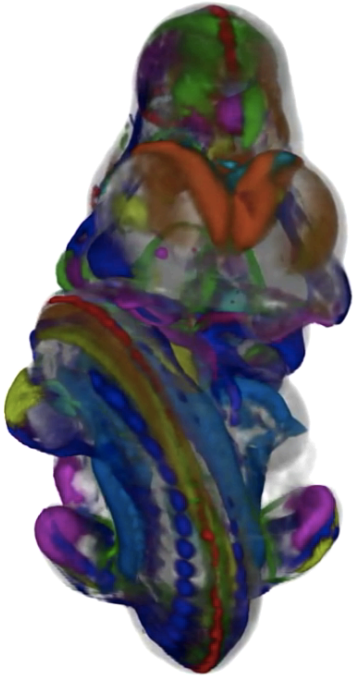
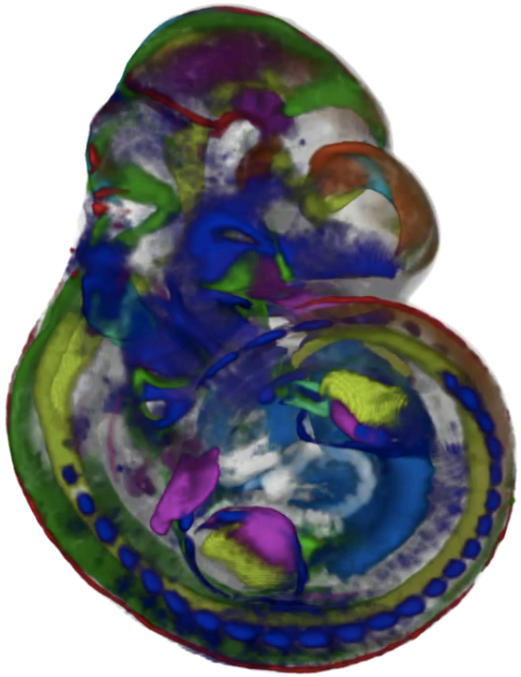
emouseatlas
www.emouseatlas.org

New Dimensions to eMouseAtlas



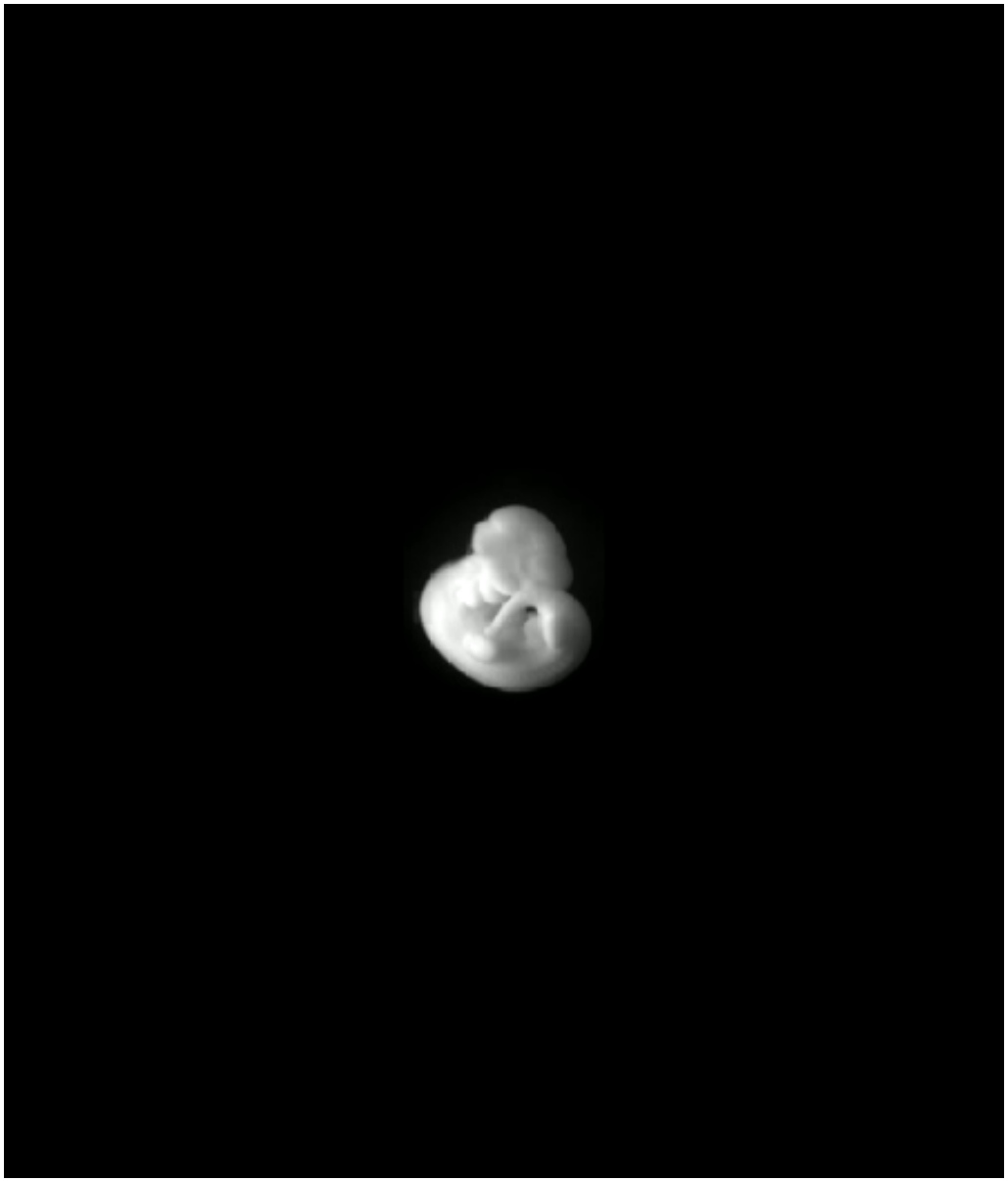


Chris Armit
Senior Editor
EMAGE Database
MRC Human Genetics Unit @ IGMM @ UoE

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

emouseatlas
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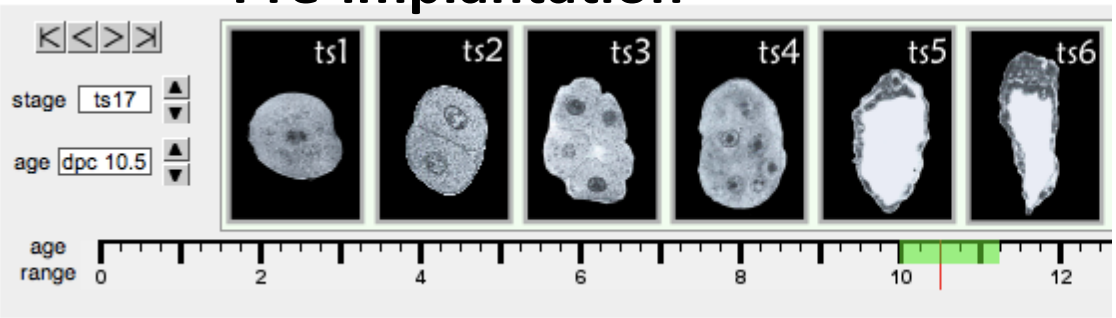
Pre-implantation



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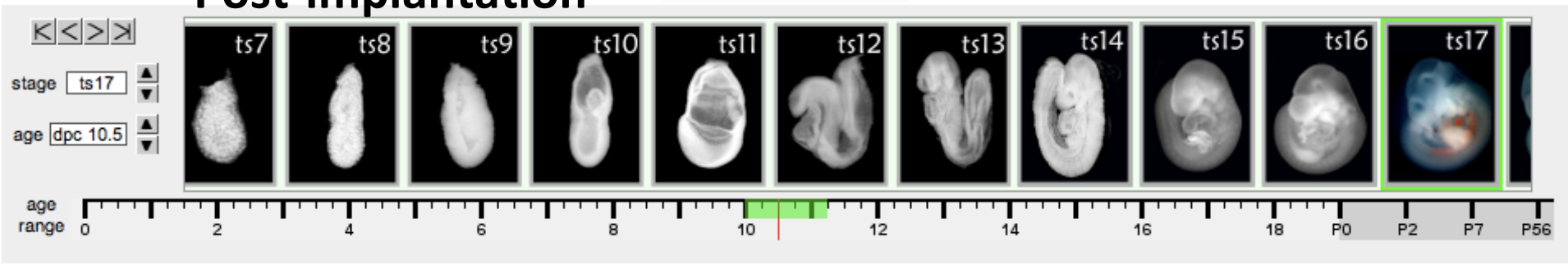

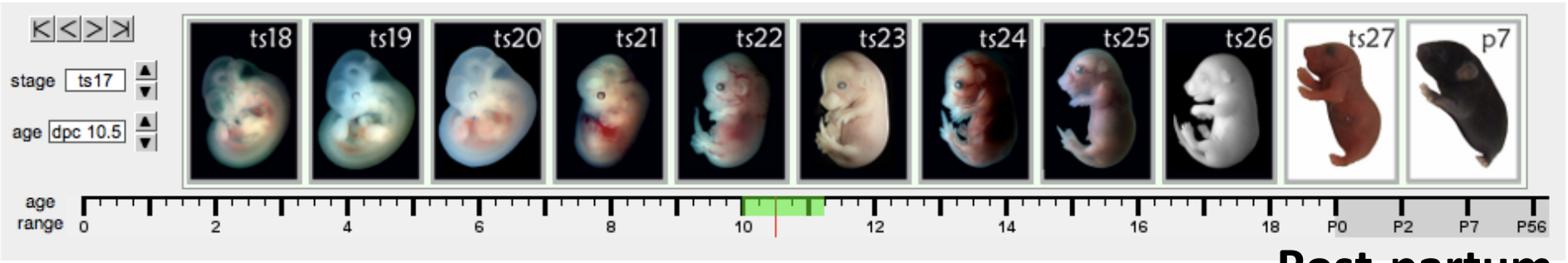

Post-partum

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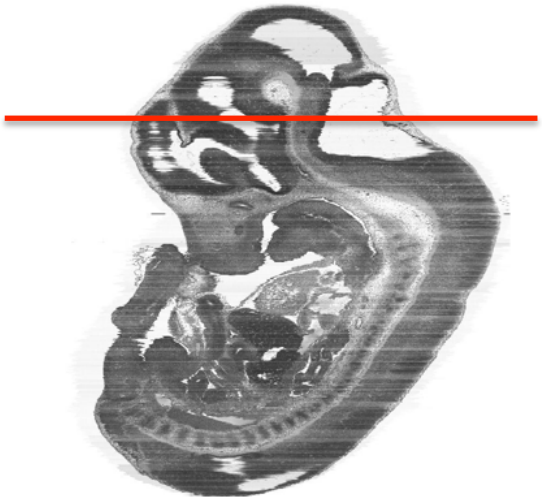

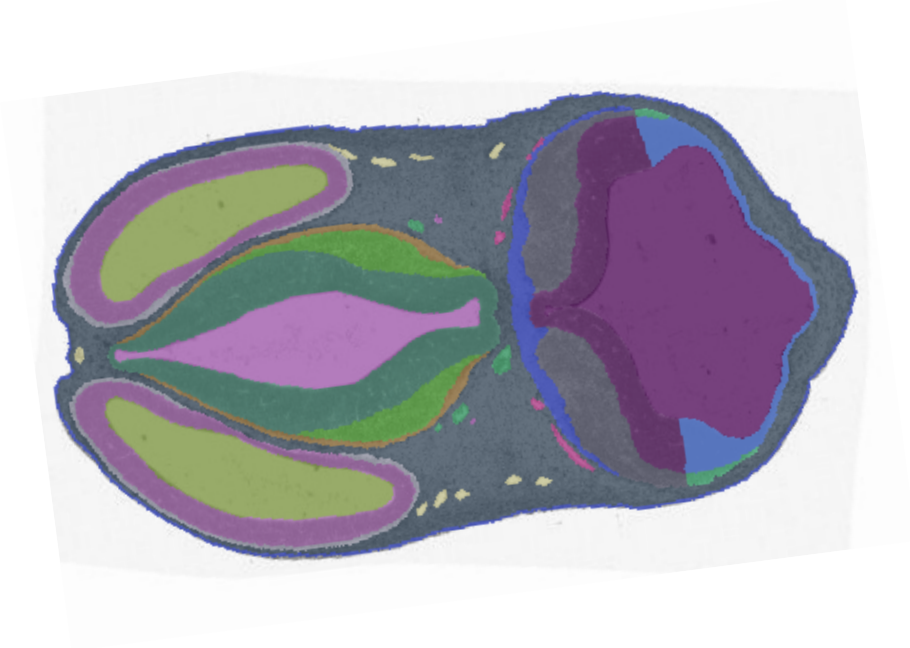

- **Delineated anatomy represented as colour domains**

Emouseatlas
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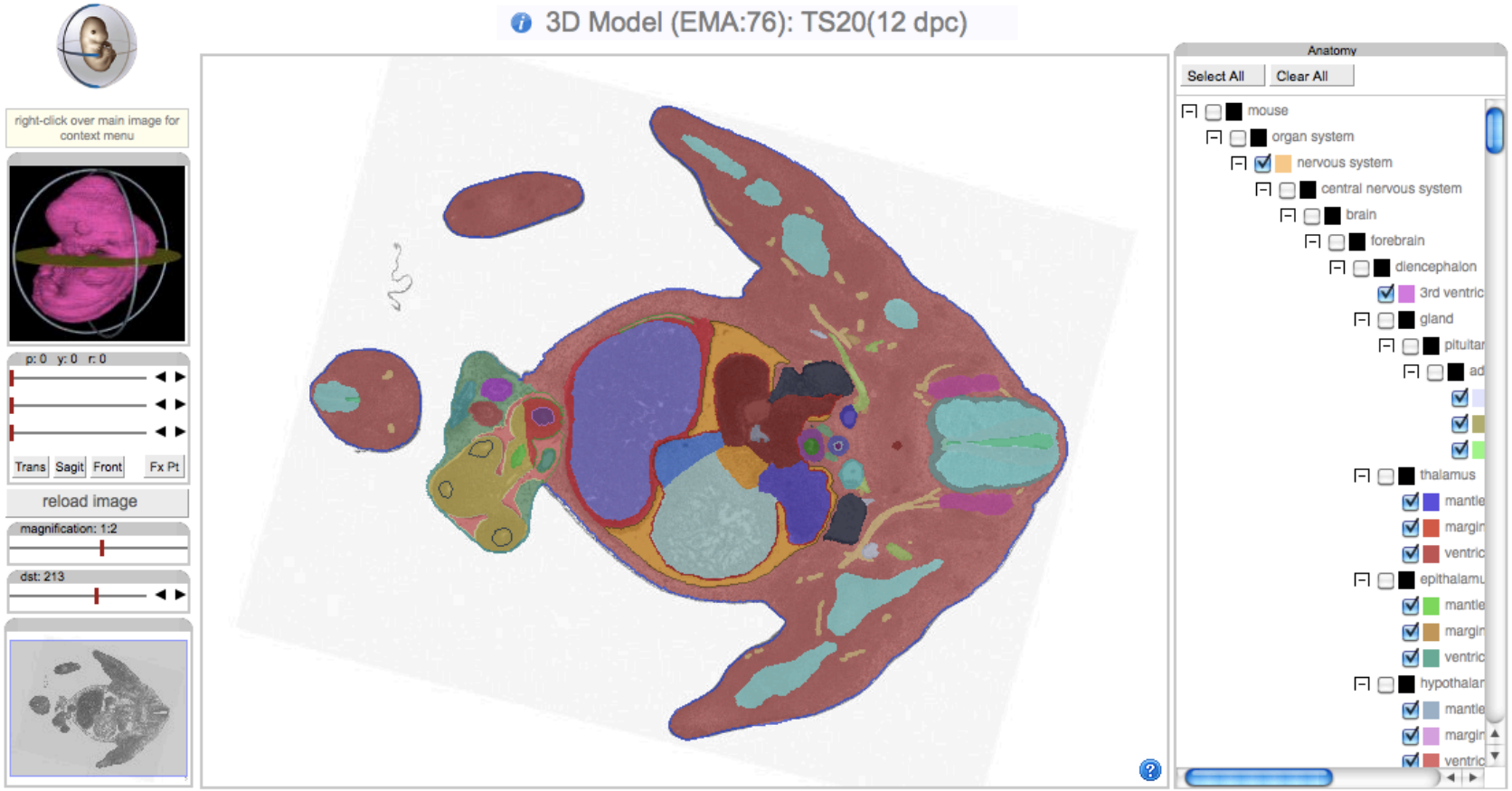

- **Delineated anatomy visualised using interactive IIP3D viewer**

Emouseatlas
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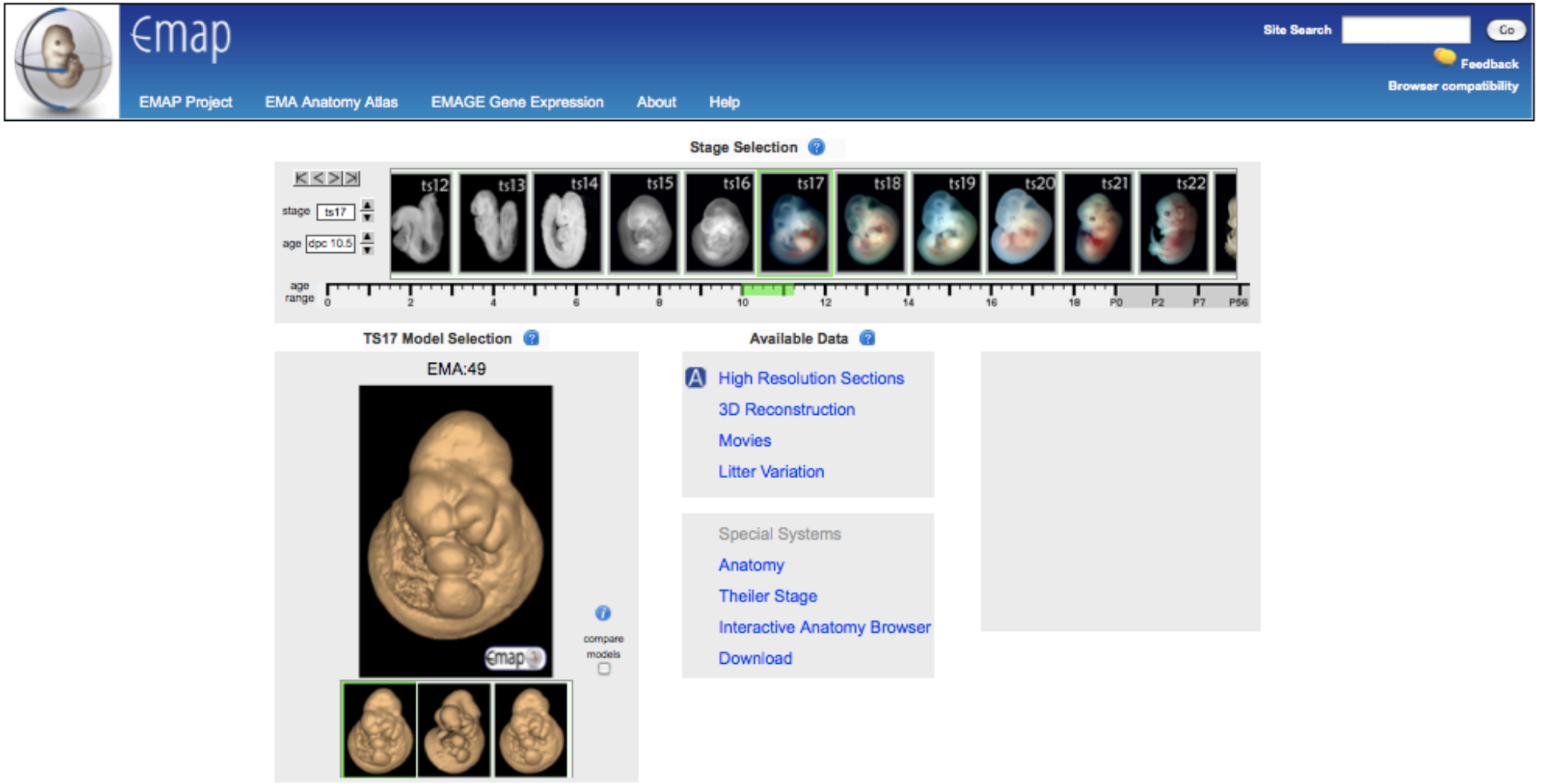

Emouseatlas
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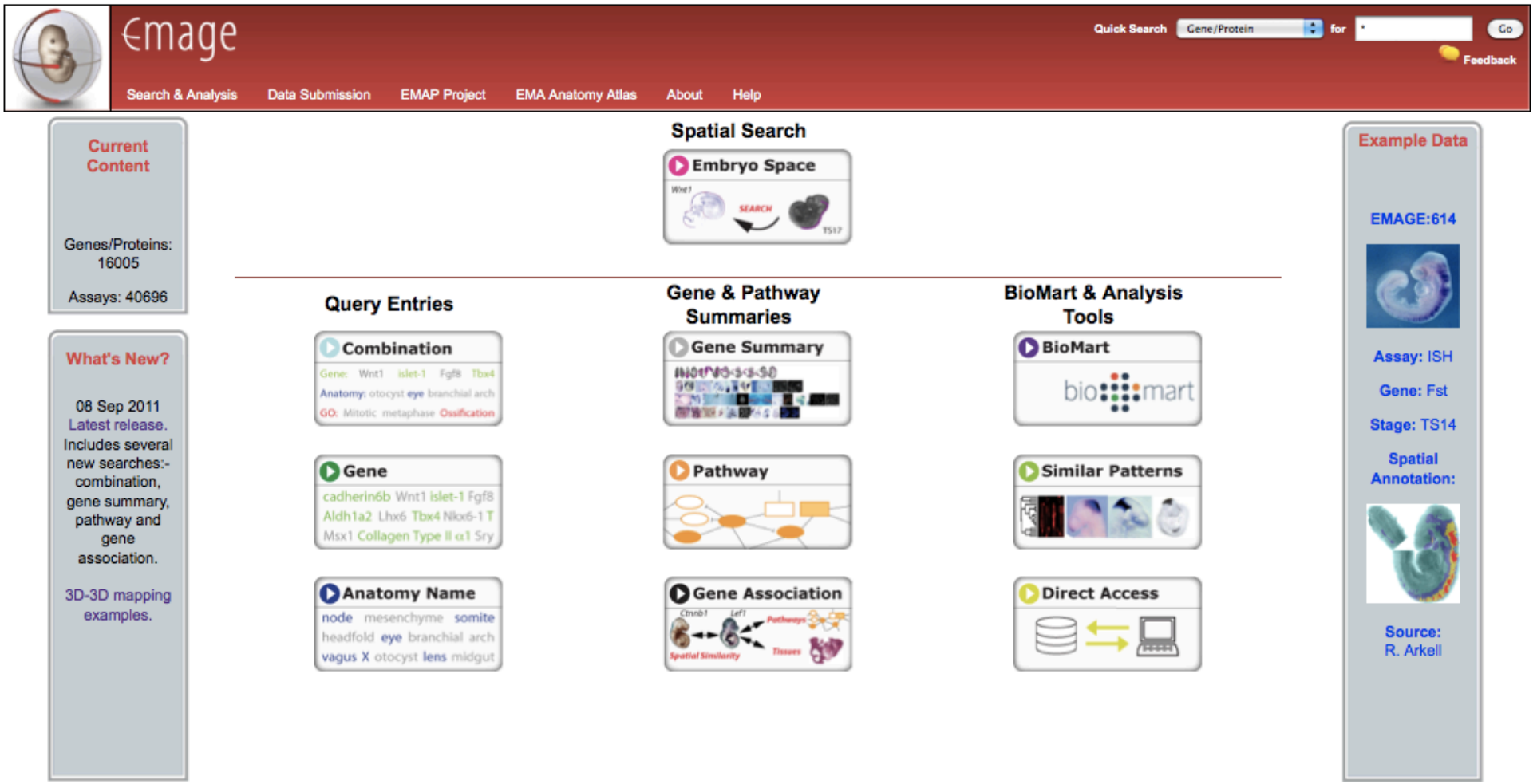
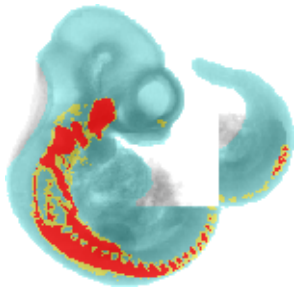
- **EMAGE Gene Expression Database**



- **EMAGE Gene Expression Database**

emouseatlas
www.emouseatlas.org

- ***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.

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- **EMAGE Gene Expression Database**

Query Entries

Combination

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

Gene

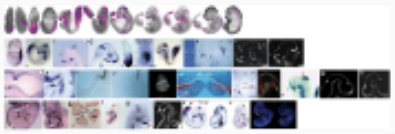
cadherin6b Wnt1 islet-1 Fgf8
Aldh1a2 Lhx6 Tbx4 Nkx6-1 T
Msx1 Collagen Type II α1 Sry

Anatomy Name

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

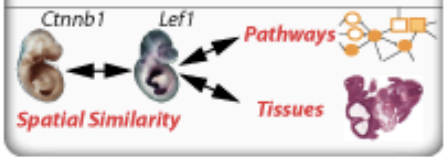
Gene & Pathway Summaries

Gene Summary



Pathway

Gene Association



BioMart & Analysis Tools

BioMart

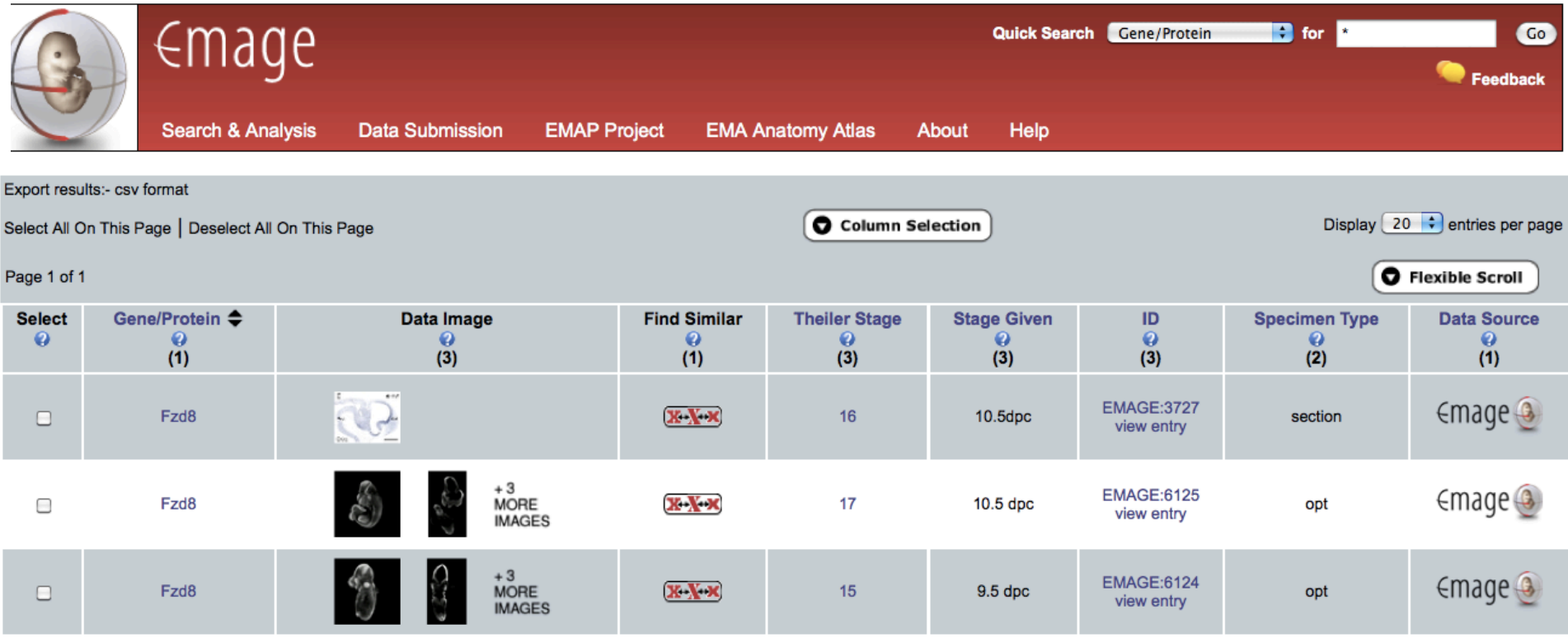
biomart

Similar Patterns

Direct Access

Emouseatlas
www.emouseatlas.org

- **EMAGE Gene Expression Database**



Emage

Quick Search Gene/Protein for * Go

Feedback

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 (1)	Data Image (3)	Find Similar (1)	Theiler Stage (3)	Stage Given (3)	ID (3)	Specimen Type (2)	Data Source (1)
☐	Fzd8			16	10.5dpc	EMAGE:3727 view entry	section	Emage
☐	Fzd8	+ 3 MORE IMAGES		17	10.5 dpc	EMAGE:6125 view entry	opt	Emage
☐	Fzd8	+ 3 MORE IMAGES		15	9.5 dpc	EMAGE:6124 view entry	opt	Emage

Emouseatlas
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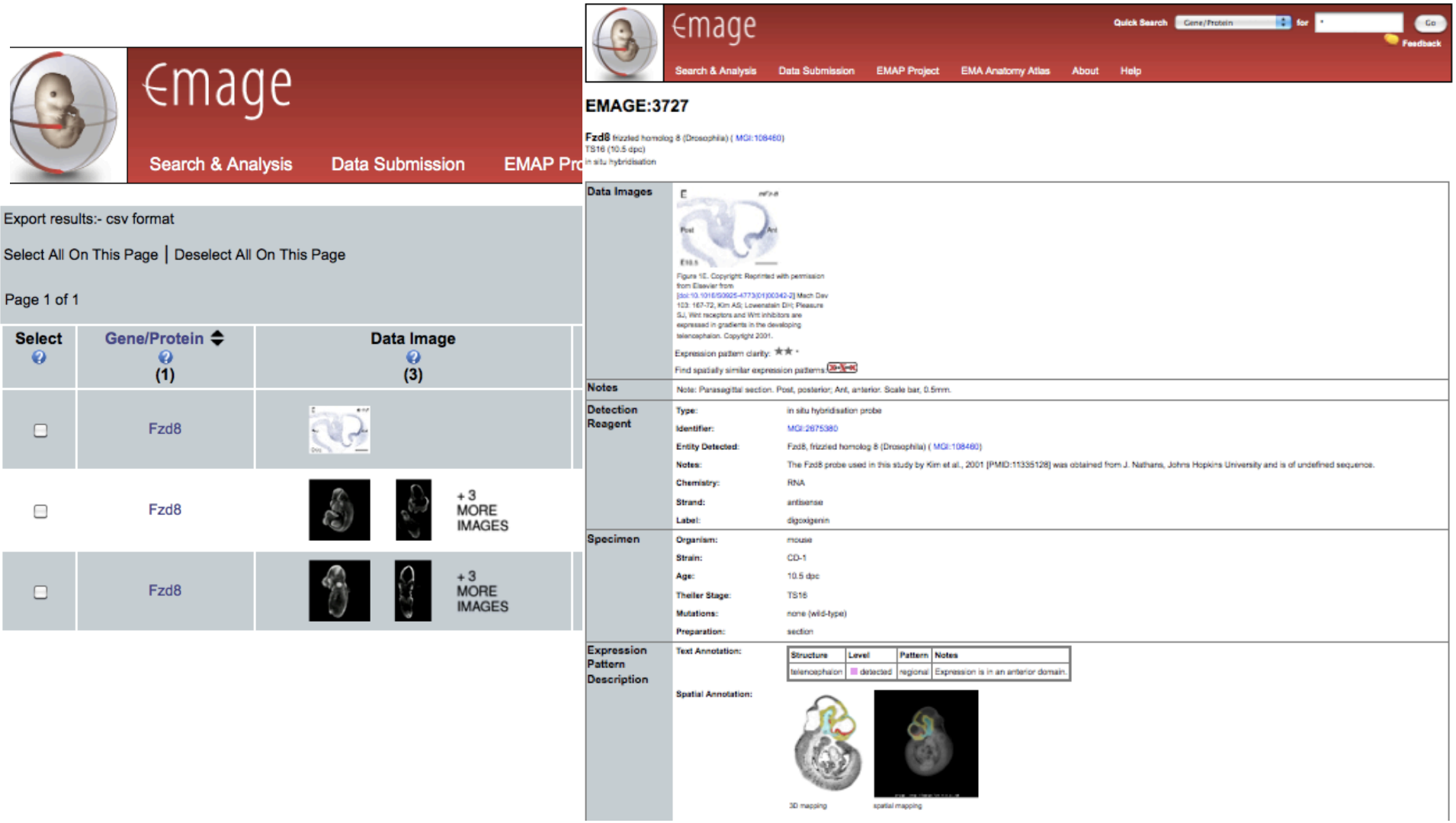
- **EMAGE Gene Expression Database**



- **EMAGE Gene Expression Database**

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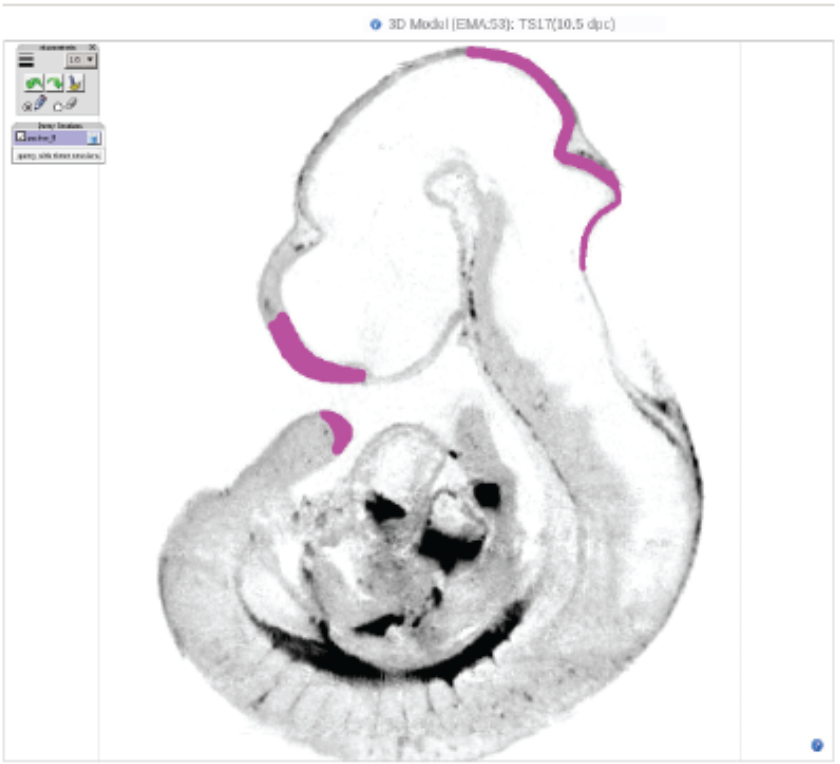
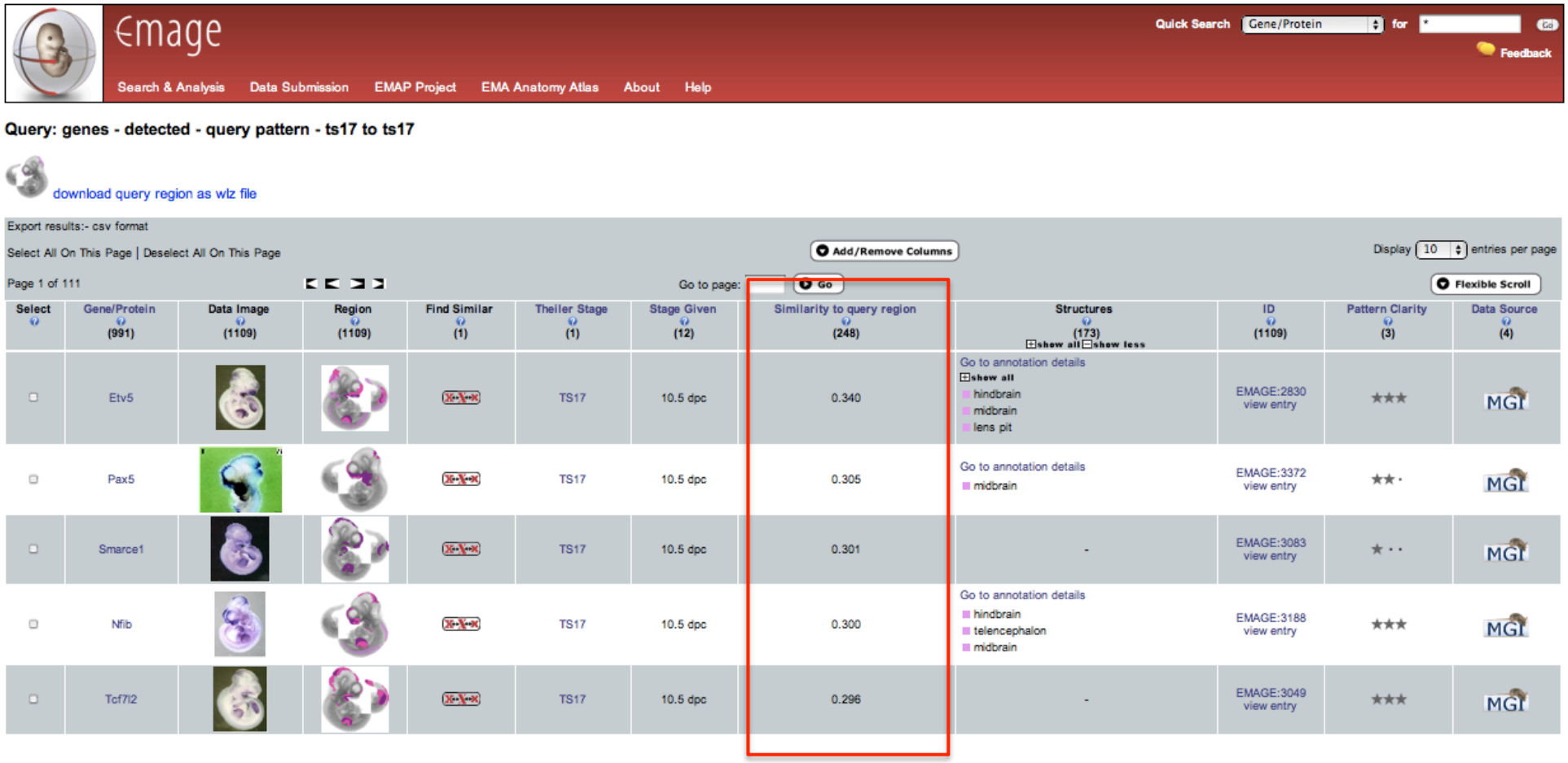


- **Using the Paint Tool is one method of generating a spatial query**

- **EMAGE Gene Expression Database**

Emouseatlas
www.emouseatlas.org



Emage

Quick Search | Gene/Protein | for | * | Go | Feedback

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 | Add/Remove Columns | Display 10 entries per page

Page 1 of 111 | Go to page: | Go | Flexible Scroll

Select	Gene/Protein (991)	Data Image (1109)	Region (1109)	Find Similar (1)	Theiler Stage (1)	Stage Given (12)	Similarity to query region (248)	Structures (173) show all / show less	ID (1109)	Pattern Clarity (3)	Data Source (4)
☐	Etv5				TS17	10.5 dpc	0.340	Go to annotation details; show all; hindbrain; midbrain; lens pit	EMAGE:2830 view entry	★★★	MGI
☐	Pax5				TS17	10.5 dpc	0.305	Go to annotation details; midbrain	EMAGE:3372 view entry	★★·	MGI
☐	Smarce1				TS17	10.5 dpc	0.301	-	EMAGE:3083 view entry	★··	MGI
☐	Nfib				TS17	10.5 dpc	0.300	Go to annotation details; hindbrain; telencephalon; midbrain	EMAGE:3188 view entry	★★★	MGI
☐	Tcf7l2				TS17	10.5 dpc	0.296	-	EMAGE:3049 view entry	★★★	MGI

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

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

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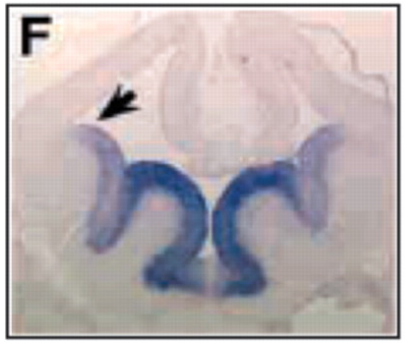
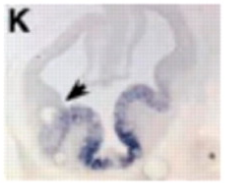
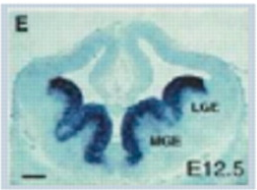
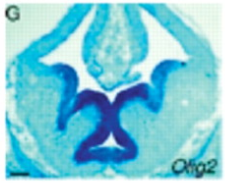
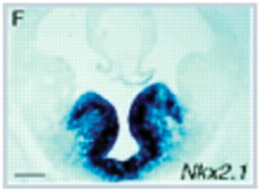


QUERY PATTERN

RESULT:

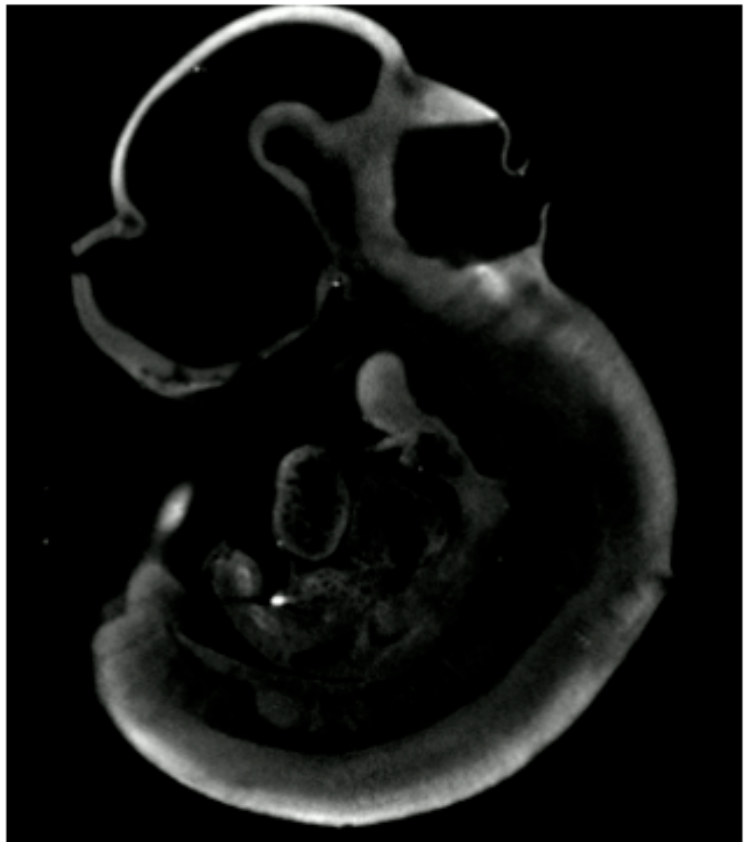
SPATIALLY SIMILAR PATTERNS

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

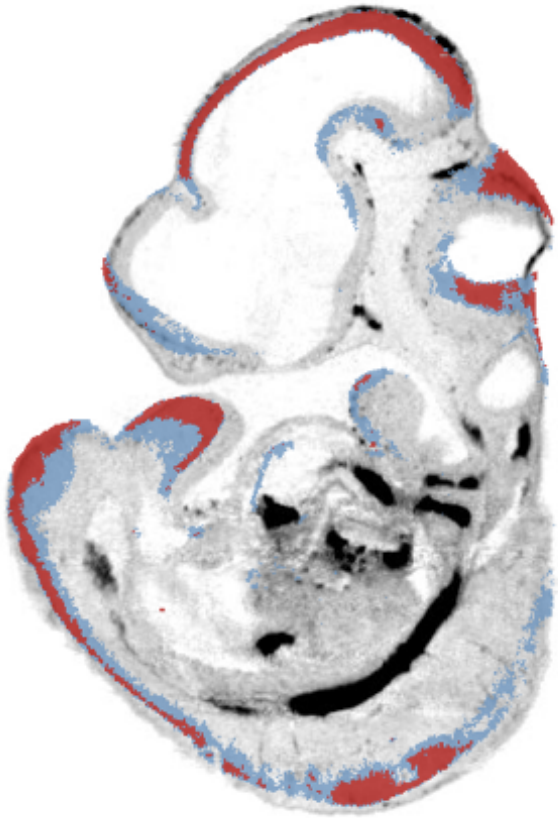
Richardson L et al. Nucl. Acids Res. 2010;38:D703-D709

Optical Projection Tomography (OPT)

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



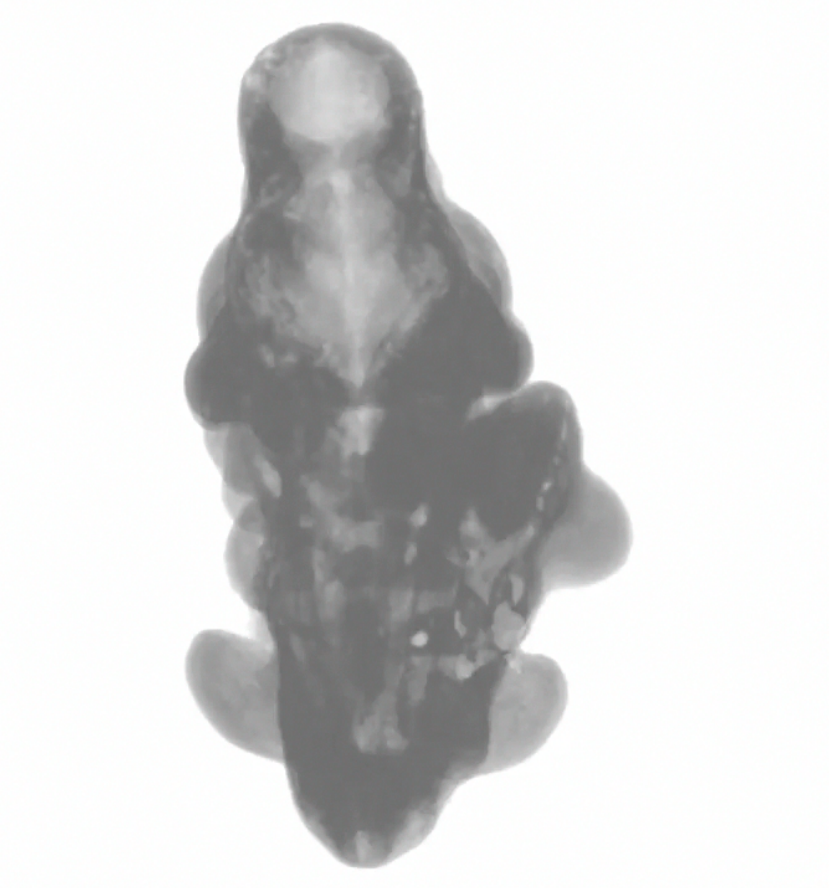
Fzd10
Theiler stage (TS) 17



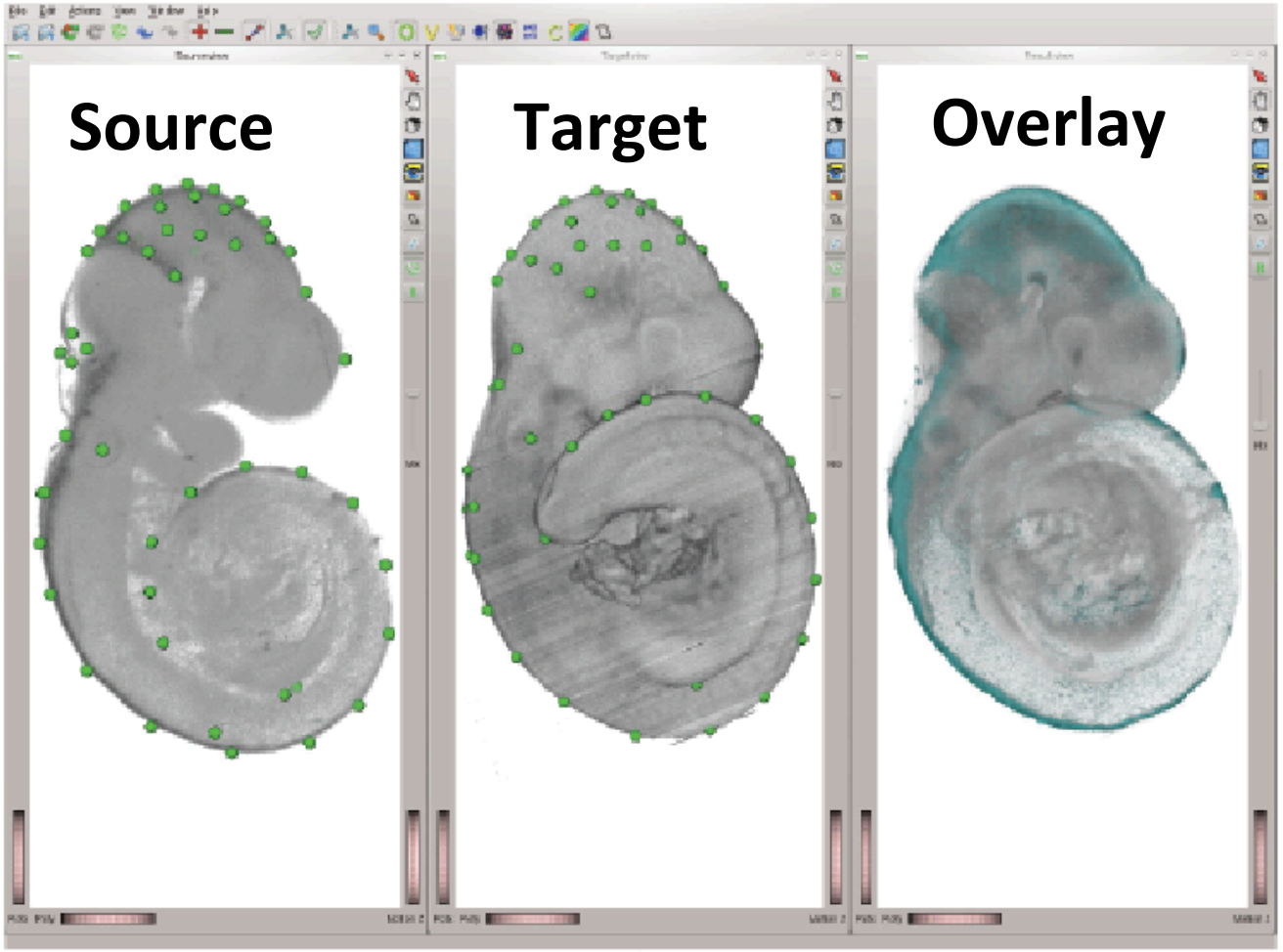
Map of Fzd10
eMouseAtlas TS17 model

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

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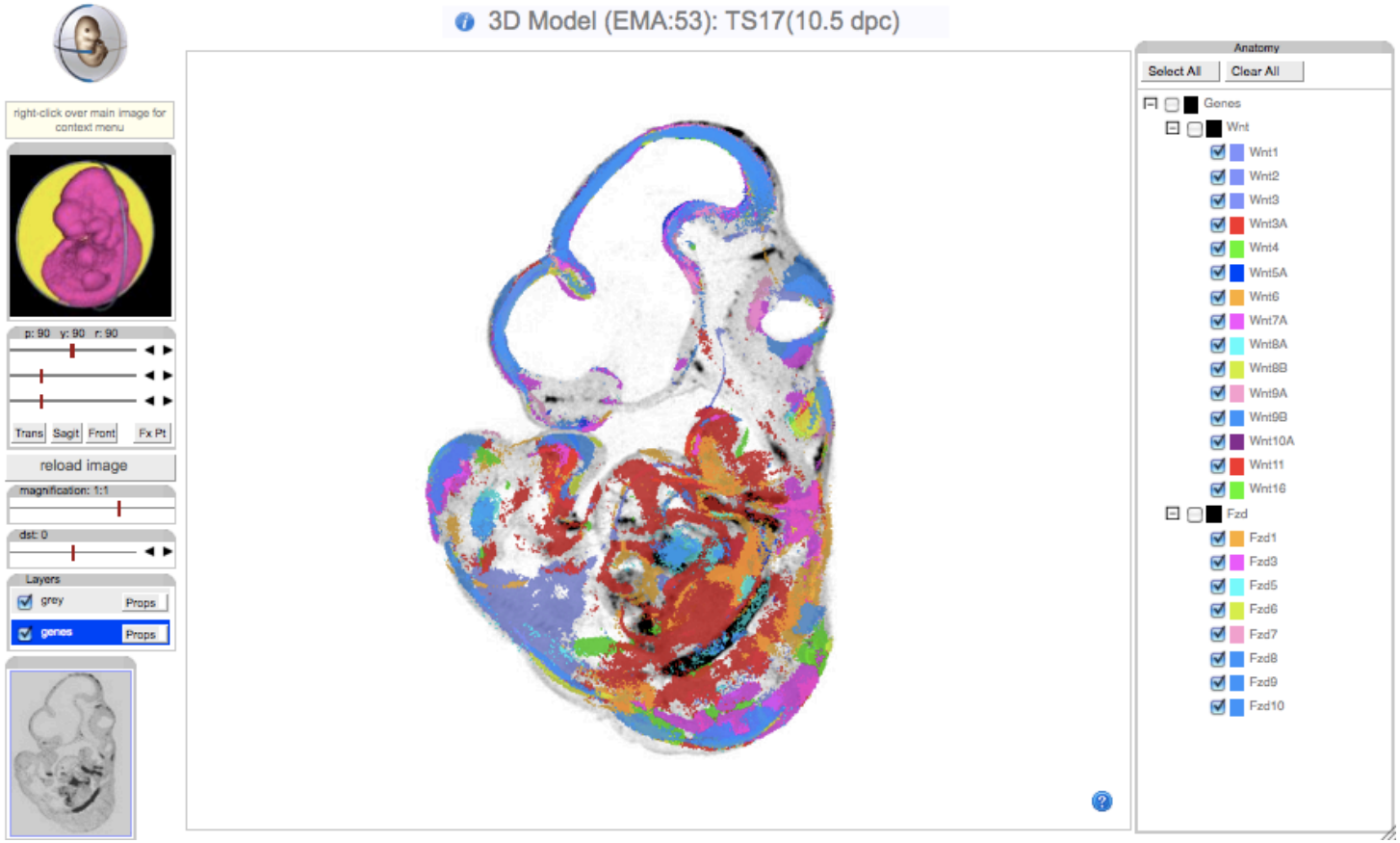

- **Maps of *in situ* hybridisation OPT gene expression patterns visualised using IIP3D viewer**

Emouseatlas
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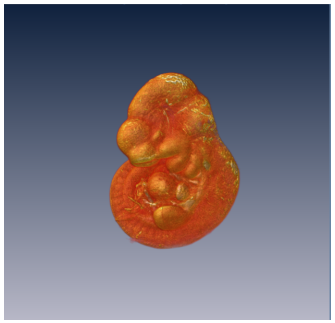
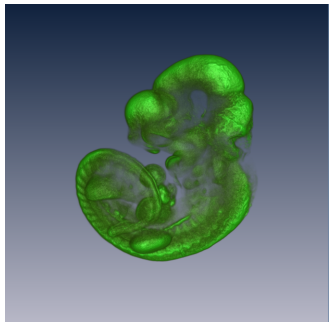
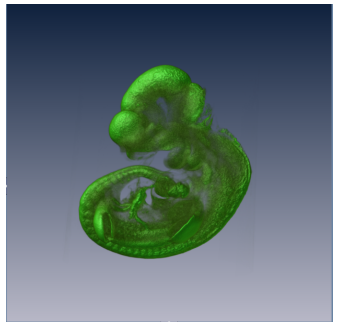


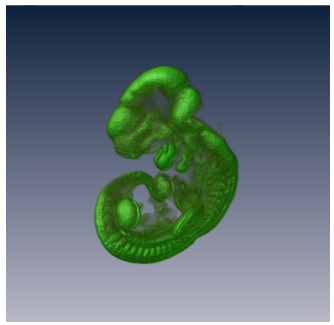
TS17 model



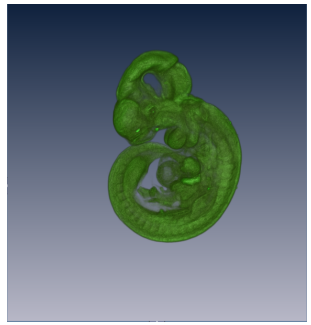
embryo 1



embryo 2



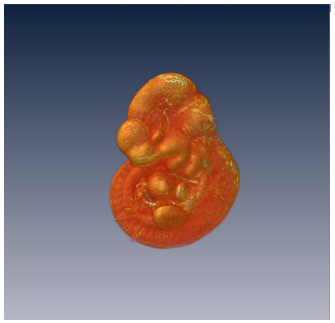
embryo 3



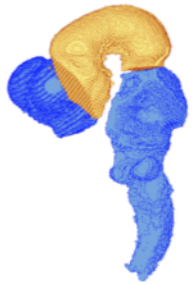
embryo 4

- **Quantitative assessment of 3D mapping**

Emouseatlas
www.emouseatlas.org



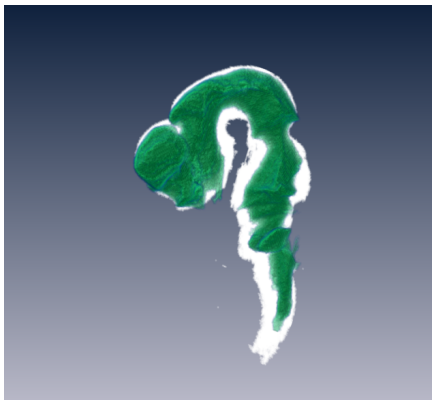
TS17 model



embryo 1

embryo 2

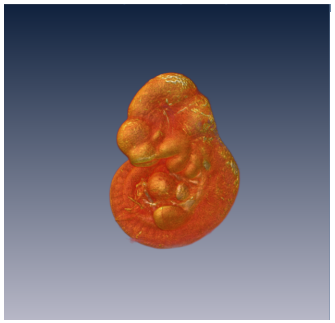
embryo 3



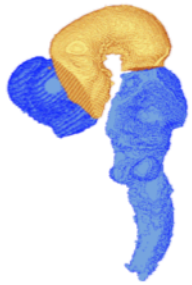
embryo 4

- **Quantitative assessment of 3D mapping**

Emouseatlas
www.emouseatlas.org



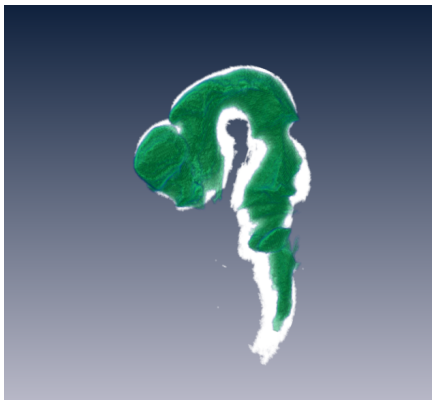
TS17 model



embryo 1
0.884

embryo 2
0.787

embryo 3
0.626



embryo 4
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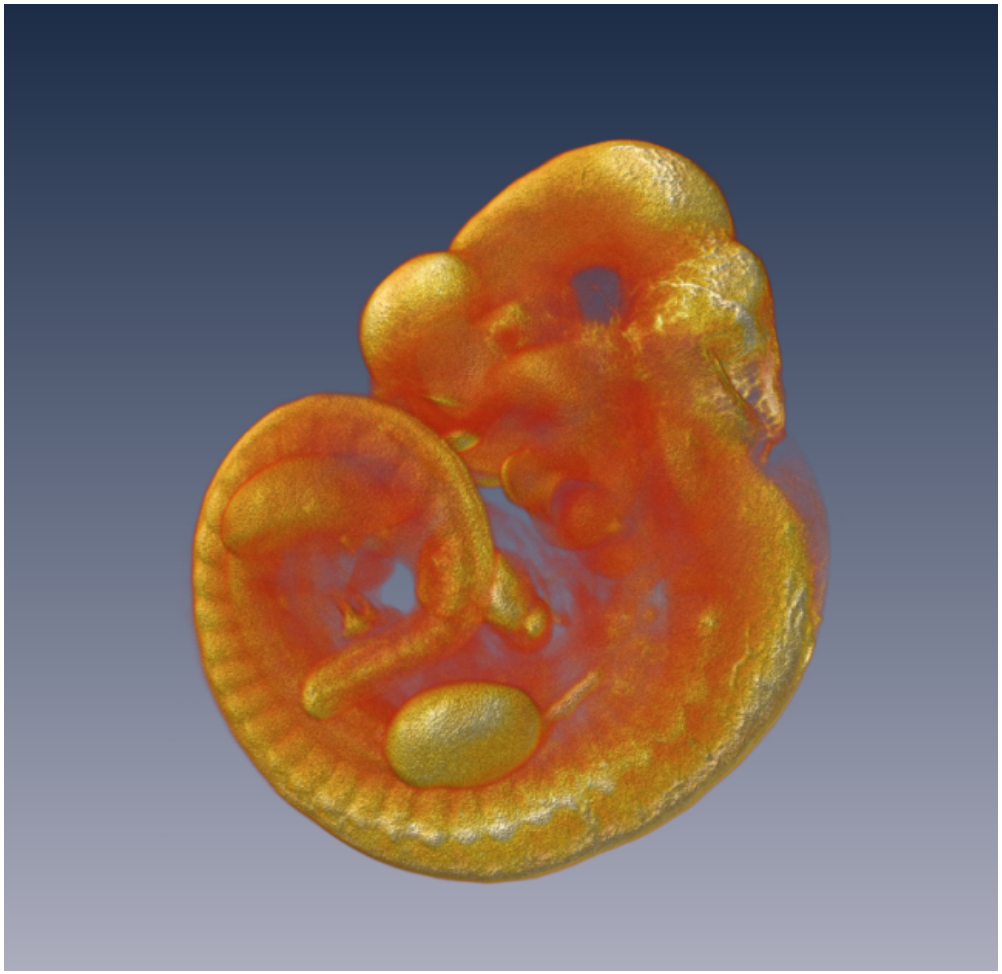
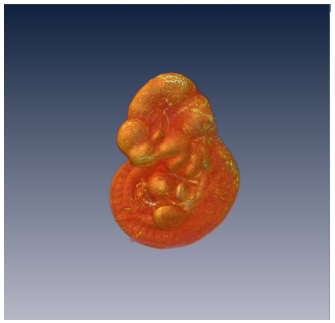
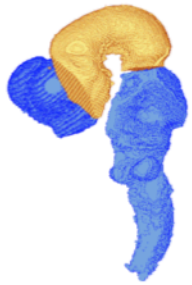
- **Intersection/target ratio**



- **Somite number**

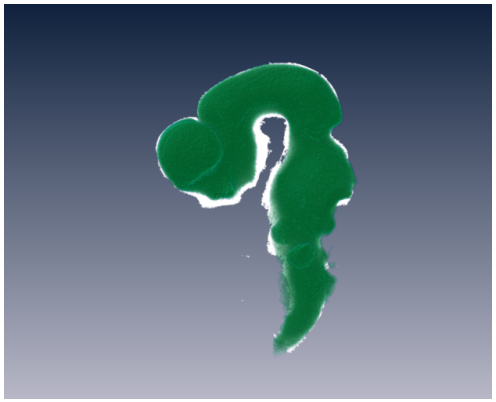
Emouseatlas
www.emouseatlas.org





TS17 model

35 somite



embryo 1

0.884

35 somite

embryo 2

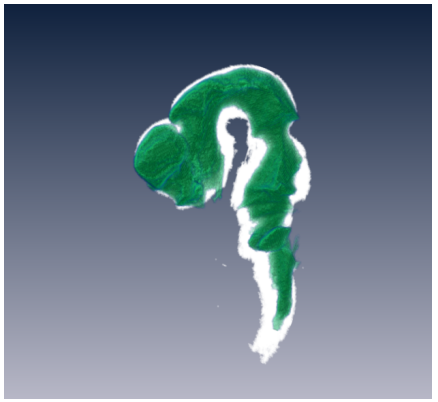
0.787

36 somite

embryo 3

0.626

36 somite



embryo 4

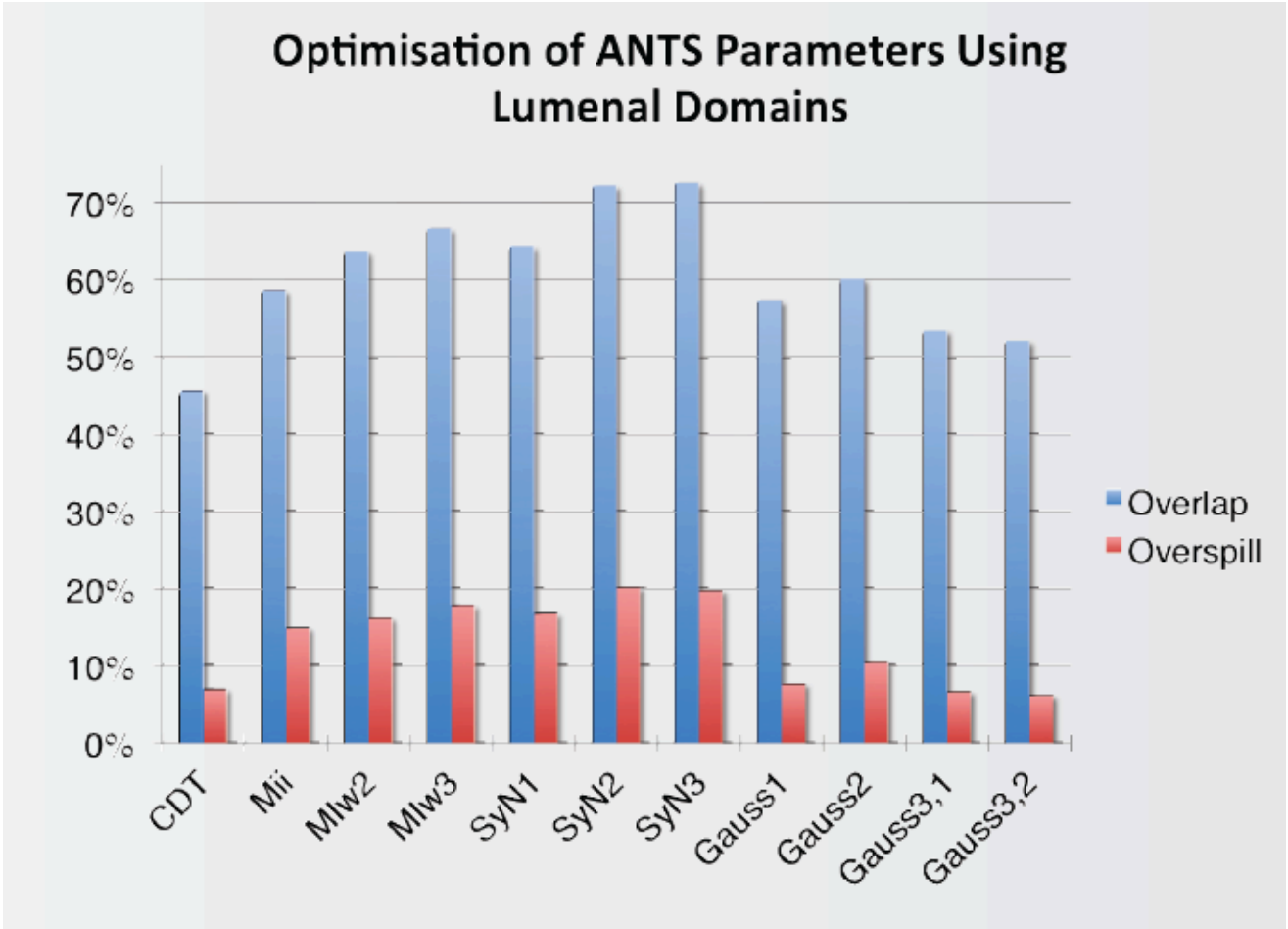
0.54

33 somite

- **Similar somite number correlates with success in warping**

emouseatlas
www.emouseatlas.org

- **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**



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

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

S_V = source volume; C_V = coordinate volume

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- **ANTS can improve success in warping**

Transcriptome tomography

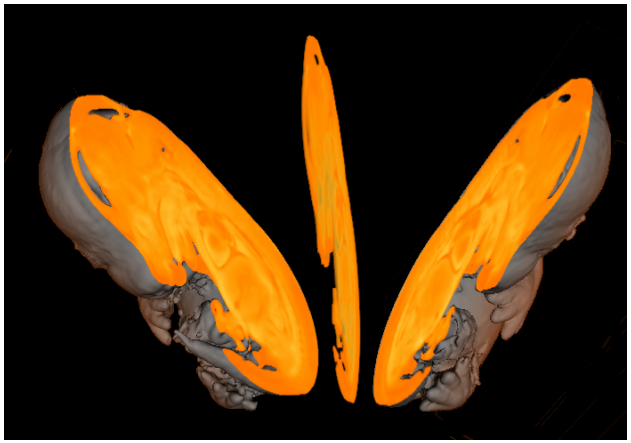
- collaboration with Dr Yuko Okamura-Oho (RIKEN)
- lo-res but complete spatial transcriptome of the 14.5dpc mouse embryo

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

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