

The human Pluripotent Stem Cell registry

Scientific and ethical qualification of pluripotent stem cells for European research

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Overview

- Qualification of Pluripotent Stem Cells
- Ethical aspects
- Scientific aspects
- Implementation in hPSCreg

PSC research publications

520

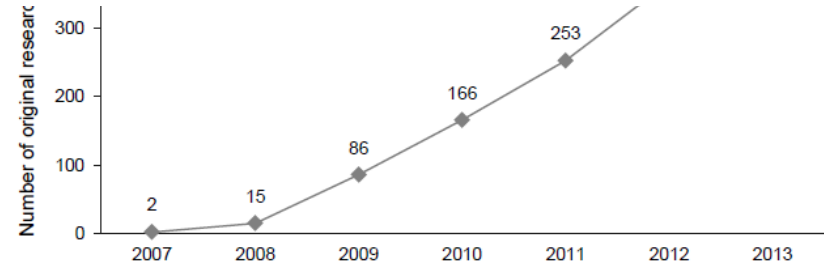
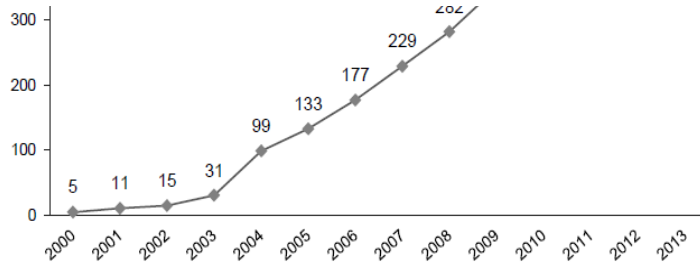
160

Number of original research papers on hESCs

Are these lines pluripotent ?

Where appropriate ethical standards applied for donation and derivation ?

How is the quality of the cells validated?



Risks if no qualification

- Lack of peer review of new (and existing) cell lines
- Widespread use of cell lines without appropriate ethical consent
- Widespread use of cross-contaminated or poorly characterized cell lines causing inheritance of misleading data
- Difficulty in locating appropriate hESC and hiPSC lines with duplication of effort and resultant waste of research funds
- Common use of only a few well characterized lines with potential distorted generalization

Ethical Qualification

The donor determines what can be done with his or her tissues and the cells derived from these tissues

Issues	
Consent	The donor needs to be informed about all aspects of the planned research and how it affects him or her
Data Protection	The donor needs to be informed about how provacy is protected and misuse of data prevented
Permitted Uses	The donor needs to permit possible usage of the cells in research and application
Regulations and Legal aspects	Rules and regulations need to be applied when consenting the donor, protecting the data, using the cells and restrict their use

Ethical Qualification

Has consent been obtained from the donor of the tissue from which iPS cells have been made?

Was the consent **voluntarily** given by the donor?

Do you (Depositor/Provider) hold a **copy of the donor Consent**?

If not, do you know who holds the original donor Consent ?

Could you obtain a copy of the signed Consent from the holder?

Could you arrange to obtain a new form of Consent, from the donor?

Can you provide us with a copy, in English, of the Consent Information provided to the donor?

Can you provide us with a copy, in its original language, of the Consent Information provided to the donor?

Was the donor informed about how her/his data will be protected?

Has the donated material been coded for traceability or pseudonymised?

Has the donated material been rendered unidentifiable (anonymised)?

Has the donor been informed that **participation will not directly influence their personal treatment**?

Ethical Qualification

Permitted Uses: Research

Does Consent pertain to one or more specific research projects?

Does Consent permit unforeseen future research, without further consent?

Is future research permitted only in relation to specified areas or types of research? If so, what are they?

Does the Consent permit uses of donated material intended for clinical treatment or human application?

Does Consent permit research by an academic institution?

Does Consent permit research by a public organisation?

Does Consent permit research by a not-for-profit company?

Does Consent permit research by a for-profit corporation?

Does Consent expressly permit derivation of iPS cells?

Ethical Qualification

Permitted Uses: Commercial Exploitation

Does Consent expressly prevent development of commercial products?

Does the Consent expressly prevent **financial gain** from any use of donated material, including products that might be developed from it?

Storage of and Access to Material

Does Consent expressly permit storage of donated material ?

Does Consent expressly permit storage of cells derived from the donated material?

Does the Consent **prevent donated material from being made available to researchers anywhere in the world?**

Does the Consent prevent cells derived from the donated material from being made available to researchers anywhere in the world?

Ethical Qualification

Benefits

Will the donor expect to receive some financial benefit, beyond reasonable expenses, in return for participation in research?

Does the Consent anticipate that the donor will be notified of results or outcomes of any research involving the donated samples, or iPS cells made from them?

Does the consent prevent the donor from receiving **financial benefit** from commercial products, which result from research with the donated material or derived cells?

Ethical Qualification

Data and Information

Does Consent expressly permit **collection of genetic information**?

Does Consent expressly permit storage of genetic information?

Does the donor Consent prevent **dissemination of genetic information**?

Was the donor informed that their donation or derived materials may be tested for the presence of microbiological agents and pathogens?

Does the donor expect to be informed by researchers if, during use of donated material, they discover something that has significant health implications for the donor (**incidental findings**)?

How is genetic information associated with the cell line accessible?

Medical Records

Does Consent permit **access to medical records of the donor**?

Does consent permit access to any other source of information about the clinical treatment or health of the donor?

Ethical Qualification for EU

Risk anticipation and mitigation

Ex-ante process

- Identifies the issues and risks
- Offers processes/solutions to mitigate them,
- Protects the researcher, the project and the funding bodies,
- Minimizes adverse impact
- Enhances consent

Risk treated as a legal hazard

Ex-post process

- Implies large budget provisions for lawsuits/litigations.
- Internal review processes have NO VALUE in court.
- Risk for researchers of being blocked by third parties – even at publication stage

Risk is inherent to research

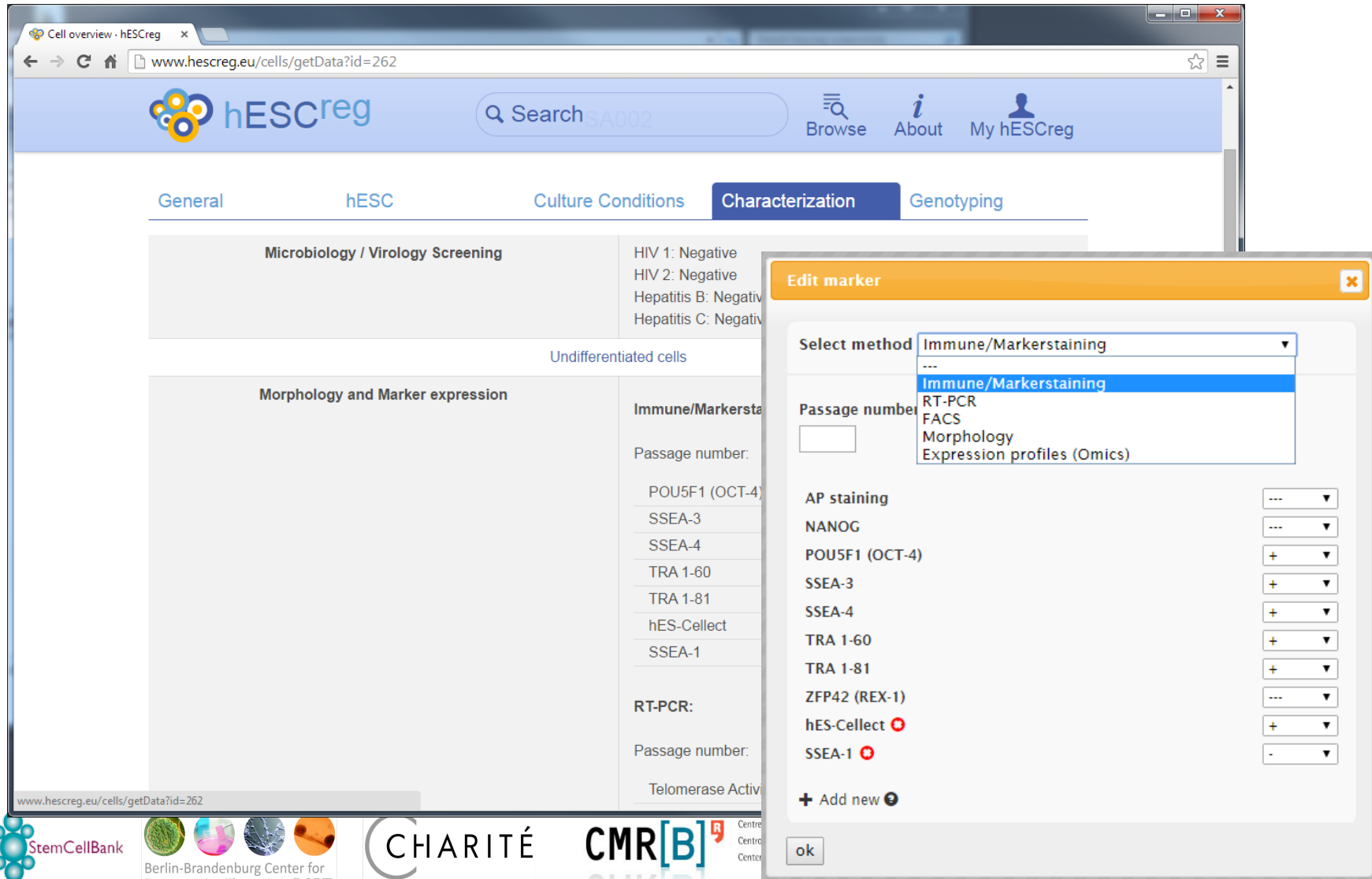
Scientific Qualification

Is there evidence of Pluripotency?

Issues	
Phenotype evidence	Expression of 'pluripotency markers' and morphology of the cells
Functional evidence	Differentiate into derivatives of the three germ layers

What is the genetic or disease background of the donor?

Scientific Qualification



The screenshot shows the hESCreg website interface. The browser address bar displays `www.hescreg.eu/cells/getData?id=262`. The page has a navigation bar with a search field containing 'SA002' and links for 'Browse', 'About', and 'My hESCreg'. Below the navigation bar are tabs for 'General', 'hESC', 'Culture Conditions', 'Characterization', and 'Genotyping'. The 'Characterization' tab is active, showing a table of markers and their status. An 'Edit marker' modal is open, allowing the user to select a method for a specific marker. The modal lists various methods such as 'Immune/Markerstaining', 'RT-PCR', 'FACS', 'Morphology', and 'Expression profiles (Omics)'. The modal also includes a 'Passage number' field and a list of markers with their respective methods and status indicators.

Microbiology / Virology Screening

HIV 1: Negative
HIV 2: Negative
Hepatitis B: Negative
Hepatitis C: Negative

Undifferentiated cells

Morphology and Marker expression

Immune/Markersta	Passage number:
POU5F1 (OCT-4)	
SSEA-3	
SSEA-4	
TRA 1-60	
TRA 1-81	
hES-Collect	
SSEA-1	
RT-PCR:	
	Passage number:
	Telomerase Activ

Edit marker

Select method: Immune/Markerstaining

Passage number:

AP staining: ...

NANOG: ...

POU5F1 (OCT-4): +

SSEA-3: +

SSEA-4: +

TRA 1-60: +

TRA 1-81: +

ZFP42 (REX-1): ...

hES-Collect: +

SSEA-1: +

+ Add new

ok

Scientific Qualification

Donor Data/Information

Is there a disease diagnosed? ?

yes no

Disease Ontology ID - [Disease Ontology](#)

DOI:11665

Disease Name:
Patau syndrome

Synonyms:

- D1 Trisomy EXACT NCI2004_11_17:C36529
- Patau's syndrome RELATED ICD9CM_2006:758.1
- trisomy 13 EXACT

[Open at Disease Ontology](#)

Additional information on disease ?

Has an abnormal karyotype been diagnosed? ?

yes no

Was the abnormal karyotype diagnosed in the donor?

yes no

Was the abnormal karyotype diagnosed in the cell line?

yes no

Are there cell lines registered from the same donor? ?

no

Internal donor ID ?

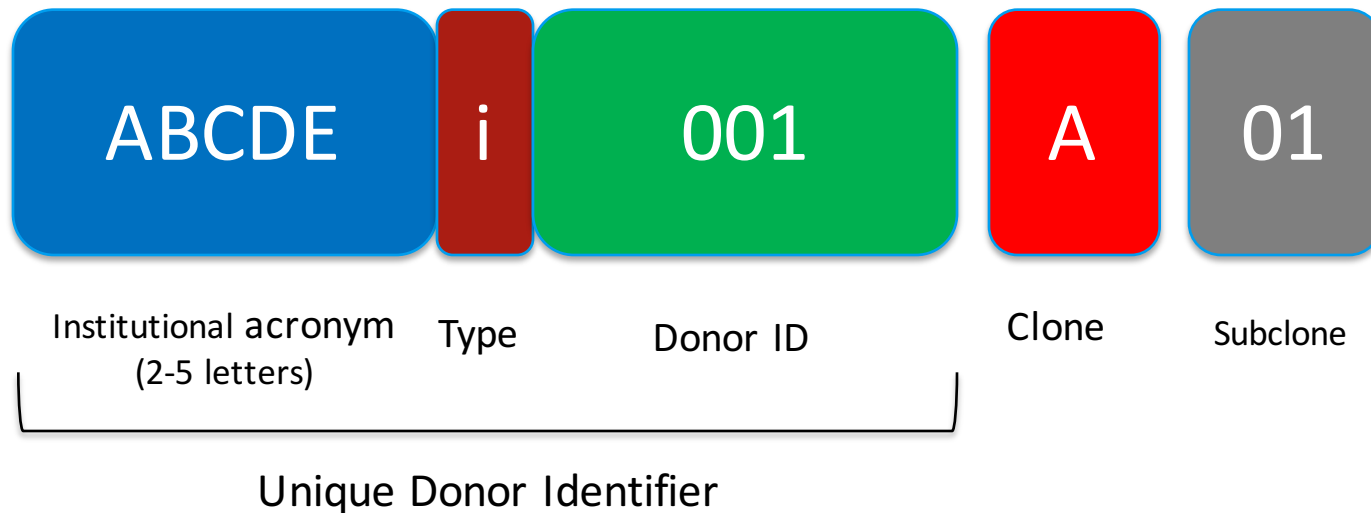
Sex

Female ▼

Country of donor origin ?

Sweden ▼

A nomenclature to provide traceability



Usage of lines

hESC Line	Year of Publication	Provider	Use in comparative research (%)	Use in overall research (% of studies)
H9	1998	WiCell	57.4	47.1
H1	1998	WiCell	29.8	24.5
H7	1998	WiCell	7.2	8.0
HES-3	2000	ES Cell International	4.8	6.5
KhES-1	2006	Kyoto University	4.8	3.1
KhES-3	2006	Kyoto University	4.6	2.5
HUES6	2004	Harvard University	4.0	1.7
HUES9	2004	Harvard University	3.8	4.3
BG01	2001	BresaGen	3.5	4.9
HES-2	2000	ES Cell International	2.9	4.5
H14	1998	WiCell	2.9	2.2

Scientific Qualification

Karyotyping

Karyotyping yes no

CGH yes no

Genotyping

HLA typing yes no

STR/Fingerprinting yes no

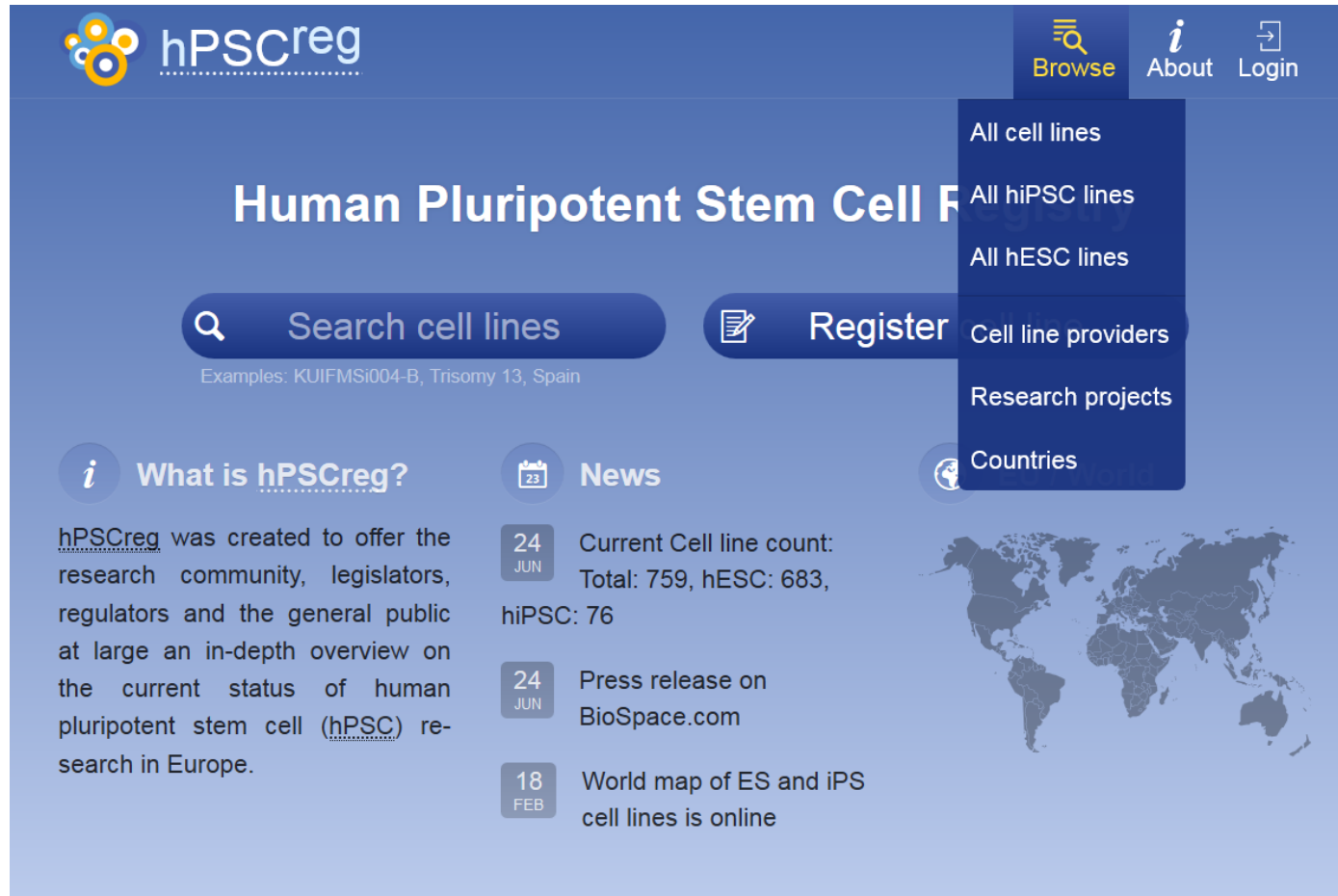
SNP yes no

Microarrays yes no

Sequencing yes no

Other yes no

Scientific Qualification



The screenshot shows the hPSCreg website with a navigation menu open. The main header includes the hPSCreg logo, a 'Browse' button with a magnifying glass icon, and 'About' and 'Login' buttons with person and key icons respectively. The main content area features the title 'Human Pluripotent Stem Cell F...', a search bar with the text 'Search cell lines' and examples 'KUIFMSi004-B, Trisomy 13, Spain', and a 'Register' button with a document icon. A dropdown menu is open over the 'Register' button, listing: 'All cell lines', 'All hiPSC lines', 'All hESC lines', 'Cell line providers', 'Research projects', and 'Countries'. Below the search bar, there are three columns: 'What is hPSCreg?' with an information icon and a paragraph about the site's purpose; 'News' with a calendar icon and three news items dated 24 JUN and 18 FEB; and 'Countries' with a globe icon and a world map.



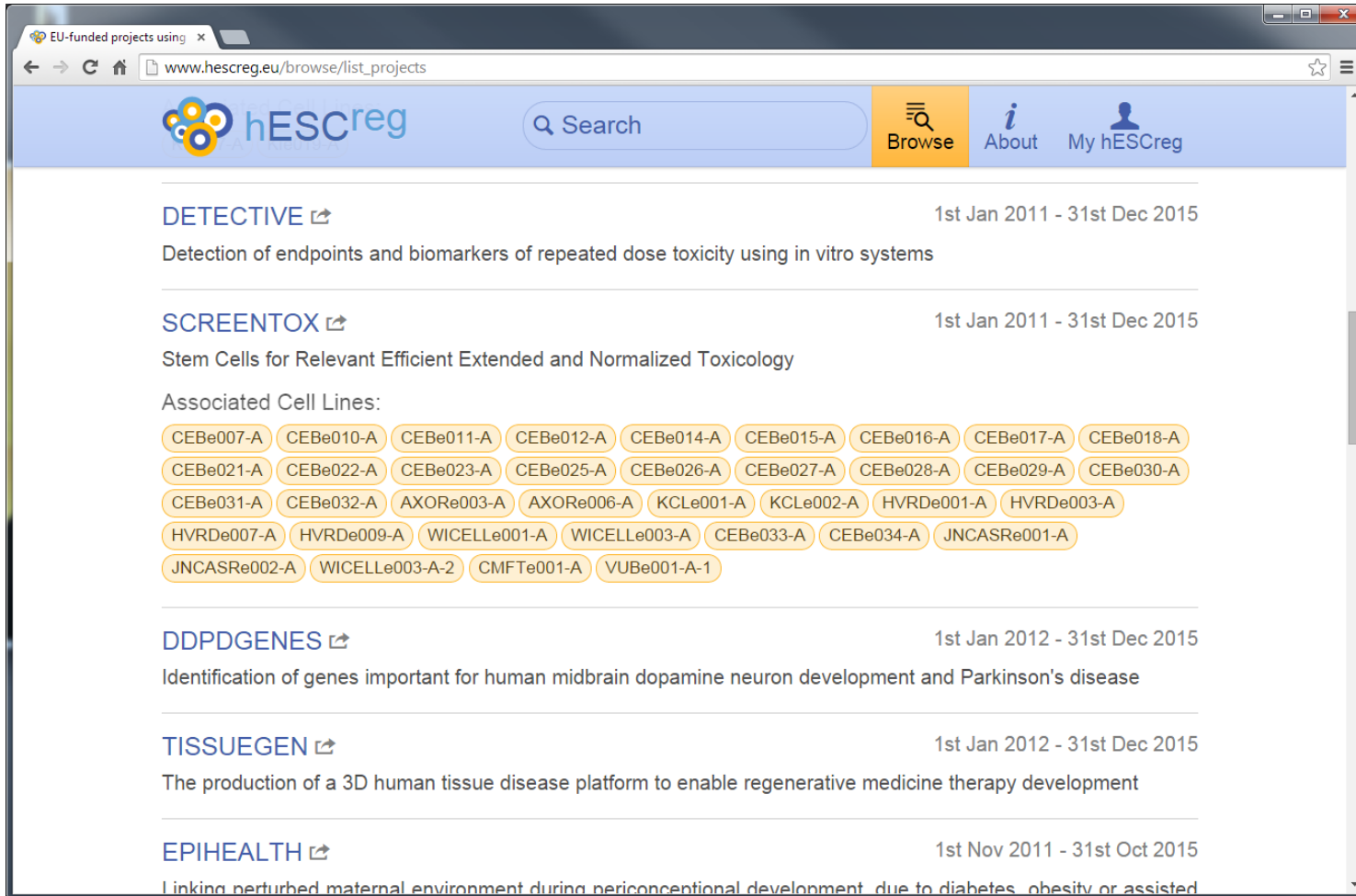
Centre de Medicina Regenerativa de Barcelona
 Centro de Medicina Regenerativa de Barcelona
 Center of Regenerative Medicine in Barcelona

Scientific Qualification

✓

	Disease	Country	Derivation Date	
	Patau syndrome (3)			
Typ	Klinefelter's syndrome (5)			
hES	Down syndrome (1)	man ES cell line		
hESC	Cellartis AB Sweden - Human ES cell line derivation	Sweden	2001-05-21	Patau syndrome
hESC	King's College - Department of Women's Health	Sweden	2001-09-01	Klinefelter's syndrome
hESC		United Kingdom	2007-04-12	Klinefelter's syndrome

Scientific Qualification



EU-funded projects using hESCreg

www.hescreg.eu/browse/list_projects

hESCreg Search Browse About My hESCreg

DETECTIVE 1st Jan 2011 - 31st Dec 2015
 Detection of endpoints and biomarkers of repeated dose toxicity using in vitro systems

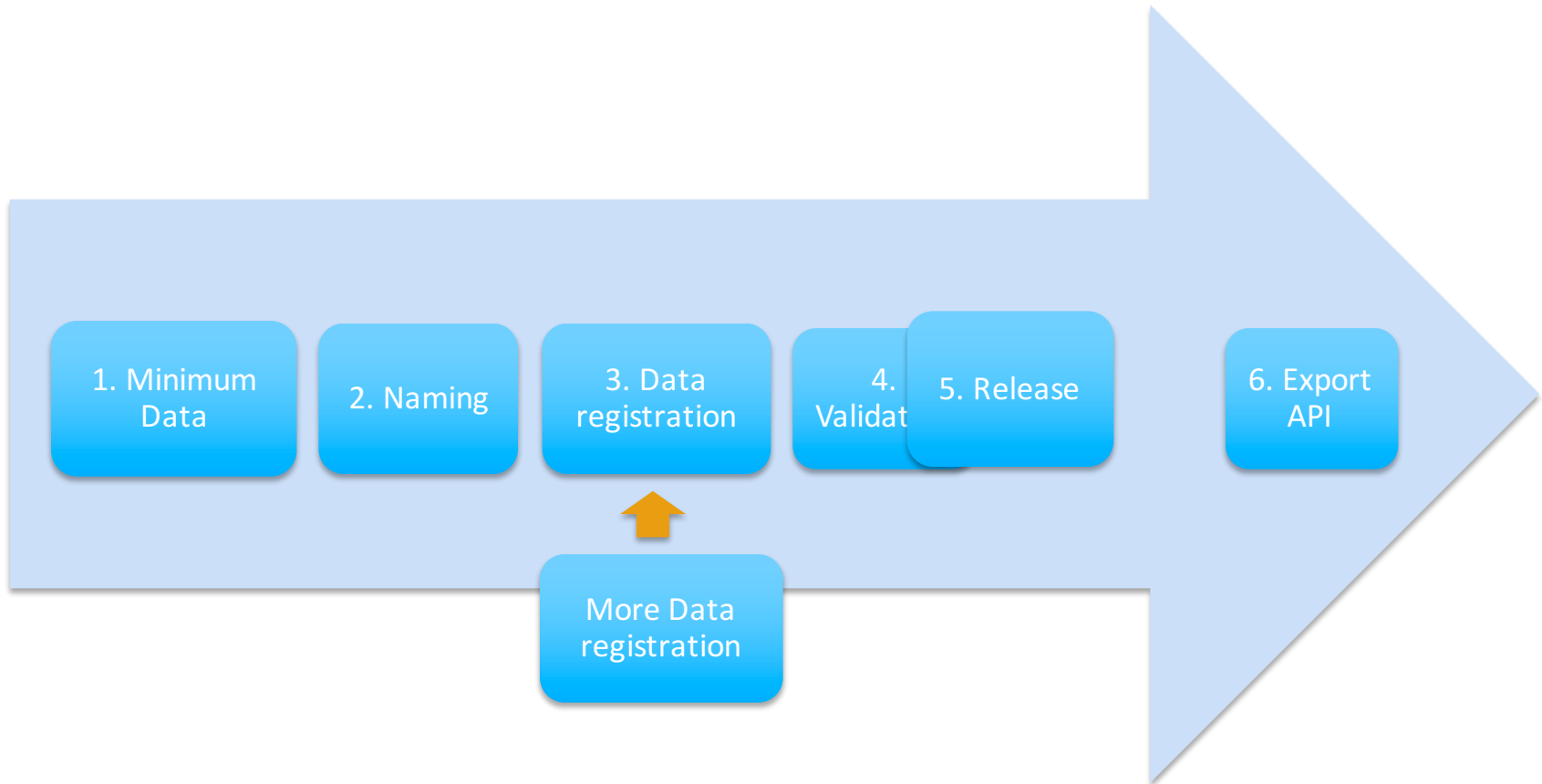
SCREENTOX 1st Jan 2011 - 31st Dec 2015
 Stem Cells for Relevant Efficient Extended and Normalized Toxicology
 Associated Cell Lines:
 CEBe007-A CEBe010-A CEBe011-A CEBe012-A CEBe014-A CEBe015-A CEBe016-A CEBe017-A CEBe018-A
 CEBe021-A CEBe022-A CEBe023-A CEBe025-A CEBe026-A CEBe027-A CEBe028-A CEBe029-A CEBe030-A
 CEBe031-A CEBe032-A AXORe003-A AXORe006-A KCLe001-A KCLe002-A HVRDe001-A HVRDe003-A
 HVRDe007-A HVRDe009-A WICELLe001-A WICELLe003-A CEBe033-A CEBe034-A JNCASRe001-A
 JNCASRe002-A WICELLe003-A-2 CMFTe001-A VUBe001-A-1

DDPDGENES 1st Jan 2012 - 31st Dec 2015
 Identification of genes important for human midbrain dopamine neuron development and Parkinson's disease

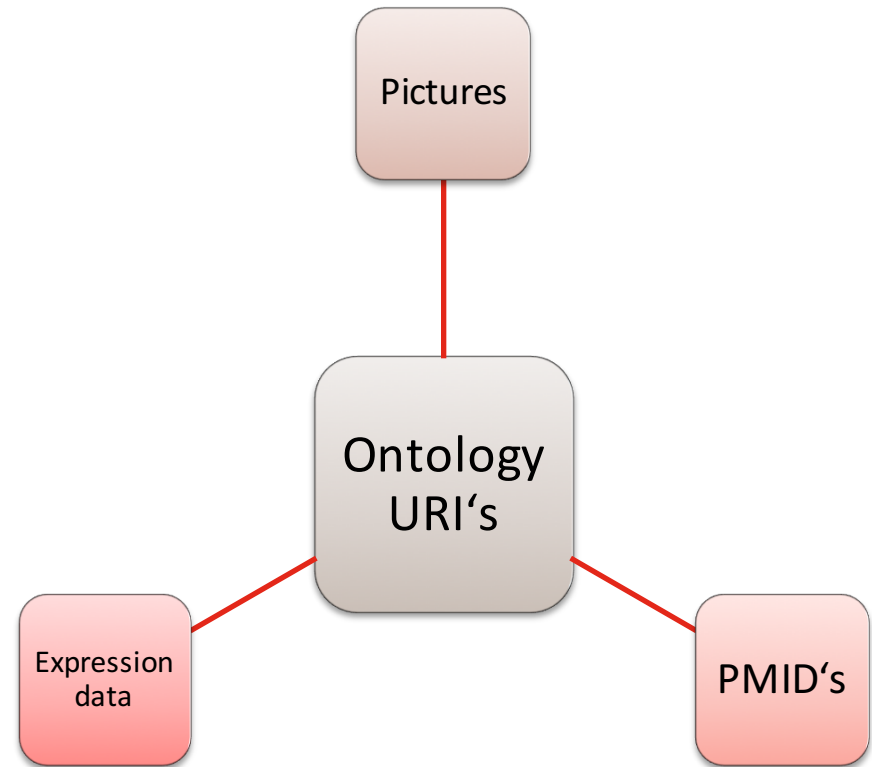
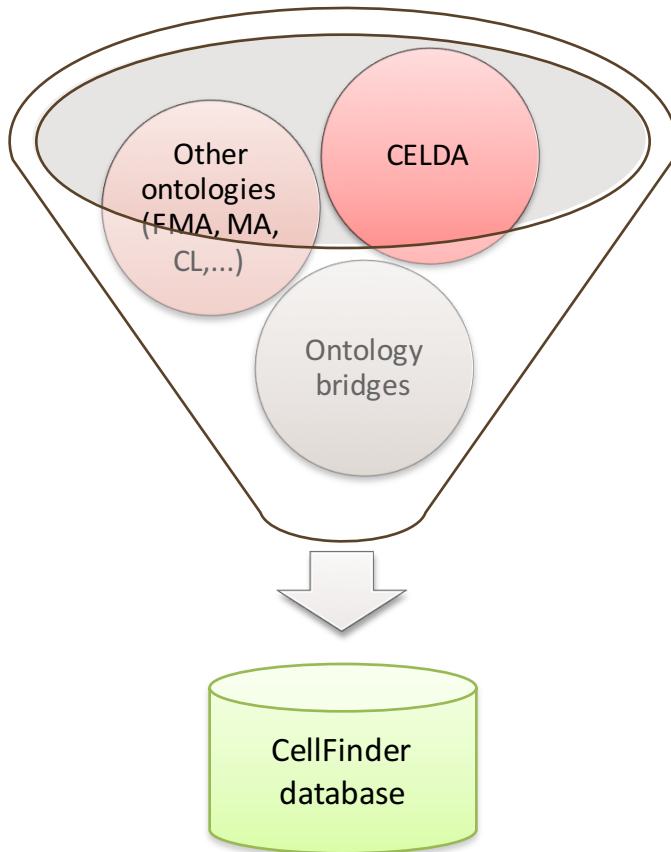
TISSUEGEN 1st Jan 2012 - 31st Dec 2015
 The production of a 3D human tissue disease platform to enable regenerative medicine therapy development

EPIHEALTH 1st Nov 2011 - 31st Oct 2015
 Linking perturbed maternal environment during periconceptional development due to diabetes, obesity or assisted

Processing of data



Integration of Data



Integration of Data

Search for an organ, tissue, cell, gene or protein

Go

Ex: [Kidney](#) [Hepatocyte](#) [Embryonic stem cell](#) [SA002](#) [FLT3LG](#)

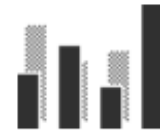
Body Browser

Graphically explore an organism's body and visualize expression profiles.



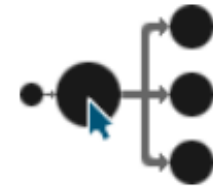
Analysis

Search for markers and compare cell types utilizing genomics and proteomics.

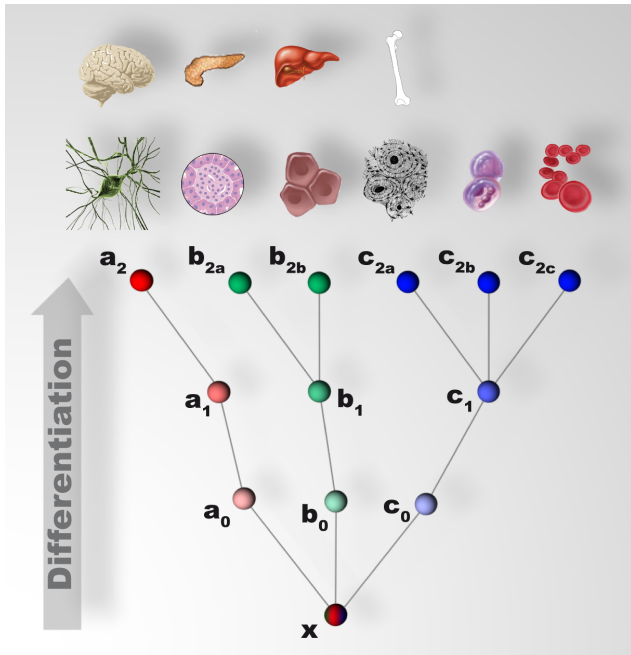


Developmental Tree

Browse the development of cell types and explore their fate.



Integration of Data



Explore an Organism



Male Human



Female Human

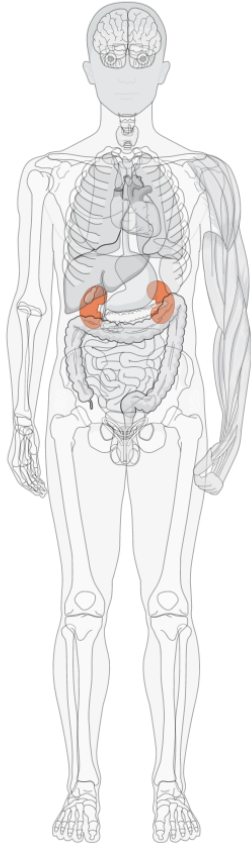
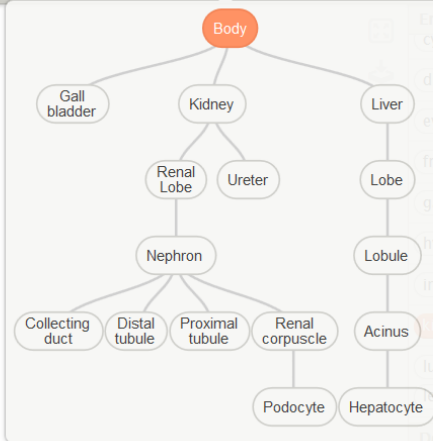


Mouse

Search for organs, anatomical parts or cells

Integration of Data

Human Adult Male Body

```

    graph TD
      Body[Body] --> GallBladder[Gall bladder]
      Body --> Kidney[Kidney]
      Body --> Liver[Liver]
      Kidney --> RenalLobe[Renal Lobe]
      Kidney --> Ureter[Ureter]
      RenalLobe --> Nephron[Nephron]
      Nephron --> CollectingDuct[Collecting duct]
      Nephron --> DistalTubule[Distal tubule]
      Nephron --> ProximalTubule[Proximal tubule]
      Nephron --> RenalCorpuscle[Renal corpuscle]
      RenalCorpuscle --> Podocyte[Podocyte]
      Liver --> Lobe[Lobe]
      Lobe --> Lobule[Lobule]
      Lobule --> Acinus[Acinus]
      Acinus --> Hepatocyte[Hepatocyte]
  
```

Search

Entities

- cystic duct
- common hepatic duct
- common bile duct
- cerebellum
- duodenum
- deferent duct
- eyeball
- eye
- esophagus
- epididymis
- frontal lobe
- gall bladder
- hypothalamus
- hyoid bone
- humerus
- heart
- intestine
- kidney
- lung
- liver
- left ventricle
- left coronary artery
- left clavicle
- atrium
- left adrenal gland
- larynx
- large intestine

DEFINITION:

The human body is the entire structure of a human organism, and consists of a head, neck, torso, two arms and two legs. By the time the human reaches adulthood, the body consists of close to 100 trillion cells, the basic unit of life. These cells are organised biologically to eventually form the whole body. *(Reference)*

DETAILS:

[CellFinder](#)

SPECIES: human

GENDER: male

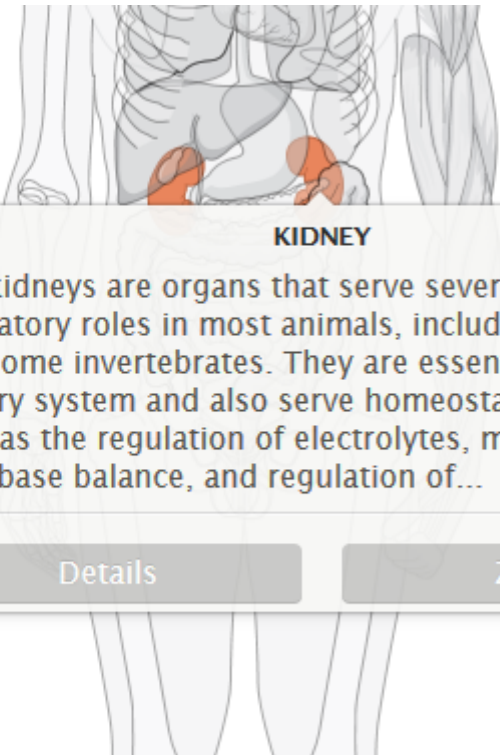
RESOLUTION: body

DEVELOPMENTAL STAGE: adult

[Heatmap](#)

[Histologic Images](#)

Integration of Data



KIDNEY

The kidneys are organs that serve several essential regulatory roles in most animals, including vertebrates and some invertebrates. They are essential in the urinary system and also serve homeostatic functions such as the regulation of electrolytes, maintenance of acid-base balance, and regulation of...

Details
Zoom

Integration of Data

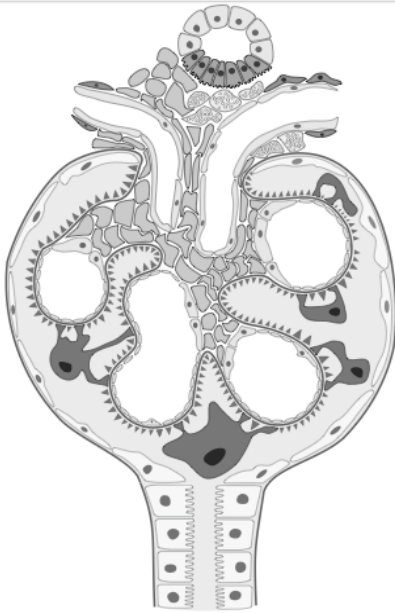
CellFinder · Browse · Semantic Body Browser

cellfinder.de/beta/browse

CellFinder **BETA** Search Compare Browse Annotation Community Help About Contact Login Register

Semantic Body Browser Developmental Tree

Human Adult Renal Corpuscle



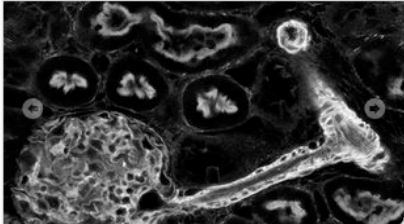
Filter Units

Units

- arterial endothelial cell afferent arteriole A
- basal lamina B
- renal corpuscle capillary endothelial cell C
- distal tubular epithelial cell D
- distal convoluted tubule
- extraglomerular mesangial cell epithelial cell E
- efferent arteriole

Information

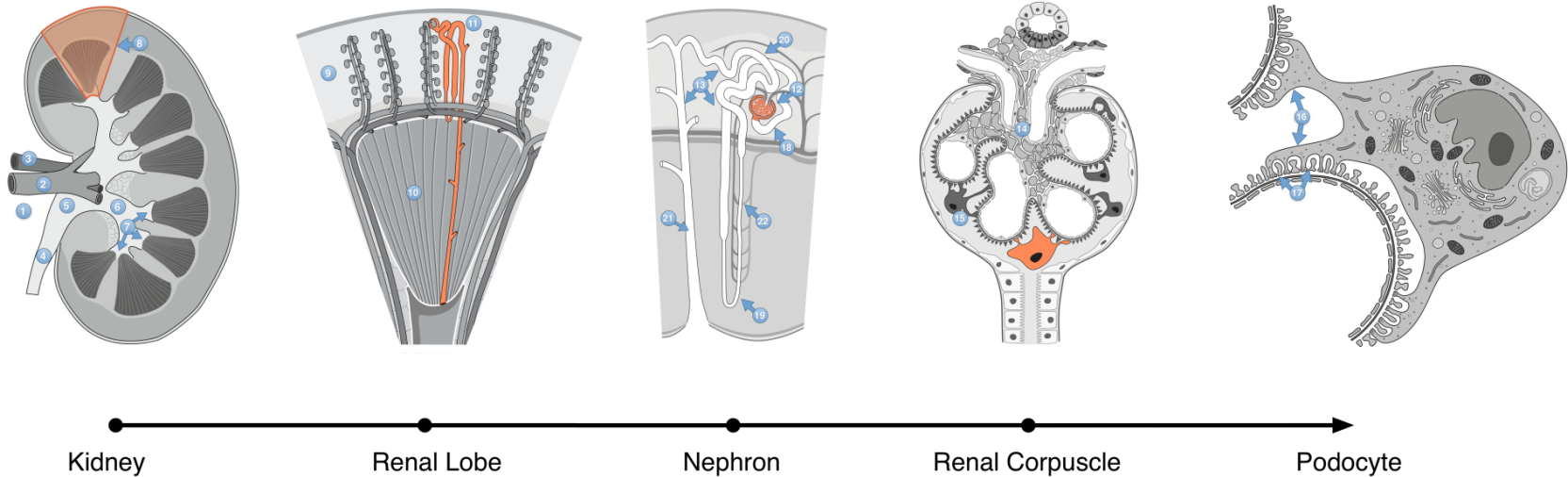
Picture



Version: 289 (Check Compatability) · Rendering Time: 0.0062

Feedback

Integration of Data

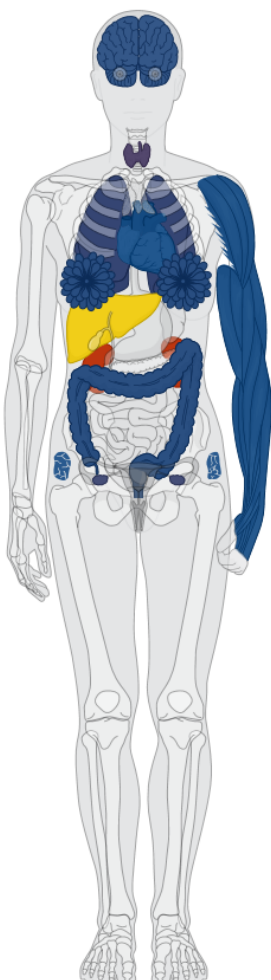


Body Browser: Gene expression

Human Adult Female Body

Search

GGT1 Heat Map Modus



Entity	Expression (TPM)
adrenal gland	0.4 / 0.5
brain	0.16 / 0.3
breast	0.14 / 0.1
heart	0.01 / 0.0
kidney	1.73 / 81.9
large intestine	0.14 / 0.1
liver	2.15 / 2.2
lung	0.29 / 0.3
ovary	0.35 / 1.7
skeletal muscle	0.03 / 0.0
thyroid gland	0.5 / 0.6

Entities

Details

Heatmap

0.01 TPM 81.9

Human BodyMap 2.0

CD24 GGT1 NPHS1 NPHS2 PAX2

Summary

- One stop information hub for established, quality controlled human PSC lines
- Validated ethical procurement of lines
- Scientific QC and characterization data for lines
- Enable access to and comparison of cell associated information
- Enable and integrate user feedback / data supplementation