Human Developmental Biology Resource (HDBR)

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Genetics Matters 27 February 2015

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HDBR

HUMAN DEVELOPMENTAL BIOLOGY RESOURCE

UCL

"An embryonic and fetal tissue bank enabling studies of human development"

wellcome trust

MRC Medical Research Council

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www.hdbr.org

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Why do we need to study human development?

- Fascination with our own species

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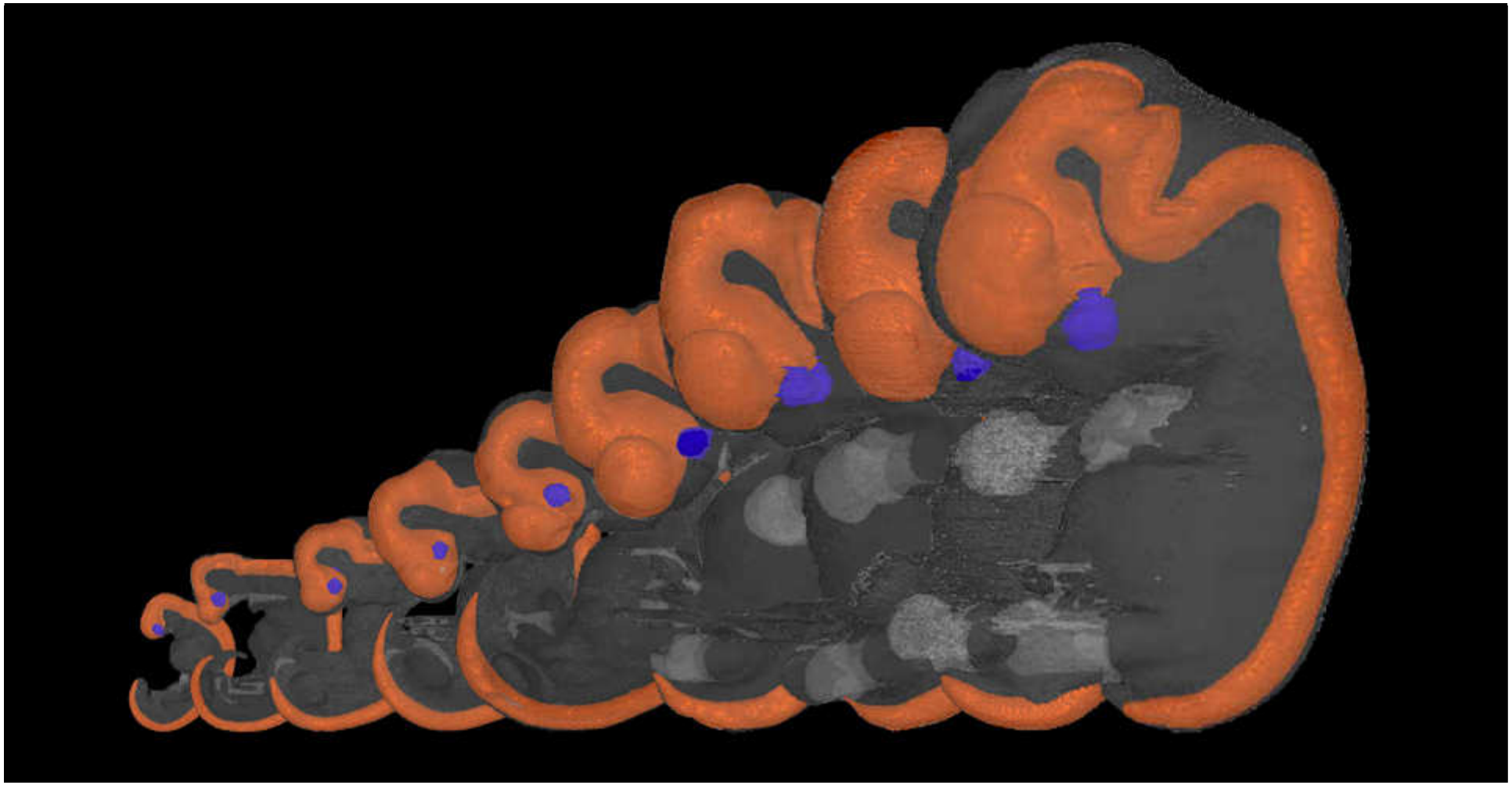
Many disorders originate during development



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What about animal models (e.g. mouse)?

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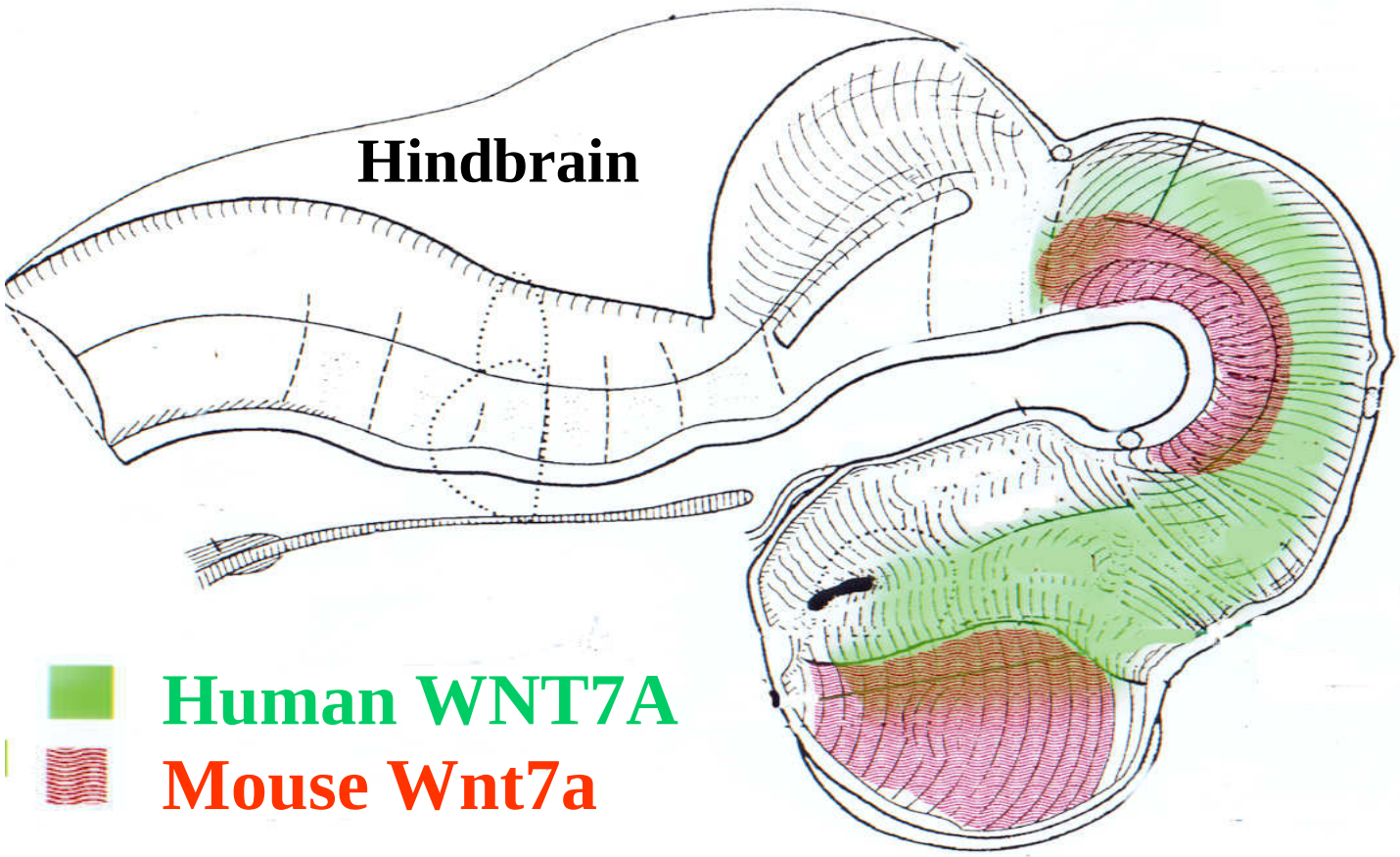
The same gene may be active in different places in human



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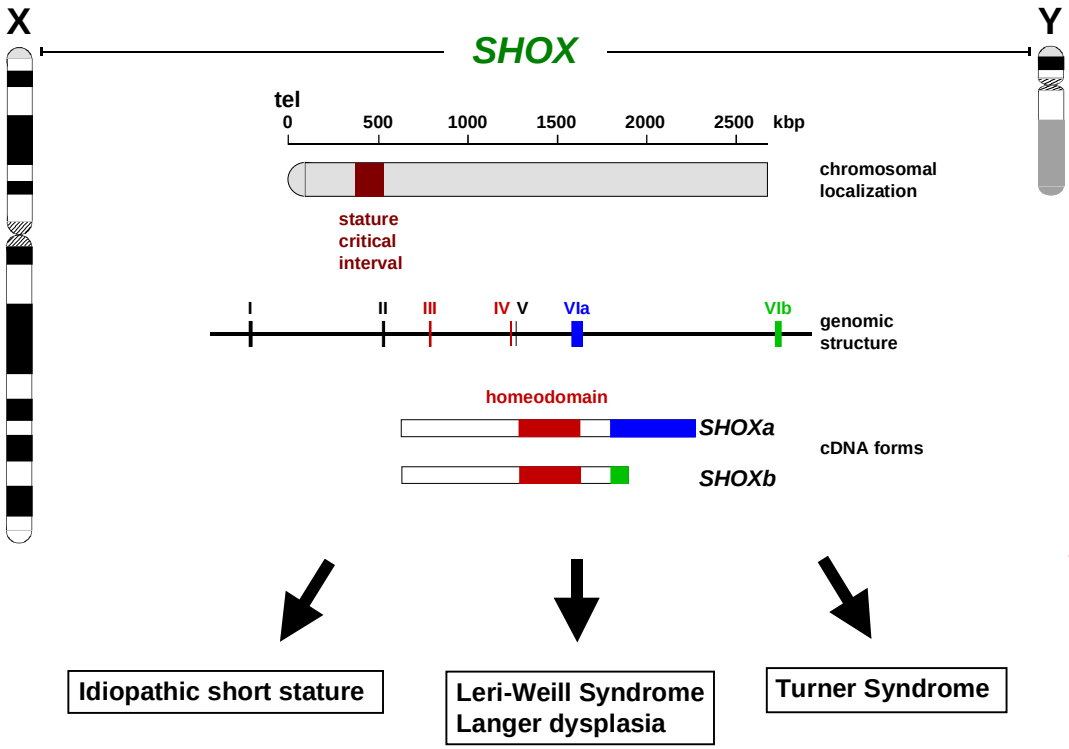
SHOX is an example of a gene present in human but not in mouse



Leri-Weill Syndrome

Idiopathic

S hort Stature

H omeobox Gene

O n the

X Chromosome

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HTA Human Tissue Authority

- HDBR governance
  - HDBR conforms to HTA codes of practice and is a licensed HTA tissue bank (part of NBB)

  - HDBR has ethical approval from REC
  - Steering committee comprised of independent scientists, HDBR funders, an ethicist and a lay member of the public – review HDBR activity at biannual meetings.

wellcome trust

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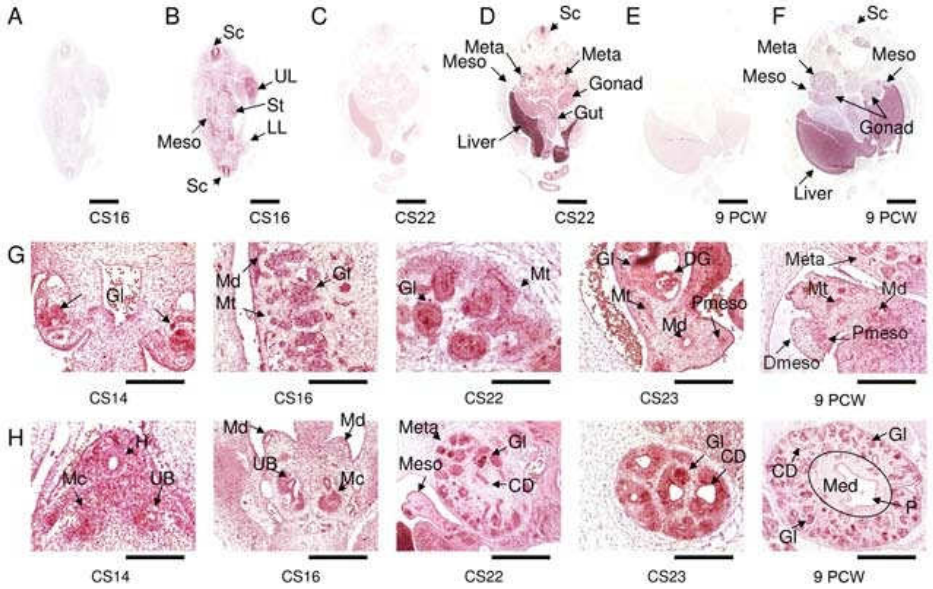
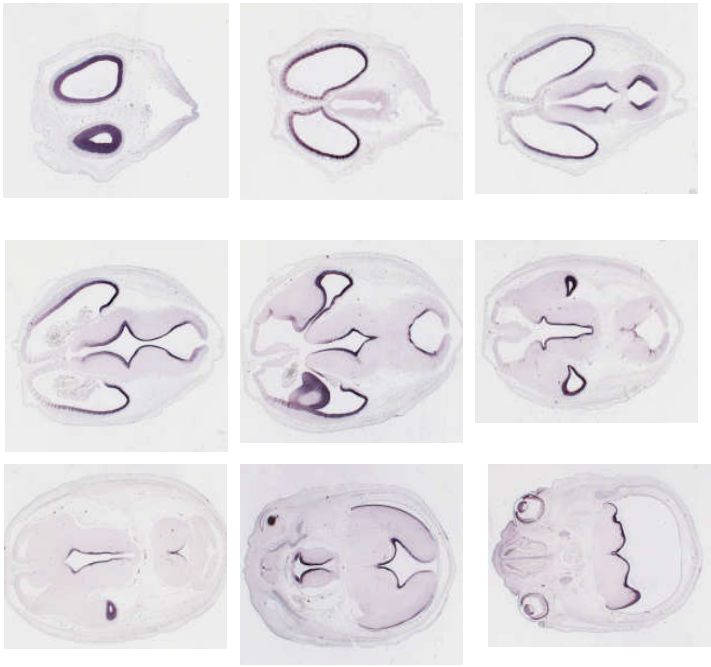
MRC Medical Research Council

HDBR material has been used by many researchers in many different kinds of research project

- Single gene studies



AHI1



FGFR3

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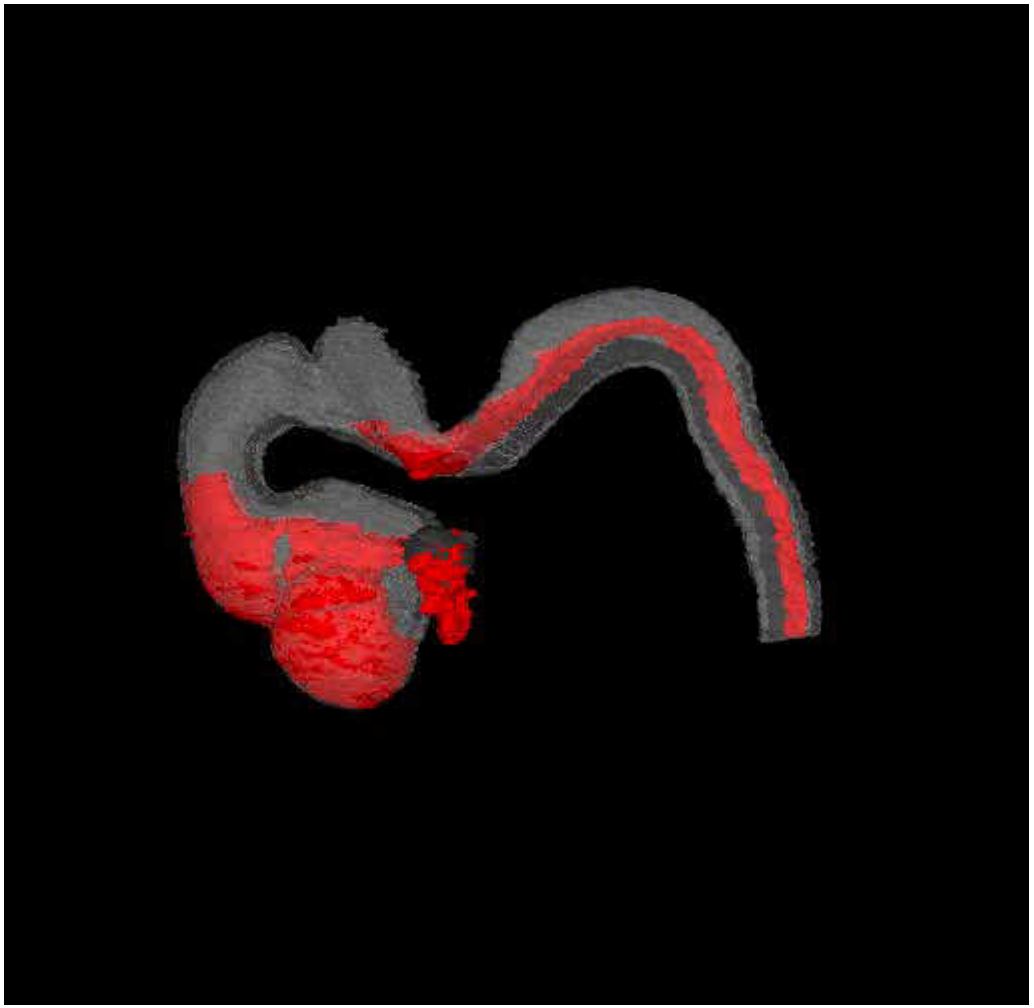
Aniridia -PAX6

Aniridia is the absence of the iris – caused by mutations in the PAX6 gene.



PAX6 gene activity (red colour) is seen in the developing eye and specific areas of the developing brain and spinal cord

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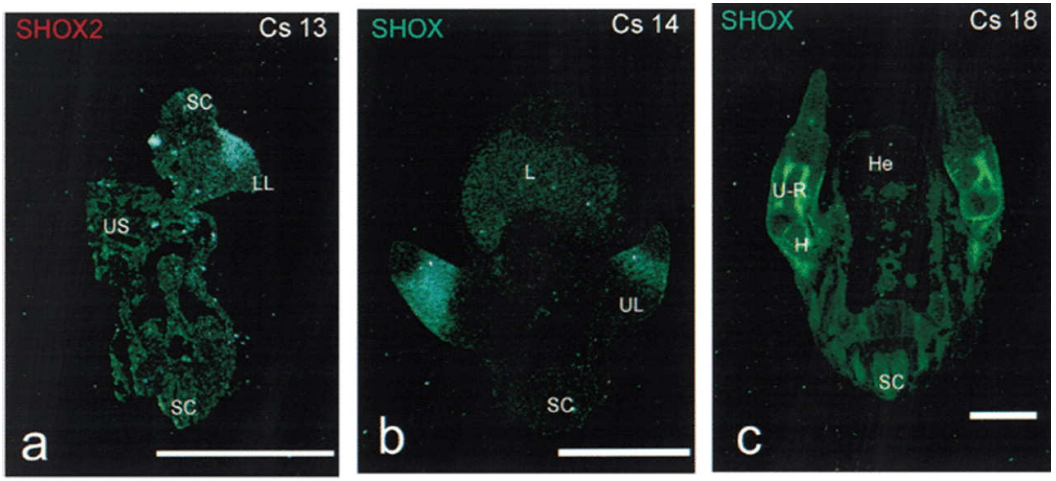
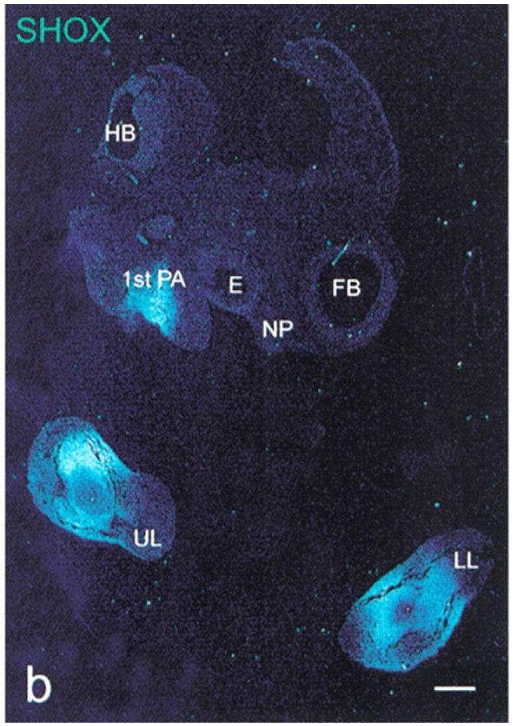
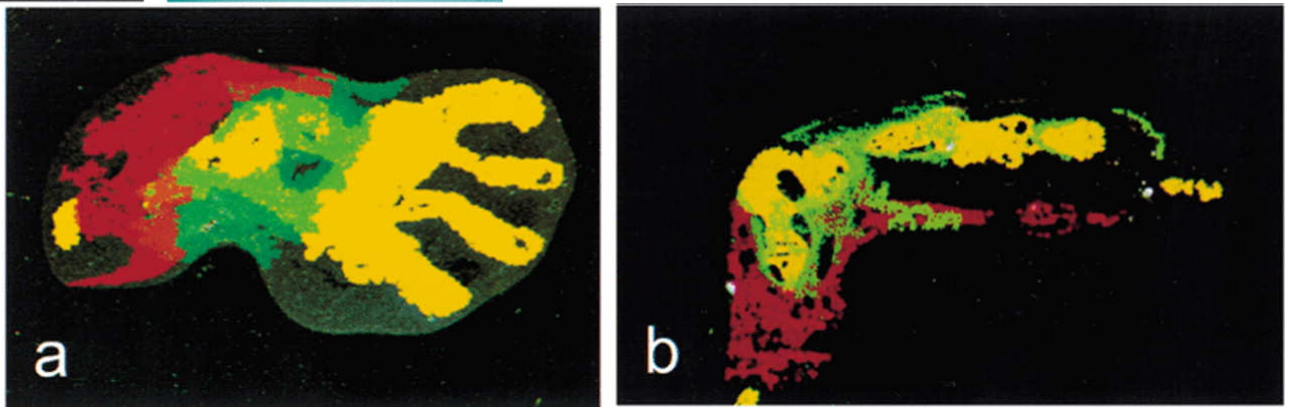




SHOX



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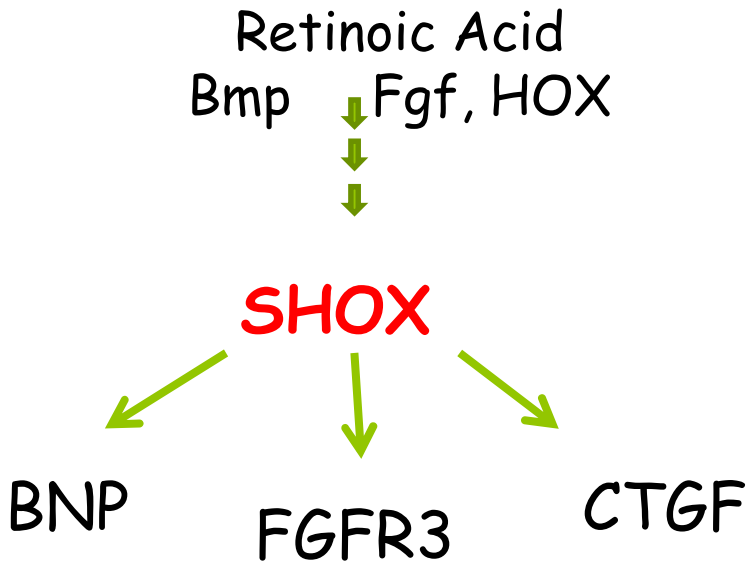
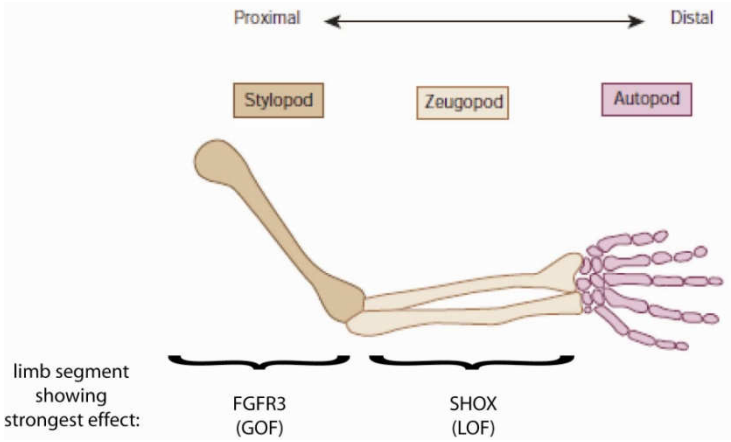
SHOX -> SHOX pathway





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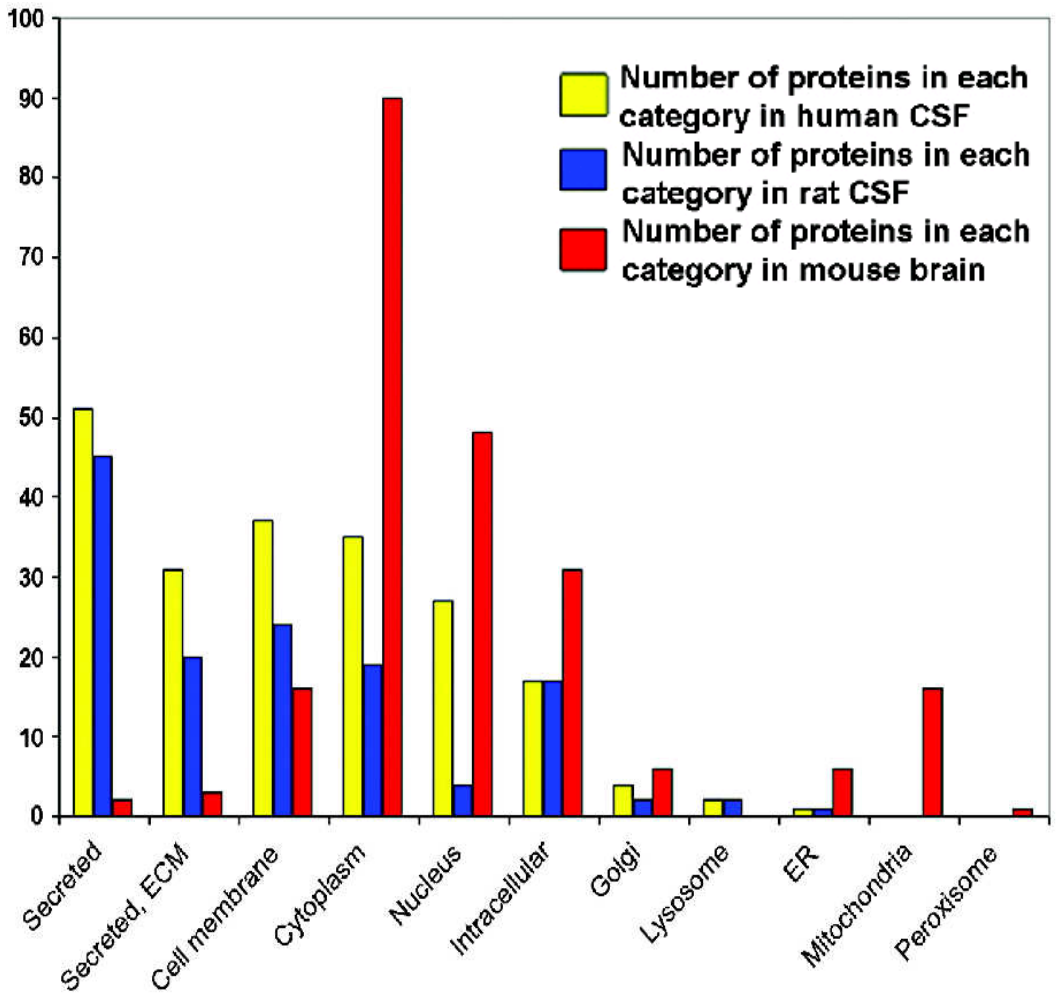
Protein studies

- Individual proteins
- Many proteins
  -proteomics



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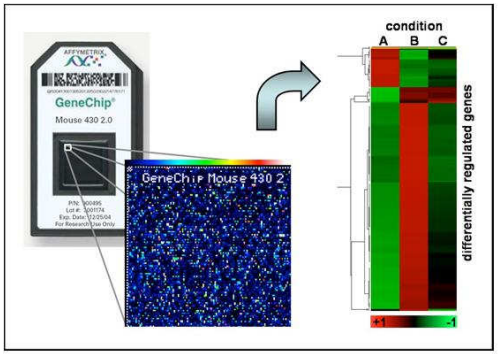
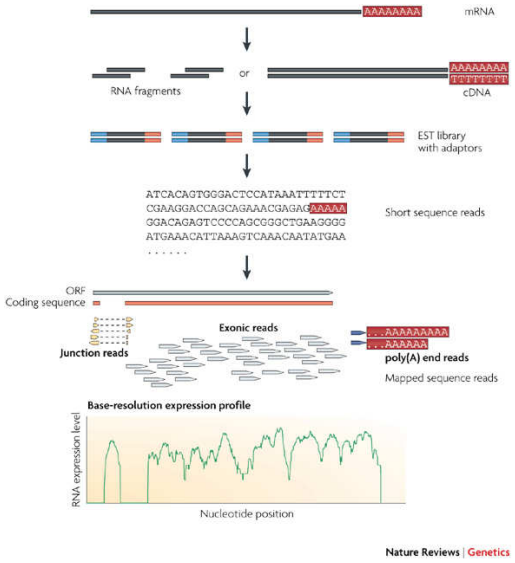
Transcriptome studies

- Identifying all the genes that are expressed in an organ/tissue/cell
  - Microarray
  - RNA-sequencing





Transcriptomics data can be "mined" multiple times by different groups and/or for different purposes

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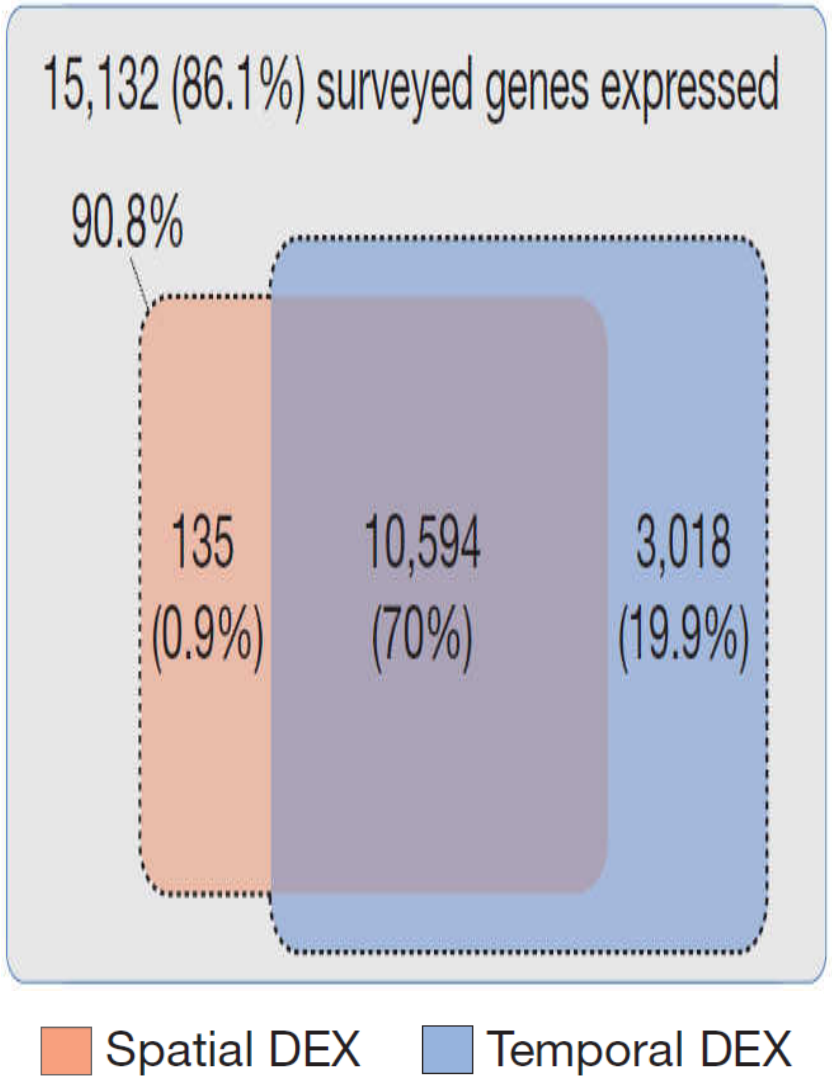
Transcriptome studies- identify genes with differential expression patterns (DEX)



RNA sequencing of 57 brain samples from 15 distinct grouped age periods - embryonic to late adulthood – across up to 16 distinct brain regions..

17,565 genes were analysed, **15,132** were expressed in at least 1 brain region in one age group.

Of the 15,132 expressed genes:

- **70.9%** of genes displayed spatial DEX.
- **89.9%** of genes displayed temporal DEX.

http://www.brainspan.org/

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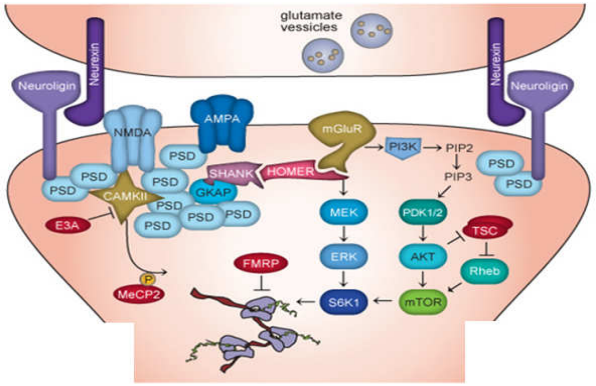
Transcriptome studies- find genes expressed in unexpected places and times of development

- Some genes implicated in Autism Spectrum Disorder are expressed in the mature synapses of the adult brain



Gene	Genotator Autism score *	SFARI gene score+	Microarray expression [14]	RNA Seq [30]
NRXN4 (CNTNAP2)	11.3	S	Moderate	High
SHANK3	11.1	S	Very Low	Low
NRXN1	9.9	1	High	Moderate
NLGN4X	6.0	2	High	Low
SHANK2	3.4	3	Moderate	Low
NRXN3	2.5	-	Moderate	Low
NLGN3	2.3	2	Low	High

- They are ALSO expressed at early stages of human cortex development

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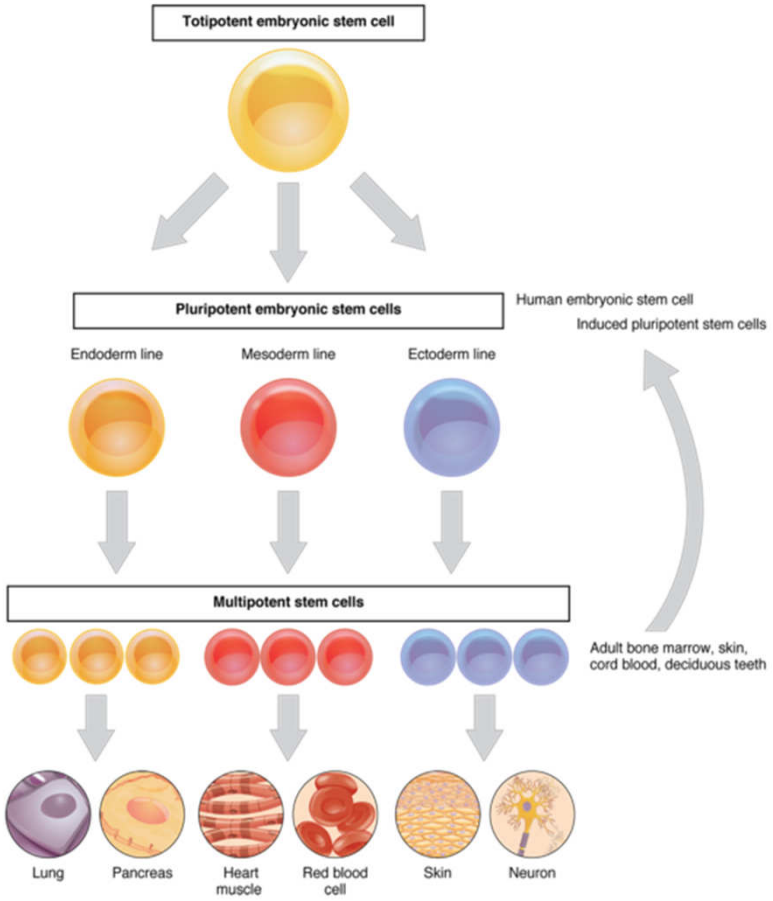
Stem cell studies



- are the different cell types generated from stem cells the same as cells in the body?
- Do they go through the same changes as developing cells?

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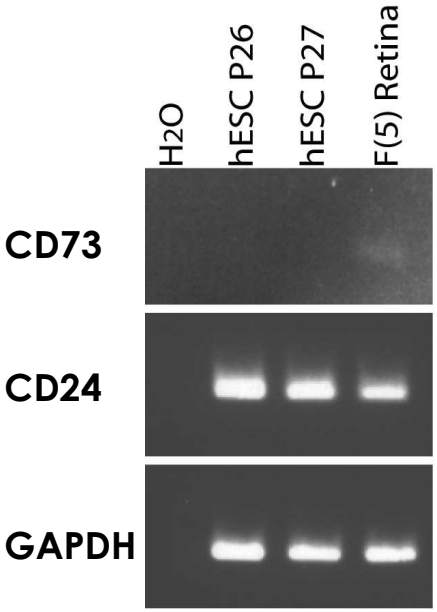
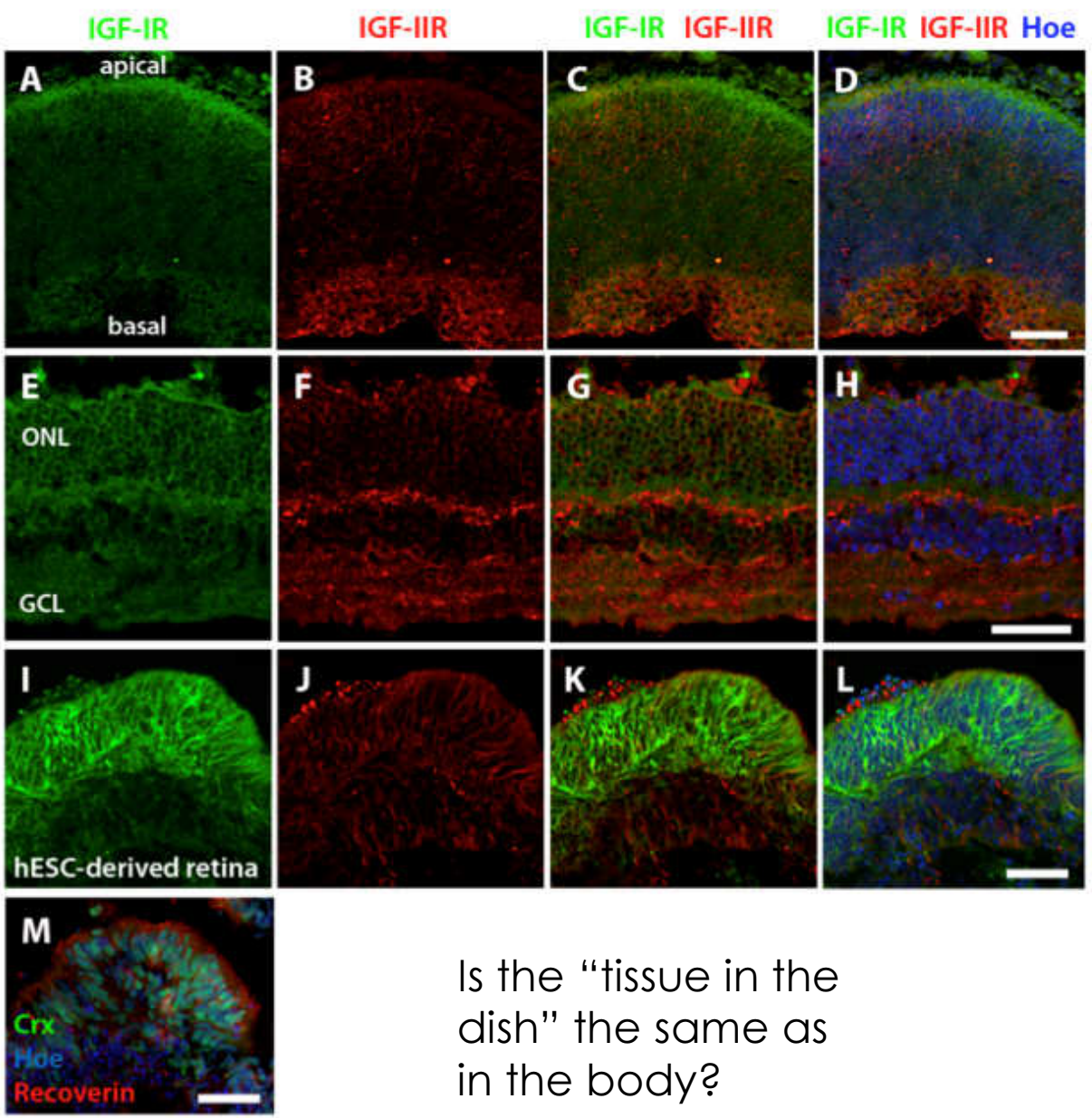
Validating cells:





Is the "tissue in the dish" the same as in the body?

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Thank you

Questions?

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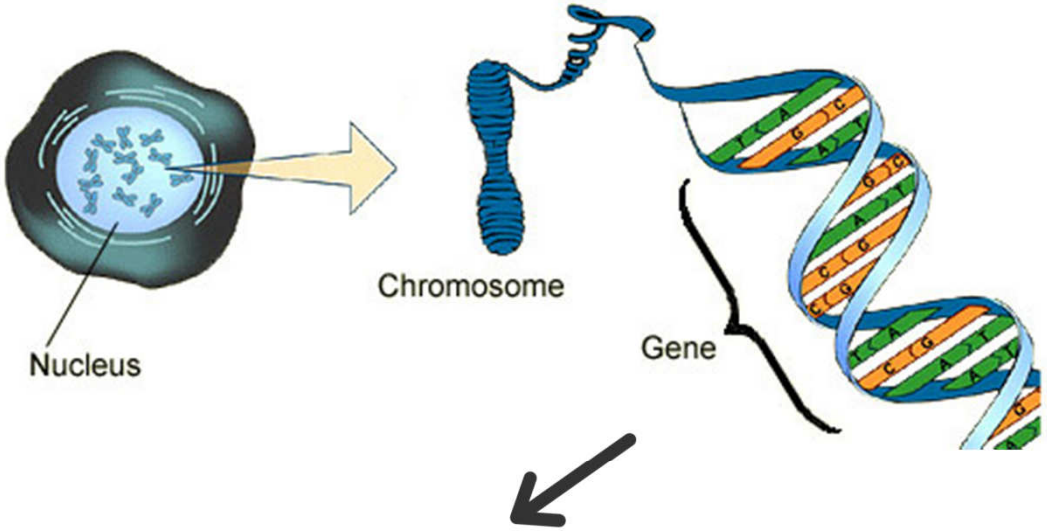
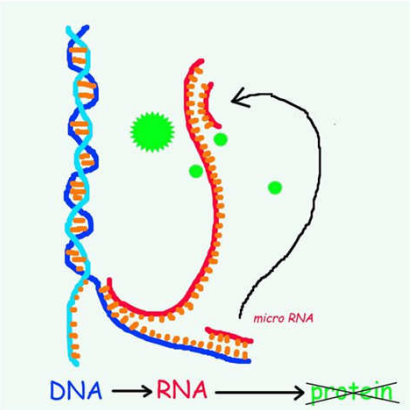
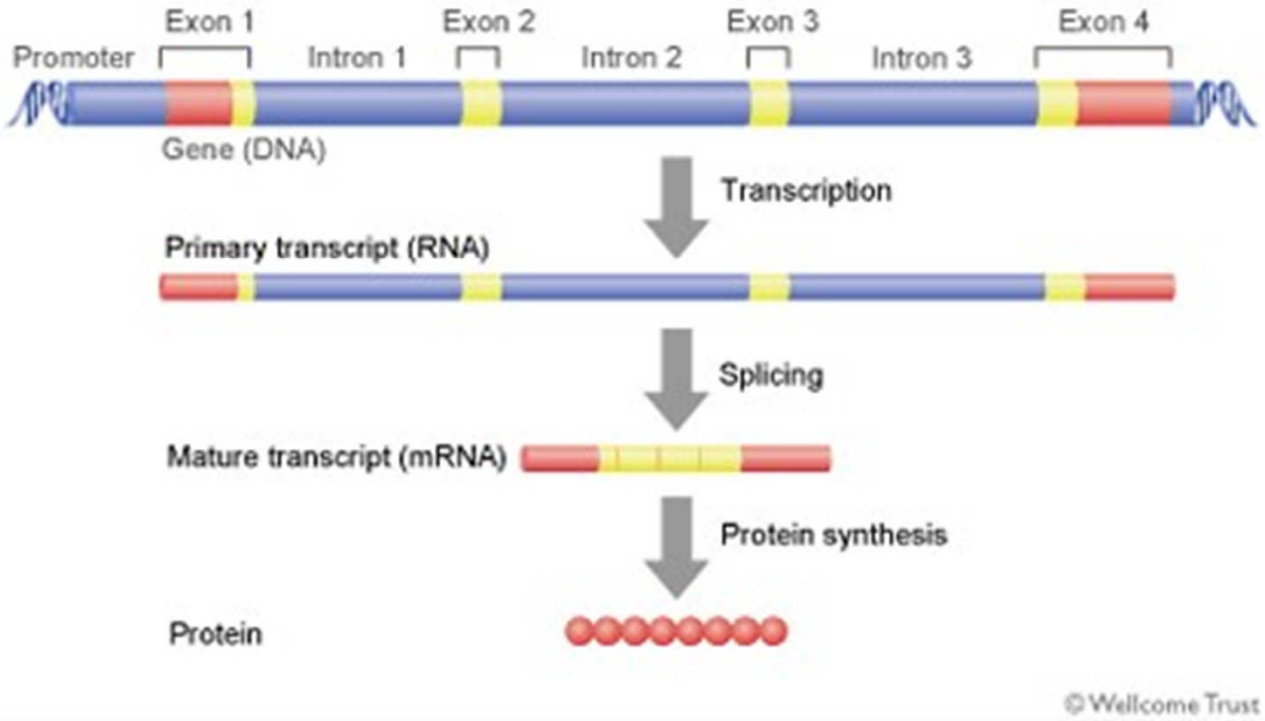




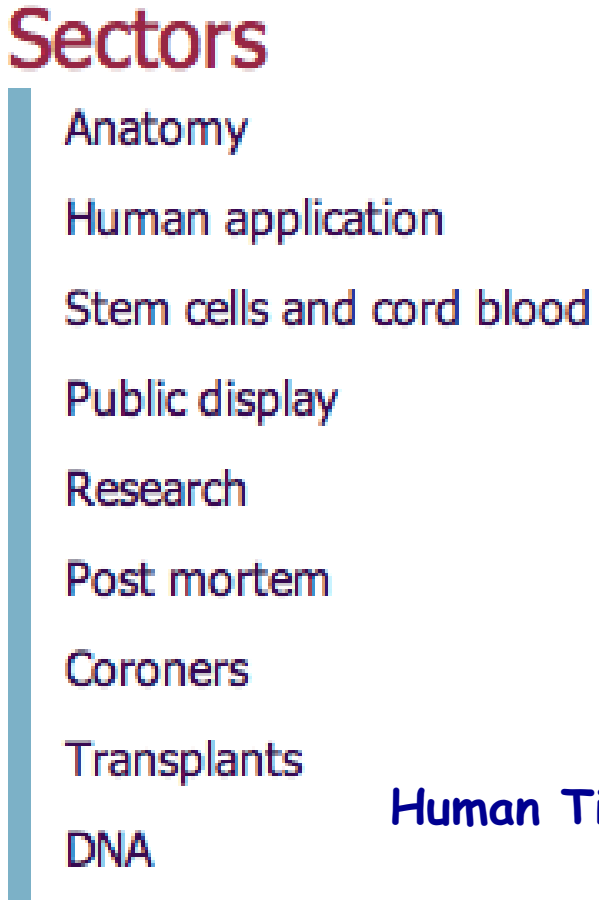
Structure of a Gene



ethical issues

- Consent
- Fundamental principles
  - Appropriate: who can give it
  - Valid: voluntary, informed, given by someone with capacity
  - Scope: generic or specific
  - Duration: enduring or time-limited
  - Ability for consent to be **withdrawn**
- What is the consent for?
  - To collect tissue
  - Type/purpose of research
  - Who is carrying out research
- Patient information sheet and consent form
- Regulatory body
  - Human Tissue Authority [HTA]

What are the activities of the HTA?



- Interpreting the Human Tissue Act
  - Codes of practice
- Implementing the Human Tissue Act
  - Licensing
  - Inspecting

Human Tissue Act (2004)

Came into force- 1st September 2006

http://www.hta.gov.uk/

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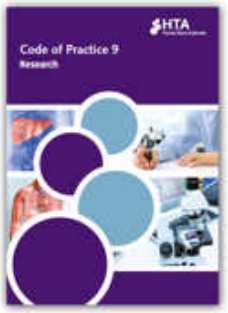
HTA codes of practice

- Codes of practice
  - Code 1 Consent
  - Code 2 Donation of organs
  - Code 3 Post mortem
  - Code 4 Anatomy
  - Code 5 Disposal
  - Code 6 Donation of bone marrow
  - Code 7 Public display
  - Code 8 Import and export
  - Code 9 Research

Code of Practice 1 - Consent

Code of practice 9 - Research



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