Conservation of a cell type specific transcriptional basin across tissues, individuals, and species.

In FANTOM4 we developed a methodology for characterising specific transcriptional basins (networks that define the stable state of a cell). Here using smooth muscle cells as a model system, we examined the levels of variation in these basins from cells isolated from different donors, different tissue locations and across multiple vertebrate species. We measure promoter expression using unamplified deepCAGE [nuclear vs cytoplasmic?] [and small non-coding RNAs by sequencing]. We find a core smooth muscle network that is conserved between individuals, tissue location and across species. In addition for each source of variation we find an extended smooth muscle network that varies with genotype, tissue development and species which is defined in terms of expression pattern and observed transcription factor

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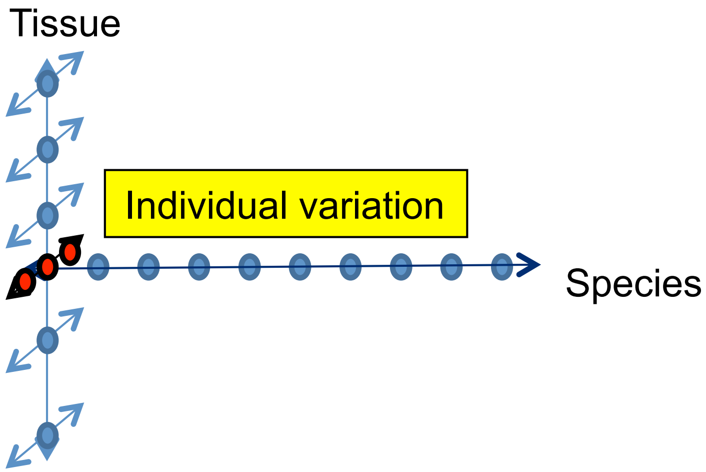
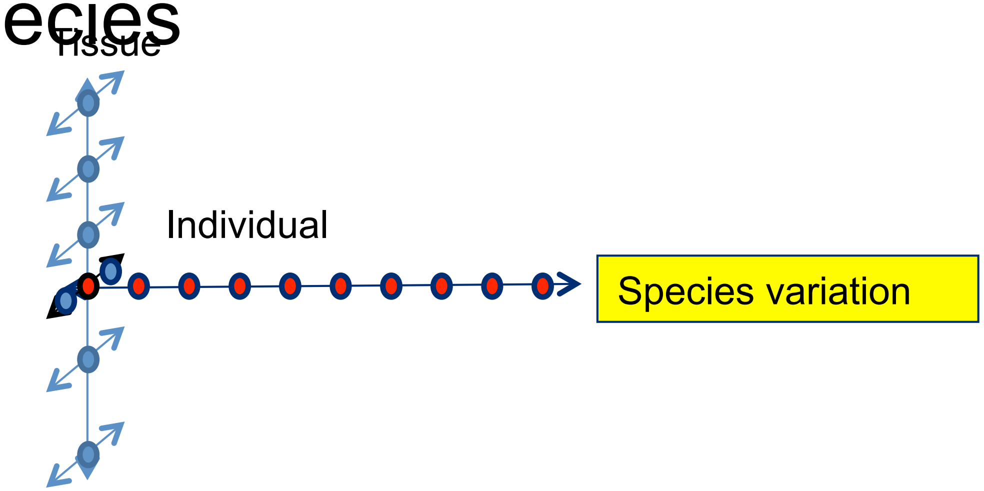
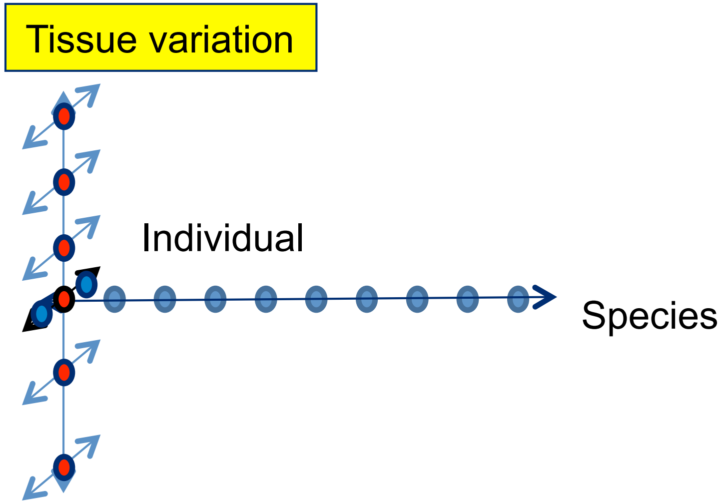
Network comparison across individuals, tissues and species



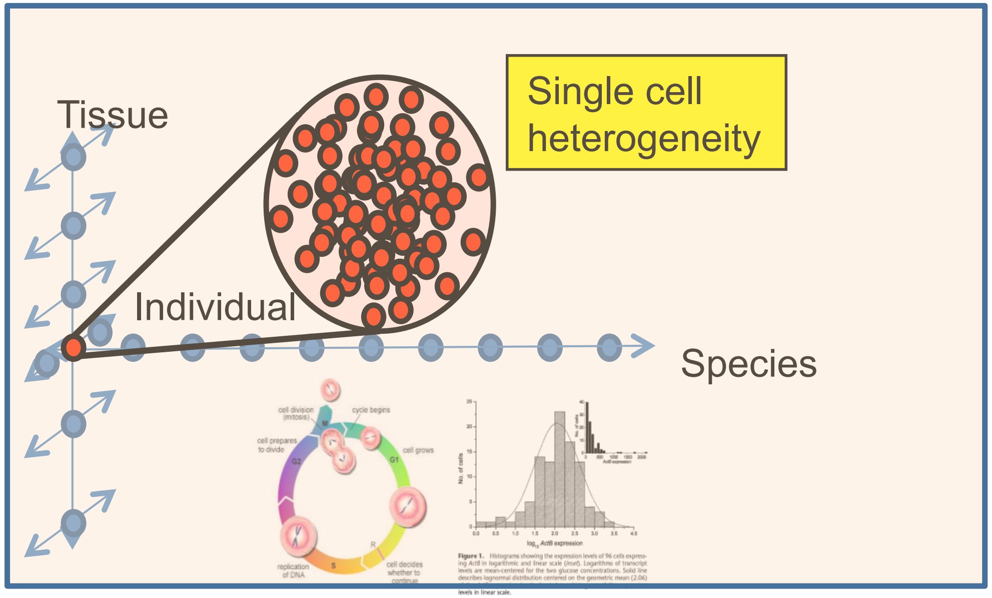
Individual variation



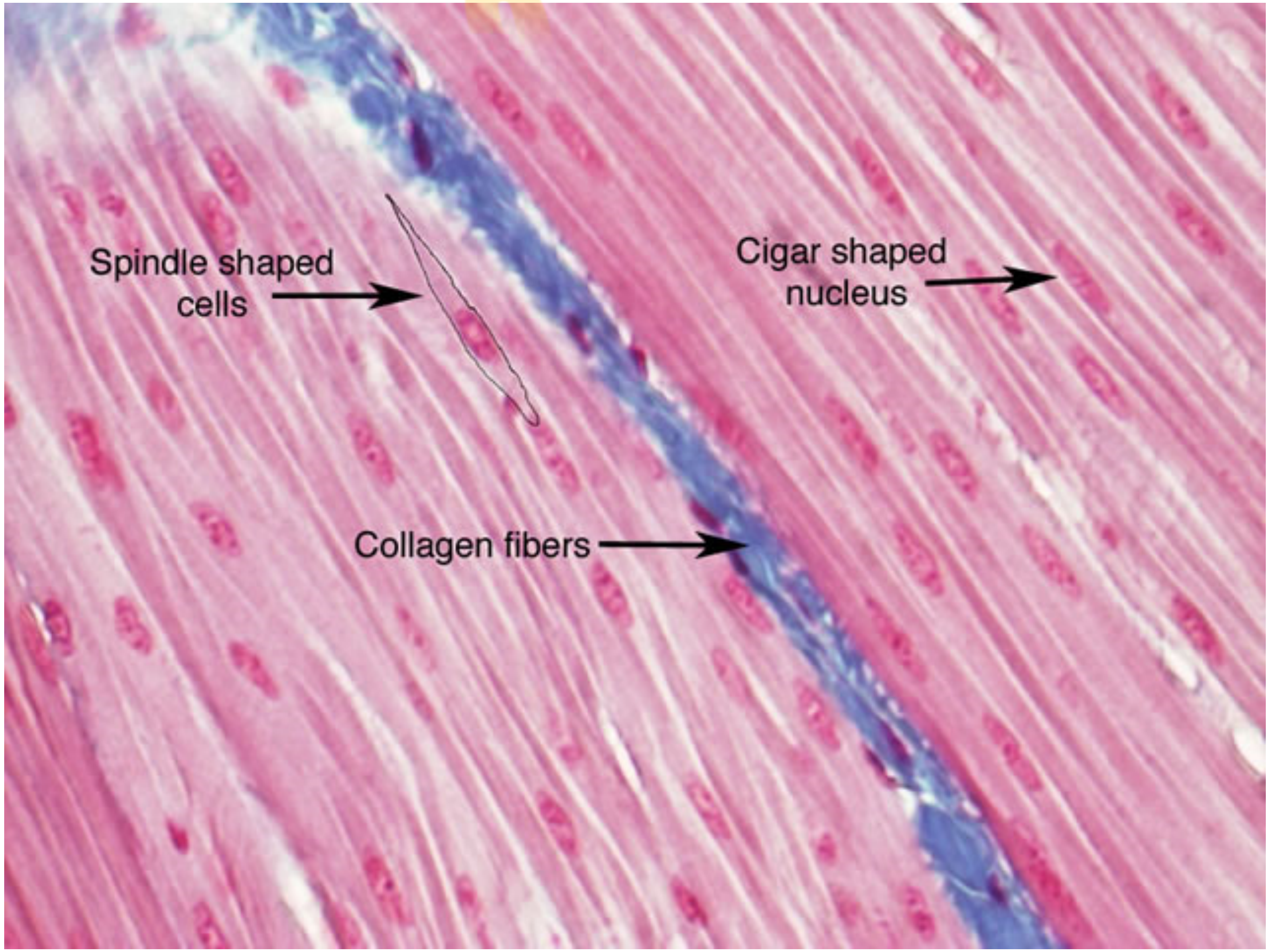
Species variation



Tissue variation



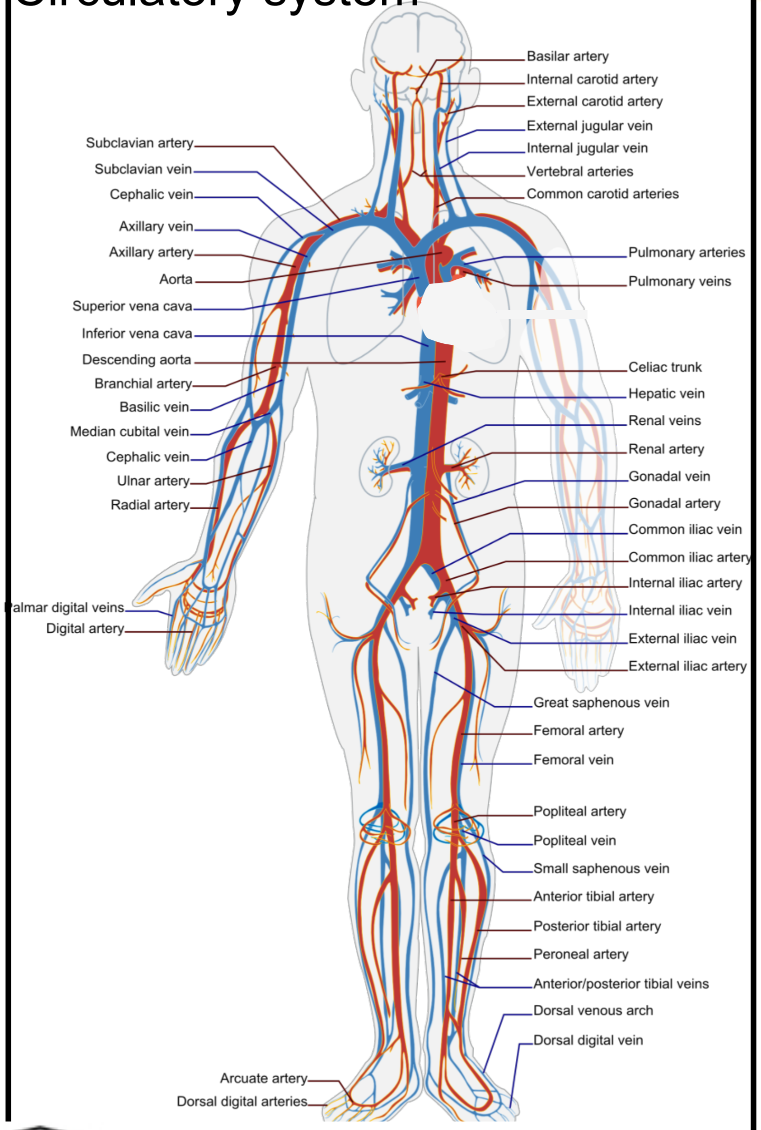
Single cell heterogeneity



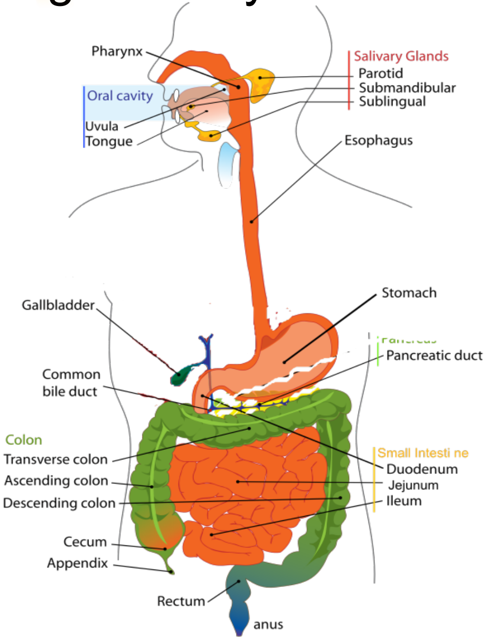
Smooth Muscle Cells

Smooth muscle locations

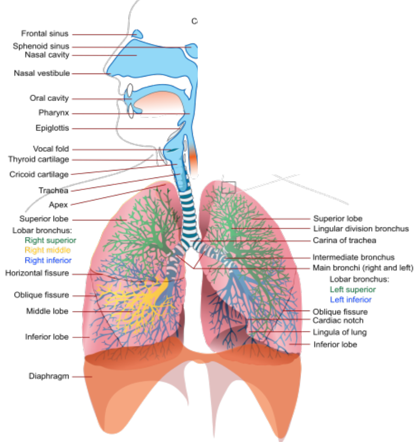
Circulatory system



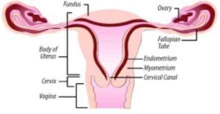
Digestive system



Respiratory system

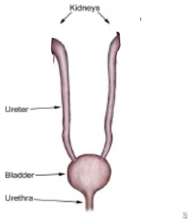


Reproductive system



Normal Uterus

Urinary system



Experimental design

Across individual

3 donors for each cell type in every study

Across location

Human SMCs from 18 locations (Aortic, Bladder, Brachiocephalic, Brain Vascular, Bronchial, Carotid, Colonic, Coronary Artery, Esophageal, Internal Thoracic Artery, Intestinal, Prostate, Pulmonary Artery, Subclavian Artery, Tracheal , Umbilical Artery, Umbilical Vein , Uterine)

Across species

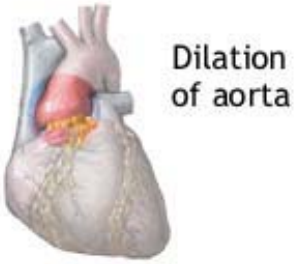
Human, Mouse, Rat, Pig, Chicken

Anatomically conserved sites – Aortic SMCs, Bone marrow derived mesenchymal stem cells, Hepatocytes

Disorders linked to smooth muscle defects

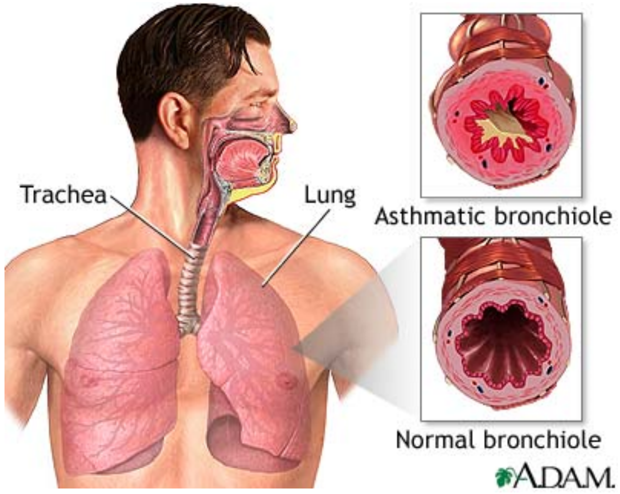
Circulatory system

- Marfan's syndrome
- Vascular Ehlers-Danlos syndrom
- Loeys-Dietz syndrome (LDS)
- Williams-Beuren Syndrome
- Williams Syndrome



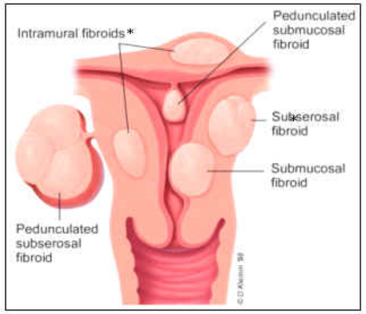
Respiratory system

- Asthma



Reproductive system

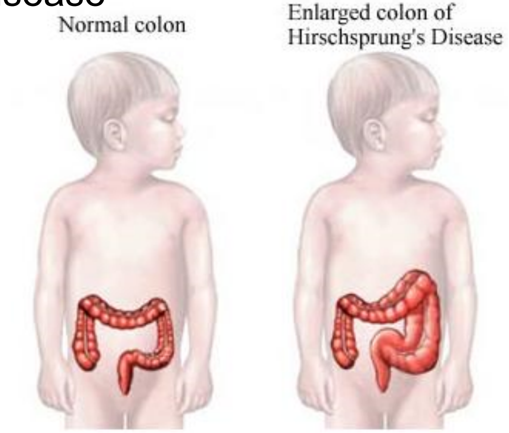
- Leiomyoma – uterine fibroids
- Leiomyosarcoma -uterine cancer



* = most common

Digestive system

- Hirschsprungs disease



Analyses needed

- Motif activity (or similar) analysis across multiple locations and species
- Homology mapping
- Cross species expression clustering
- Promoter conservation
- Network conservation
- Cross species perturbation?