

# How to mend a broken heart...

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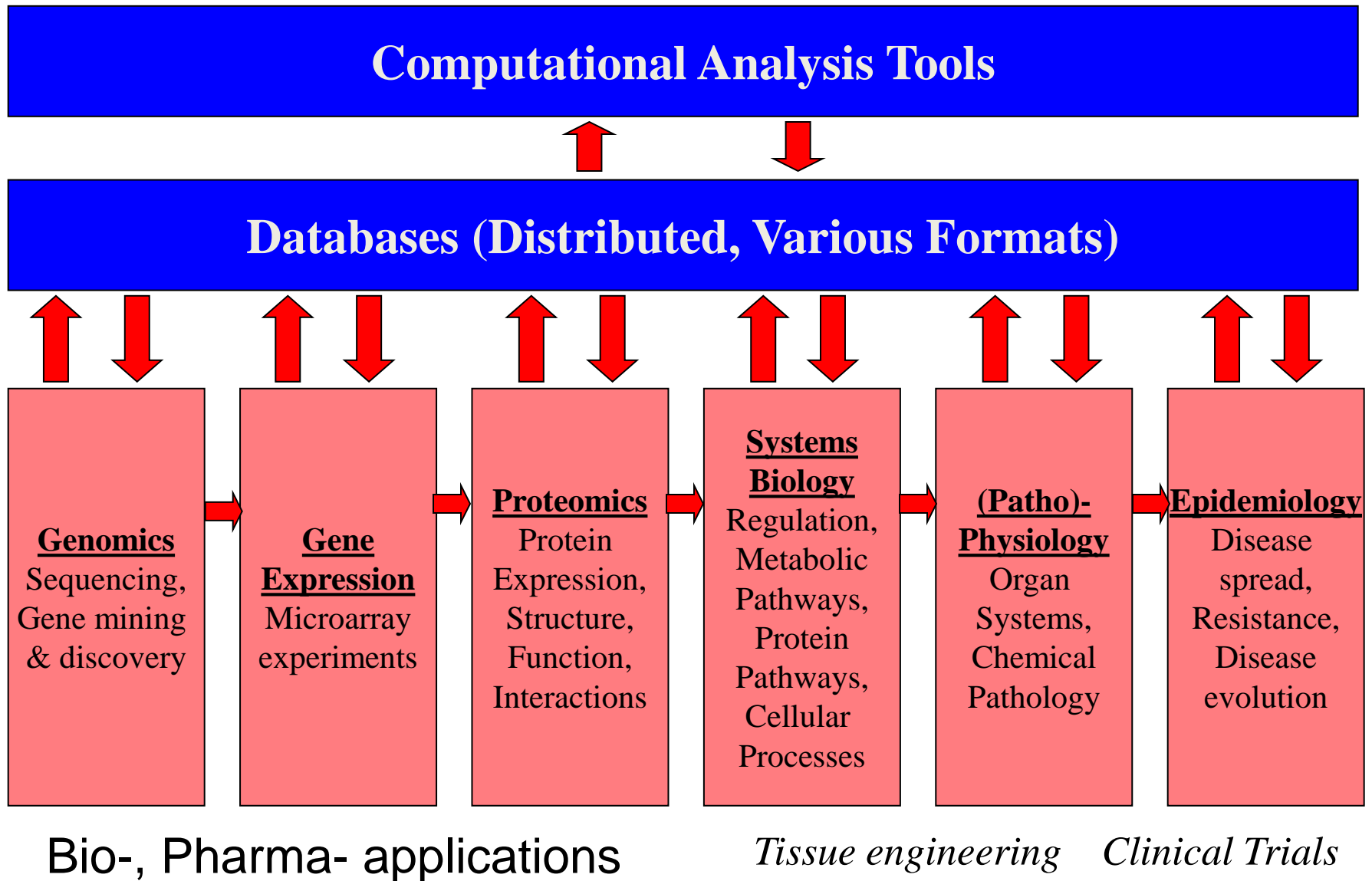
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# 1. Acknowledgements

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- Dr Fanny Bajolle (Paris)
- Dr Tariq Abdulla (Warwick)

# 2. Genesis of Multiscale Engineering Concept



**Information-driven discovery**

## 2. Genesis of Multiscale Engineering Concept

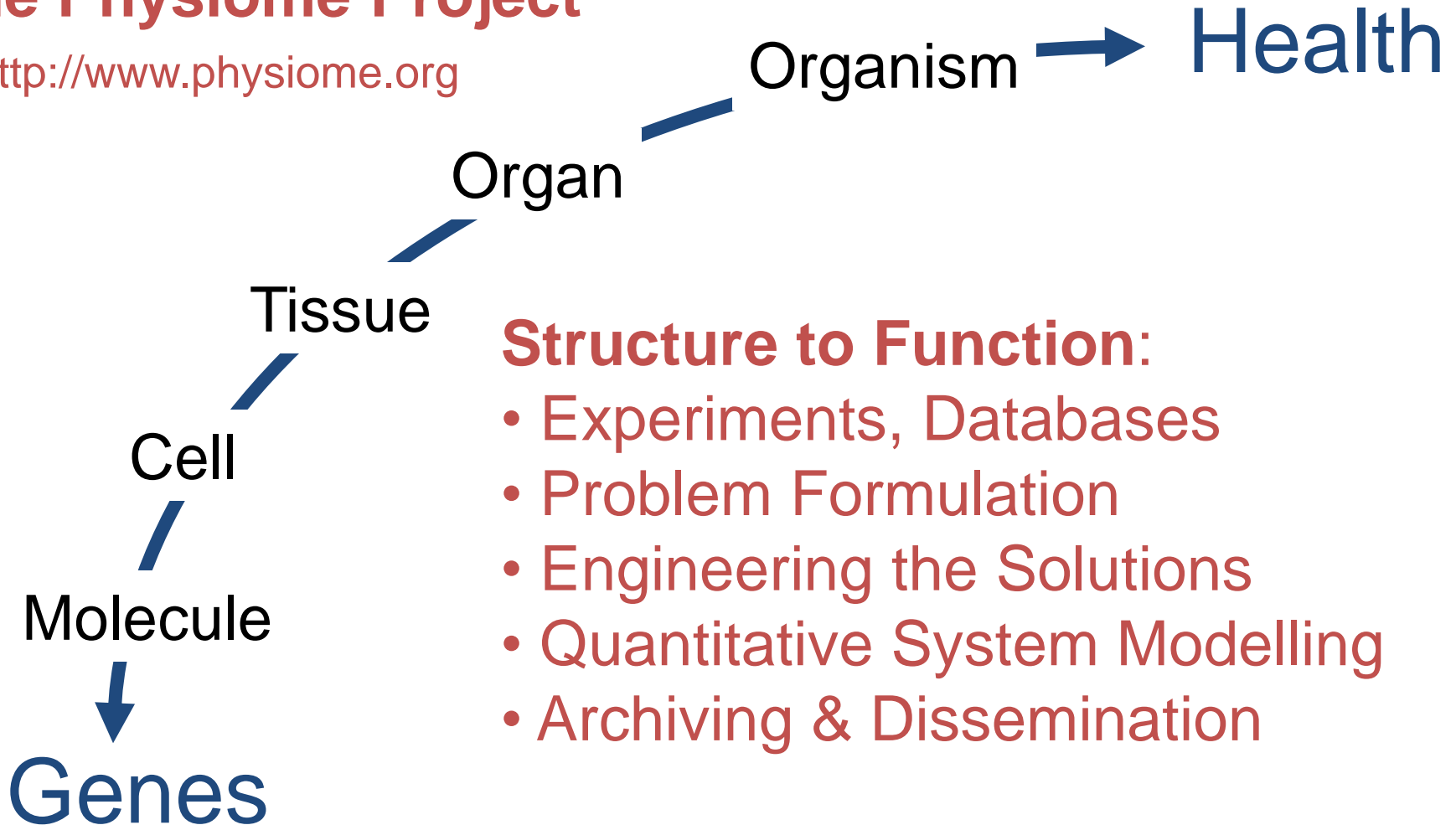
### Definition of multiscale modelling

“...multiscale modelling is the field of solving physical problems which have important features at multiple scales, particularly multiple spatial and (or) temporal scales”.

# 3. Physiological Context

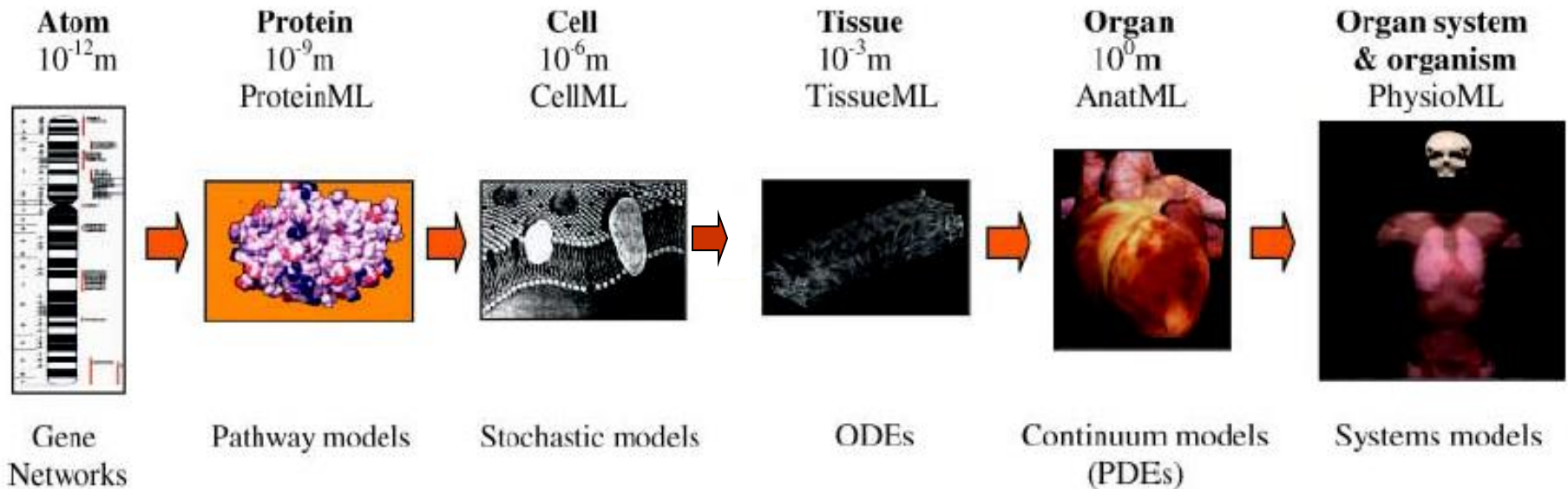
## The Physiome Project

<http://www.physiome.org>



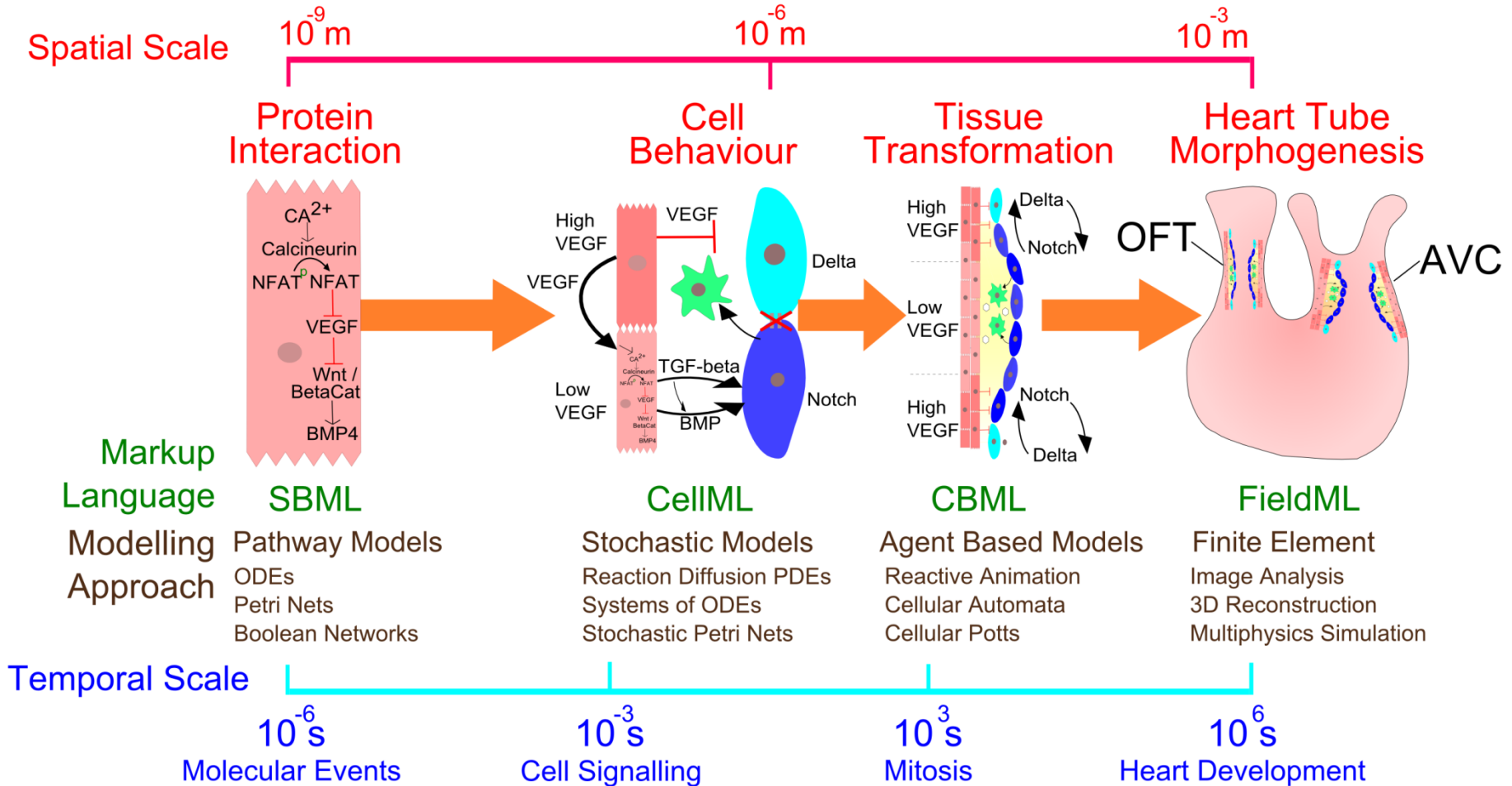
**From Genome to Function**

# 3. Physiological Context



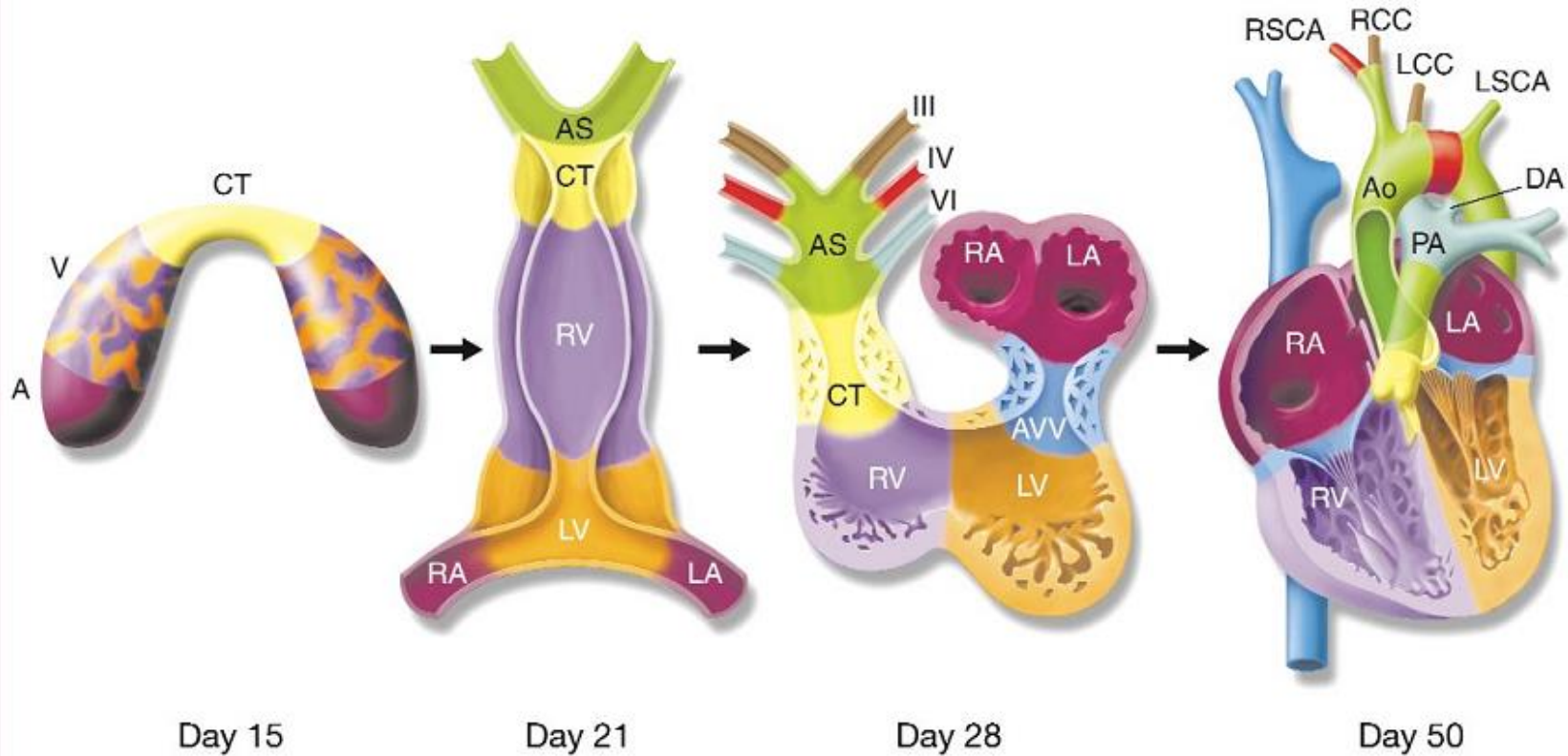
## The Physiome Project

# 3. Physiological Context



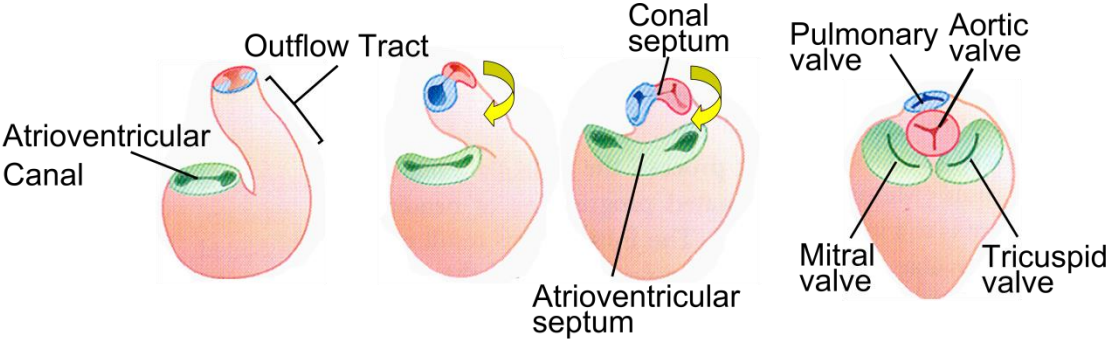


# 4. Normal Heart Development

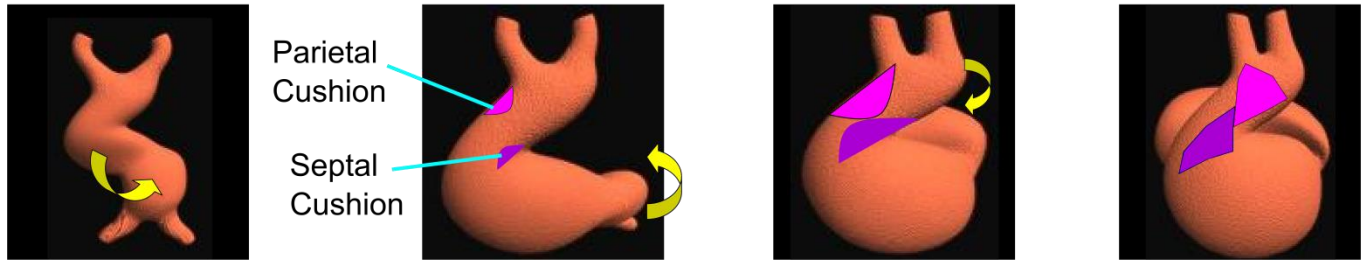


# 4. Normal Heart Development

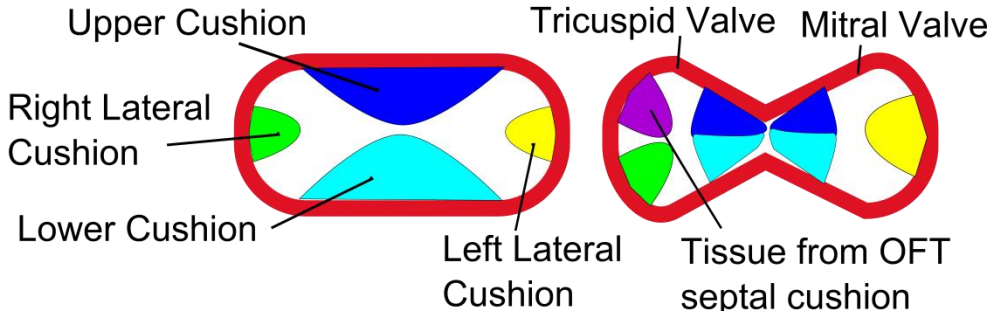
Heart Looping (Rear View)



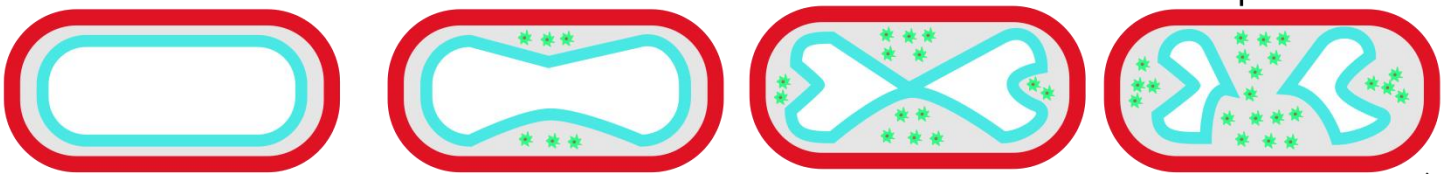
Outflow Tract



AV Valves



AV Canal



Human Embryonic Day

E24

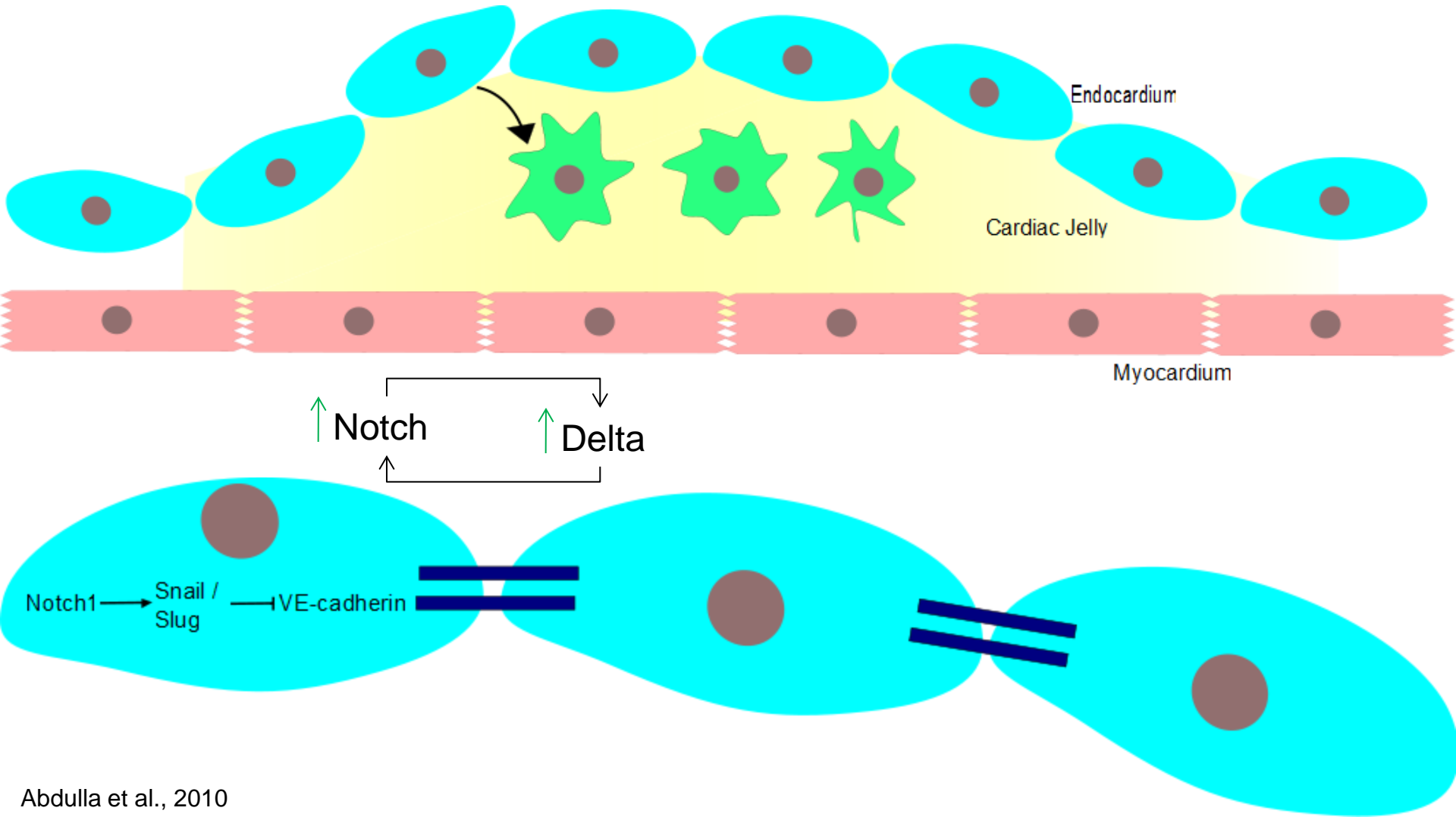
E26

E28

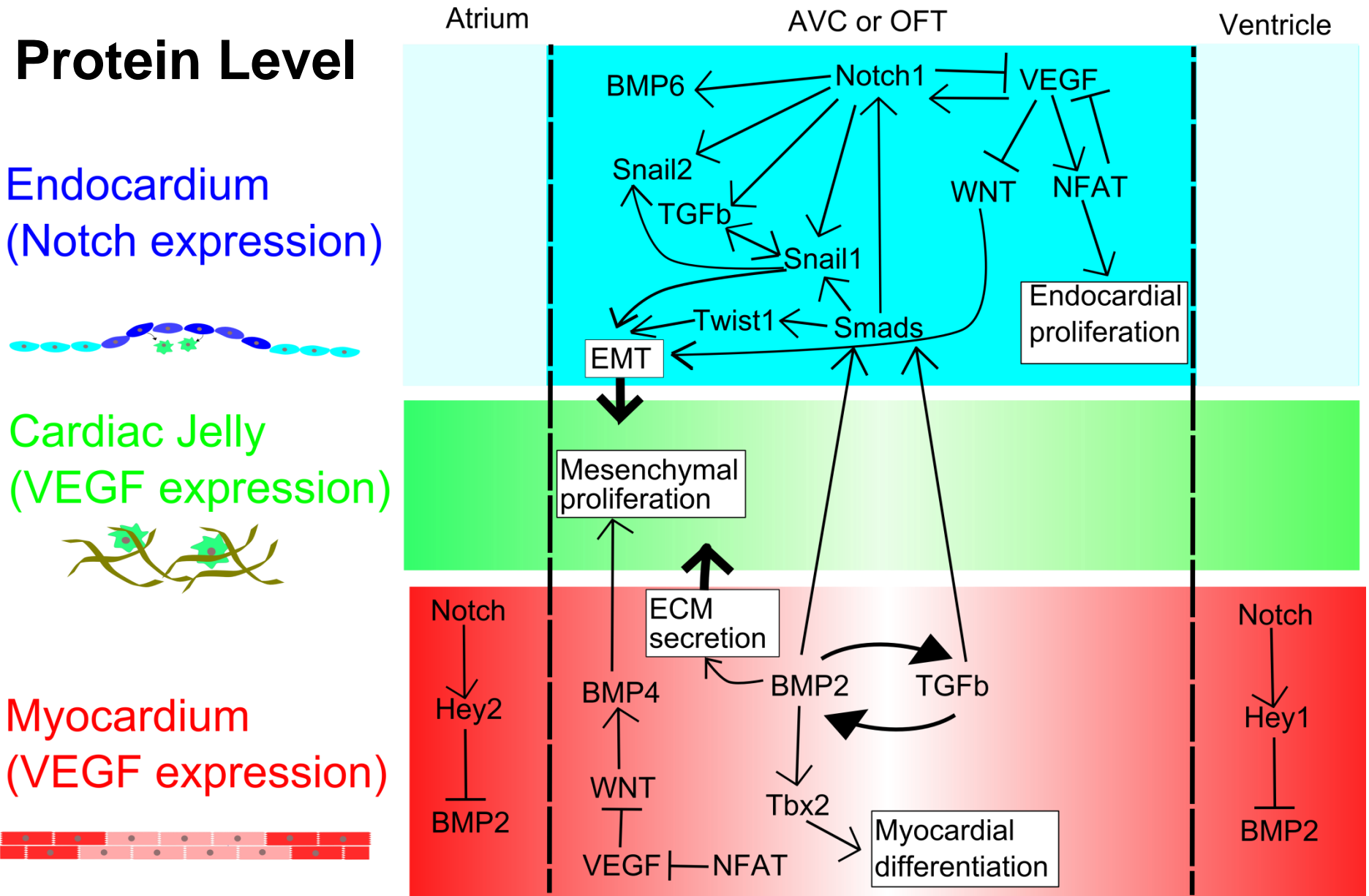
E32

# 4. Normal Heart Development

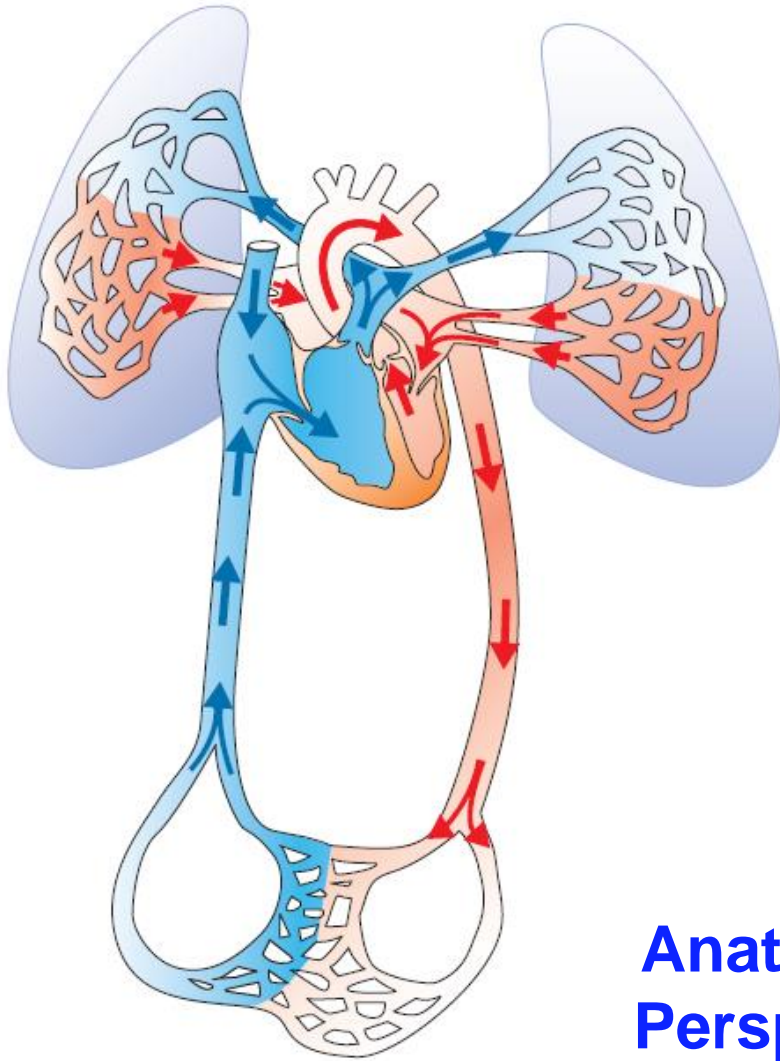
## Epithelial to Mesenchymal Transition



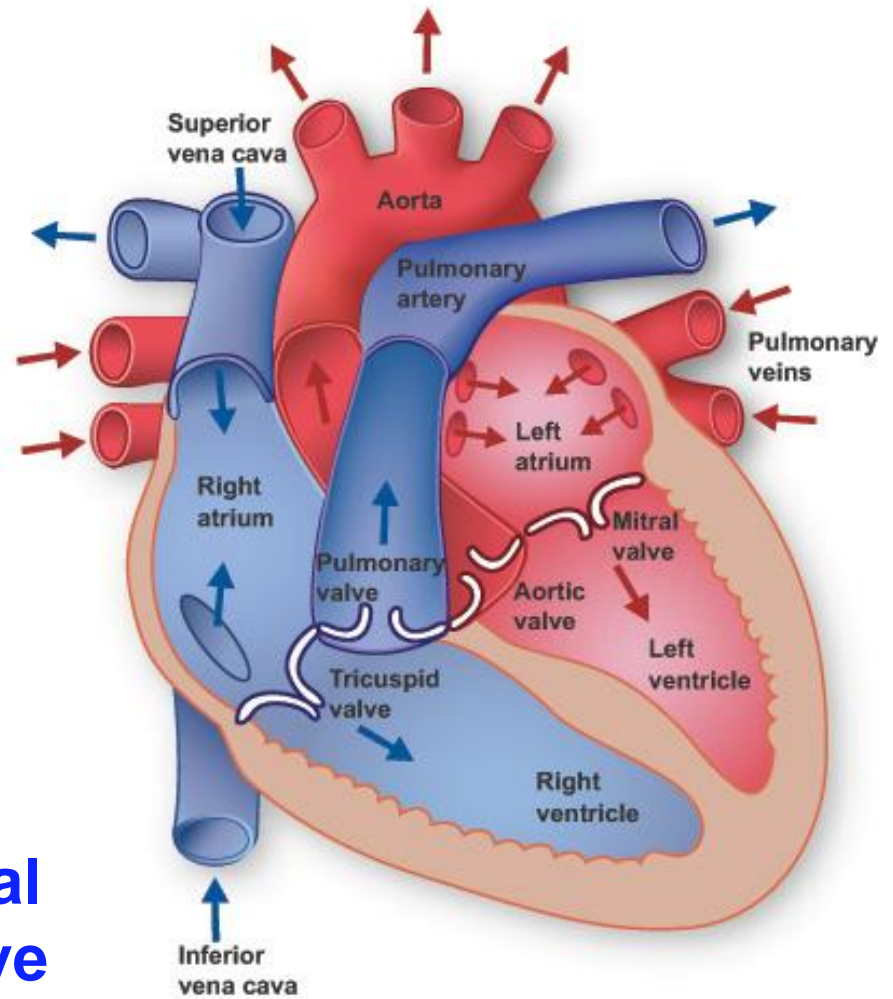
# 4. Normal Heart Development



# 4. Normal Heart Development

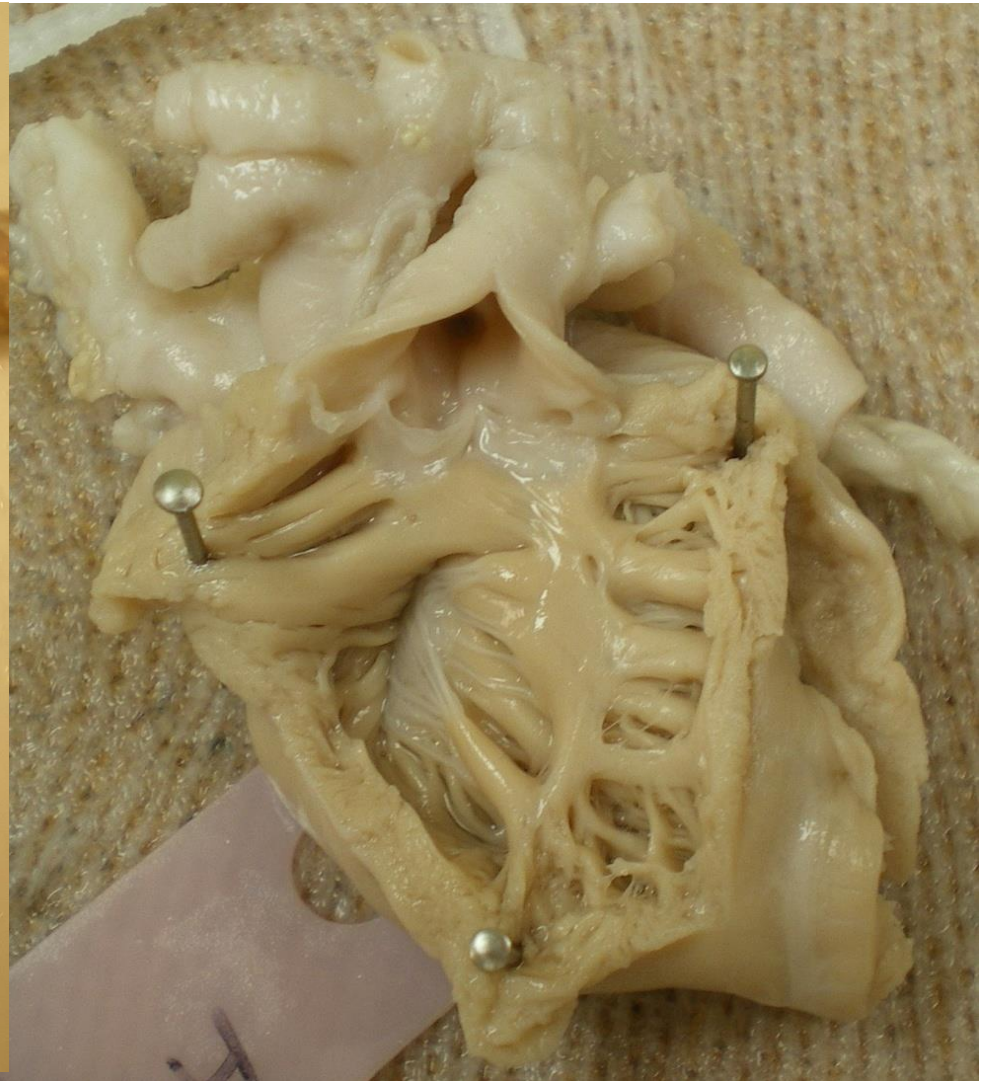
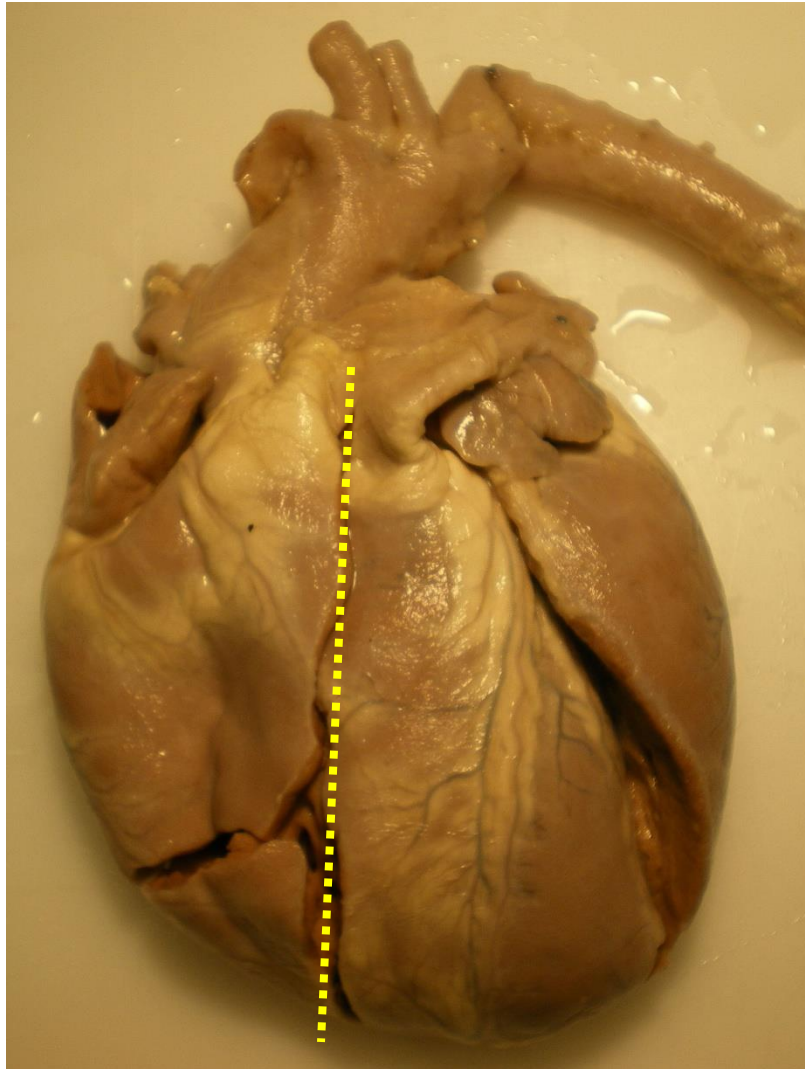


**Anatomical  
Perspective**





## 4. Normal Heart Development



# 5. Development in Congenital Heart Disease

## Clinical drivers for an engineering intervention:

- Why is it important to better understand congenital heart defects ?
- What is the Tetralogy of Fallot from an anatomical standpoint ?
- Which embryological processes are involved in the formation of the Tetralogy of Fallot ?

# 5. Development in Congenital Heart Disease

Why is it important to know more about congenital heart defects and particularly about the Tetralogy of Fallot ?

Congenital heart defects are the *most common congenital anomaly* observed in newborns – about *5-10 per 1000 births*

⇒ 10% of childhood mortality

Tetralogy of Fallot is the *most common form of cyanotic congenital heart disease*. It affects 9%-15% of all infants with congenital heart disease...

...and represents *55-70% of cyanotic congenital malformations*

We need to improve our knowledge about this abnormality





# 5. Development in Congenital Heart Disease

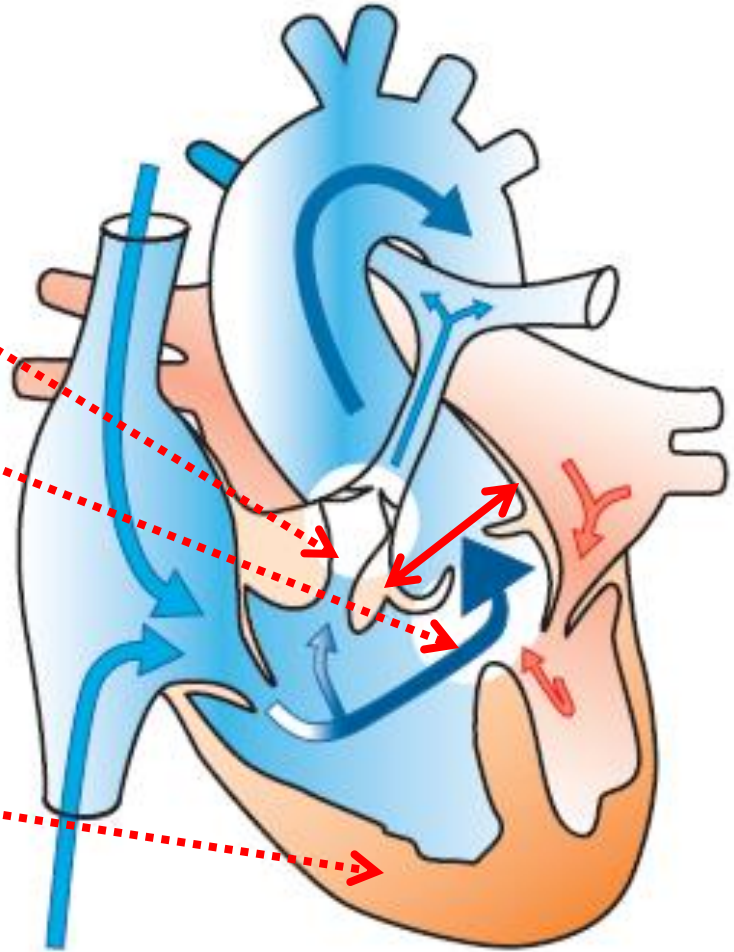
## Tetralogy of Fallot

Pulmonary Stenosis

Ventricular Septal Defect by malalignment

Dextroposition of the Aorta  
(aortic overriding)

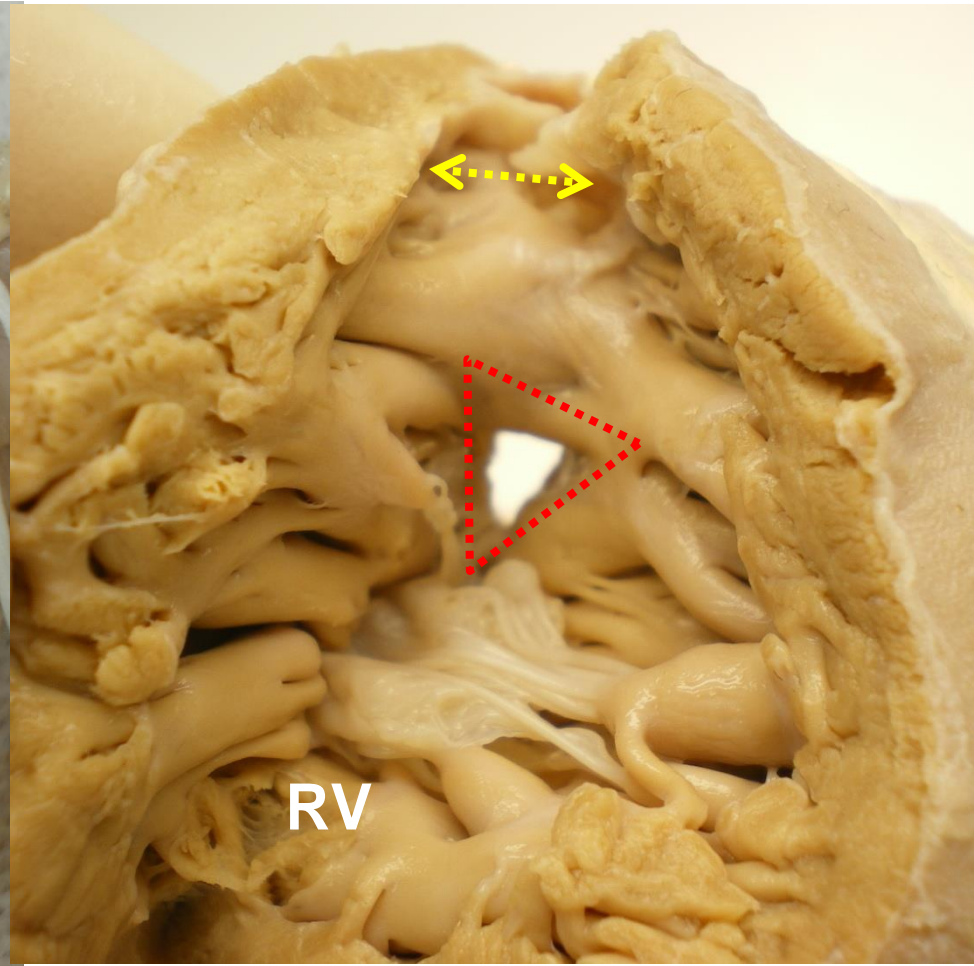
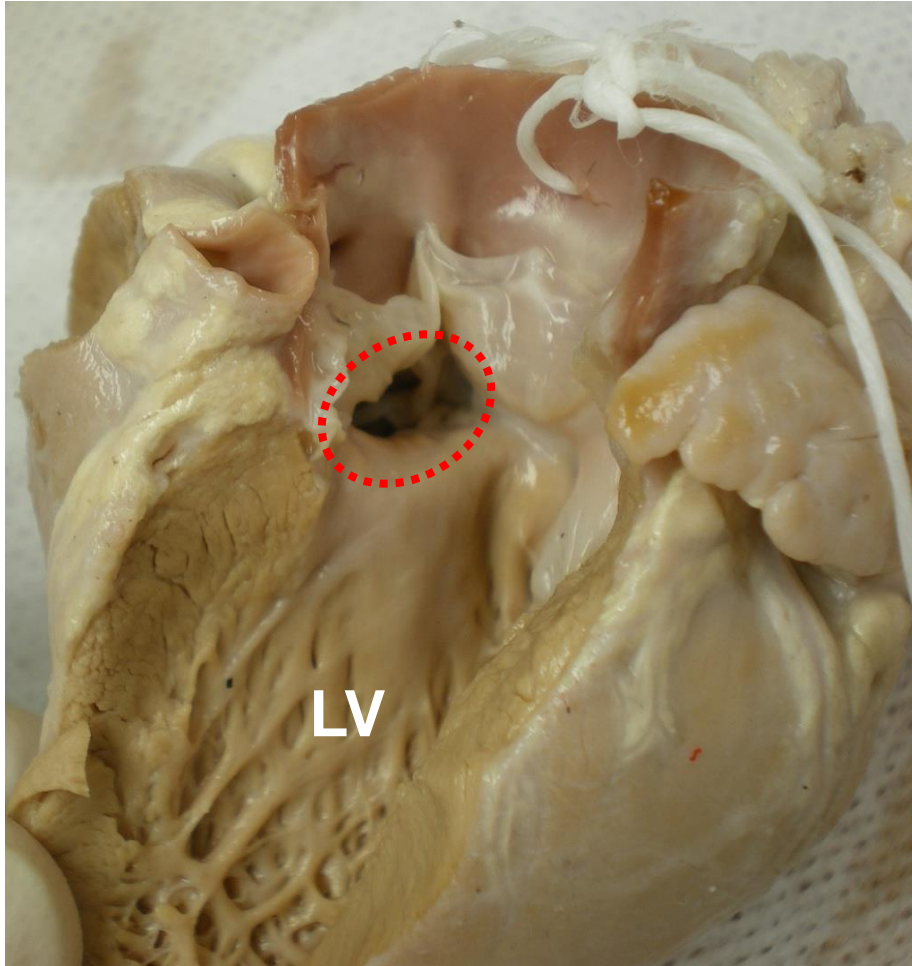
Right ventricular hypertrophy



# 5. Development in Congenital Heart Disease

Inter-ventricular septal defect

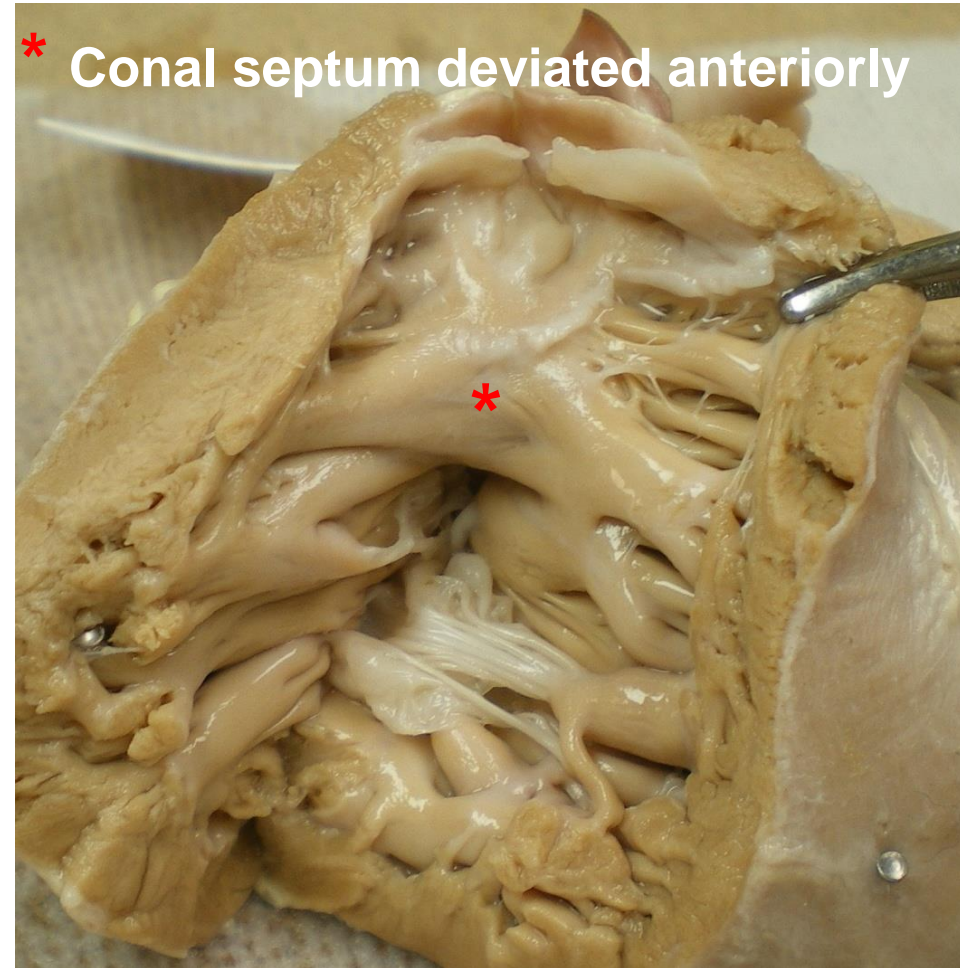
Pulmonary stenosis



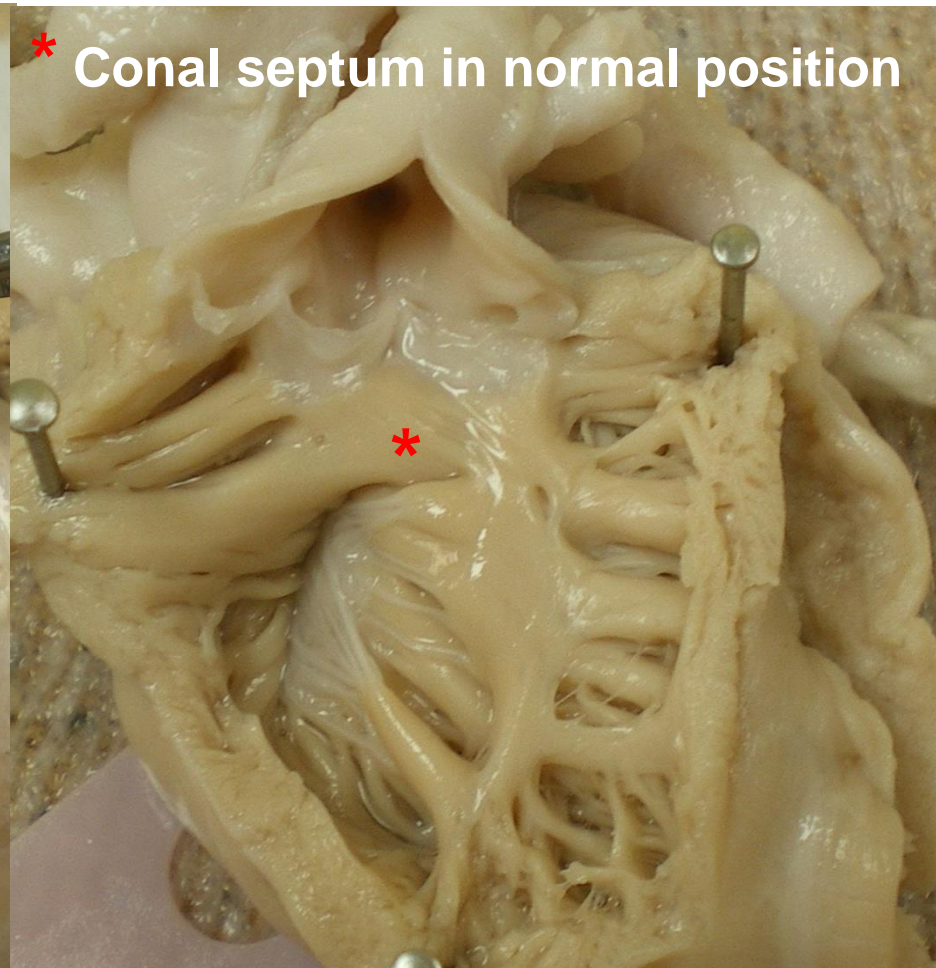
Anatomy of the Tetralogy of Fallot



# 5. Development in Congenital Heart Disease



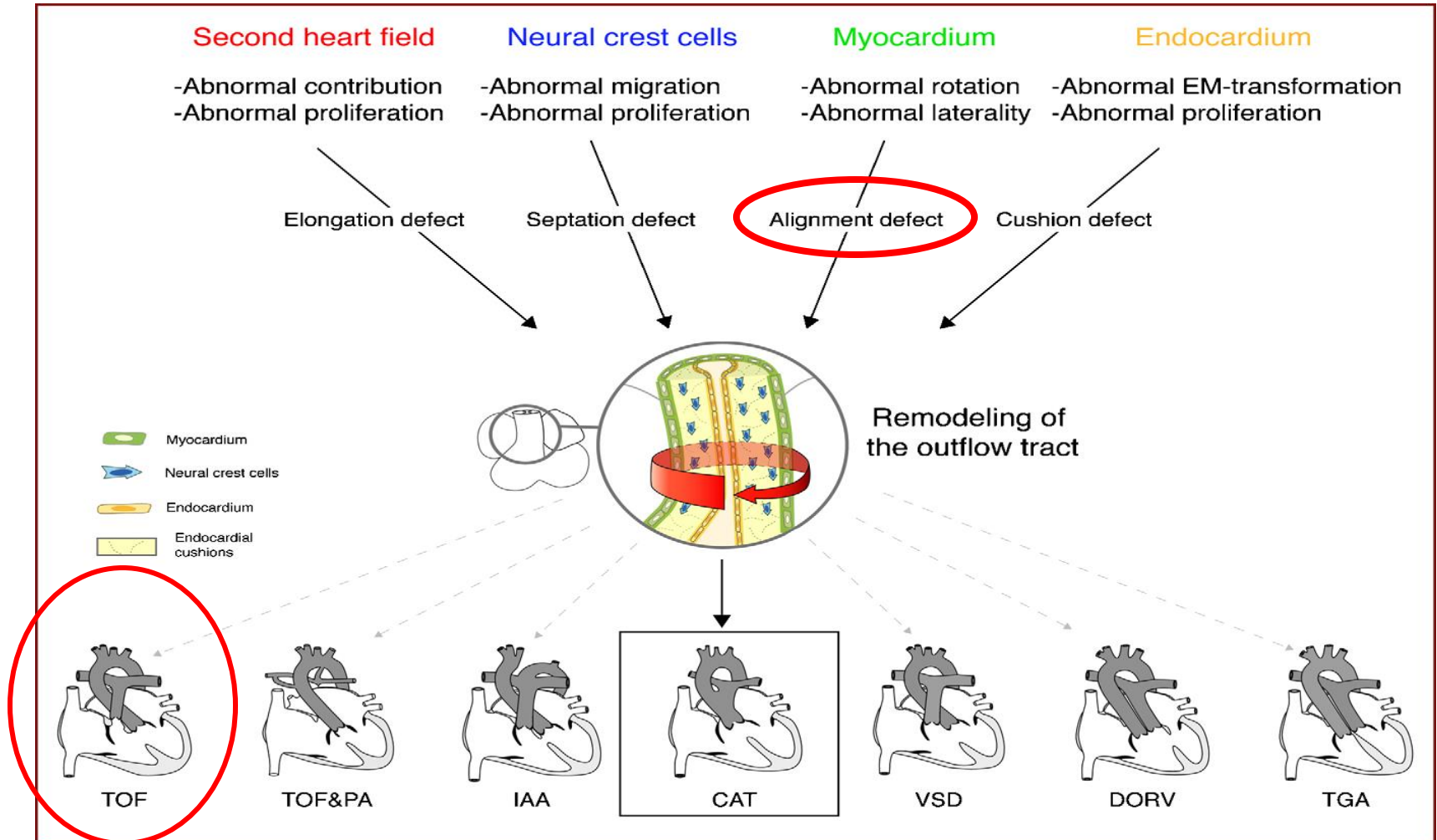
**Tetralogy of Fallot**



**Normal Heart**

# 5. Development in Congenital Heart Disease

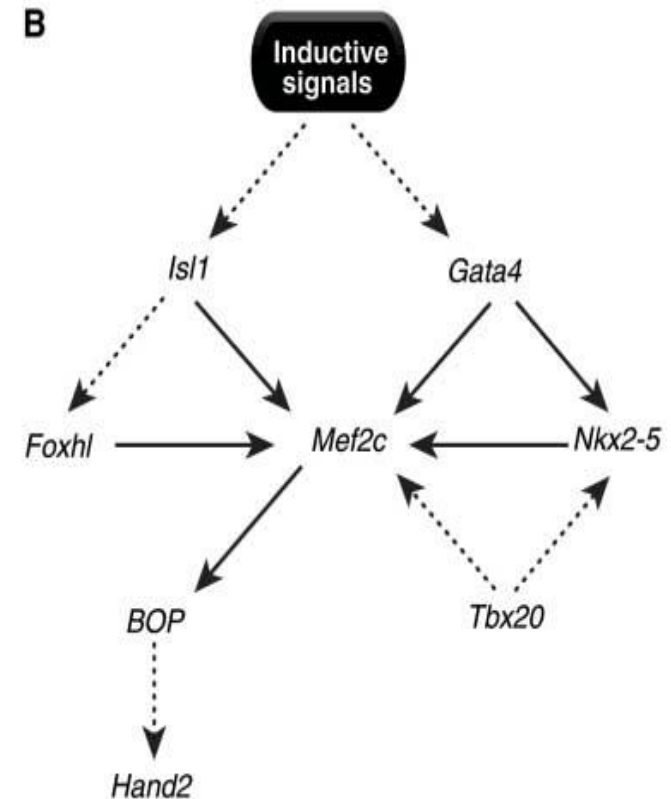
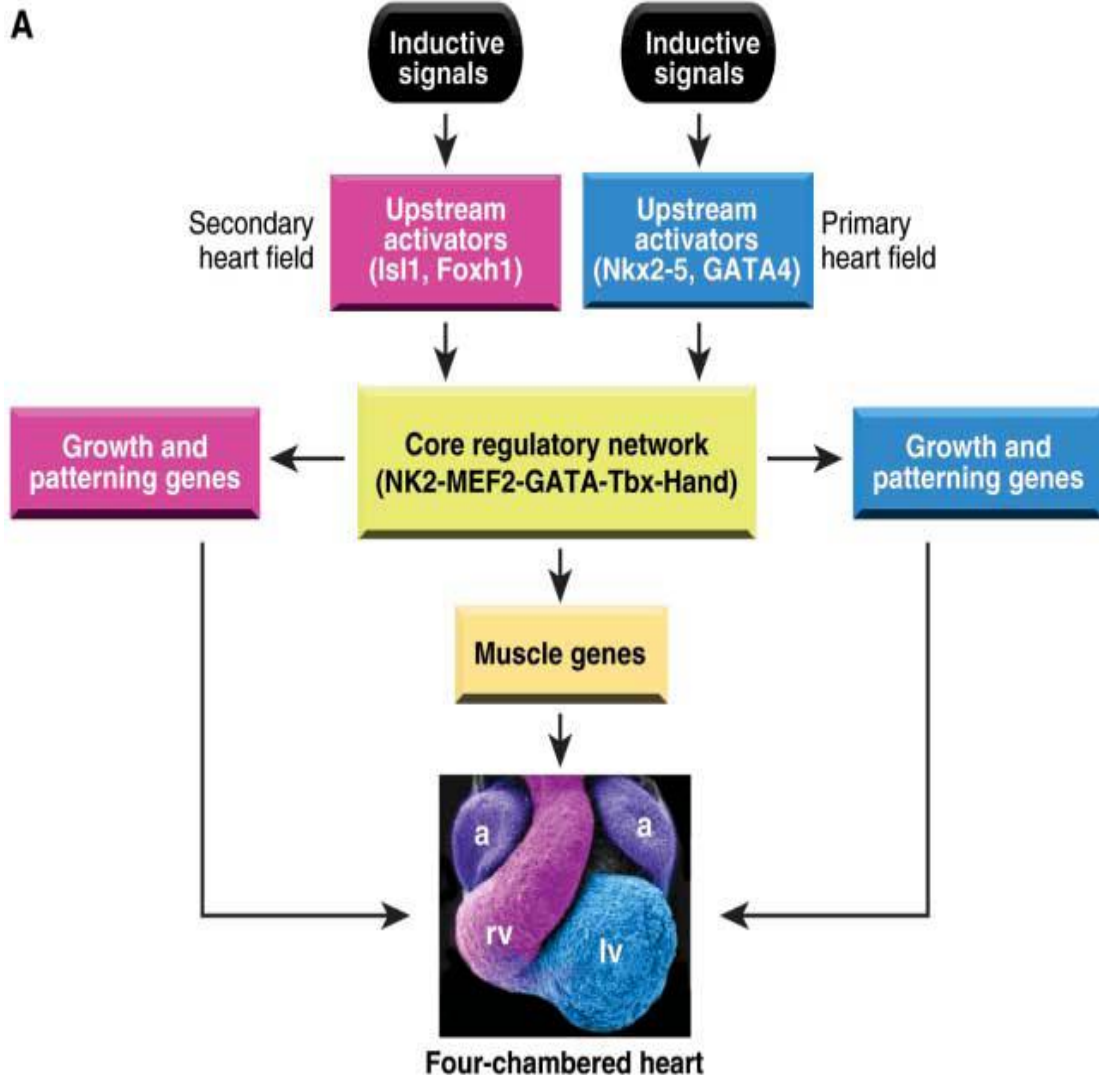
Which embryological processes are involved in the Tetralogy of Fallot ?  
Scale of tissue and cells



# 5. Development in Congenital Heart Disease

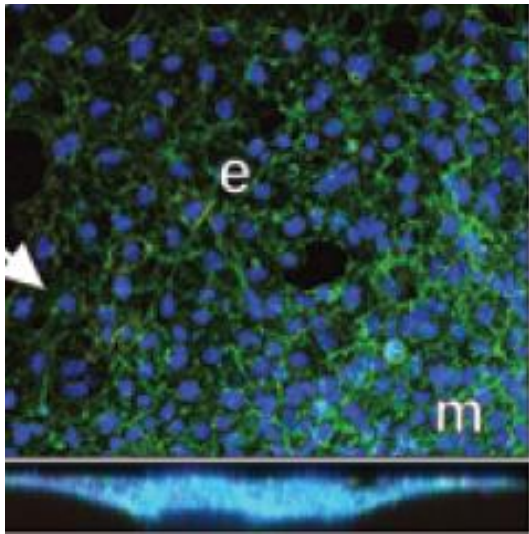
Which embryological processes are involved in the Tetralogy of Fallot ?

Scale of genetic signalling

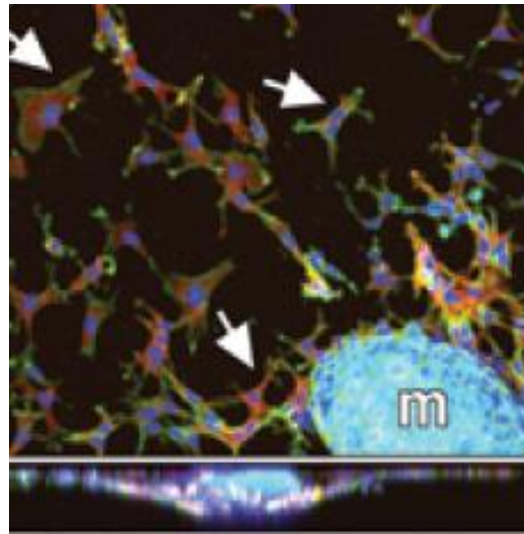




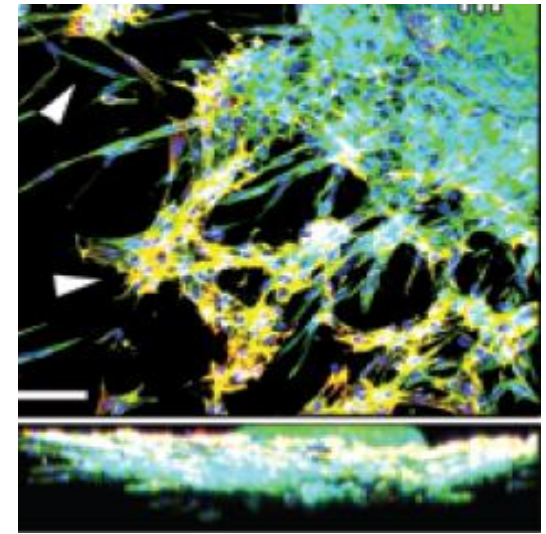
# 6. Modelling & Simulation



Wildtype



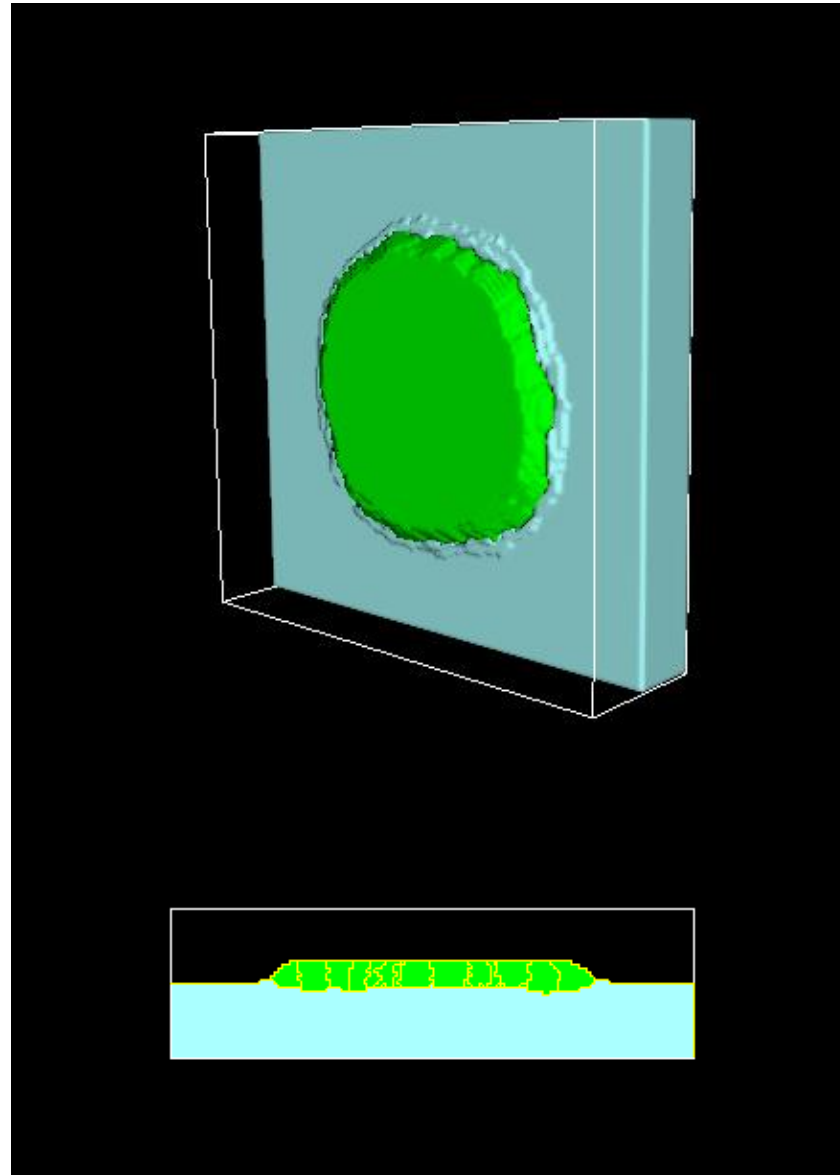
Notch1



BMP2

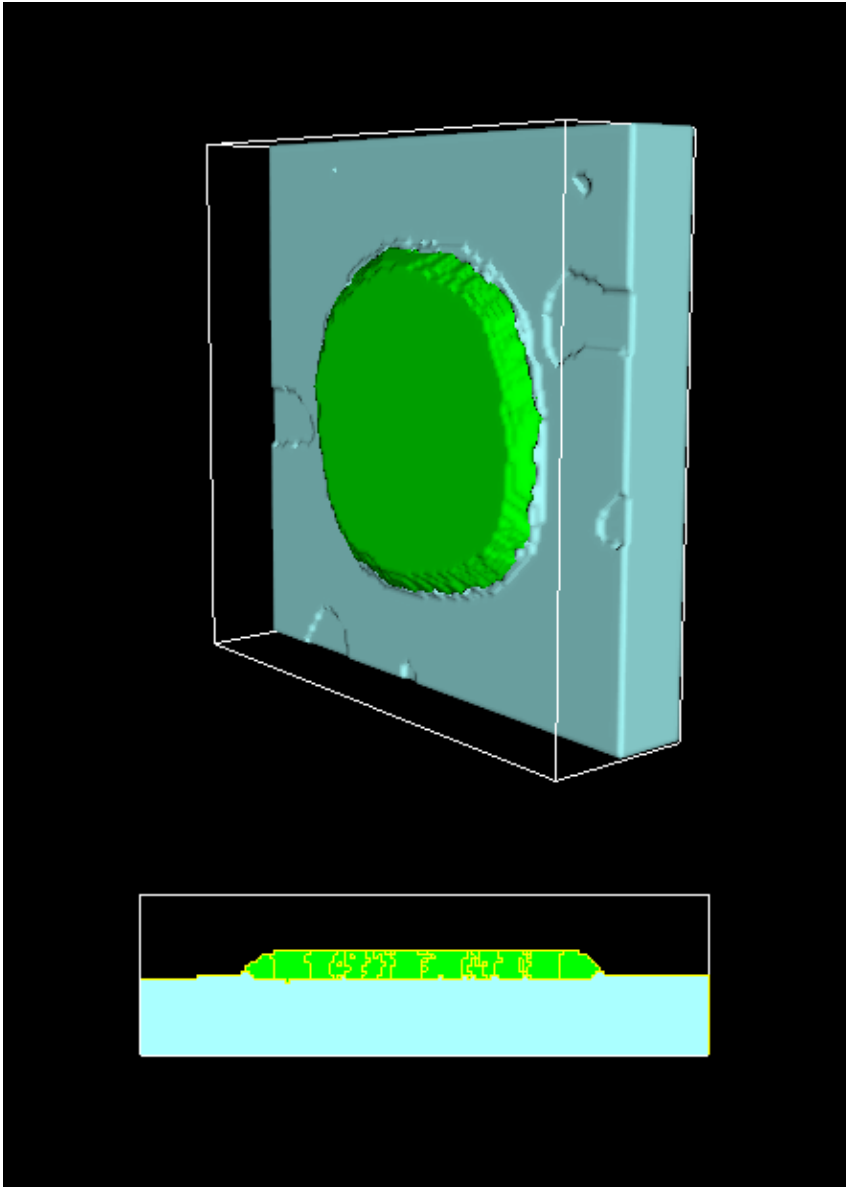
*in vitro* Epithelial to Mesenchymal Transition

# 6. Modelling & Simulation



Wildtype

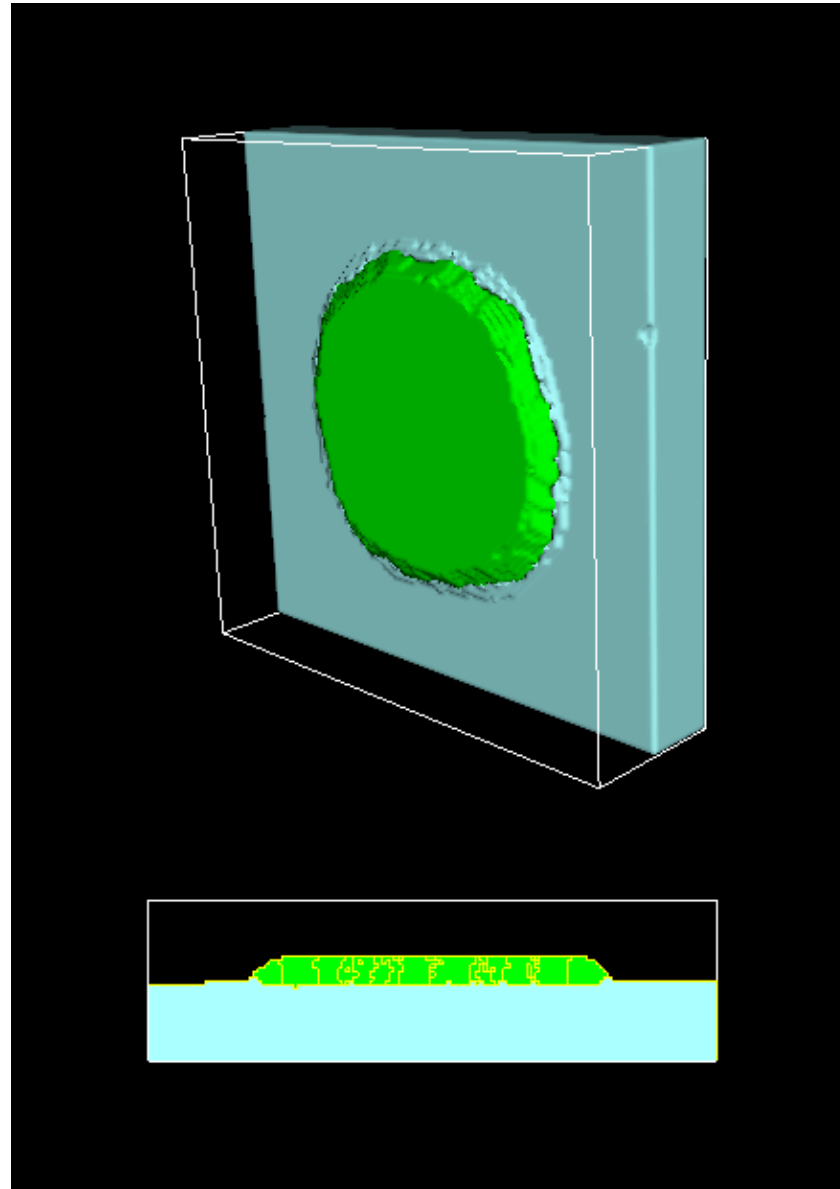
# 6. Modelling & Simulation



Notch1

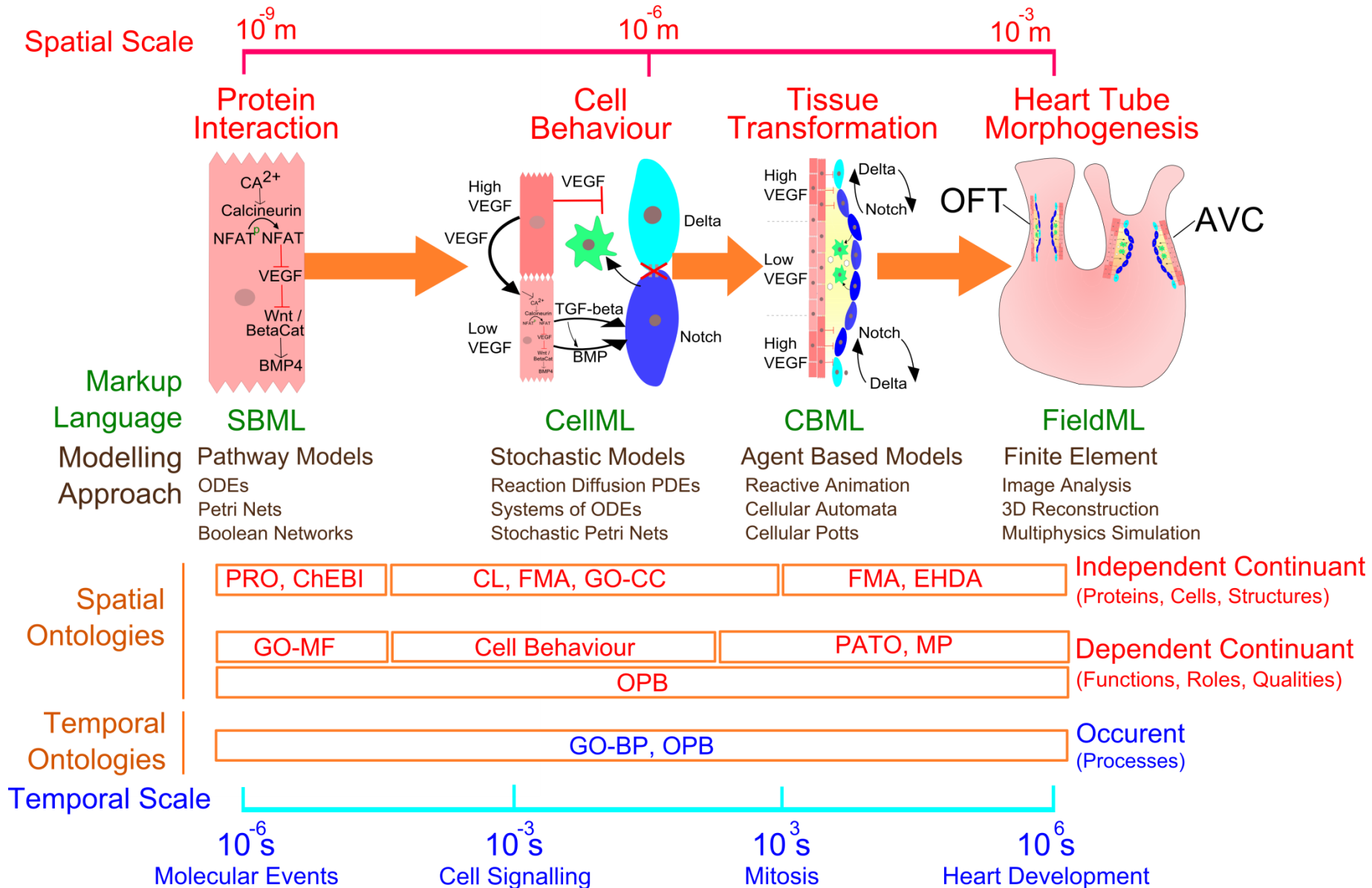


# 6. Modelling & Simulation



BMP2

# 7. Possible Future Scenarios



## Scale Linking

# 7. Possible Future Scenarios



**Anatomic Re-determination of Tetralogy of Fallot**

# 8. Identifying the Engineering Components

- Systems Engineering Contribution
  - Multiscale Framework
  - Methodology
  - Cybernetics
- Modelling & Simulation
  - Cellular Potts models
- *in vivo* & *in vitro* samples
  - Microscopy



# 8. Identifying the Engineering Components



Olympus Fluoview FV-1000 Laser Scanning Confocal Microscope

## 8. Identifying the Engineering Components



# Thank You!



He's not just a fish  
He's hope



  
British Heart  
Foundation

Mending  
broken  
hearts  
appeal

Sponsor hope   
Find out more 



# References

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