Symetrie vs. asymetrie v morfogenezi

Obsah

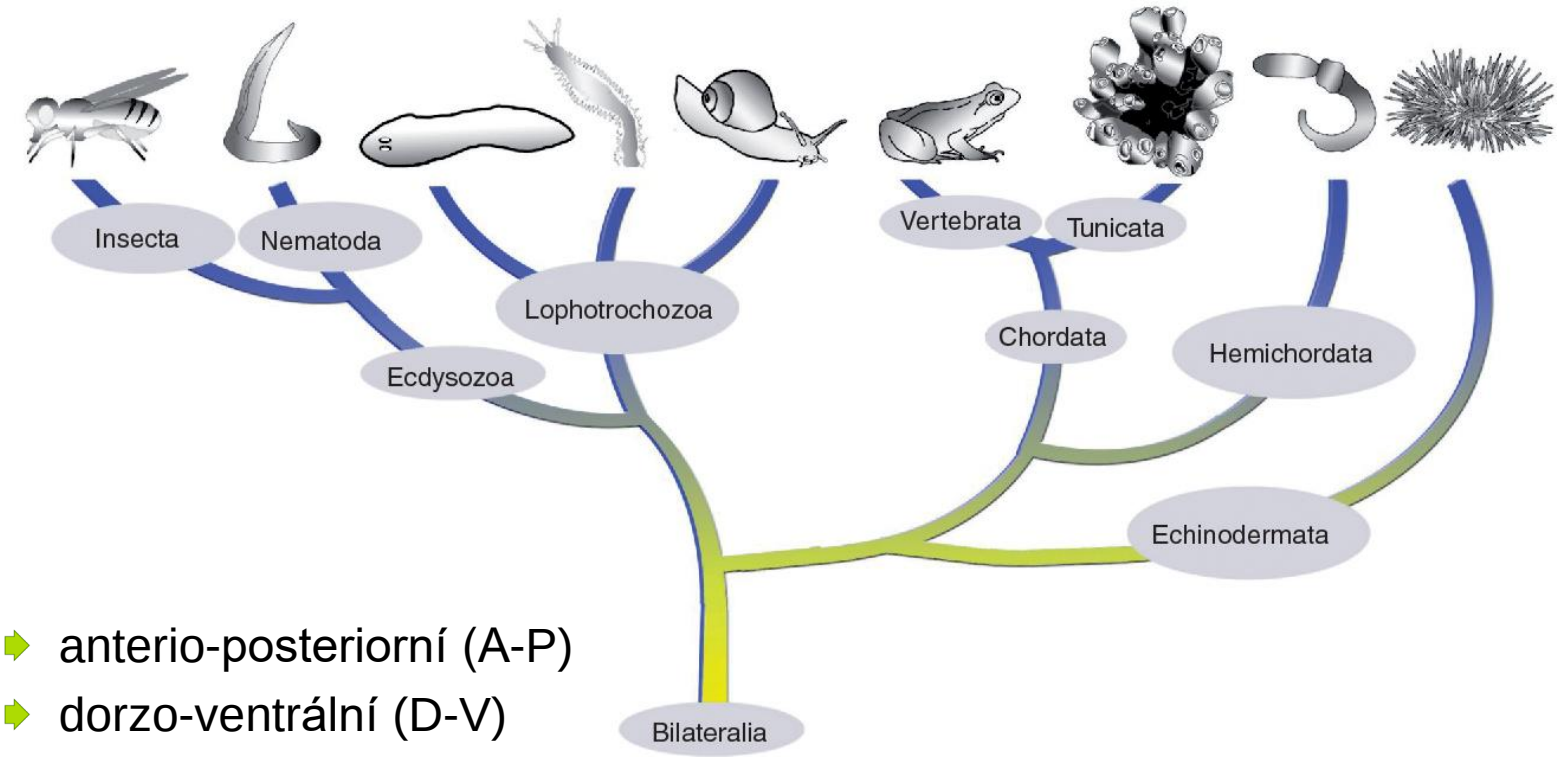
- buněčné mechanismy přispívající k determinaci symetrie/asymetrie
- molekulární regulace symetrie
- modely regulace
- příklady poruch symetrie a asymetrie (situs ambiguus, situs inversus, ..)

Hlavní otázky

- Jak embrya uspořádávají/orientují L/P osu s ohledem na další dvě osy a střední linii těla?
- Kdy to nastává a kdy embryo začne rozlišovat svou pravou a levou stranu?
- Jak se tato informace šíří tkáněmi a řídí regiony s levou a pravou identitou?
- Jaký je vztah mezi chiralitou (chováním buněk v kultuře) a směrovou asymetrií (např. tělesná stavba u obratlovců)?
- Jaký je vztah lateralizace jiných aspektů těla (behaviorální, imunologický, uspořádání proudů chlupů) k signalizačním drahám, které ustanovují polohu orgánu?
- Jak konzervované jsou tyto mechanizmy napříč živočichy a jaký je evoluční vztah mezi různými způsoby jak tento problém řeší různé živočišné skupiny?

- Cílem je i nalezení vývojových příčin způsobujících kongenitální poruchy laterality

Determinace os

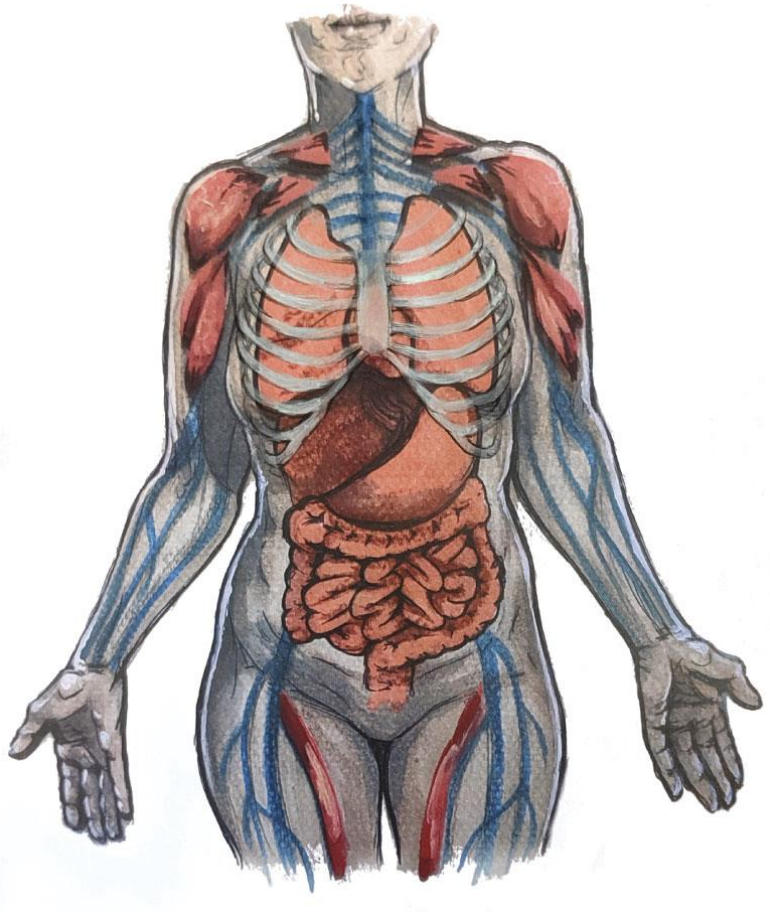


- anterio-posteriorní (A-P)
- dorzo-ventrální (D-V)
- levá a pravá strana

Grimes 2019

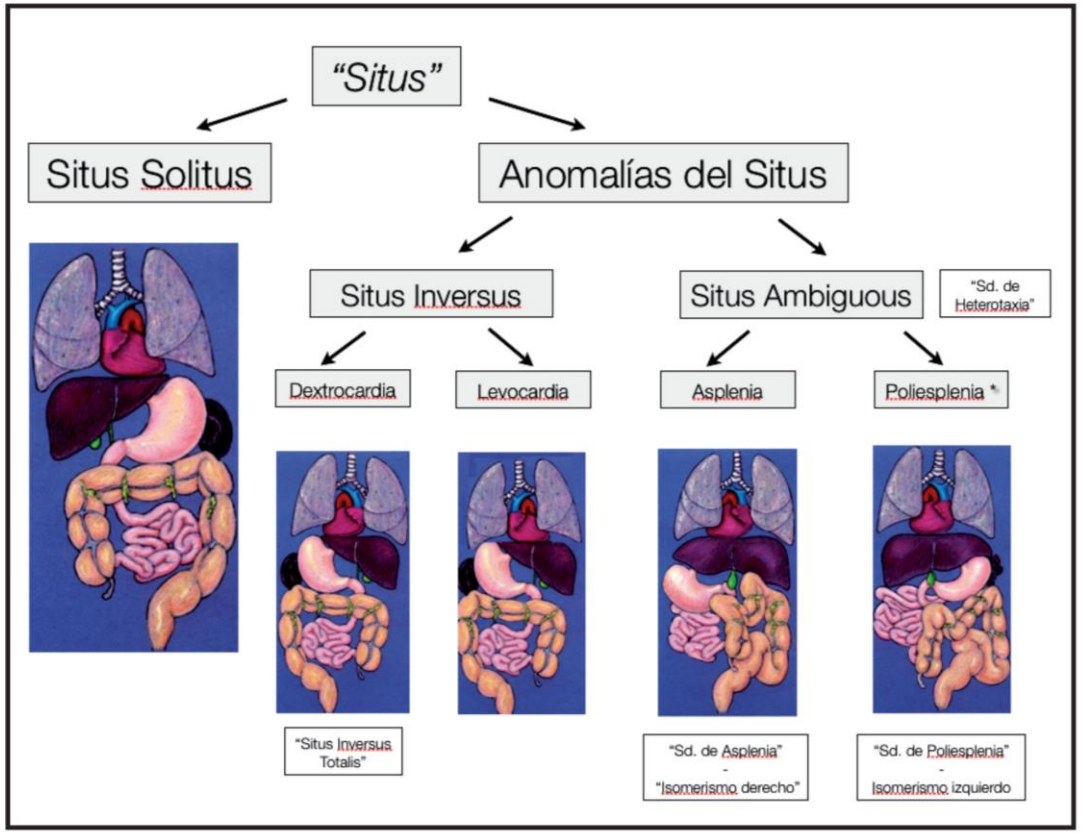
Asymetrie ve vývoji

- (1) fluktující asymetrie
- (2) anti-symetrie
- (3) směrové asymetrie



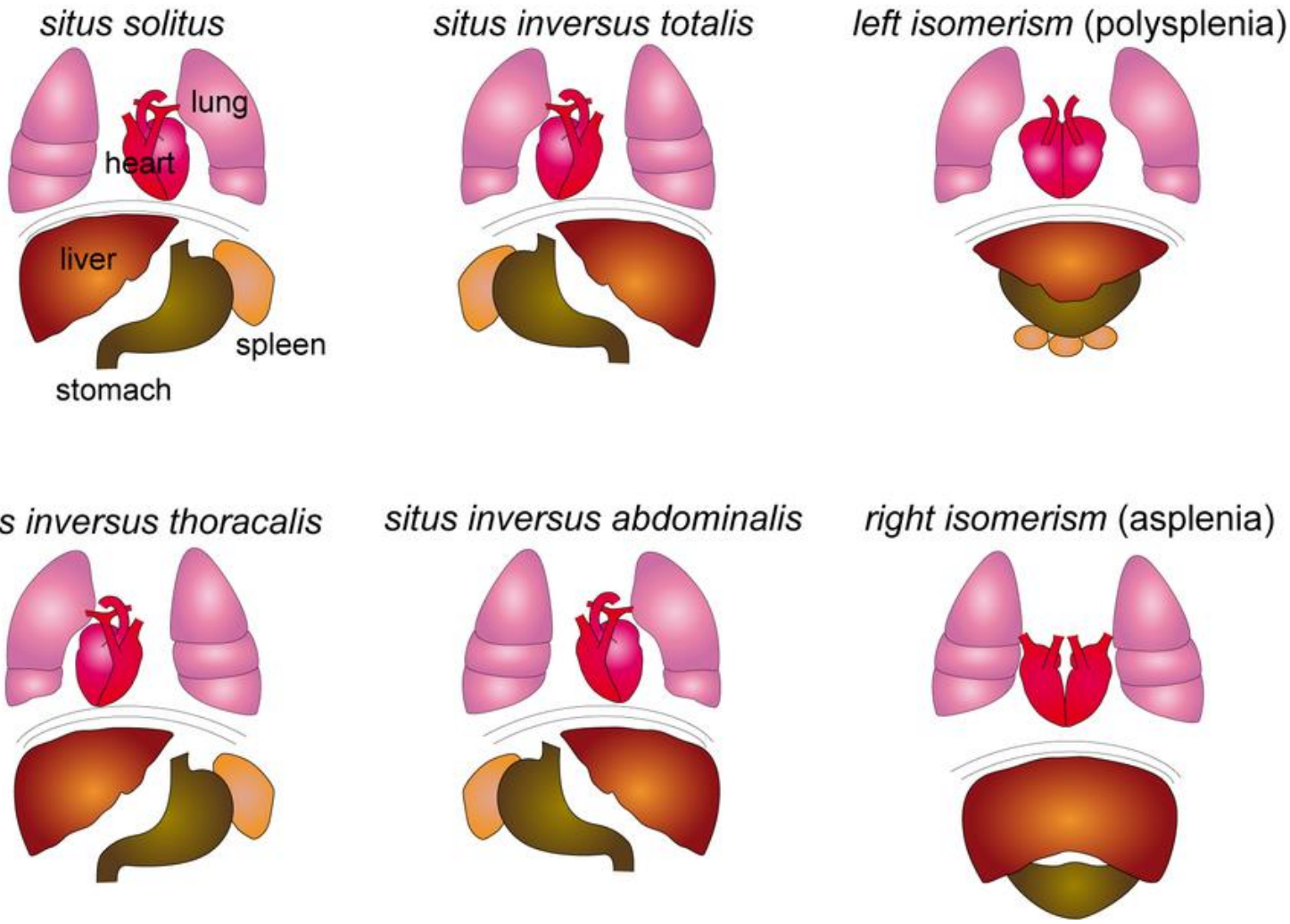
Poruchy asymetrie

- situs ambiguus
- situs inversus

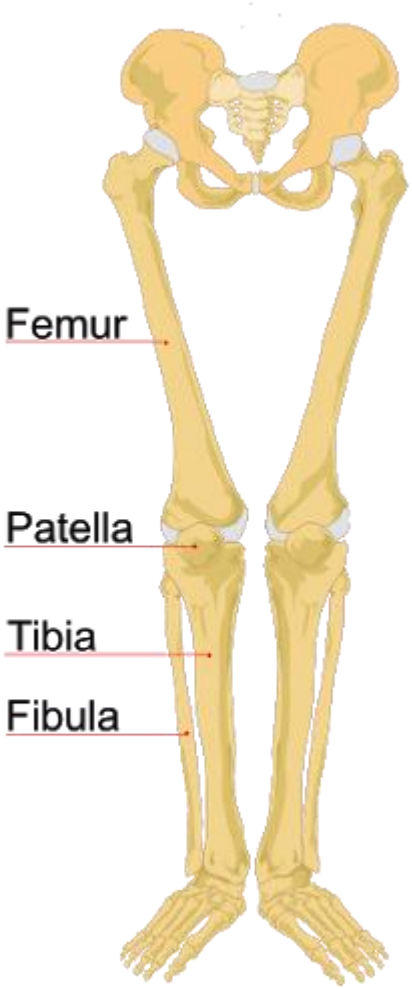


Corral et al. 2013

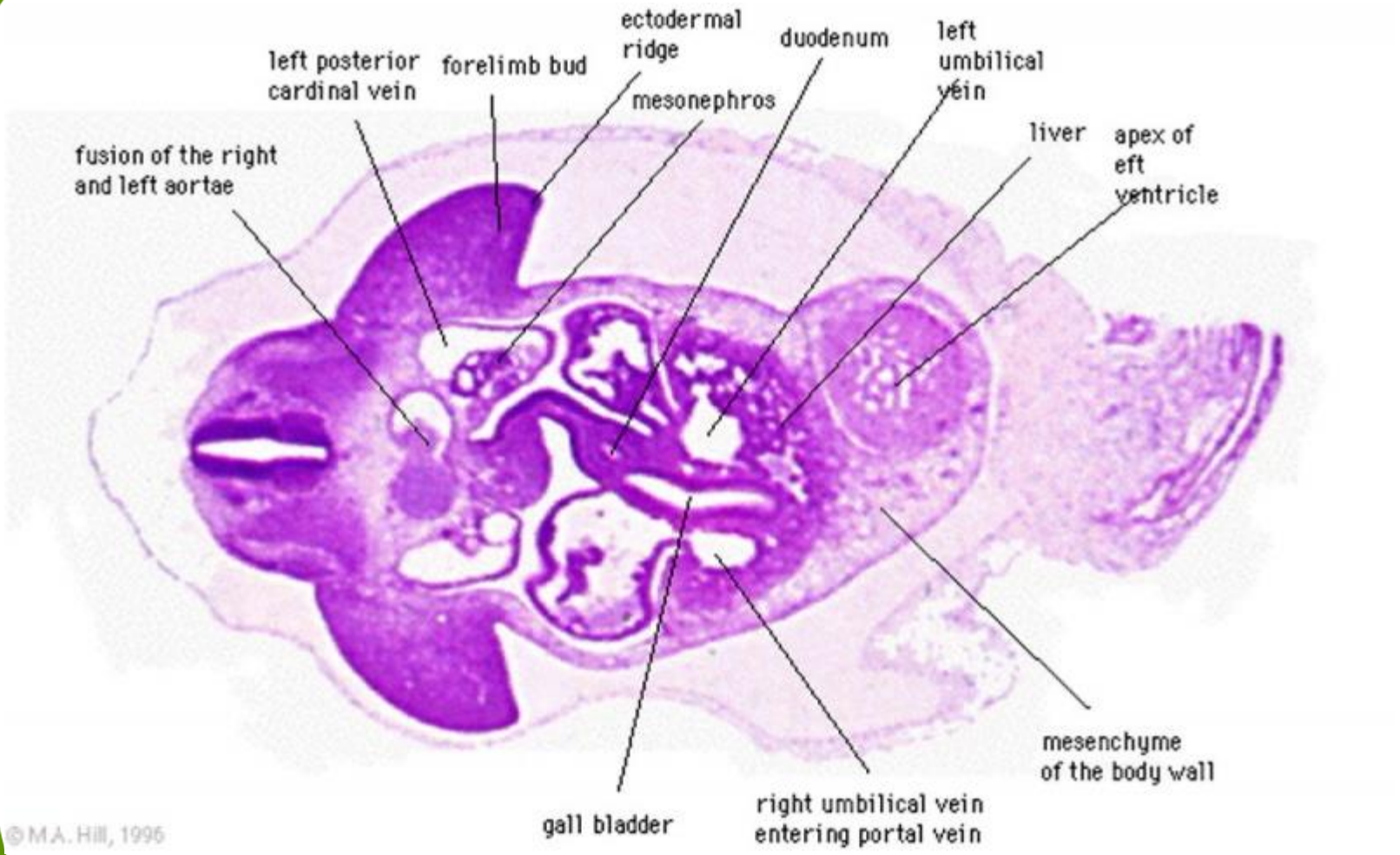
Poruchy asymetrie



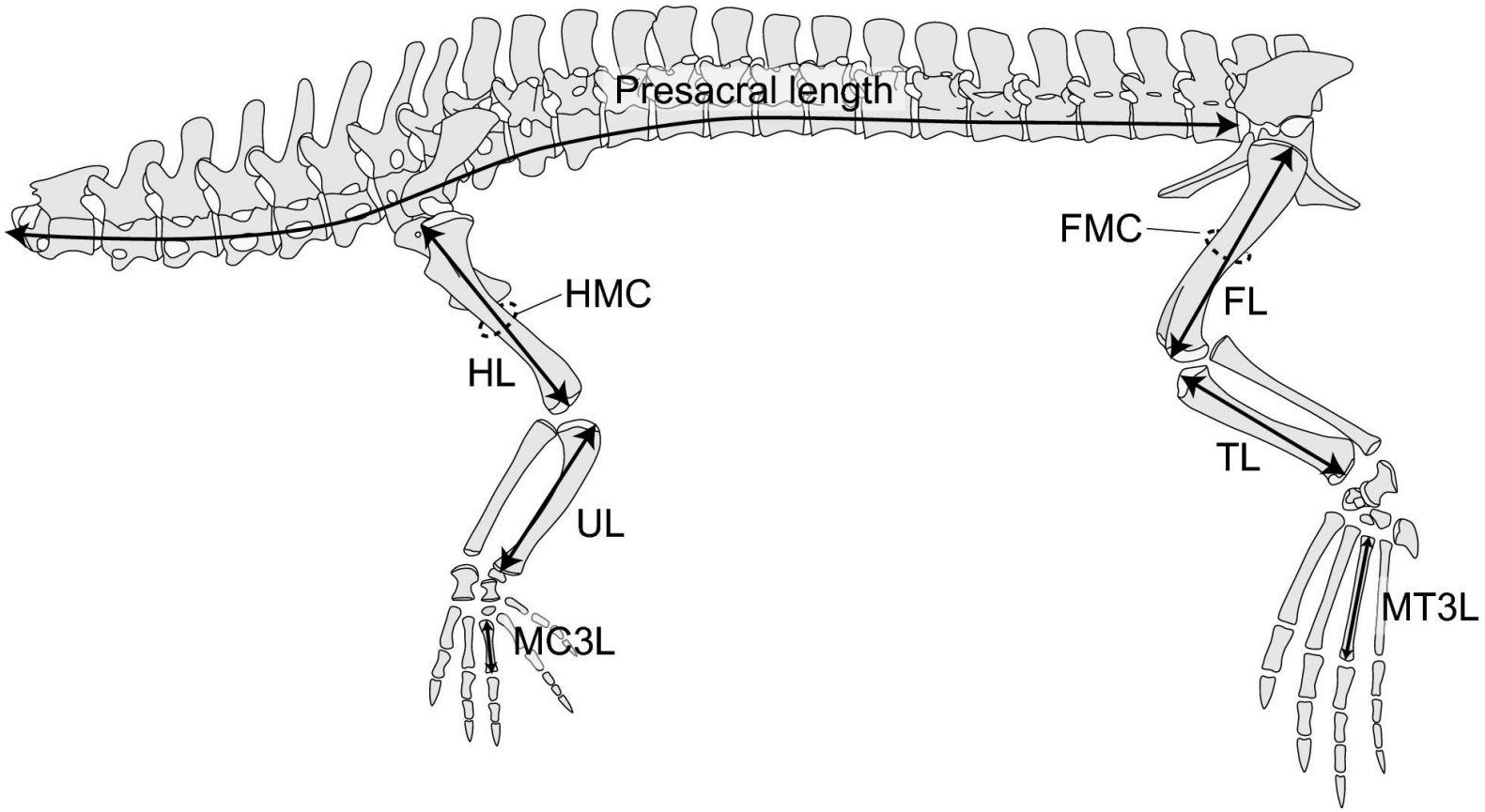
Symetrie ve vývoji



Symetrie vs. asymetrie



Symetrie vs. asymetrie

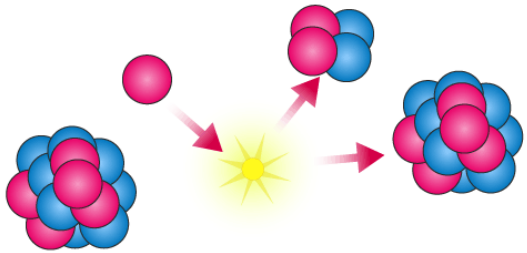


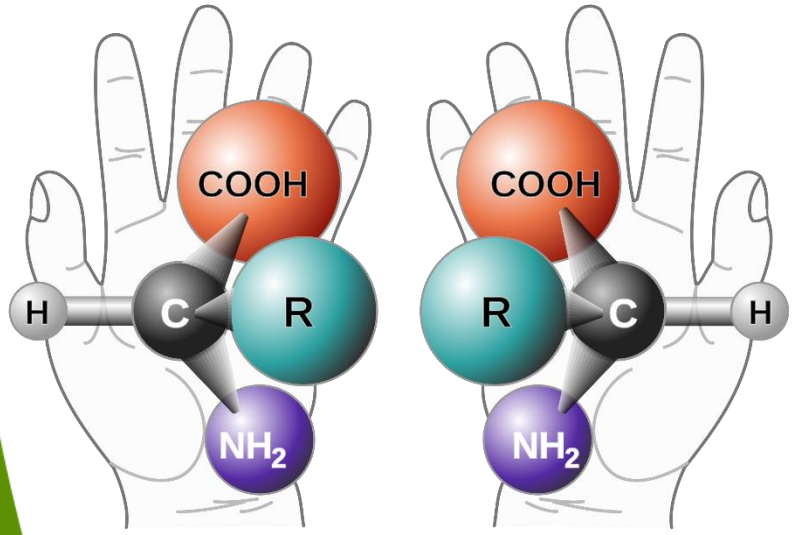
Poruchy symetrie

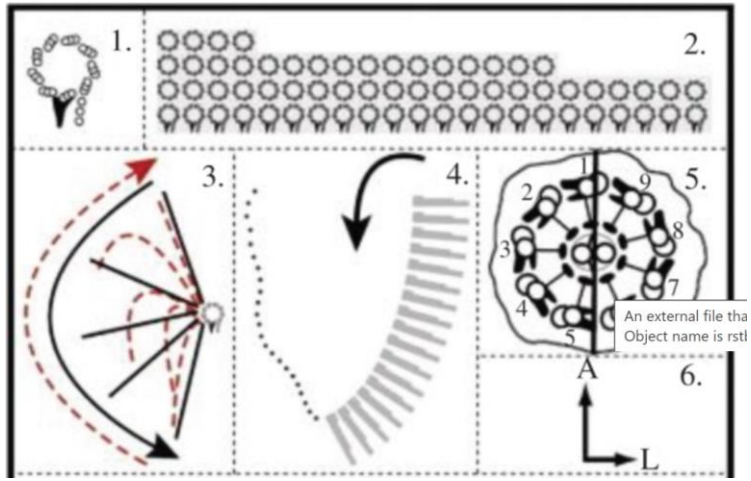
- Holt-Oram syndrom
- Idiopatická skolióza

Narušení symetrie: od asymetrických molekul k asymetrickým embryím

- Slabé jaderné síly
- Chiralita molekul (L- nebo D- AMK)
- Chiralita organel (centriol)

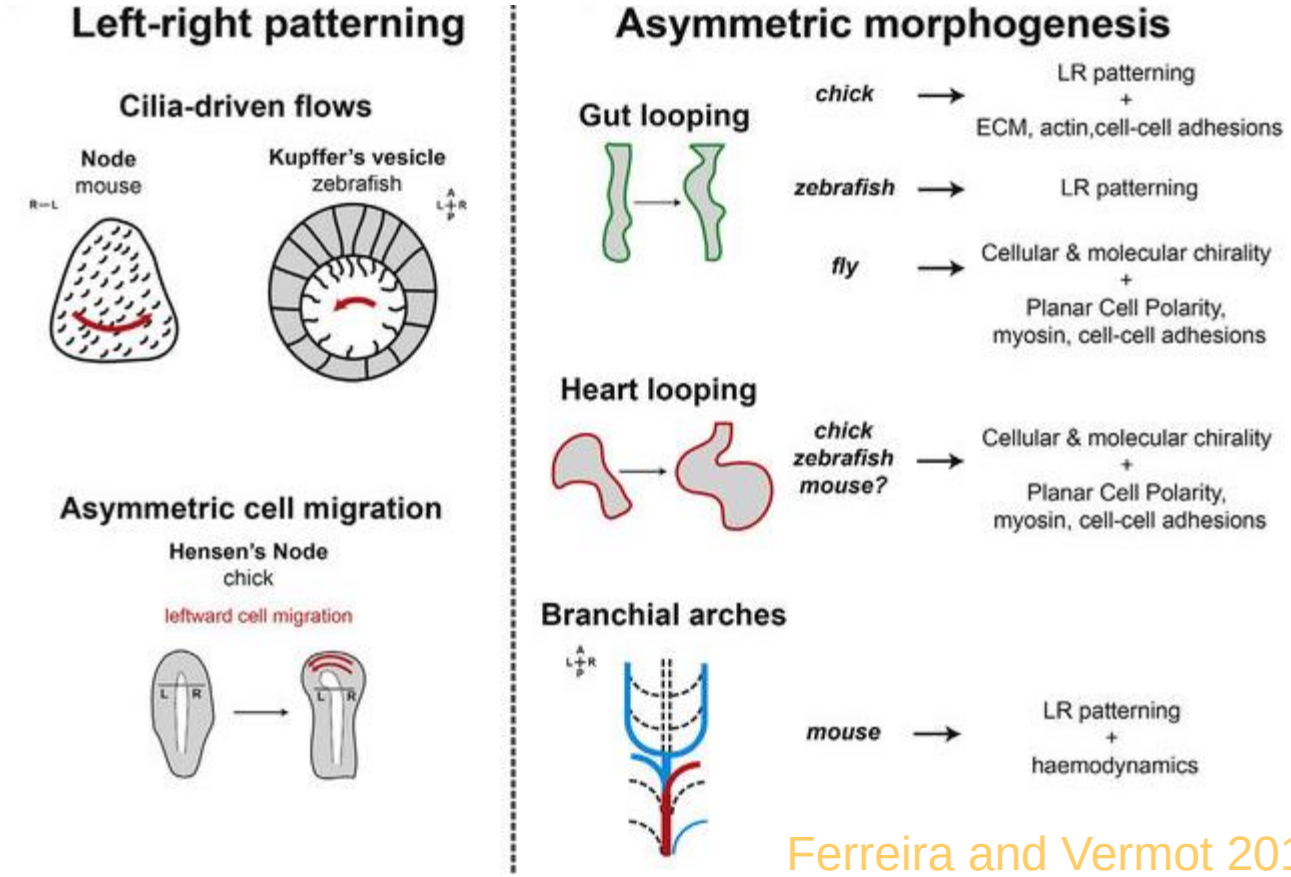






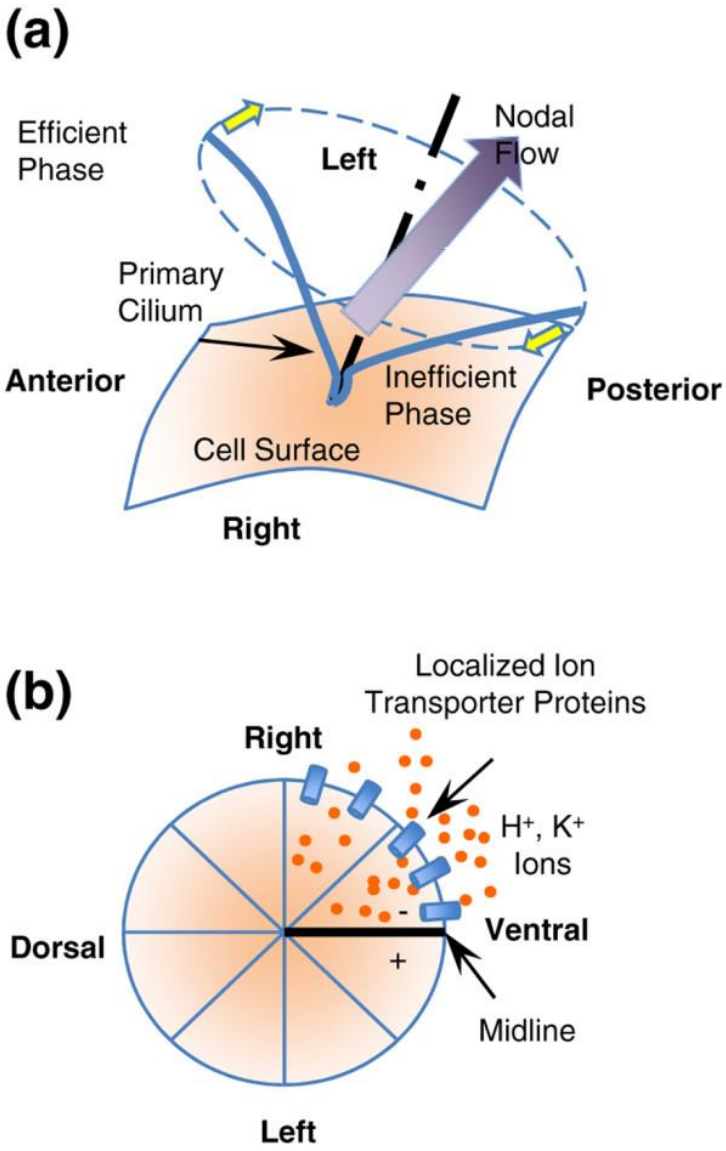
Narušení symetrie: od asymetrických molekul k asymetrickým embryím

- asymetrie morfologie buněk, nebo jejich chování
- vnitřní vlastnosti tkání (adheze mezi buňkami, uspořádání jednotlivých komponent cytoskeletu jako je aktin a myosin)

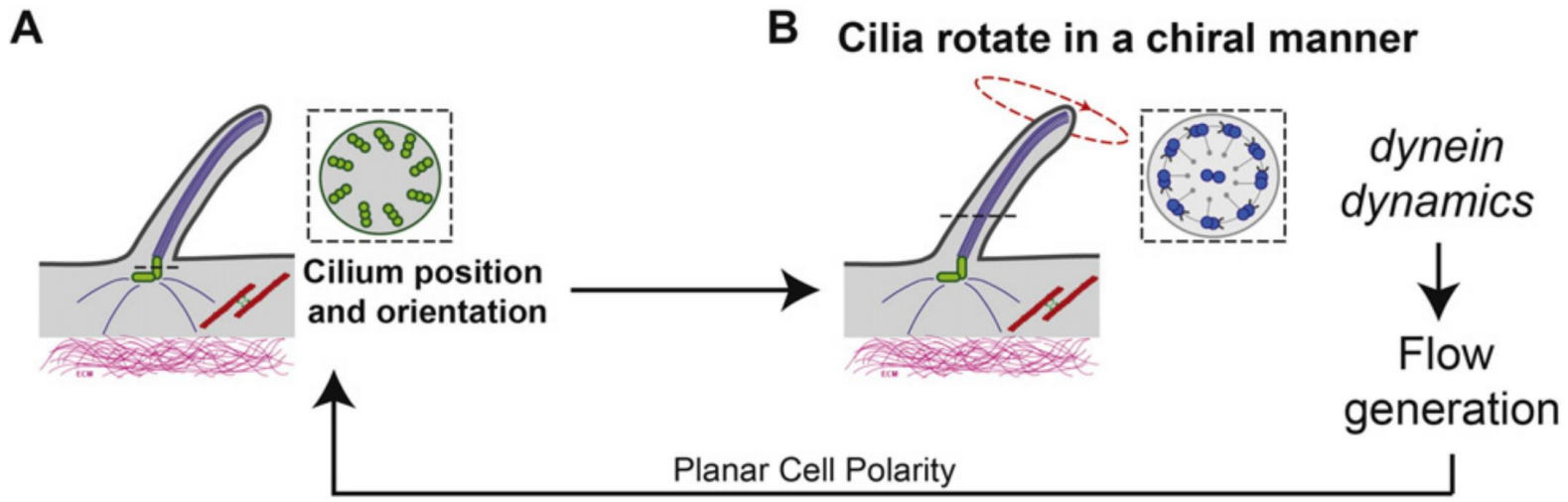


Ferreira and Vermot 2016

Modely vzniku asymetrie

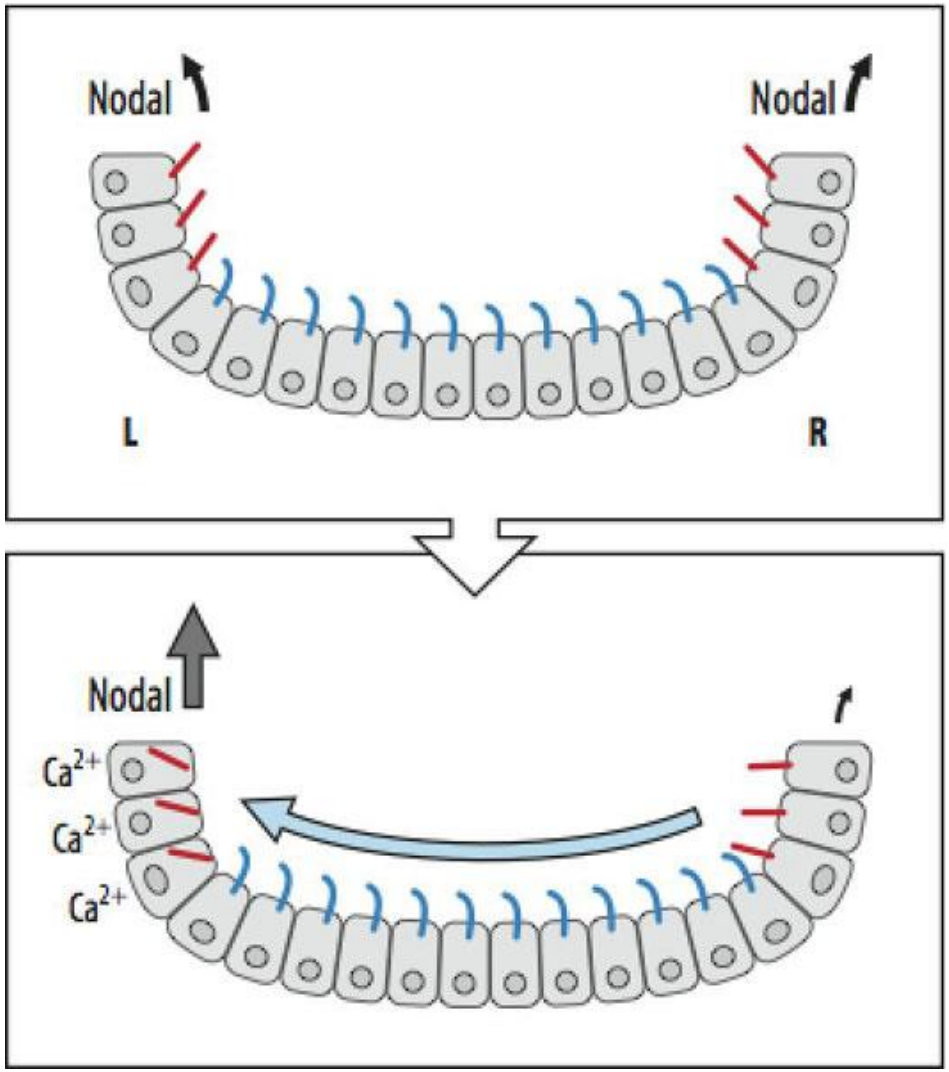


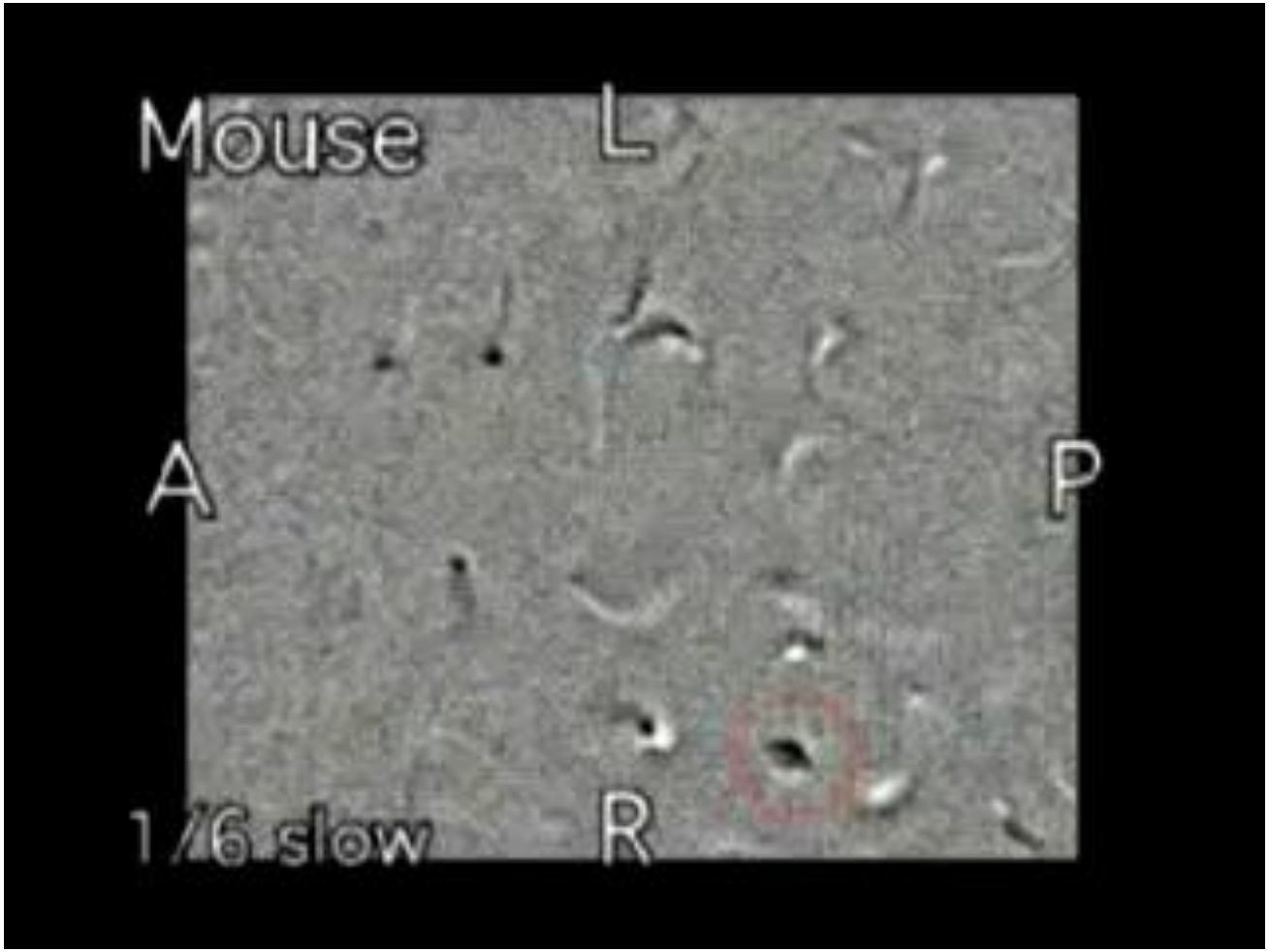
Rotace cilií

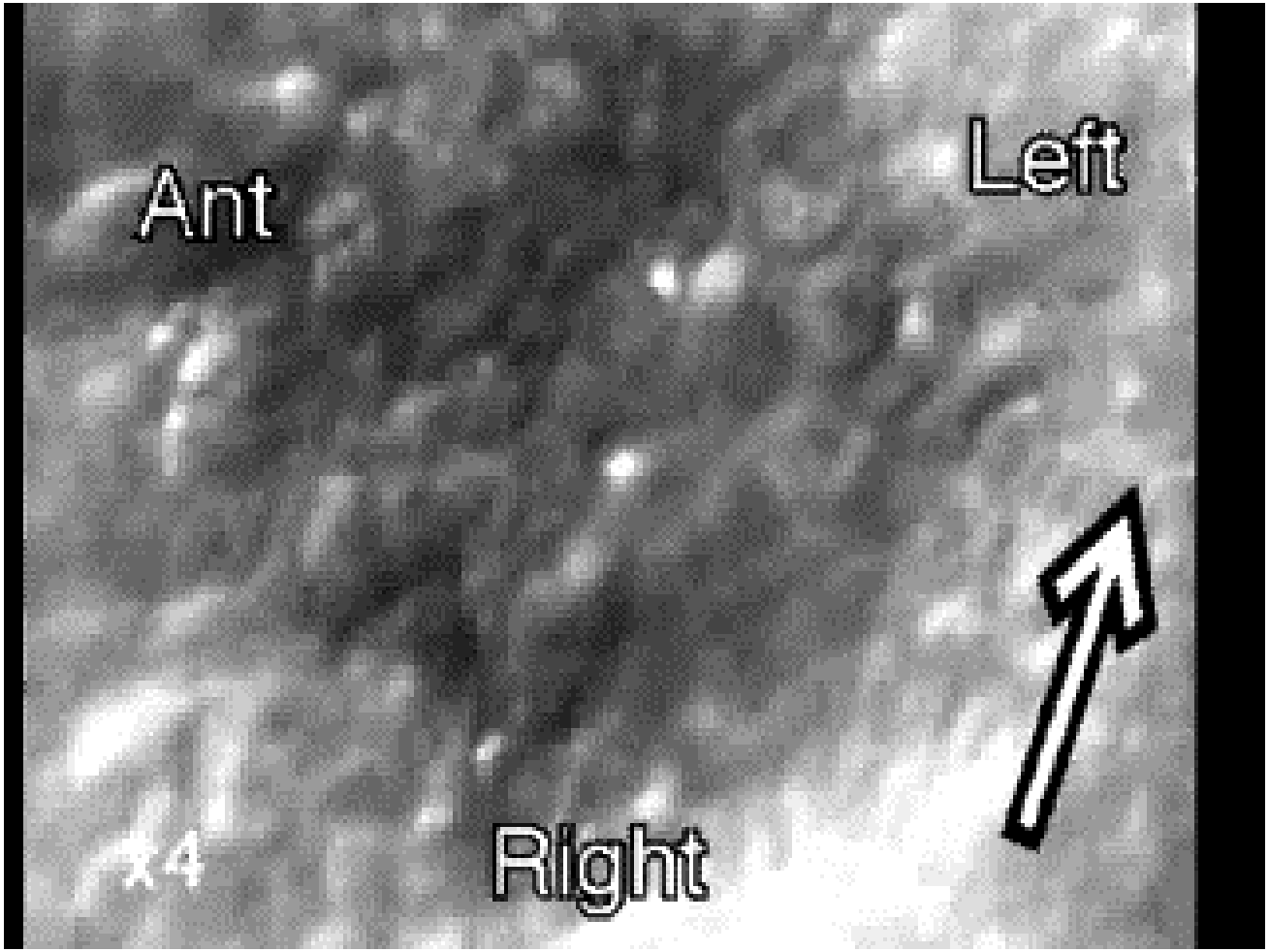


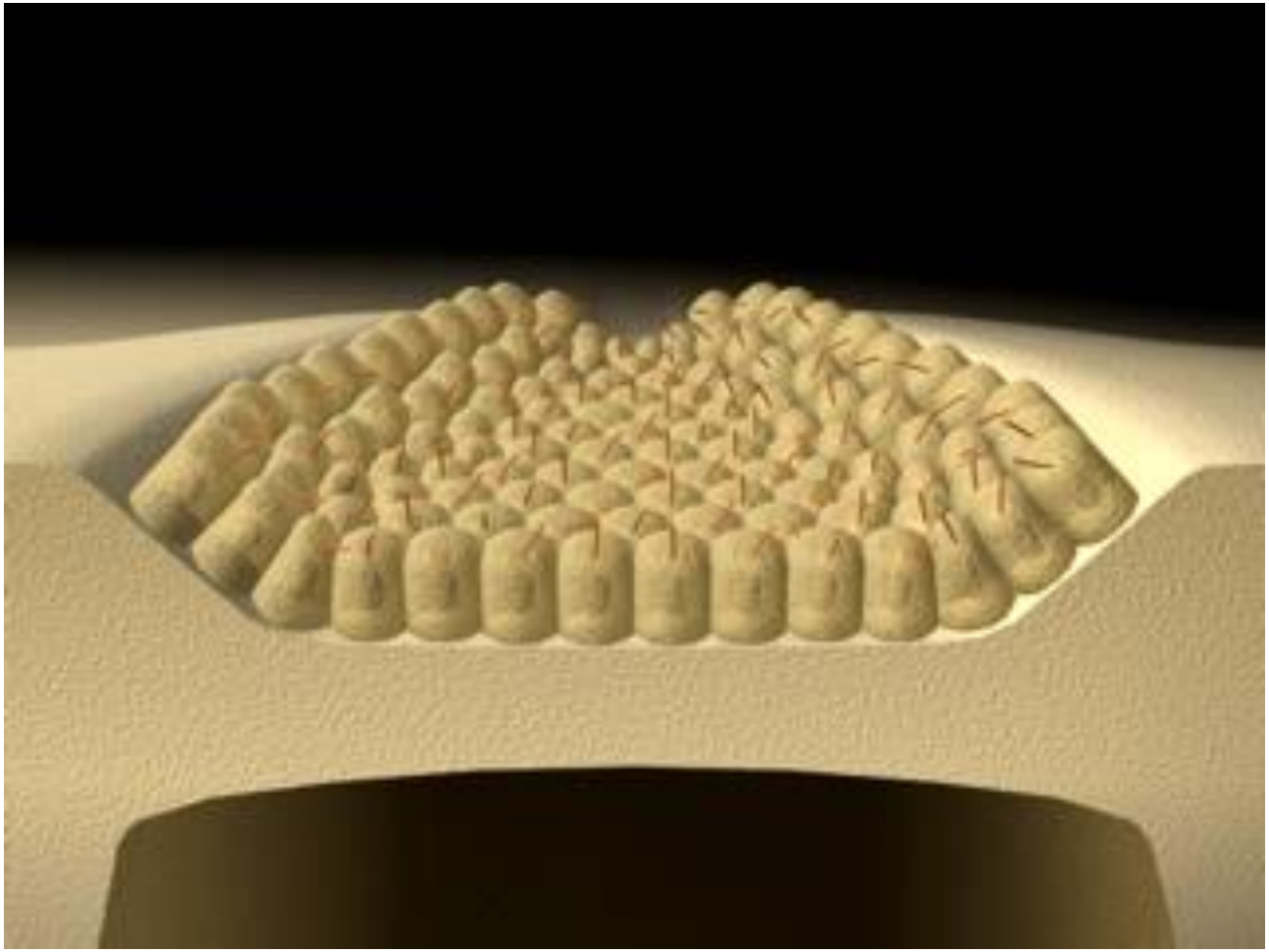
Ferreira and Vermot 2016

Rotace cilií



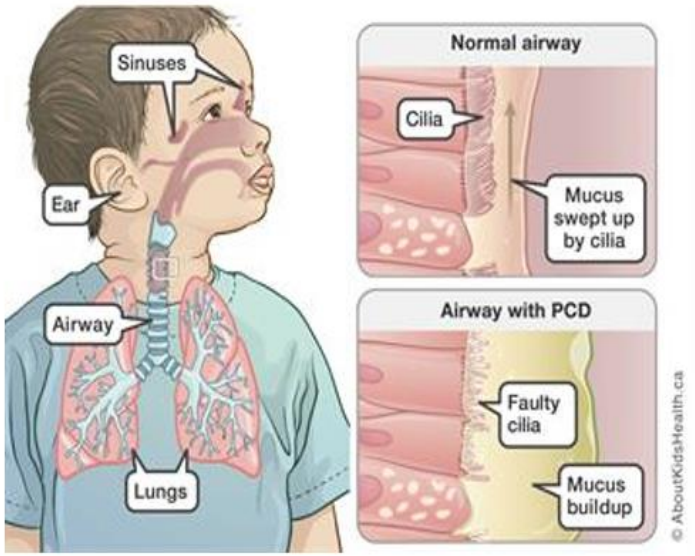

Mouse
L
A
P
1/6 slow
R

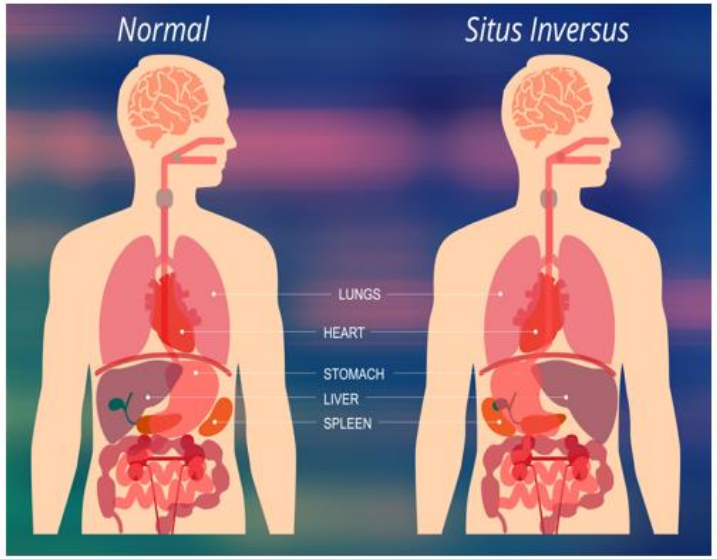

Ant
Left
Right
x4



Poruchy funkce cilií

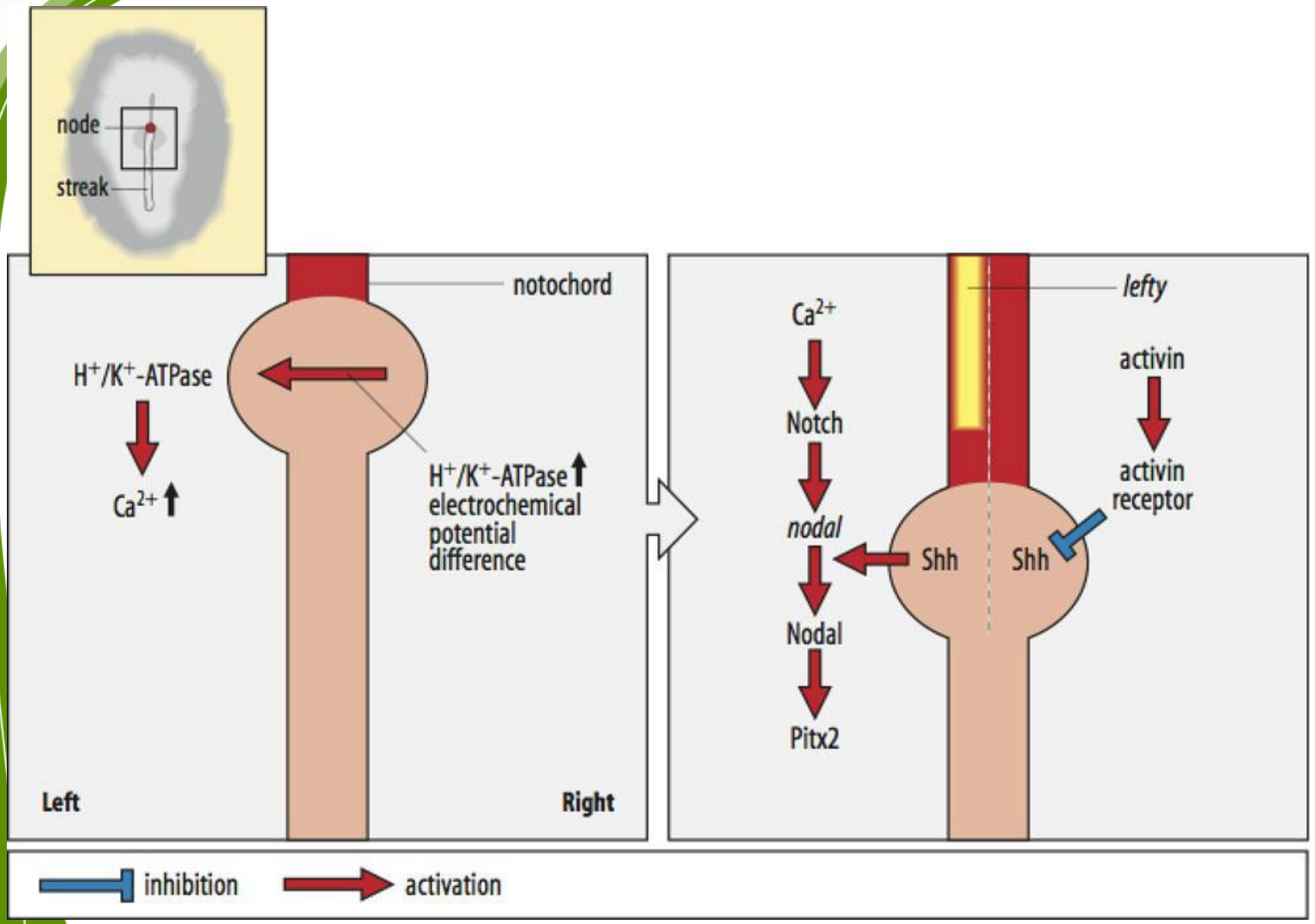
- Kartagenerův syndrom
- iv myší model



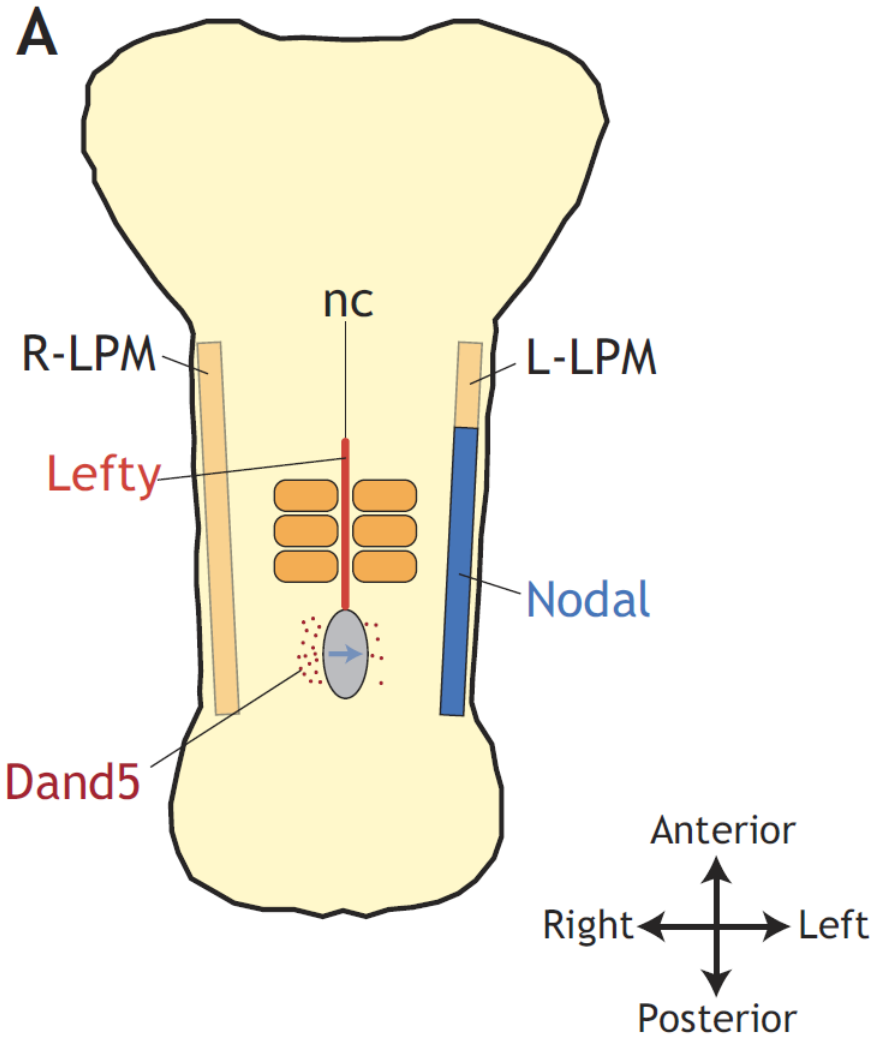


Primary ciliary dyskinesia and situs inversus are two main characteristic of kartagener syndrome.

„Ion flux model“

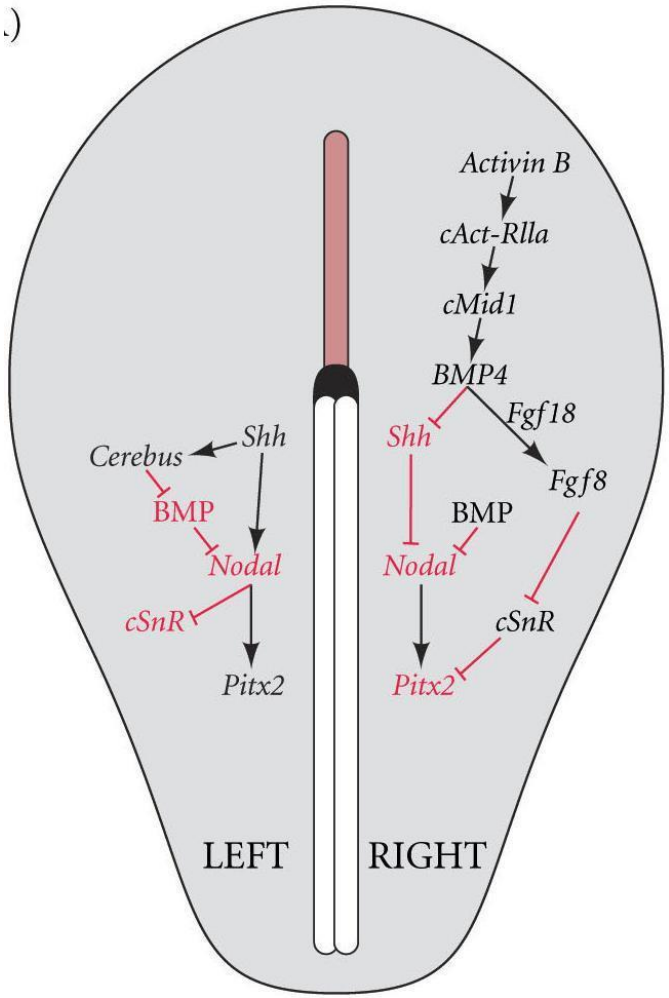


L-P organizátor (LRO)

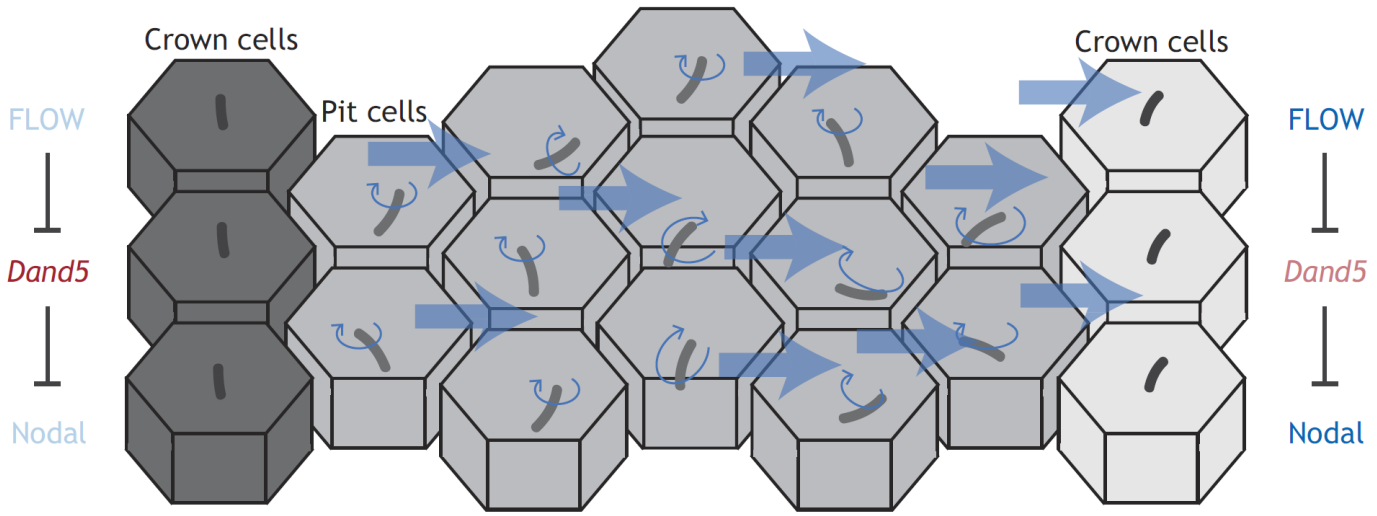


Grimes 2019

L-P organizátor (LRO)

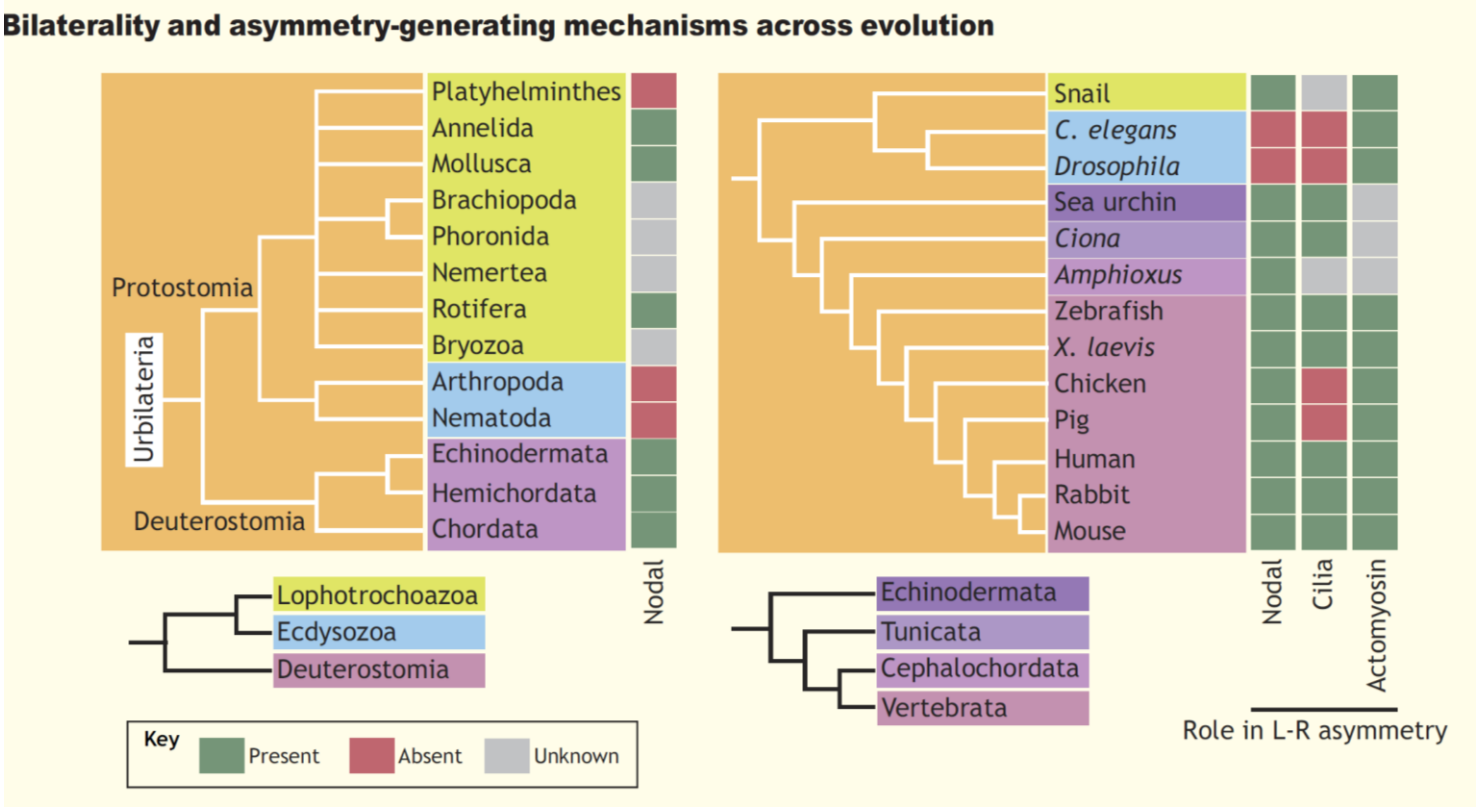


Asymetrické proudění tekutin



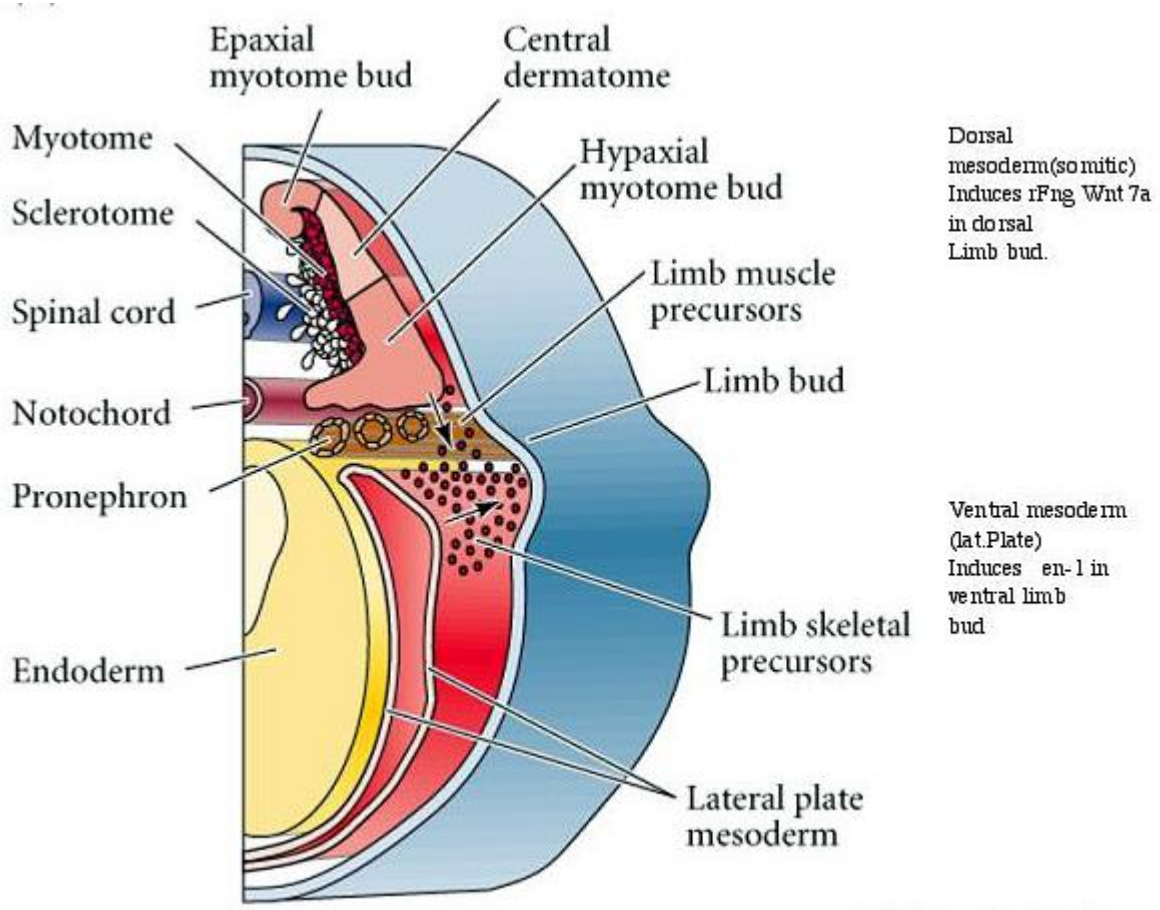
Grimes 2019

Fylogeneze



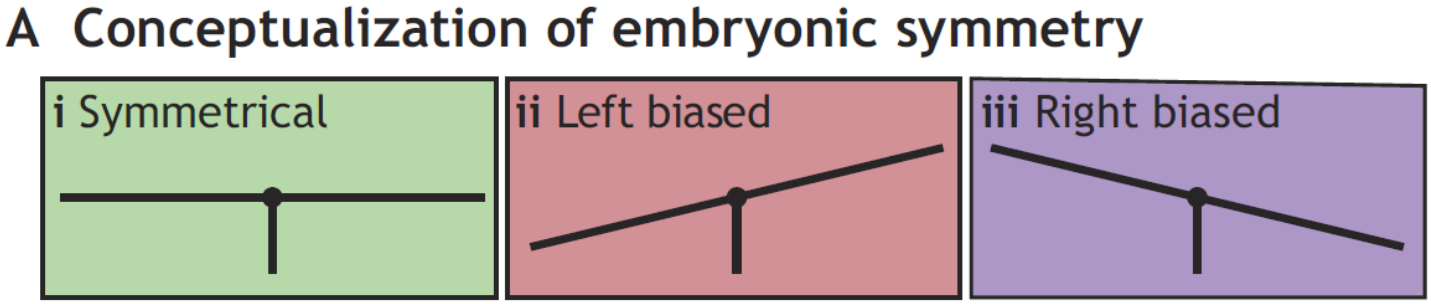
Grimes 2019

Tvorba symetrie: ochrana symetrických struktur od asymetrických vlivů



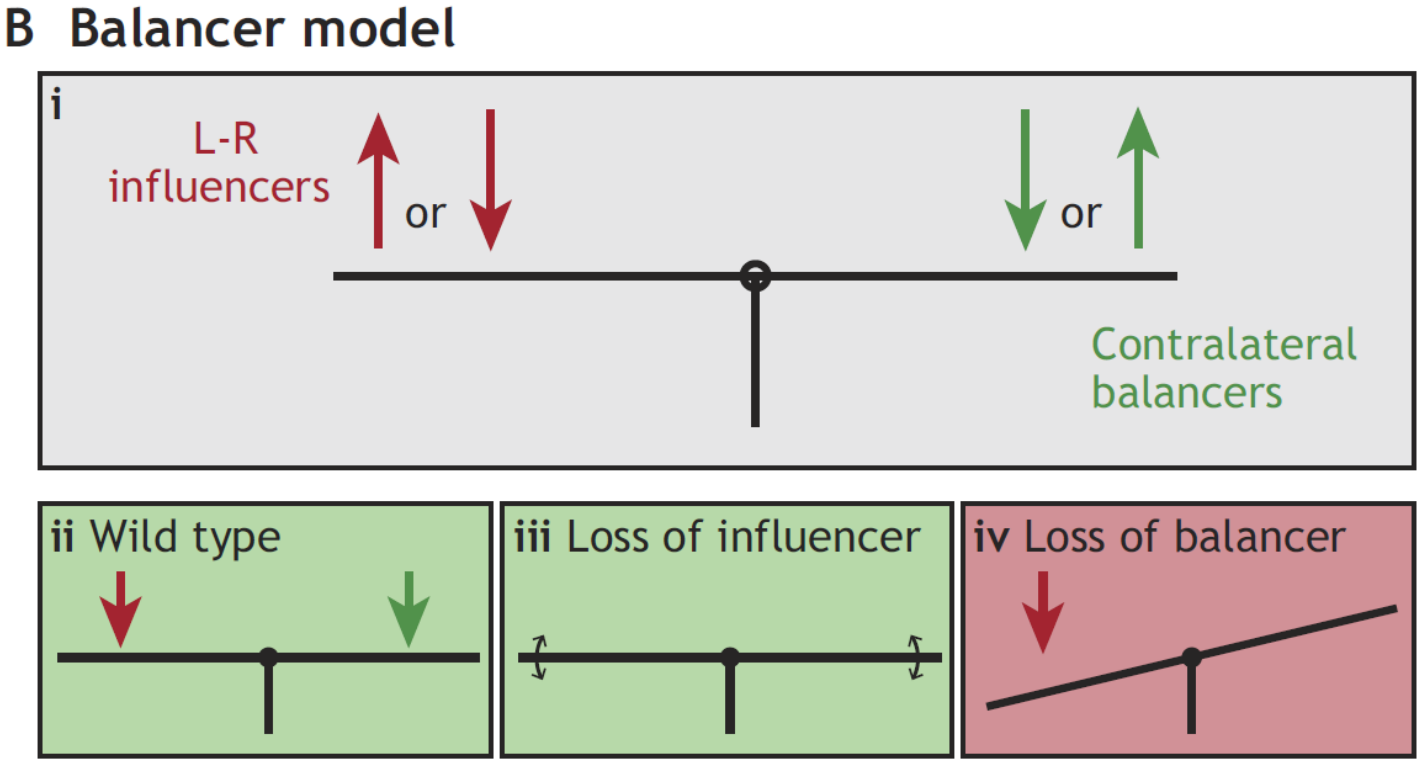
Gilbert 2010

Koncept vývoje symetrických struktur



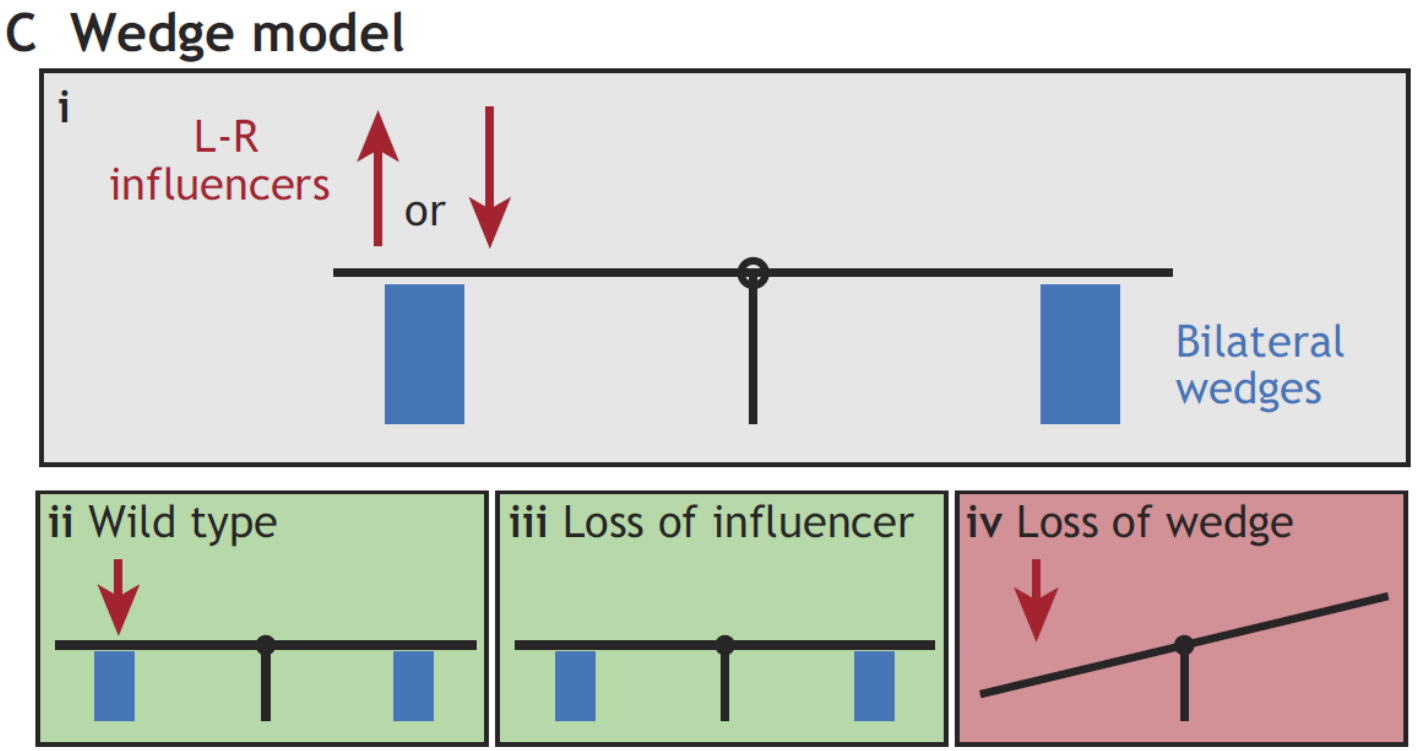
Grimes 2019

Kyvadlový model



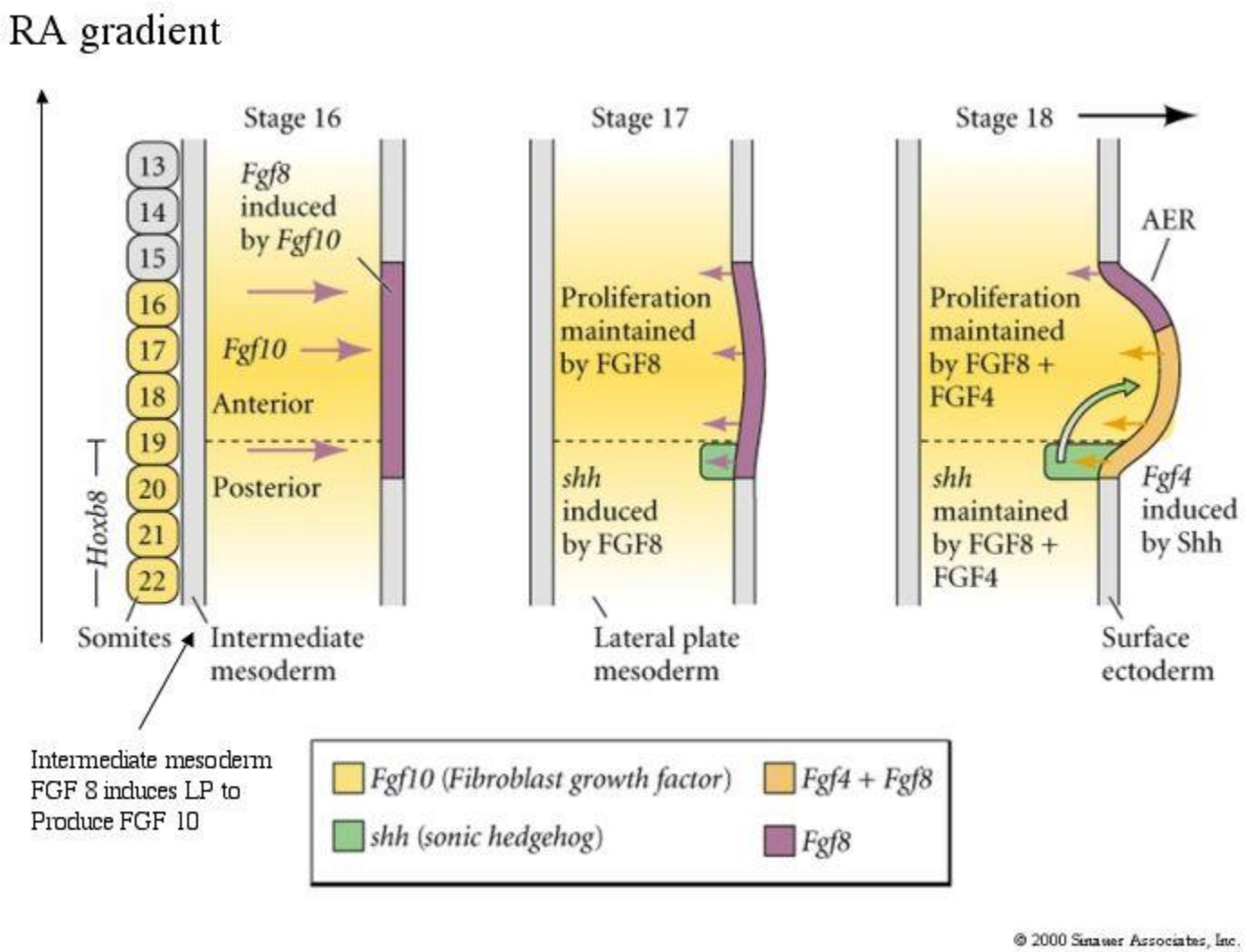
Grimes 2019

Klínový model



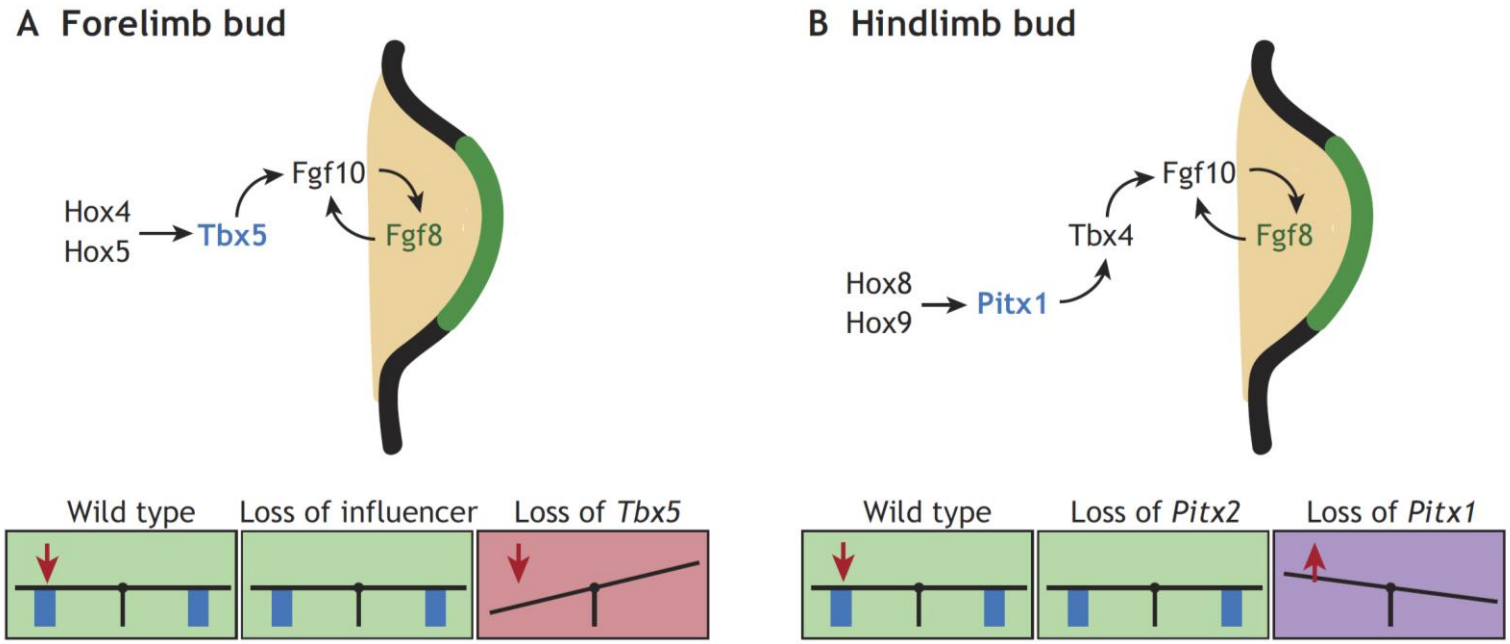
Grimes 2019

Udržení symetrického růstu končetinových pupenů



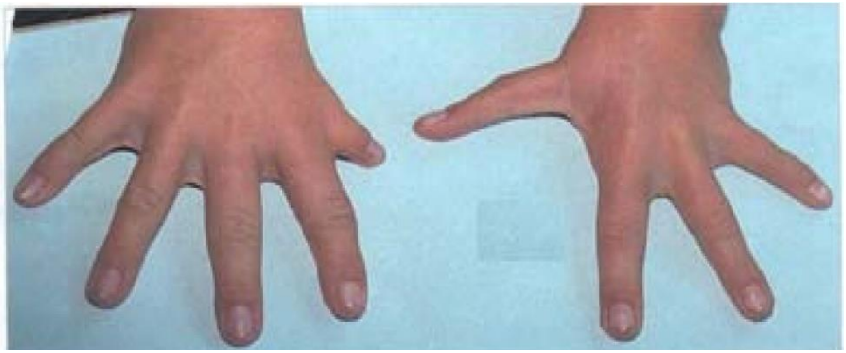
Gilbert 2010

Regulace vývoje končetinového pupene



Grimes 2019

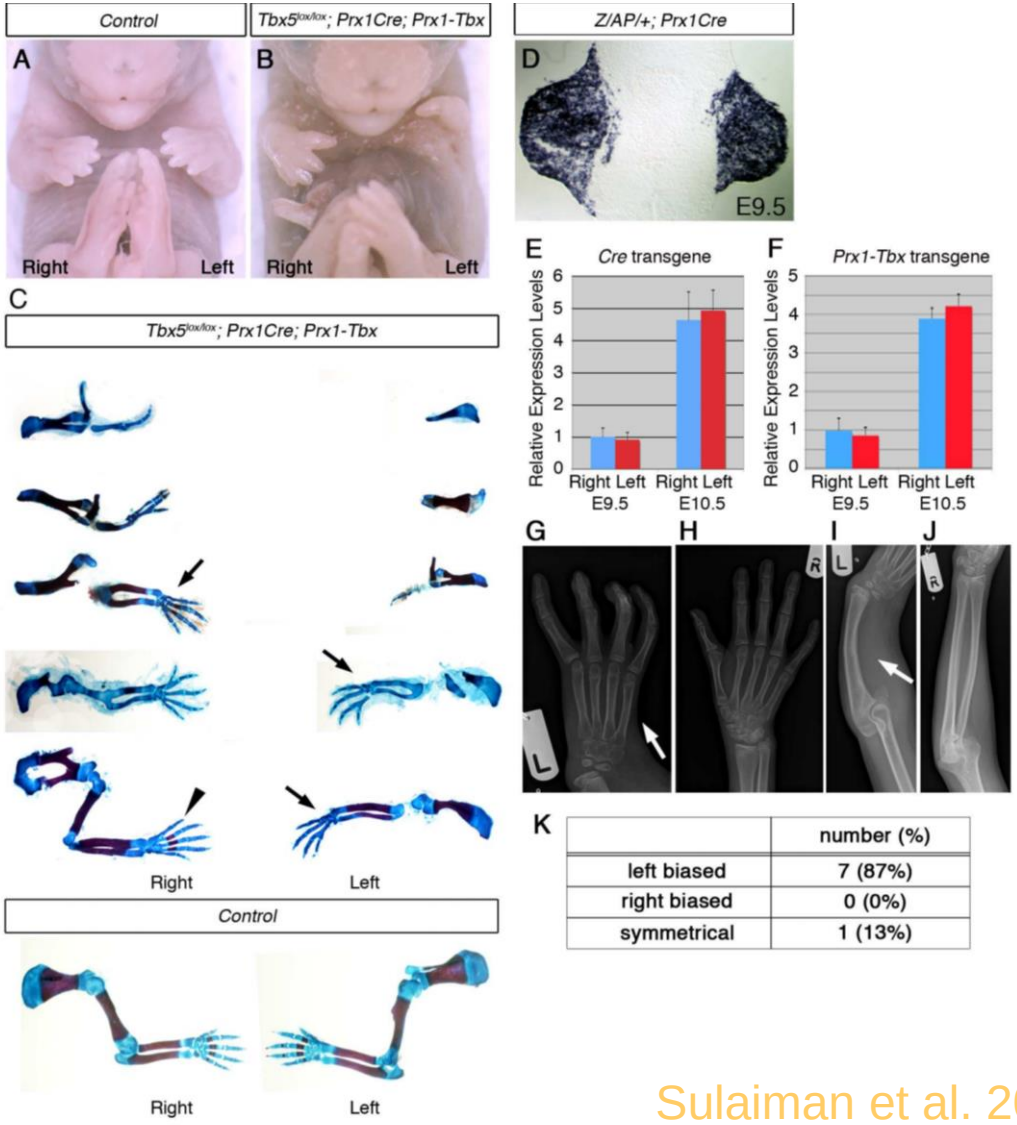
Holt-Oram syndrom



A

B

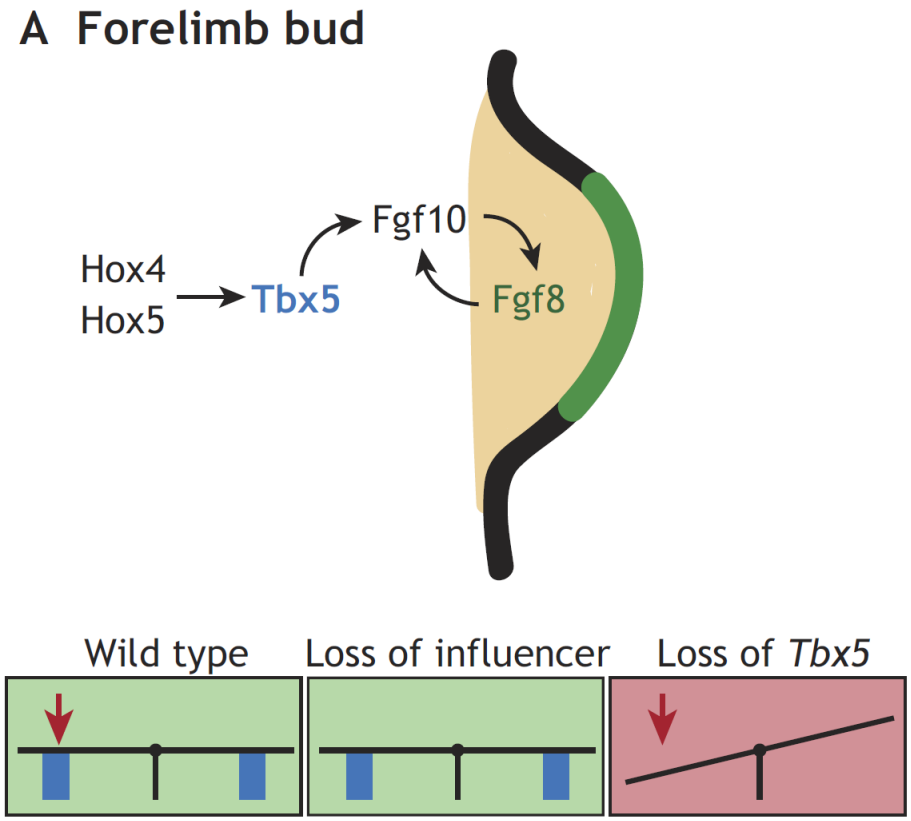
Holt-Oram syndrom



	number (%)
left biased	7 (87%)
right biased	0 (0%)
symmetrical	1 (13%)

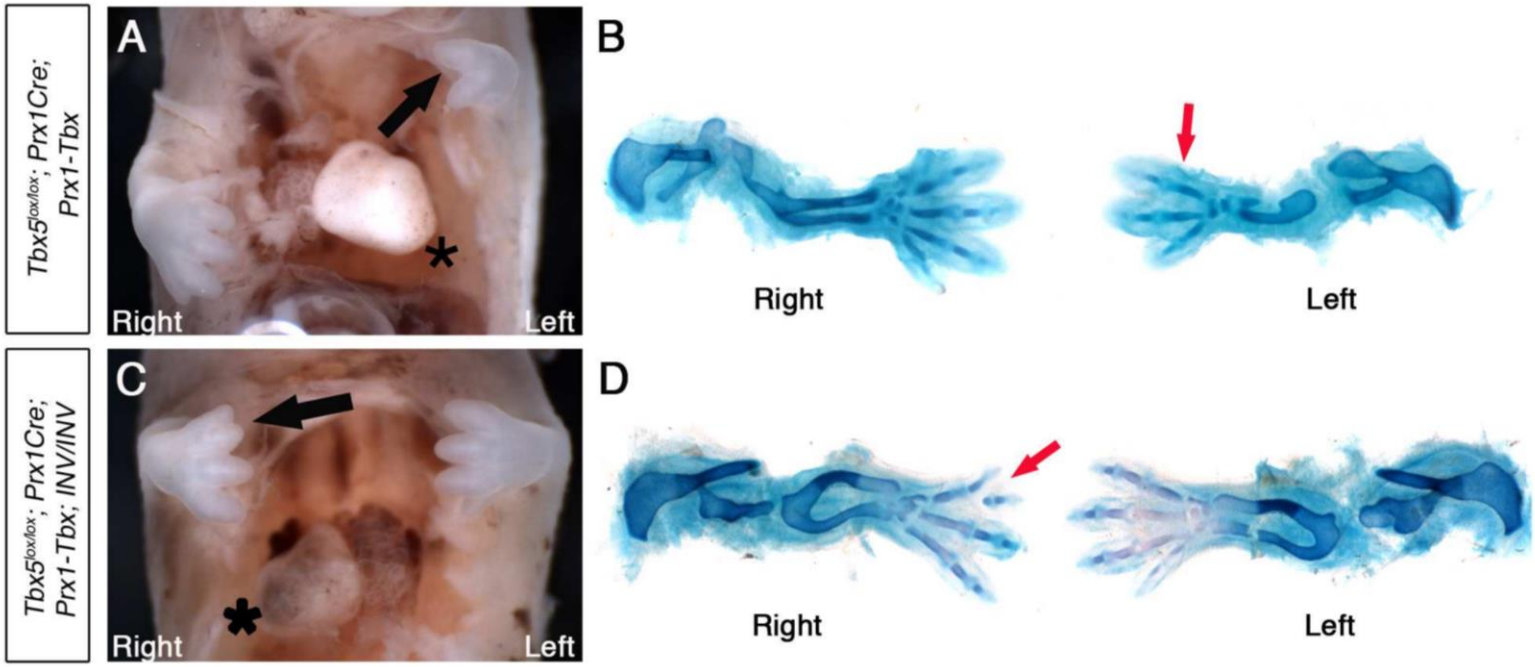
Sulaiman et al. 2016

Hrudní končetina



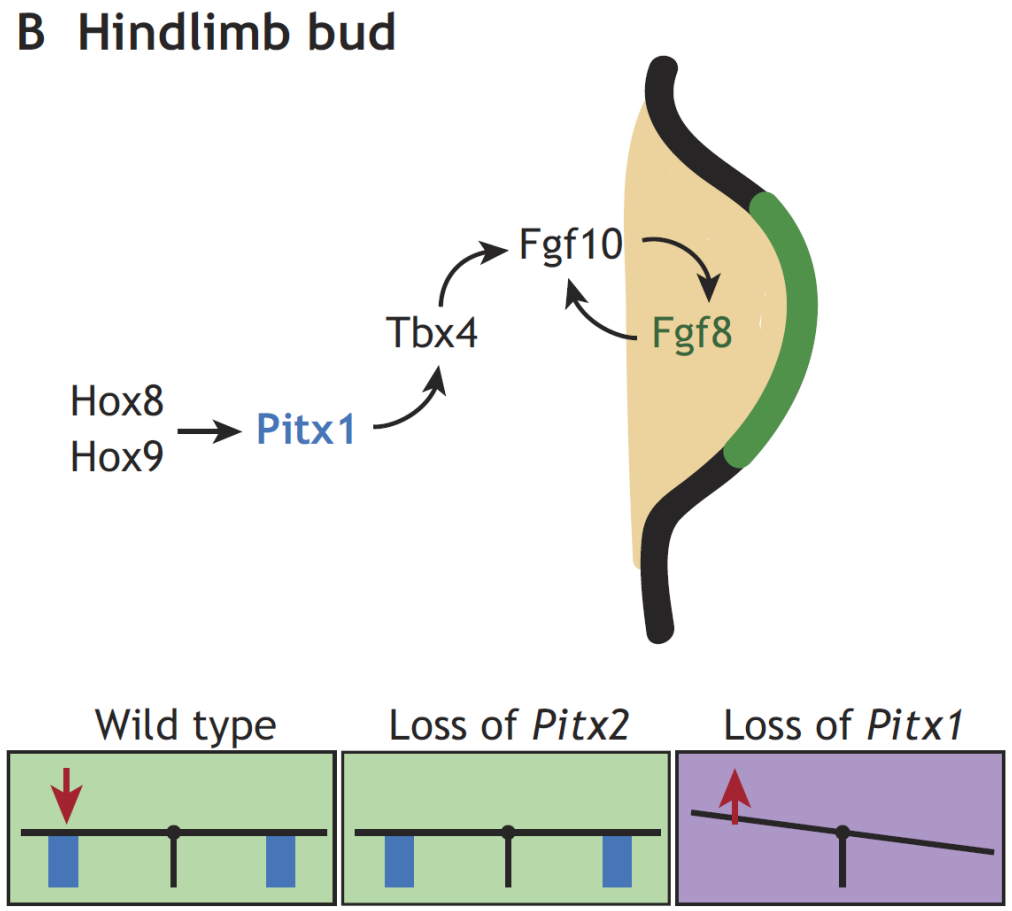
Grimes 2019

Obrácení fenotypu



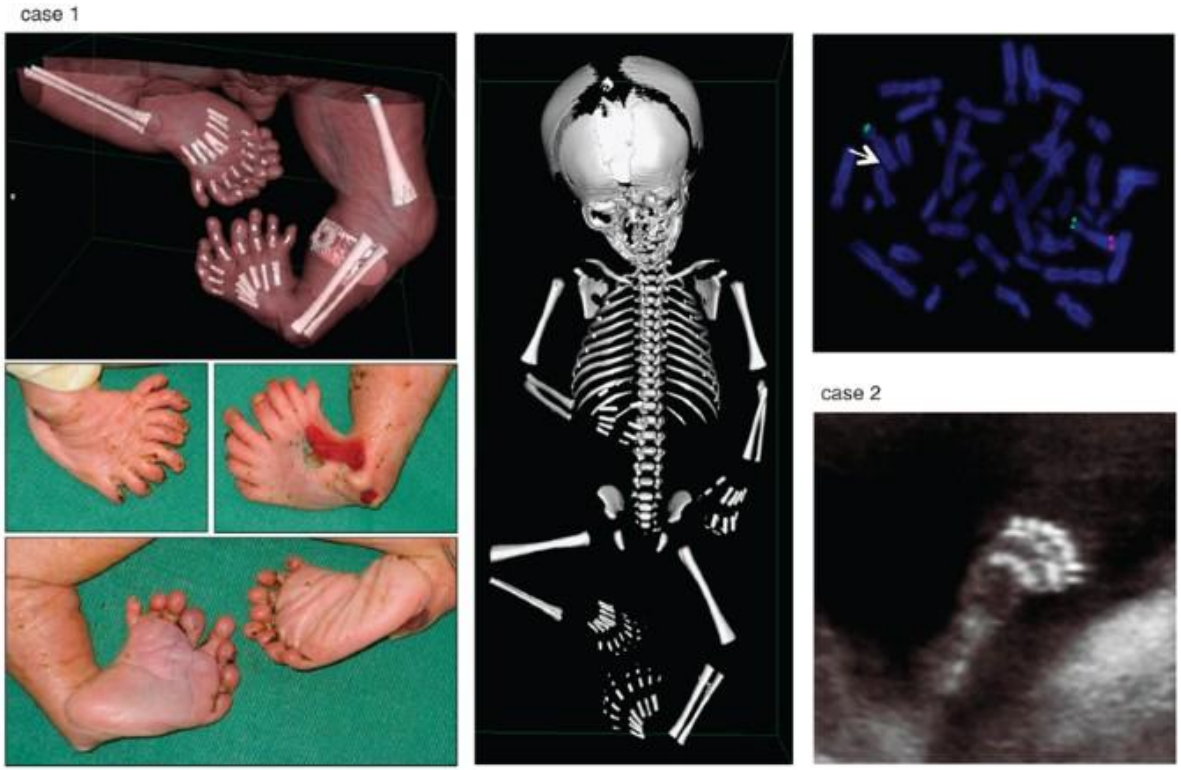
Sulaiman et al. 2016

Pánevní končetina

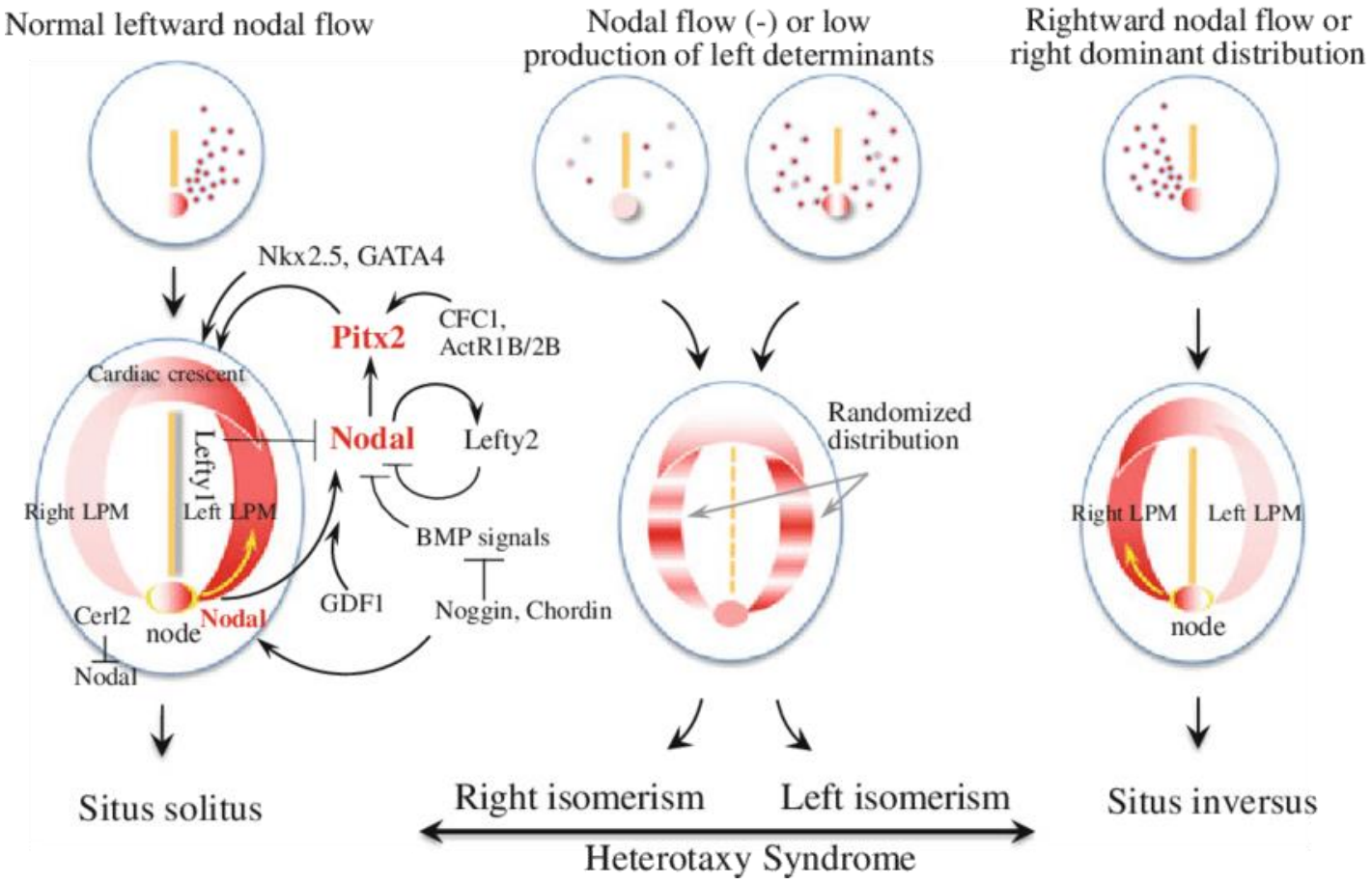


Grimes 2019

Pitx1 ve vývoji pánevní končetiny

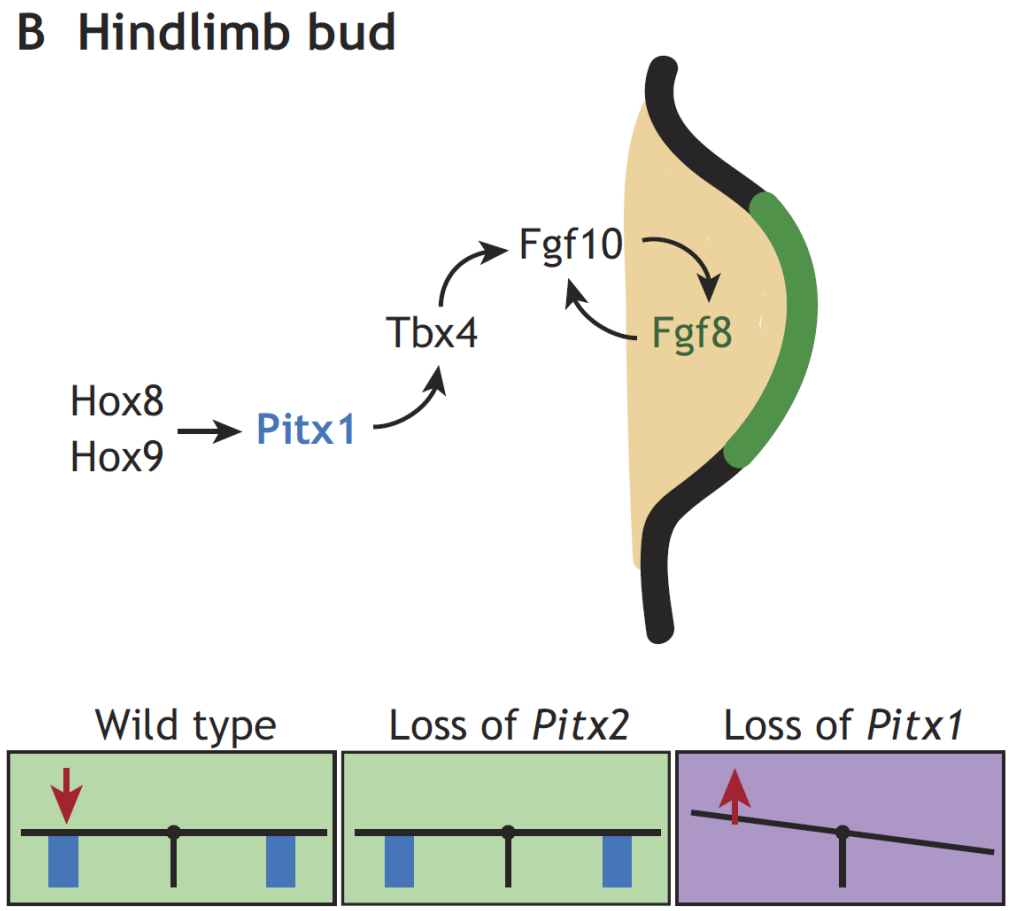


Kompenzace díky Pitx2



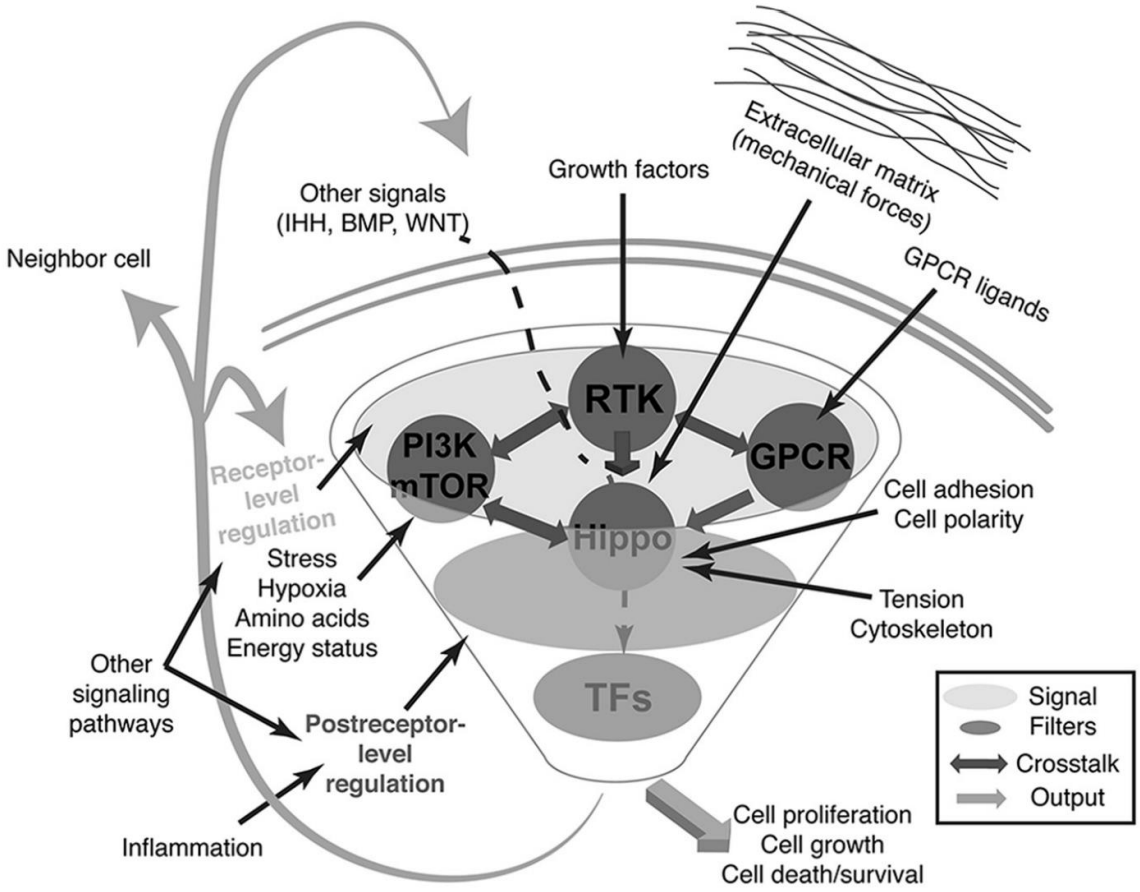
Shiraishi and Ichikawa, 2012

Kompenzace díky Pitx2

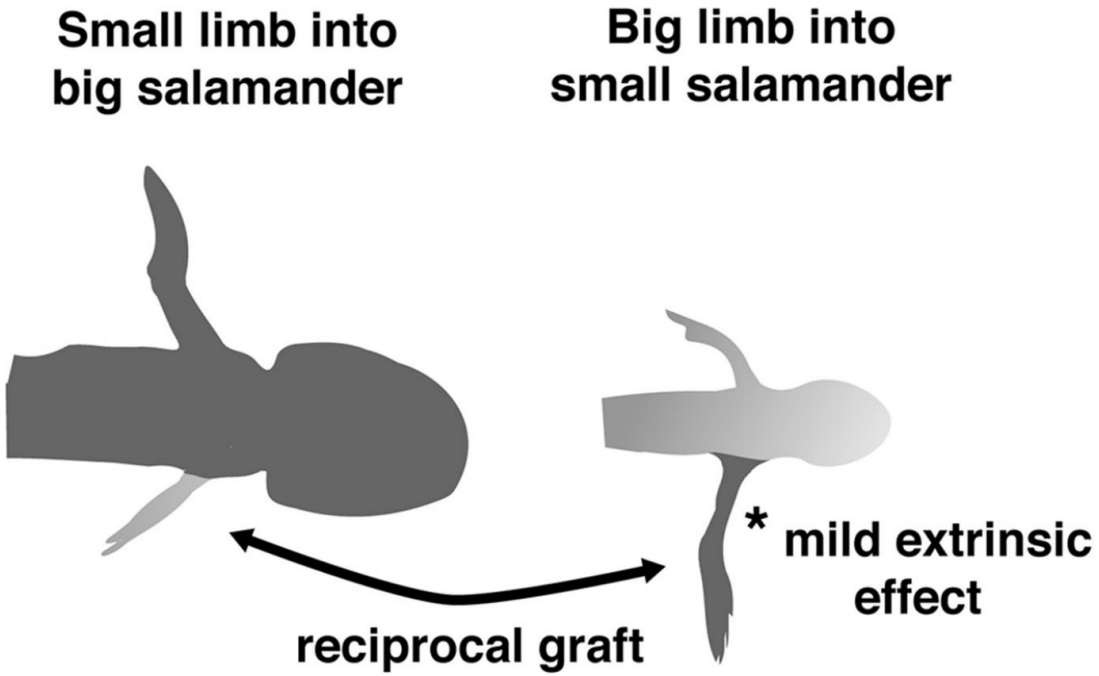


Grimes 2019

Regulace symetrického růstu

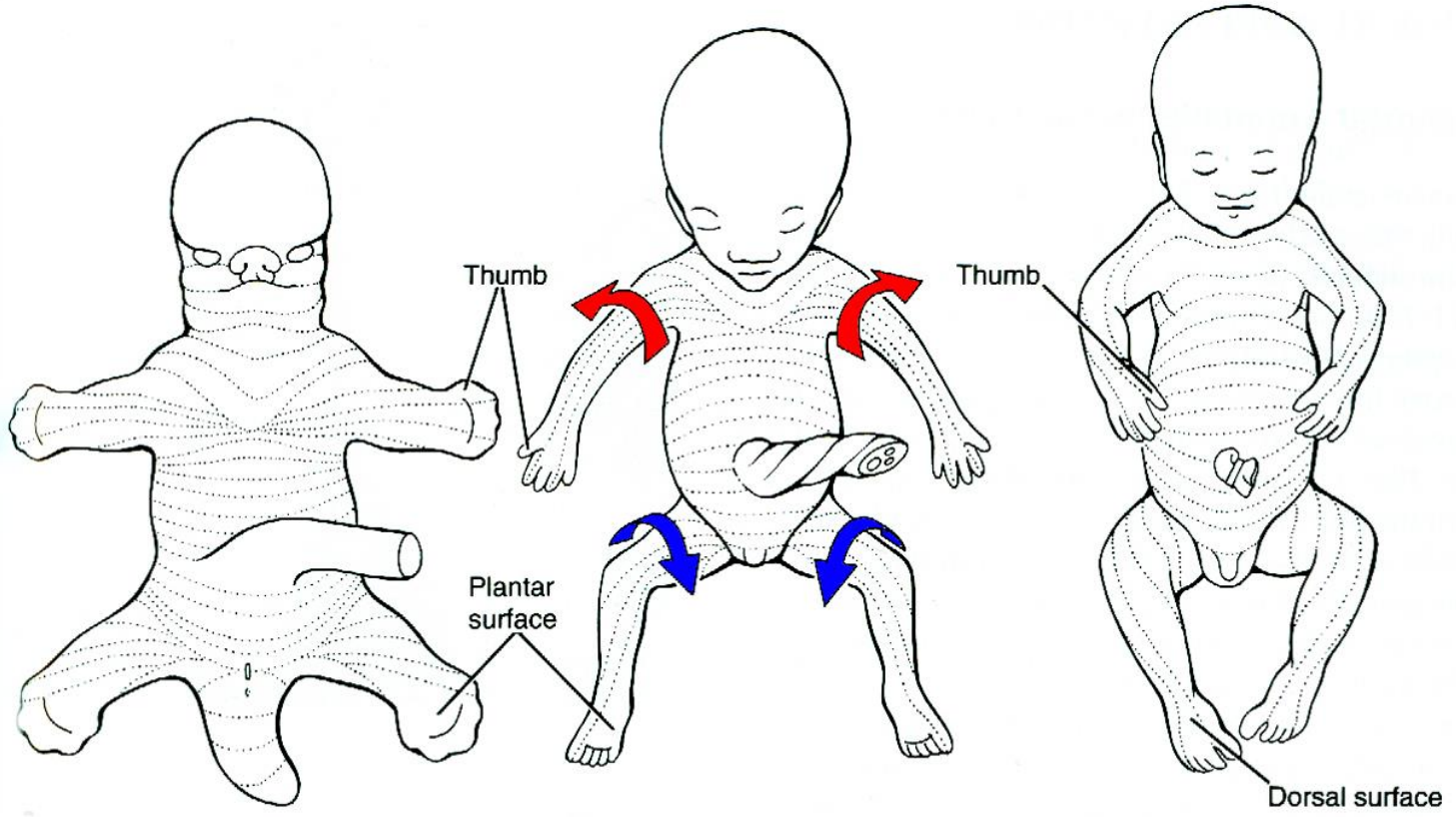


Roselló-Díez and Joyner, 2015

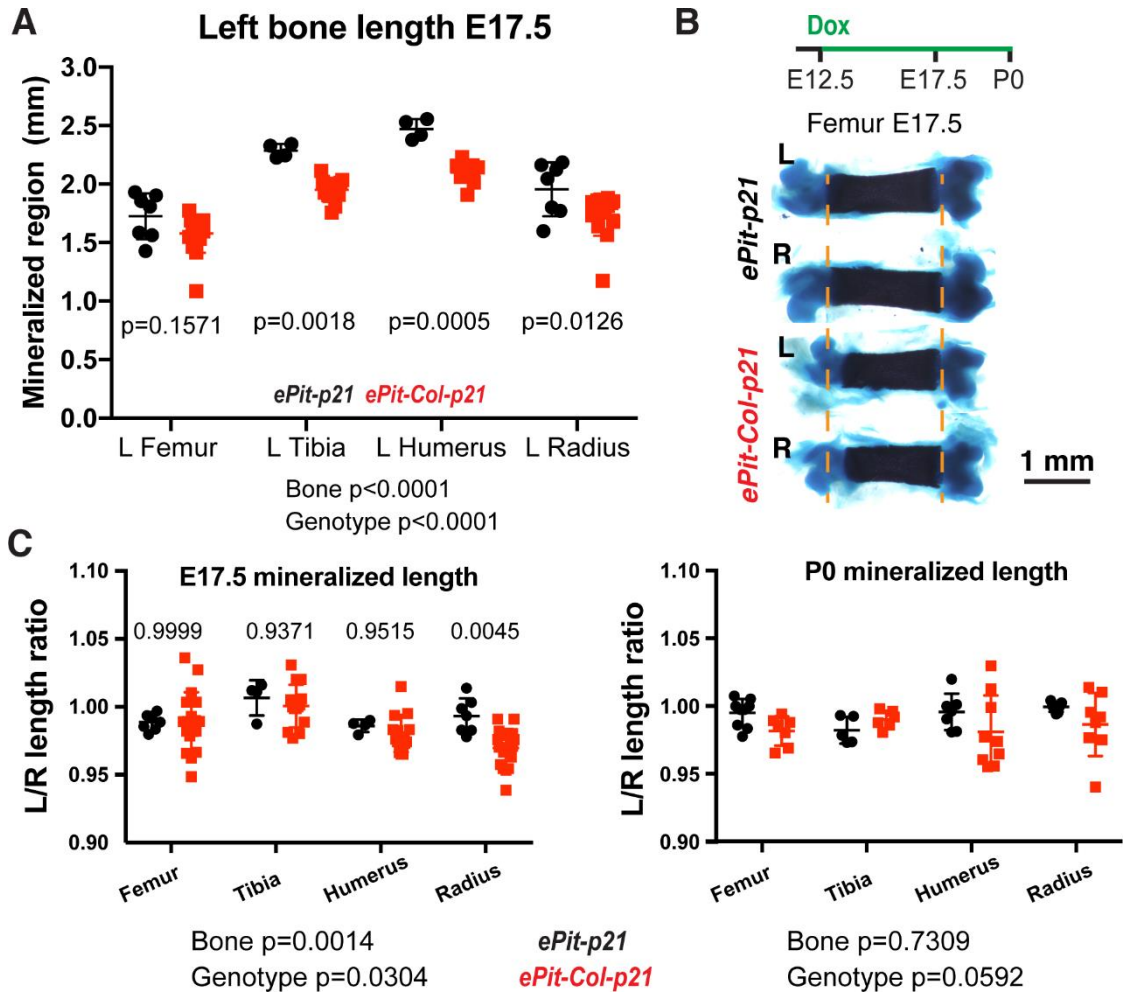


Roselló-Díez and Joyner, 2015

„Catch-up growth“

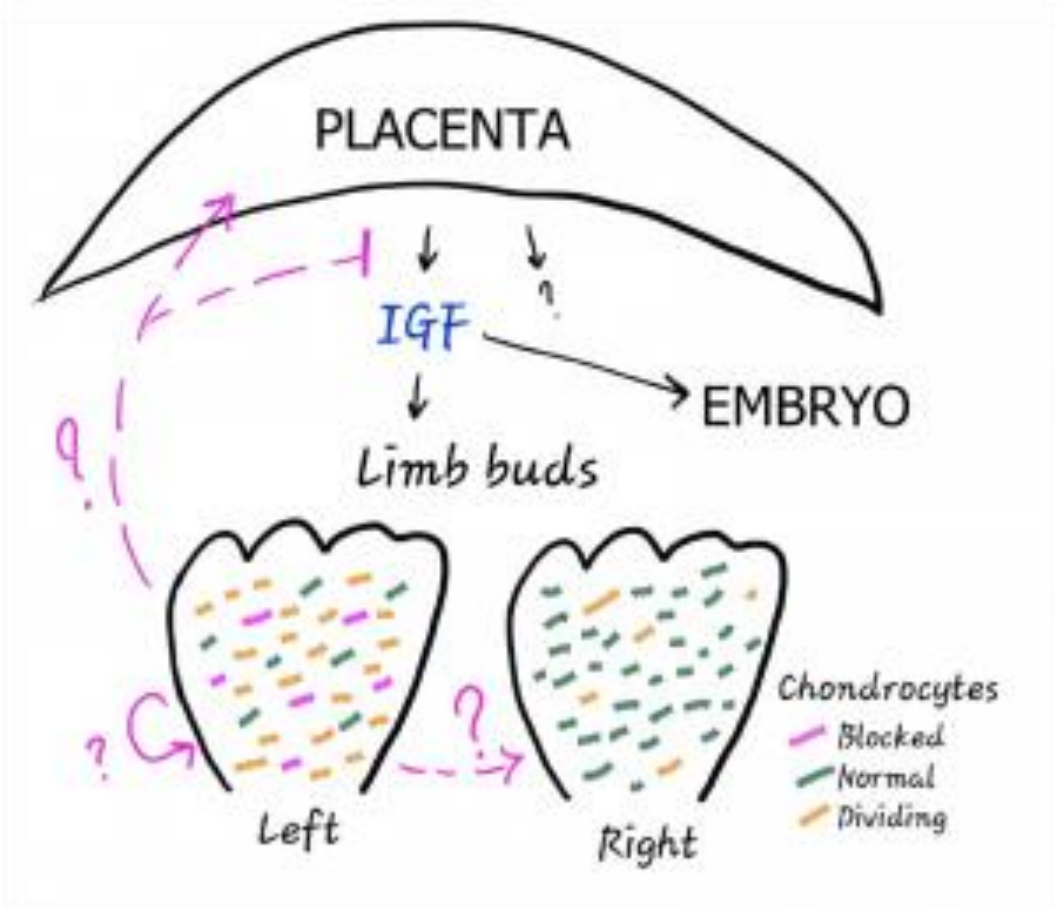


„Catch-up growth“

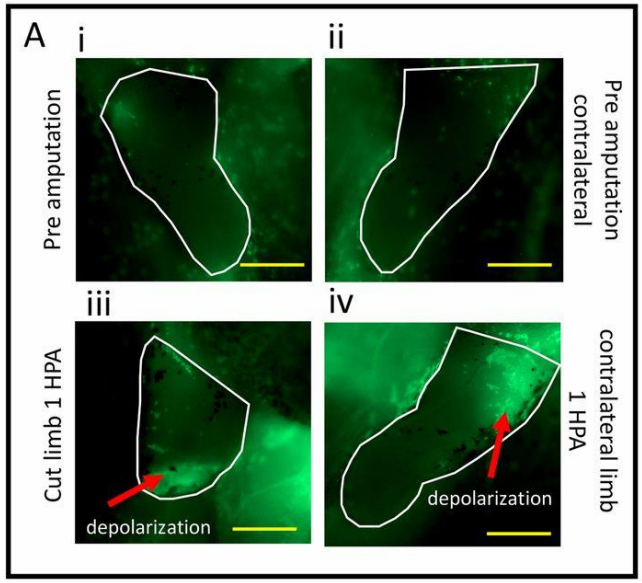


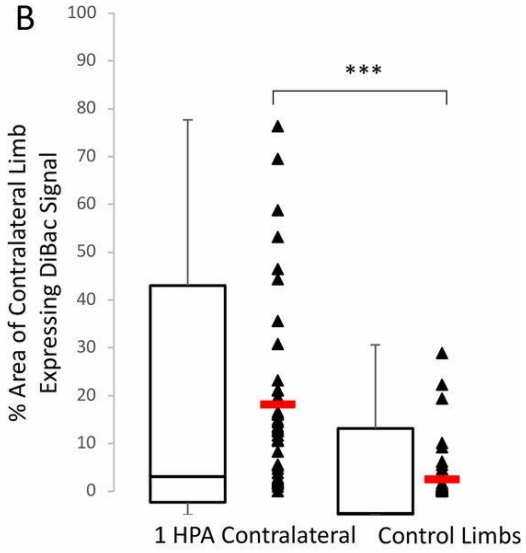
Rosello-Diez et al. 2018

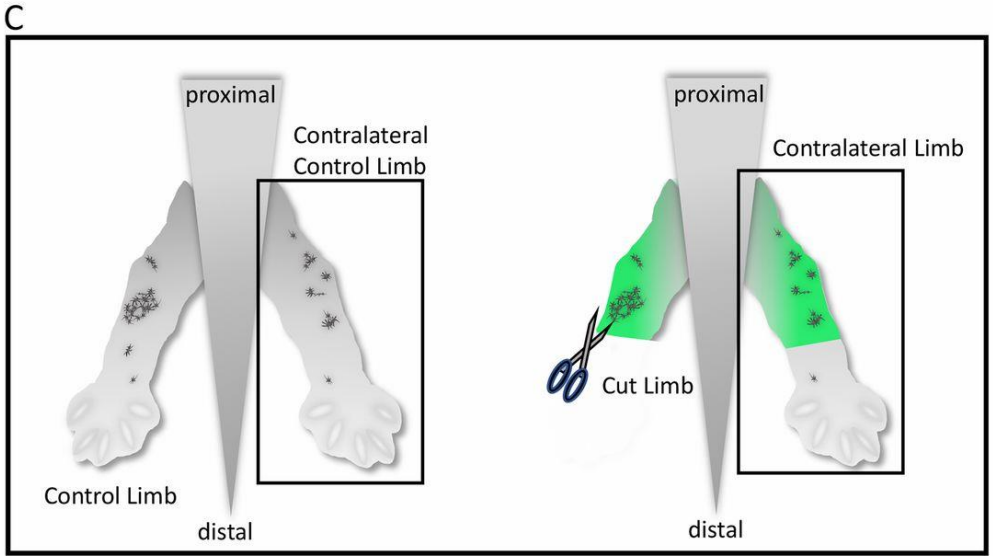
„Catch-up growth“



Vliv na kontralaterální stranu

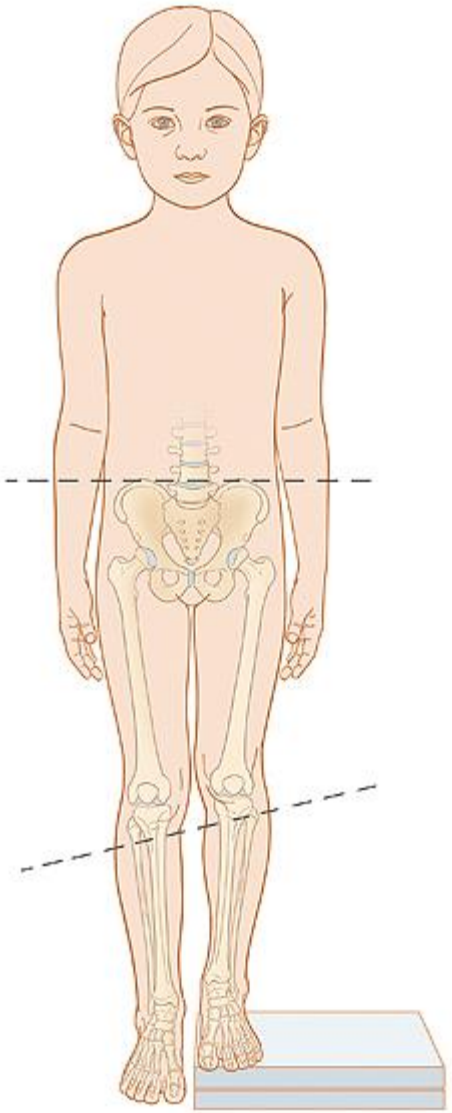


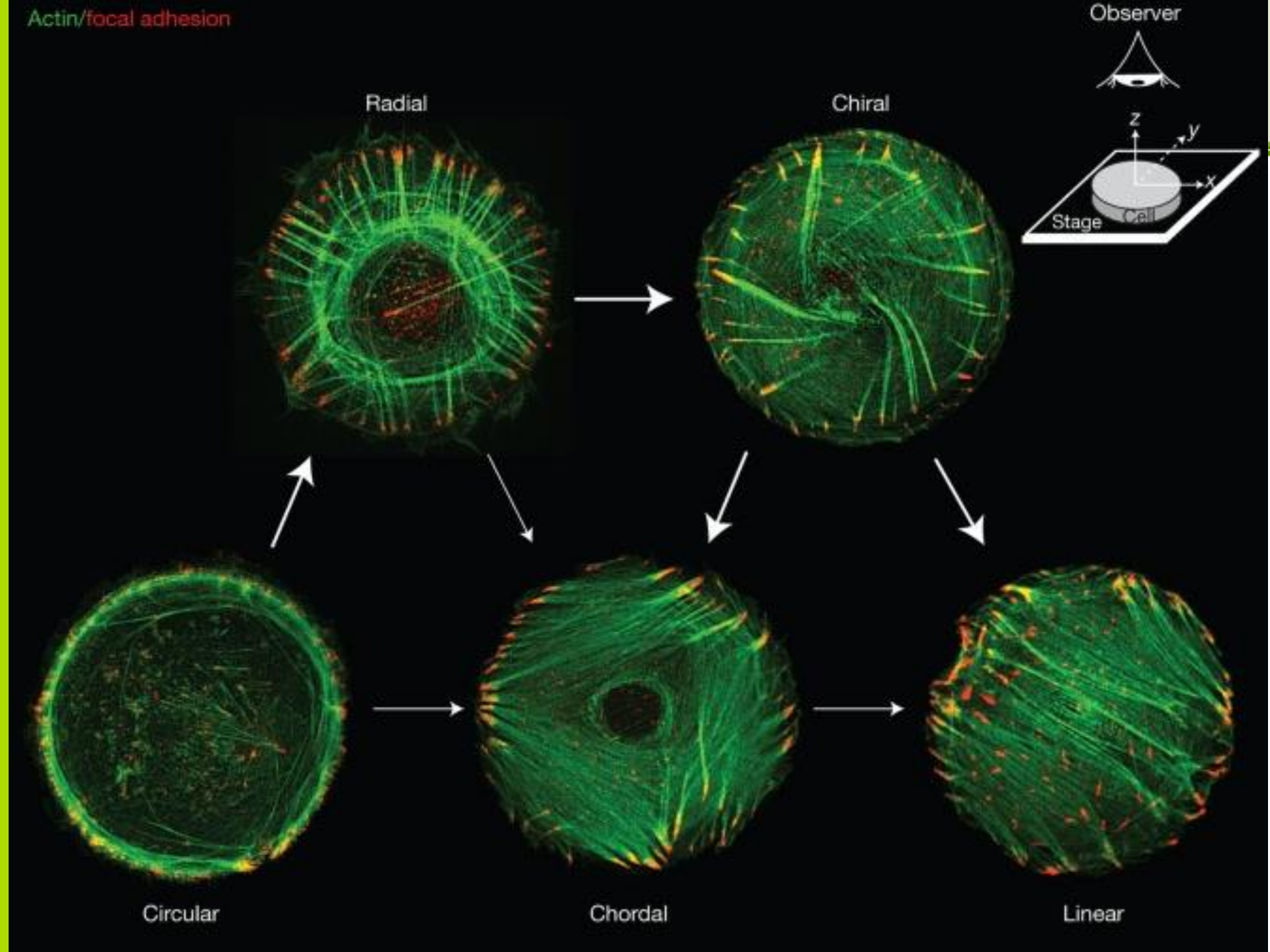




Busse et al. 2018

„Limb length discrepancy“ (LLD)




Actin/focal adhesion
Observer
Radial
Chiral
z
y
x
Stage
Cell
Circular
Chordal
Linear