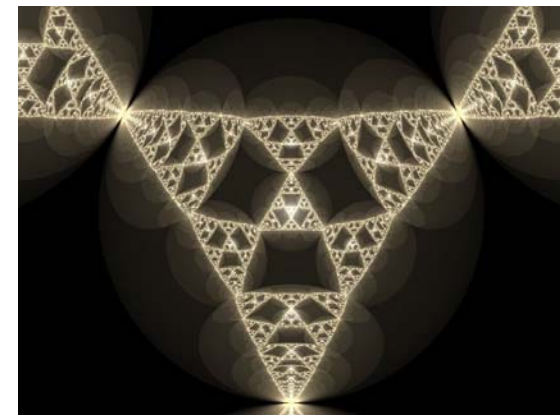


Knowledge base for v-Embryo:



information infrastructure for *in silico* modeling

Singh² AV, Shah¹ I, Kavlock¹ RJ, and Knudsen¹ TB

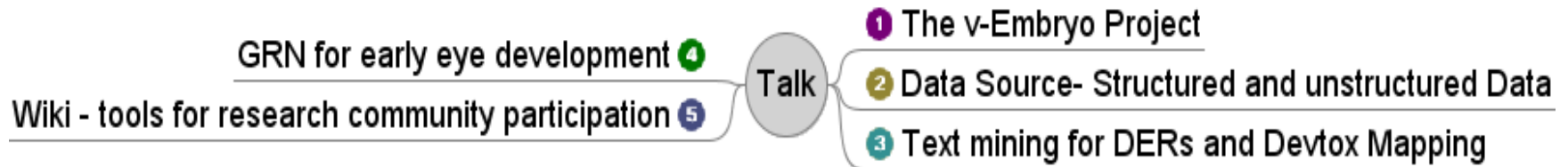
¹National Center for Computational Toxicology - EPA

²Lockheed Martin
Research Triangle Park, NC

Teratology Society, July 2, 2008 - Monterey CA

DISCLAIMER: views reflect those of the presenter and not EPA policy; any reference to commercial products or tradenames does not constitute endorsement

1 The Virtual Embryo Project

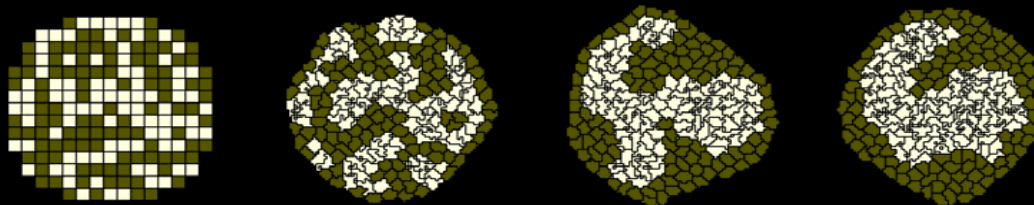


- ❖ “... far reaching new research program to develop a sophisticated computer model of a (mammalian) embryo ...” - *Risk Policy Report, Vol 15, No.2 - January 8 2008*
- ❖ virtual tissues and artificial life simulators as models to study morphogenesis and predict defects *in silico*
- ❖ addresses how mechanisms at one scale (cellular) interact to produce higher level (tissue) phenomena

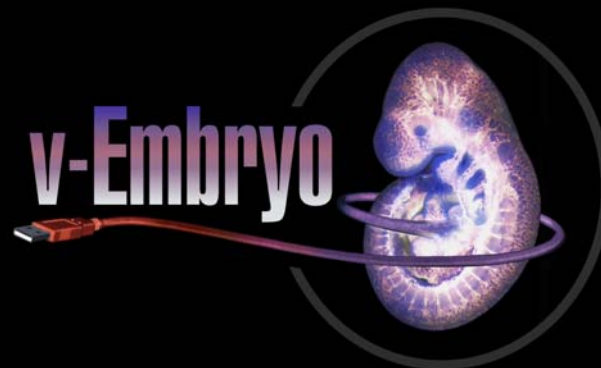
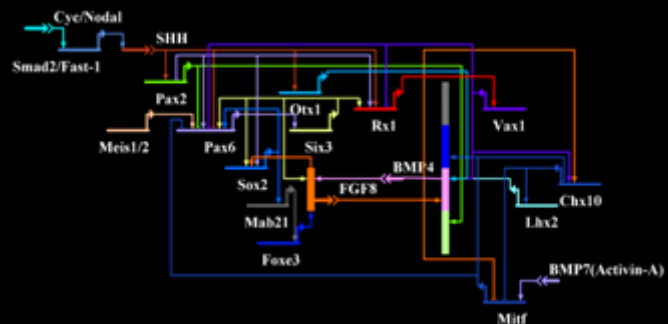
traditional prenatal studies



artificial life simulators



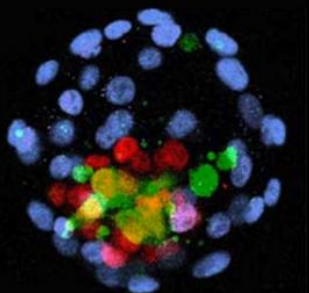
developmental pathways



HTP screening assays

stem cells

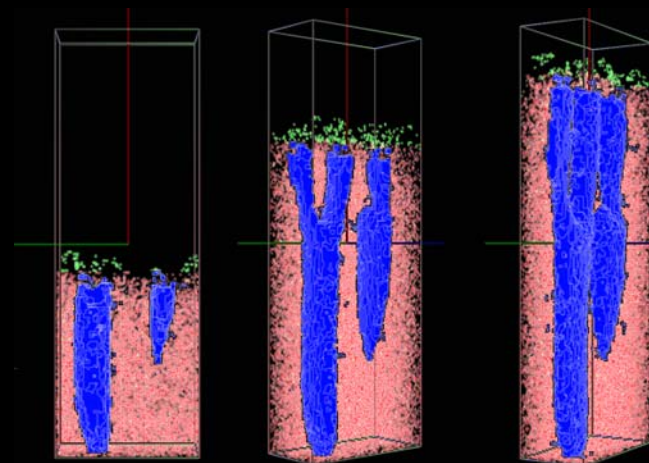
Z-fish embryos



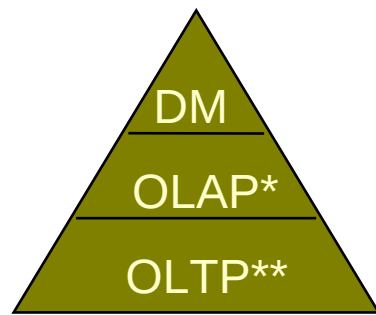
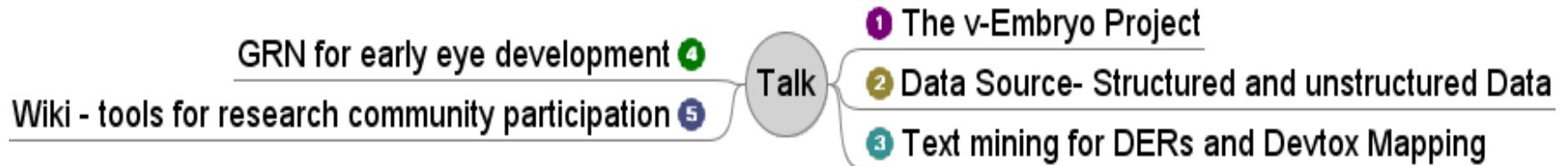
ToxCast™ & BDSM



in silico morphogenesis (CC3D)



2 Data Sources

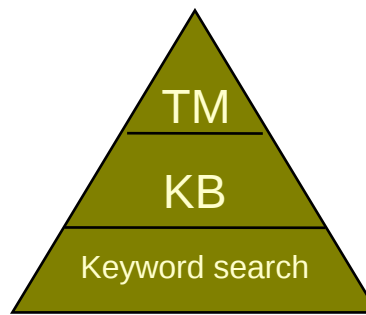


structured data

* Online analytical processing

**Online transaction processing

+



unstructured data

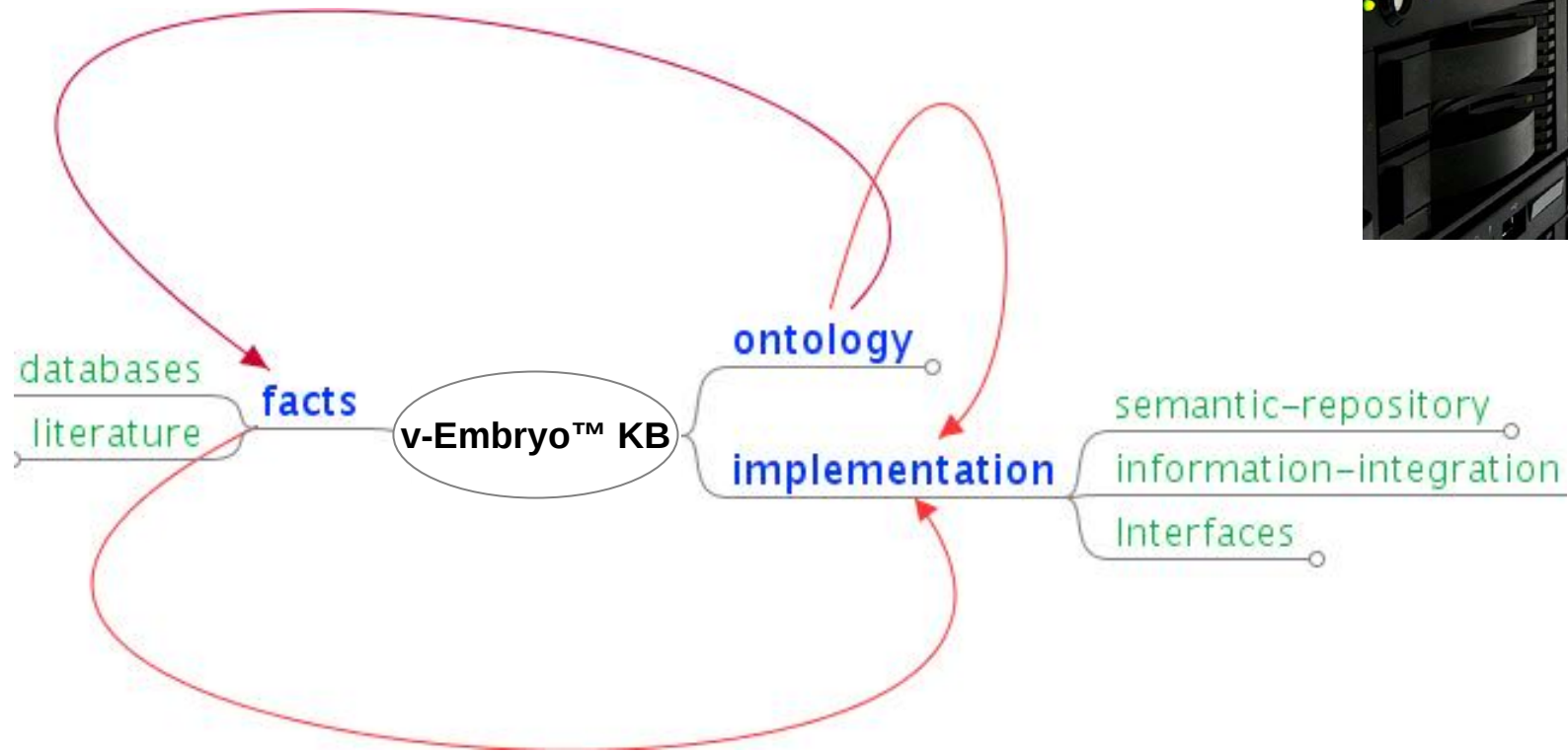
=

- Summarization
- Classification
- Clustering
- Ontologies
- NLP
- Concepts
- Correlations
- Causality

- databases
- computable
- easier to manage
- QA/QC curation
- semantics/metadata
- *accurate but slow*

- non-uniform format (literature)
- algorithms needed to put in computable form
- difficult to manage and control
- noisy (filtering becomes essential)
- ambiguous - **cricket the game** or **cricket the bug**?
- *preliminary but fast*

Information infrastructure: normal and abnormal embryogenesis



Source: Imran Shah, NCCT – EPA

3

4

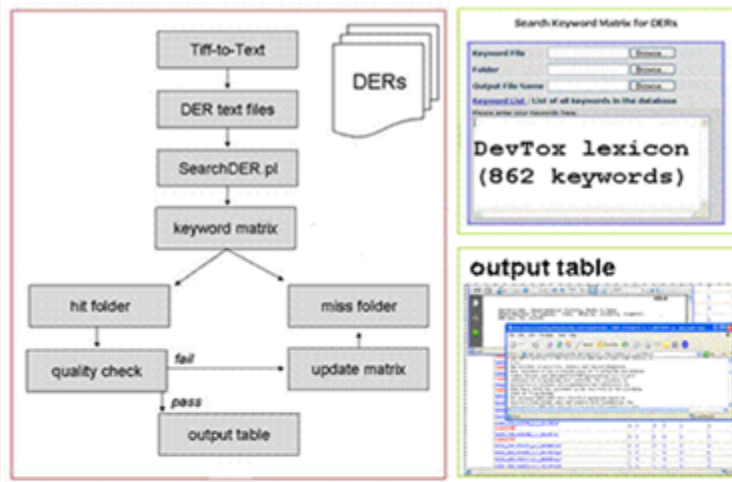
5

Talk

1 The v-Embryo Project

2 Data Source- Structured and unstructured Data

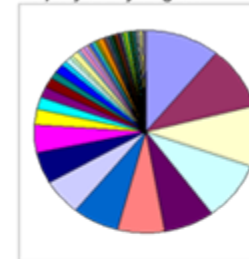
3 Text mining for DERs and Devtox Mapping



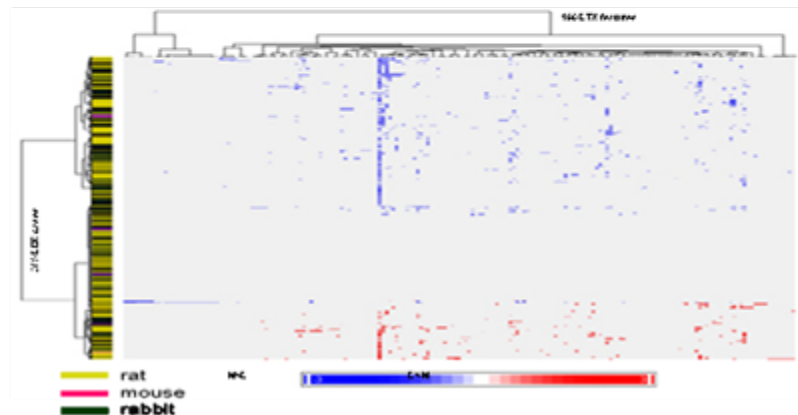
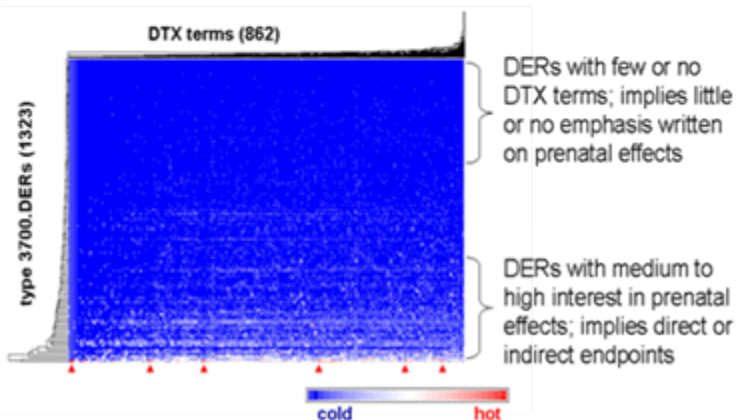
862 DTX keywords run through 1323 prenatal DERs

HRs	Rat	Mouse	Rabbit	Hamster	Total
DER counts	461	20	394	3	878
Feature counts	1705	28	493	3	2229
Features / DER	3.70	1.40	1.25	1.00	2.54

displayed by region

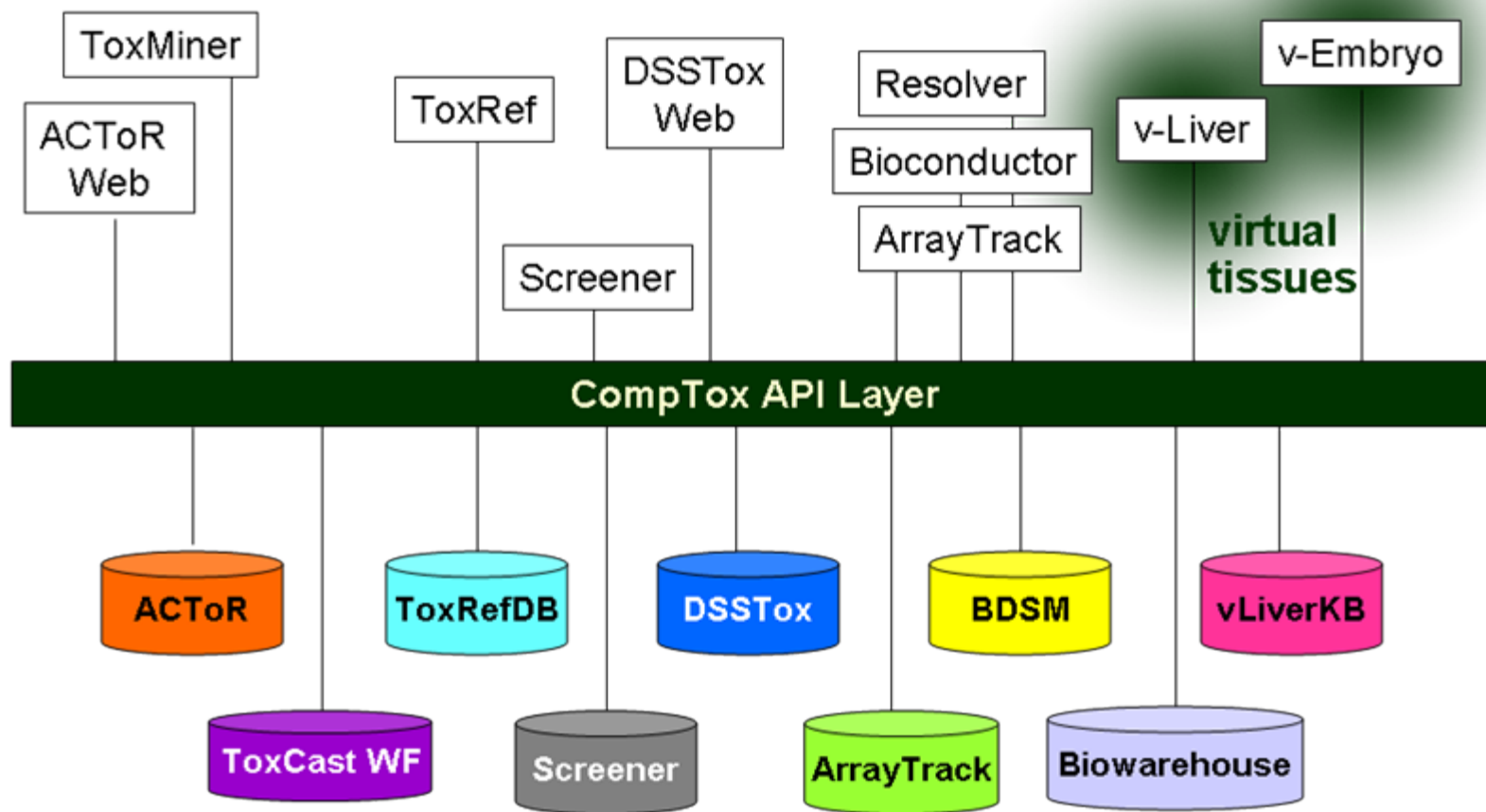


ranked by phenotype

[illegible]

EPA's COMPTOX APPLICATION FRAMEWORK

developmental toxicity module ported from BDSM*



SOURCE: Richard Judson, NCCT

***Singh et al. (2005) Computational systems analysis of developmental toxicity: design, development and implementation of a birth defects systems manager (BDSM). Reprod Toxicol 19:421-439**

Gene regulatory networks

GRN for early eye development 4

Wiki - tools for research community participation 5

Talk

1 The v-Embryo Project

2 Data Source- Structured and unstructured Data

3 Text mining for DERs and Devtox Mapping

emap <http://genex.hgu.mrc.ac.uk/> 3D digital atlas | TS14

HOME 3D DIGITAL ATLAS EMAGE DATABASE RESOURCES CONTACT SITE SEARCH

☐ 3D Navigation ☒ Navigation Window ☒ Section Window ☒ Anatomy Window Theiler Stage **TS14**

No component selected

TS14

- embryo
 - branchial arch
 - cavities and their linings
 - ectoderm
 - limb
 - mesenchyme
 - notochord*
 - organ system
 - cardiovascular system
 - nervous system
 - sensory organ
 - ear
 - eye**
 - nose
 - visceral organ
 - primitive streak
 - tail bud
 - extraembryonic component*

< Contract Expand >

More Theiler 14 (E9) resources:

[Information on this model](#) [Help with the Browsers](#) [FAQ](#)

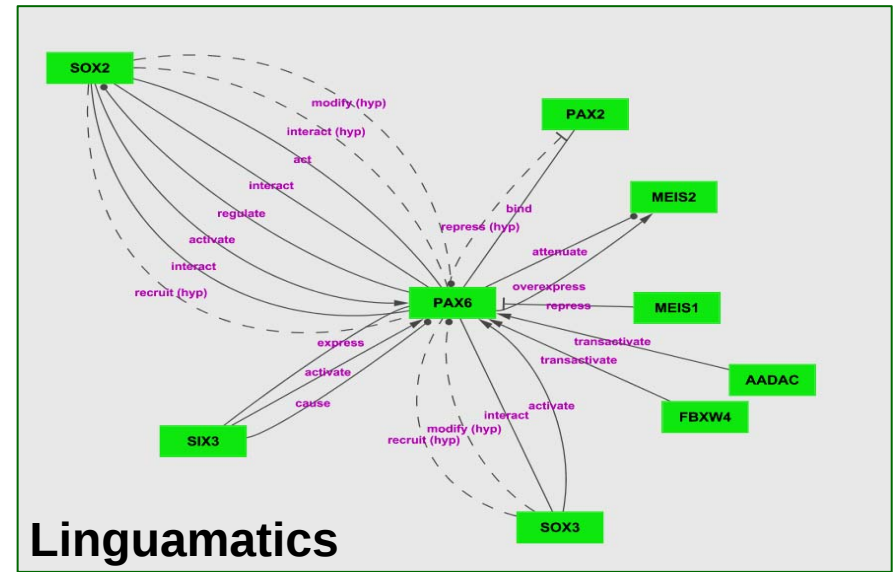
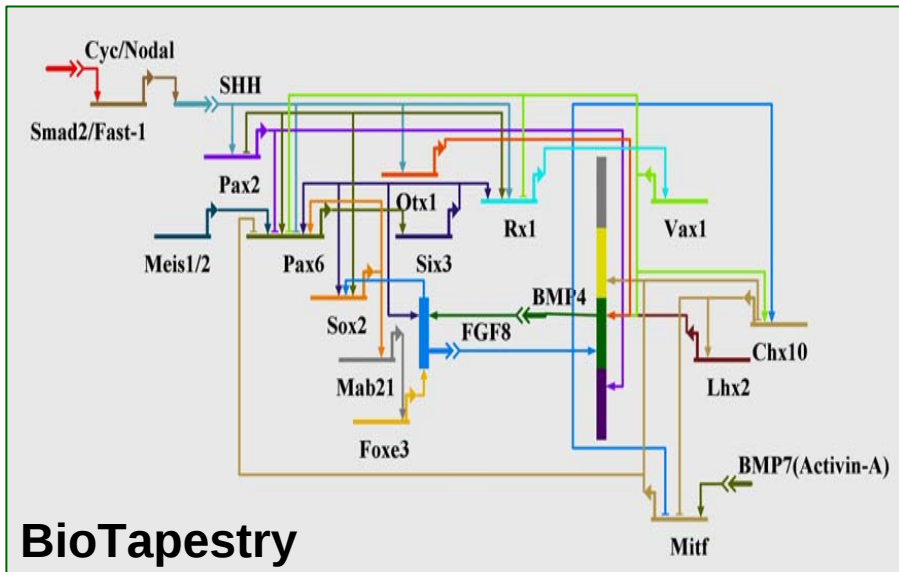
Stage Definition	Section Movies:	Embryo View:	High-resolution Section Images:	Anatomy Nomenclature Database	CD-ROM
	Transverse ~Frontal ~Sagittal	 More		Java Browser Plain Text XML	

Web page contact: genexweb@hgu.mrc.ac.uk Last modified: 01/03/2004

63 genes (TS12-18)
captures 2164 PMIDs

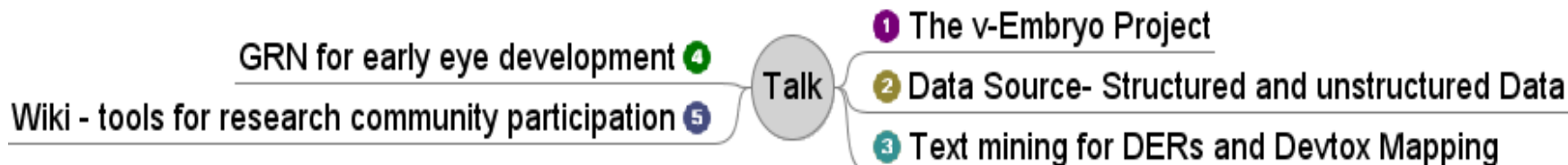
S.No.	Gene 1	Gene 2	Search 1	Search 2	PMID	Web link	Title	Authors	Read	Relevant	New Inform
1	Cyc	Shh	total or embryo	mouse or mic	1223892	Web browser	A transcription factor	Capra A, Yan Y	Y	N	N
2	Cyc	Shh	total or embryo	mouse or mic	1083387	Web browser	Direct factor of the	Watt F, Albr Y	Y	N	N
3	Cyc	Shh	total or embryo	mouse or mic	1068427	Web browser	Tan distal cell	Colbran J, Y Y	N	N	N
4	Cyc	Shh	total or embryo	mouse or mic	1045241	Web browser	Expression of	Steffe U, Be Y	N	N	N
5	Cyc	Shh	total or embryo	mouse or mic	1074418	Web browser	Complex	Watt F, Albr Y	N	N	N
6	Cyc	Shh	total or embryo	mouse or mic	1173484	Web browser	Sept, the	Watt F, Albr Y	N	N	N
7	Shh	Shh	total or embryo	mouse or mic	1060336	Web browser	Vad, a	Watt F, Albr Y	Y	Y	Y
8	Shh	Shh	total or embryo	mouse or mic	1060336	Web browser	Sonic	Watt F, Albr Y	Y	Y	Y
9	Shh	Shh	total or embryo	mouse or mic	1060336	Web browser	Shh	Watt F, Albr Y	Y	Y	Y
10	Shh	Shh	total or embryo	mouse or mic	1060336	Web browser	Shh	Watt F, Albr Y	Y	Y	Y
11	Shh	Shh	total or embryo	mouse or mic	1060336	Web browser	Shh	Watt F, Albr Y	Y	Y	Y
12	Shh	Shh	total or embryo	mouse or mic	1060336	Web browser	Shh	Watt F, Albr Y	Y	Y	Y
13	Shh	Shh	total or embryo	mouse or mic	1060336	Web browser	Shh	Watt F, Albr Y	Y	Y	Y
14	Shh	Shh	total or embryo	mouse or mic	1060336	Web browser	Shh	Watt F, Albr Y	Y	Y	Y
15	Shh	Shh	total or embryo	mouse or mic	1060336	Web browser	Shh	Watt F, Albr Y	Y	Y	Y
16	Shh	Shh	total or embryo	mouse or mic	1060336	Web browser	Shh	Watt F, Albr Y	Y	Y	Y
17	Shh	Shh	total or embryo	mouse or mic	1060336	Web browser	Shh	Watt F, Albr Y	Y	Y	Y
18	Shh	Shh	total or embryo	mouse or mic	1060336	Web browser	Shh	Watt F, Albr Y	Y	Y	Y
19	Shh	Shh	total or embryo	mouse or mic	1060336	Web browser	Shh	Watt F, Albr Y	Y	Y	Y
20	Shh	Shh	total or embryo	mouse or mic	1060336	Web browser	Shh	Watt F, Albr Y	Y	Y	Y
21	Shh	Shh	total or embryo	mouse or mic	1060336	Web browser	Shh	Watt F, Albr Y	Y	Y	Y
22	Shh	Shh	total or embryo	mouse or mic	1060336	Web browser	Shh	Watt F, Albr Y	Y	Y	Y
23	Shh	Shh	total or embryo	mouse or mic	1060336	Web browser	Shh	Watt F, Albr Y	Y	Y	Y
24	Shh	Shh	total or embryo	mouse or mic	1060336	Web browser	Shh	Watt F, Albr Y	Y	Y	Y
25	Shh	Shh	total or embryo	mouse or mic	1060336	Web browser	Shh	Watt F, Albr Y	Y	Y	Y
26	Shh	Shh	total or embryo	mouse or mic	1060336	Web browser	Shh	Watt F, Albr Y	Y	Y	Y
27	Shh	Shh	total or embryo	mouse or mic	1060336	Web browser	Shh	Watt F, Albr Y	Y	Y	Y
28	Shh	Shh	total or embryo	mouse or mic	1060336	Web browser	Shh	Watt F, Albr Y	Y	Y	Y
29	Shh	Shh	total or embryo	mouse or mic	1060336	Web browser	Shh	Watt F, Albr Y	Y	Y	Y
30	Shh	Shh	total or embryo	mouse or mic	1060336	Web browser	Shh	Watt F, Albr Y	Y	Y	Y
31	Shh	Shh	total or embryo	mouse or mic	1060336	Web browser	Shh	Watt F, Albr Y	Y	Y	Y
32	Shh	Shh	total or embryo	mouse or mic	1060336	Web browser	Shh	Watt F, Albr Y	Y	Y	Y
33	Shh	Shh	total or embryo	mouse or mic	1060336	Web browser	Shh	Watt F, Albr Y	Y	Y	Y
34	Shh	Shh	total or embryo	mouse or mic	1060336	Web browser	Shh	Watt F, Albr Y	Y	Y	Y
35	Shh	Shh	total or embryo	mouse or mic	1060336	Web browser	Shh	Watt F, Albr Y	Y	Y	Y
36	Shh	Shh	total or embryo	mouse or mic	1060336	Web browser	Shh	Watt F, Albr Y	Y	Y	Y
37	Shh	Shh	total or embryo	mouse or mic	1060336	Web browser	Shh	Watt F, Albr Y	Y	Y	Y
38	Shh	Shh	total or embryo	mouse or mic	1060336	Web browser	Shh	Watt F, Albr Y	Y	Y	Y
39	Shh	Shh	total or embryo	mouse or mic	1060336	Web browser	Shh	Watt F, Albr Y	Y	Y	Y
40	Shh	Shh	total or embryo	mouse or mic	1060336	Web browser	Shh	Watt F, Albr Y	Y	Y	Y
41	Shh	Shh	total or embryo	mouse or mic	1060336	Web browser	Shh	Watt F, Albr Y	Y	Y	Y
42	Shh	Shh	total or embryo	mouse or mic	1060336	Web browser	Shh	Watt F, Albr Y	Y	Y	Y
43	Shh	Shh	total or embryo	mouse or mic	1060336	Web browser	Shh	Watt F, Albr Y	Y	Y	Y
44	Shh	Shh	total or embryo	mouse or mic	1060336	Web browser	Shh	Watt F, Albr Y	Y	Y	Y
45	Shh	Shh	total or embryo	mouse or mic	1060336	Web browser	Shh	Watt F, Albr Y	Y	Y	Y
46	Shh	Shh	total or embryo	mouse or mic	1060336	Web browser	Shh	Watt F, Albr Y	Y	Y	Y
47	Shh	Shh	total or embryo	mouse or mic	1060336	Web browser	Shh	Watt F, Albr Y	Y	Y	Y
48	Shh	Shh	total or embryo	mouse or mic	1060336	Web browser	Shh	Watt F, Albr Y	Y	Y	Y
49	Shh	Shh	total or embryo	mouse or mic	1060336	Web browser	Shh	Watt F, Albr Y	Y	Y	Y
50	Shh	Shh	total or embryo	mouse or mic	1060336	Web browser	Shh	Watt F, Albr Y	Y	Y	Y
51	Shh	Shh	total or embryo	mouse or mic	1060336	Web browser	Shh	Watt F, Albr Y	Y	Y	Y
52	Shh	Shh	total or embryo	mouse or mic	1060336	Web browser	Shh	Watt F, Albr Y	Y	Y	Y
53	Shh	Shh	total or embryo	mouse or mic	1060336	Web browser	Shh	Watt F, Albr Y	Y	Y	Y
54	Shh	Shh	total or embryo	mouse or mic	1060336	Web browser	Shh	Watt F, Albr Y	Y	Y	Y
55	Shh	Shh	total or embryo	mouse or mic	1060336	Web browser	Shh	Watt F, Albr Y	Y	Y	Y
56	Shh	Shh	total or embryo	mouse or mic	1060336	Web browser	Shh	Watt F, Albr Y	Y	Y	Y
57	Shh	Shh	total or embryo	mouse or mic	1060336	Web browser	Shh	Watt F, Albr Y	Y	Y	Y
58	Shh	Shh	total or embryo	mouse or mic	1060336	Web browser	Shh	Watt F, Albr Y	Y	Y	Y
59	Shh	Shh	total or embryo	mouse or mic	1060336	Web browser	Shh	Watt F, Albr Y	Y	Y	Y
60	Shh	Shh	total or embryo	mouse or mic	1060336	Web browser	Shh	Watt F, Albr Y	Y	Y	Y
61	Shh	Shh	total or embryo	mouse or mic	1060336	Web browser	Shh	Watt F, Albr Y	Y	Y	Y
62	Shh	Shh	total or embryo	mouse or mic	1060336	Web browser	Shh	Watt F, Albr Y	Y	Y	Y
63	Shh	Shh	total or embryo	mouse or mic	1060336	Web browser	Shh	Watt F, Albr Y	Y	Y	Y

Self-regulating gene network for early eye development: built with EMAGE, PMID



SOURCE: Knudsen and Singh (2008), manuscript in preparation

Community knowledge environment



Software

Open Access

Calling on a million minds for community annotation in WikiProteins

Barend Mons^{*†‡§}, Michael Ashburner[¶], Christine Chichester^{†‡¥}, Erik van Mulligen^{**}, Marc Weeber[‡], Johan den Dunnen[†], Gert-Jan van Ommen[†], Mark Musen[‡], Matthew Cockerill^{**}, Henning Hermjakob^{††}, Albert Mons[‡], Abel Packer^{††}, Roberto Pacheco^{§§}, Suzanna Lewis[¶], Alfred Berkeley[‡], William Melton[‡], Nickolas Barris[‡], Jimmy Wales, Gerard Meijssen[§], Erik Moeller[§], Peter Jan Roes[‡], Katy Borner and Amos Bairoch[¥]

Addresses: ^{*}Erasmus Medical Centre, Department of Medical Informatics, Dr. Molewaterplein 40/50, NL-3015 GE Rotterdam, the Netherlands. [†]Department of Human Genetics, Centre for Medical Systems Biology, Leiden University Medical Centre, 2300 RC Leiden NL, Einthovenweg 20, 2333 ZC Leiden, the Netherlands. [‡]Knewco Inc., Falls Grove Drive, Rockville, MD 20850, USA. [§]Open Progress Foundation, Olstgracht, 1315 BH Almere, the Netherlands. [¶]The GO consortium, EMBL-European Bioinformatics Institute, Hinxton, Cambridge, and Department of Genetics, University of Cambridge, Hinxton, CB10 1SD, UK; and Berkeley Bioinformatics Open-source Projects, Lawrence Berkeley National Laboratory, Cyclotron Road, Berkeley, CA 94720, USA. [¥]Swiss Institute of Bioinformatics, Swiss-Prot Group and Department of Structural Biology and Bioinformatics, University of Geneva, CMU - Rue Michel-Servet, 1211 Genève 4, Switzerland. ^{**}Stanford Medical Informatics, NCBO, Campus Drive, Stanford, CA 94305-5479, USA. ^{††}BioMed Central, Cleveland Street, London W1T 4LE, UK. ^{‡‡}EMBL - European Bioinformatics Institute, IntAct database, Hinxton, Cambridge CB10 1SD, UK. ^{§§}SciELO, BIREME/PAHO/WHO, Rua Botucatu, 862, Vila Clementino 04023-901, São Paulo SP, Brazil. ^{¶¶}Instituto Stela, Rua Prof. Ayrton Roberto de Oliveira, 32, 7º andar Itacorubi, Florianópolis-SC, 88034-050, Brazil. The Wikimedia Foundation, San Francisco, CA 94107-8350, USA. Indiana University, S. Indiana Ave, Bloomington, IN 47405-7000, USA.

Correspondence: Barend Mons. Email: b.mons@erasmusmc.nl

Published: 28 May 2008

Genome *Biology* 2008, 9:R89 (doi:10.1186/gb-2008-9-5-r89)

The electronic version of this article is the complete one and can be found online at <http://genomebiology.com/2008/9/5/R89>

Received: 3 October 2007

Revised: 3 March 2008

Accepted: 28 May 2008

© 2008 Mons et al.; licensee BioMed Central Ltd.

This is an open access article distributed under the terms of the Creative Commons Attribution License (<http://creativecommons.org/licenses/by/2.0>), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.



SOURCE: <http://genomebiology.com/content/pdf/gb-2008-9-5-r89.pdf>

v-Embryo™ Wiki:

coming soon ... let's share our minds



v-embryo

- About v-Embryo™
- Community portal
- Current events
- Recent changes
- Random page
- Help
- Donations

toolbox

- What links here
- Related changes
- Special pages
- Printable version
- Permanent link
- CategoryTree

search

WikiSysop my talk my preferences my watchlist my contributions log out

page discussion edit history delete move protect watch

About v-Embryo

The Virtual Embryo Project (v-Embryo™):

A computational framework for developmental toxicity [edit]

Prenatal development may be perturbed by agents that a pregnant mother is exposed to. The Virtual Embryo Project (v-Embryo™) is a far reaching new research program at EPA to develop a sophisticated computer model of a mammalian embryo that can be used to better understand the prenatal risks posed by environmental chemicals and to ultimately predict a chemical's potential developmental toxicity in silico.

The basic concept of v-Embryo™ is a public portal, knowlegebase, and computational infrastructure for modeling genetic-cellular networks and developmental toxicity pathways. Affiliated computational techniques fall into two general areas of knowledge-discovery and computer simulation. As such, the project aligns with other systems biology research initiatives at the National Center for Computational Toxicology (NCCT) including ACToR, ToxCast™, and Virtual Liver.

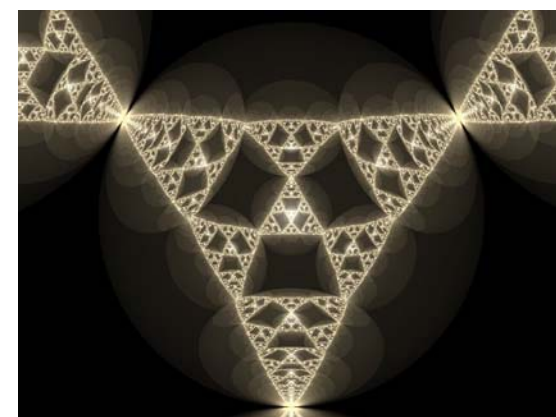


This page was last modified 12:04, June 19, 2008. This page has been accessed 128 times. Content is available under [GNU Free Documentation License 1.2](#). [Privacy policy](#) [About v-Embryo](#) [Disclaimers](#)



US EPA National Center for Computational Toxicology

<http://www.epa.gov/ncct/index.html>



v-Embryo development team

Amar Singh (LM)	singh.amarv@epa.gov
Imran Shah	shah.imran@epa.gov
Bob Kavlock	kavlock.robert@epa.gov
Richard Judson	judson.richard@epa.gov
Michael Rountree	routree.michael@epa.gov
Matt Martin	martin.matt@epa.gov
David Dix	dix.david@epa.gov
Tom Knudsen	knudsen.thomas@epa.gov
Sid Hunter	hunter.sid@epa.gov
Stephanie Padilla	padilla.stephanie@epa.gov

DISCLAIMER: views reflect those of the presenter and not EPA policy; any reference to commercial products or tradenames does not constitute endorsement