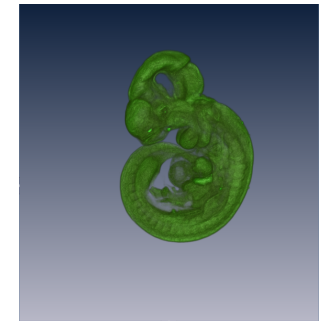
embryo 1



embryo 2



embryo 3

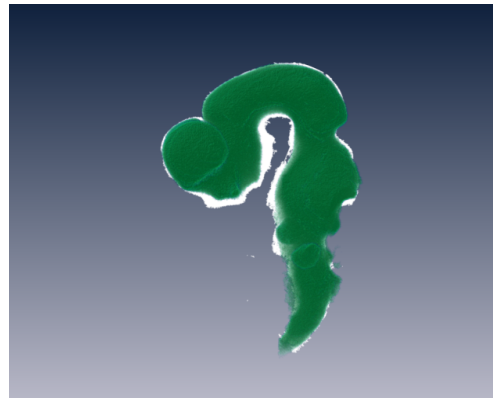
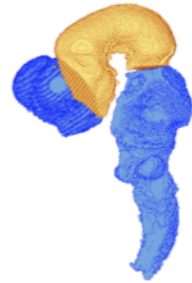


embryo 4

- **Quantitative assessment of 3D mapping**



TS17 model



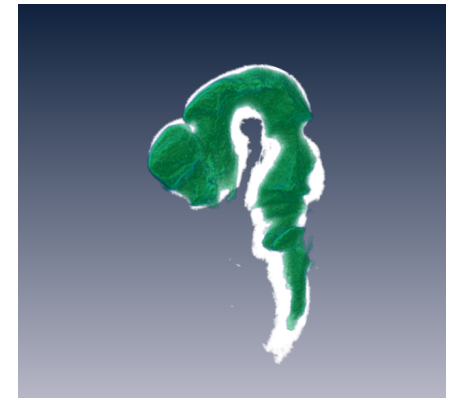
embryo 1



embryo 2



embryo 3

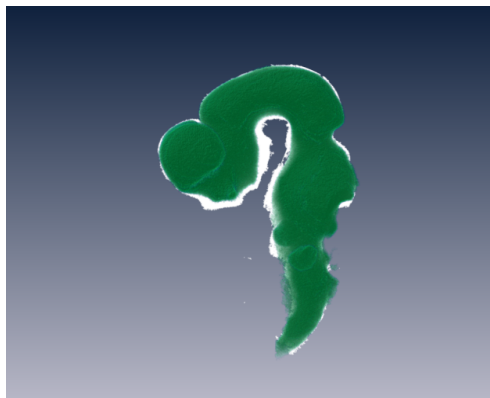


embryo 4

- **Quantitative assessment of 3D mapping**



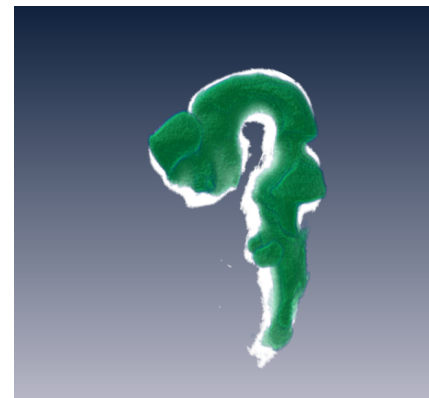
TS17 model



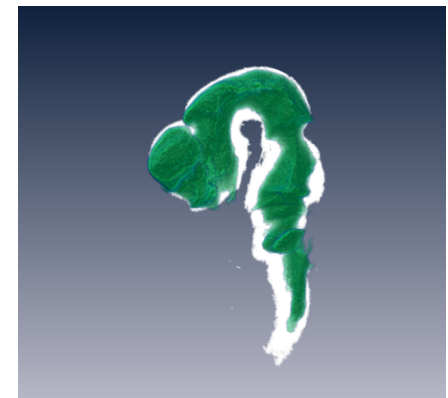
embryo 1
0.884



embryo 2
0.787

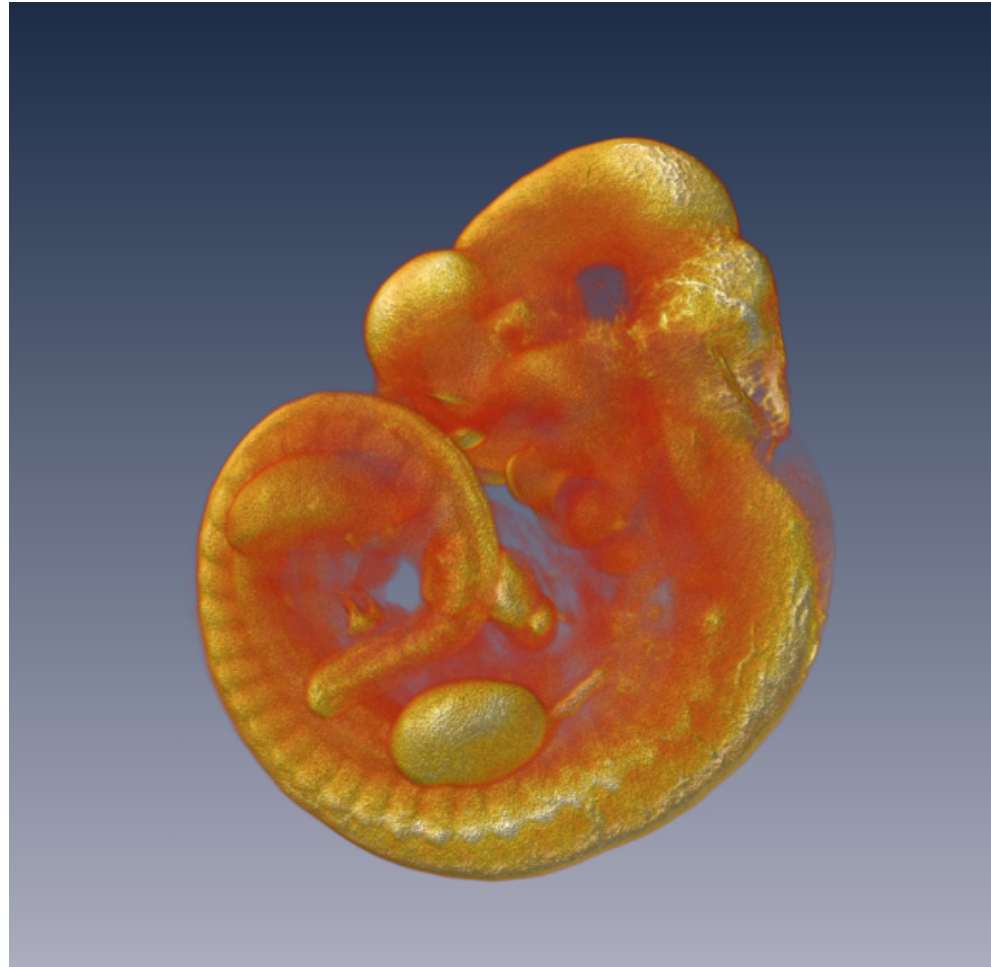


embryo 3
0.626



embryo 4
0.54

- **Intersection/target ratio**



- **Somite number**



TS17 model
35 somite



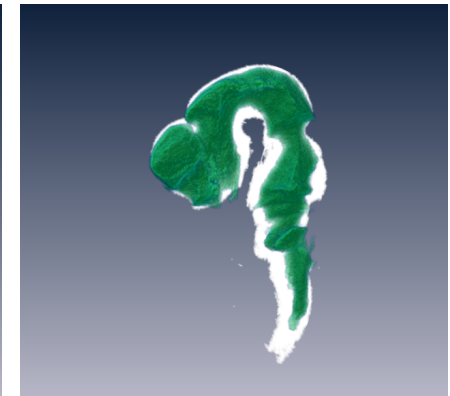
embryo 1
0.884
35 somite



embryo 2
0.787
36 somite



embryo 3
0.626
36 somite

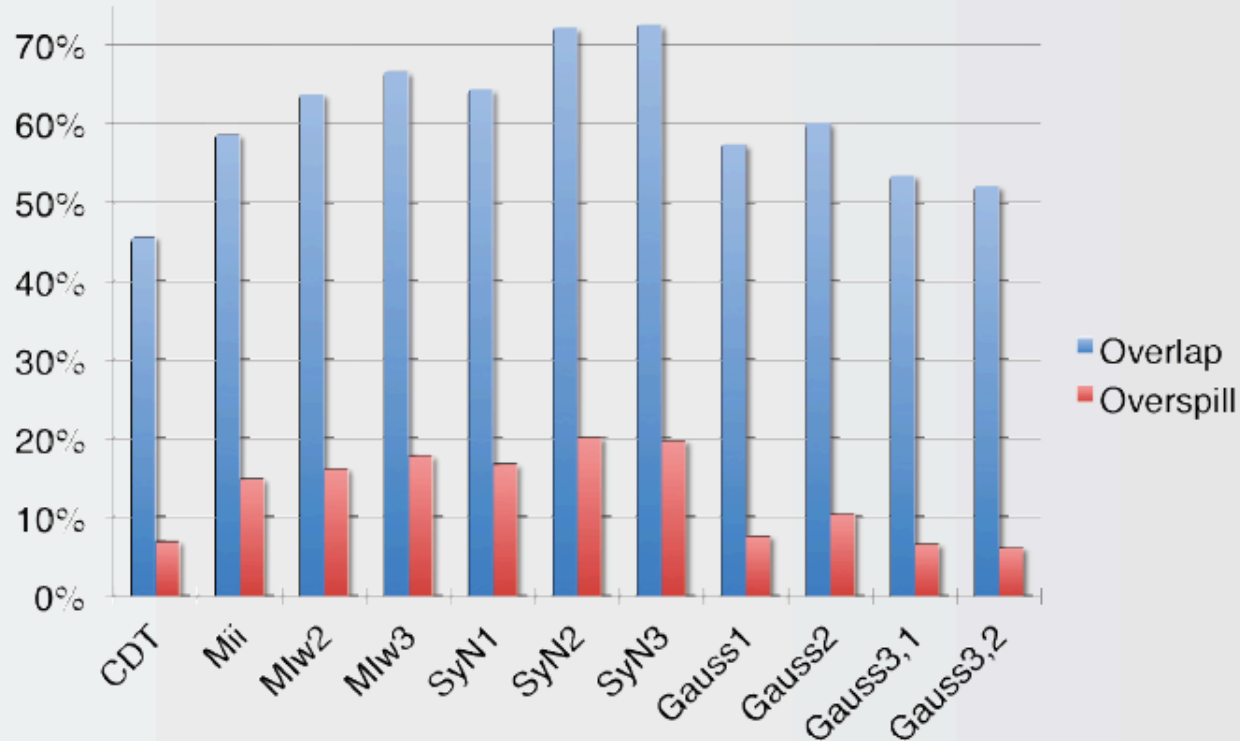


embryo 4
0.54
33 somite

- Similar somite number correlates with success in warping

- **Advanced Normalisation Tools (ANTs)**
- **Image registration tools used primarily for brain mapping**
- **Mutual information similarity matrix is used to match the source object to the target object (in this instance a warped coordinate object)**
- **A diffeomorphic transformation field is generated between source and target**

Optimisation of ANTS Parameters Using Luminal Domains



- **ANTS can improve success in warping**

$$TO_L = (C_V \cap S_V) / C_V$$

$$TO_S = (S_V - (C_V \cap S_V)) / S_V$$

S_V = source volume; C_V = coordinate volume

Transcriptome tomography

- collaboration with Dr Yuko Okamura-Oho (RIKEN)
- lo-res but complete spatial transcriptome of the 14.5dpc mouse embryo



*Specimen 1
frontal*



*Specimen 2
transverse*



*Specimen 3
sagittal*



To generate a 3D map, embryos are serially sectioned in each of three orthogonal planes - frontal, transverse, or sagittal. Gene expression densities are assayed on sectioned samples using Next Gen RNA-Seq. Section reconstructions are registered into the same 3D space to allow tomographic reconstruction.

- Tomography is used to average RNA-Seq densities across samples
- Expression profiles of single transcripts can be viewed as a heatmap

eMouseAtlas

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OPT *in situ* hybridisation

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- Dr Kristen Summerhurst