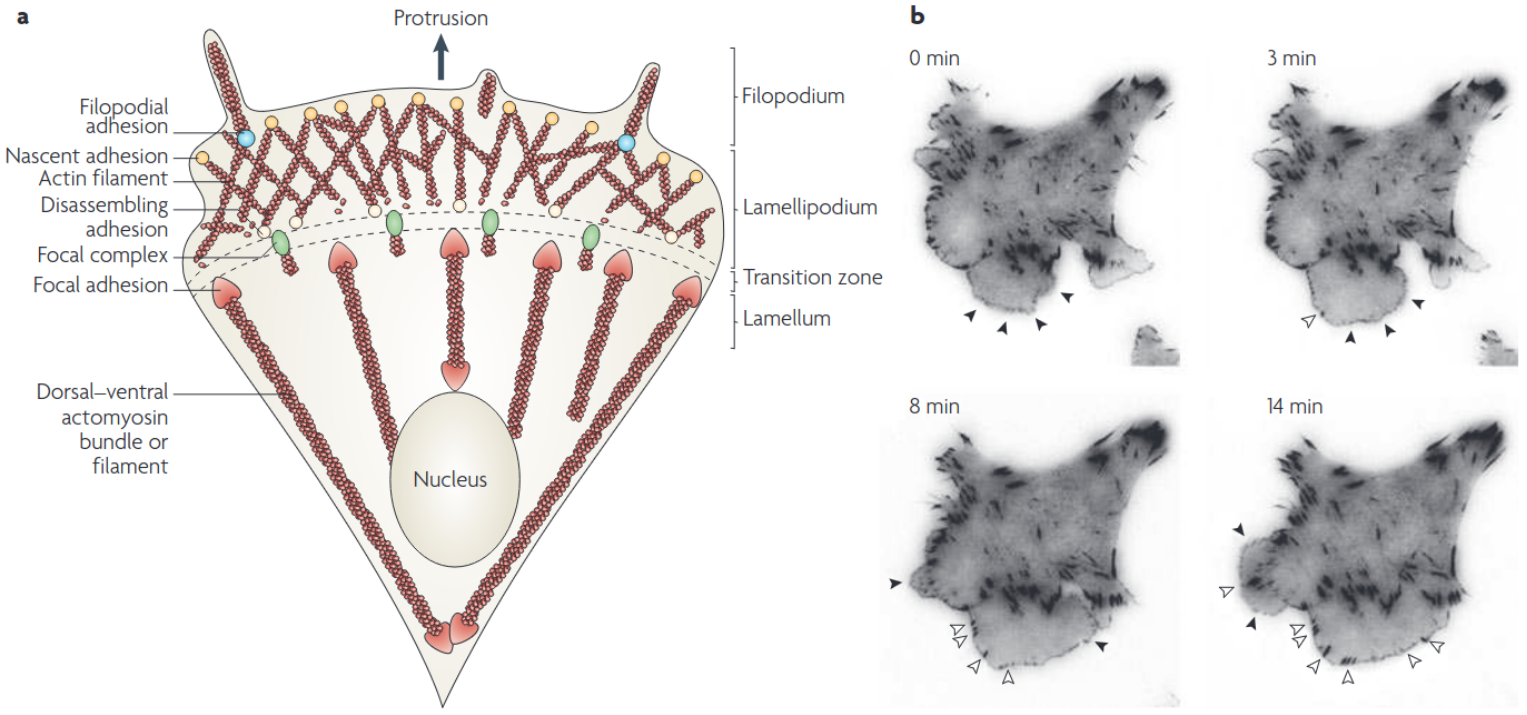
Cell adhesion to substrate

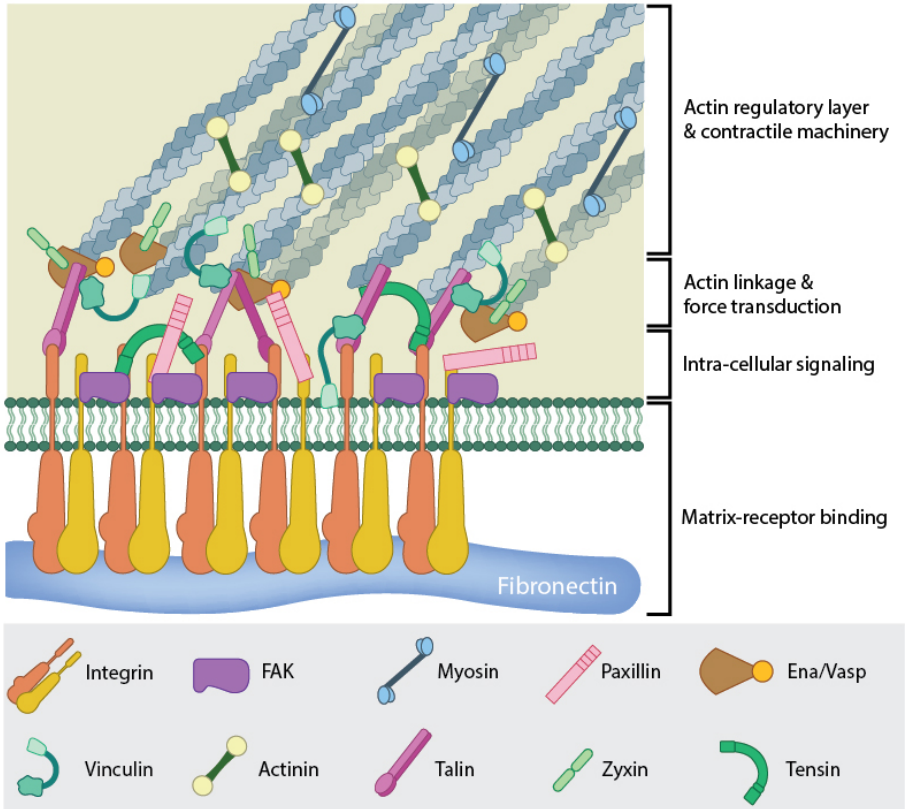
Elements of a migrating cell



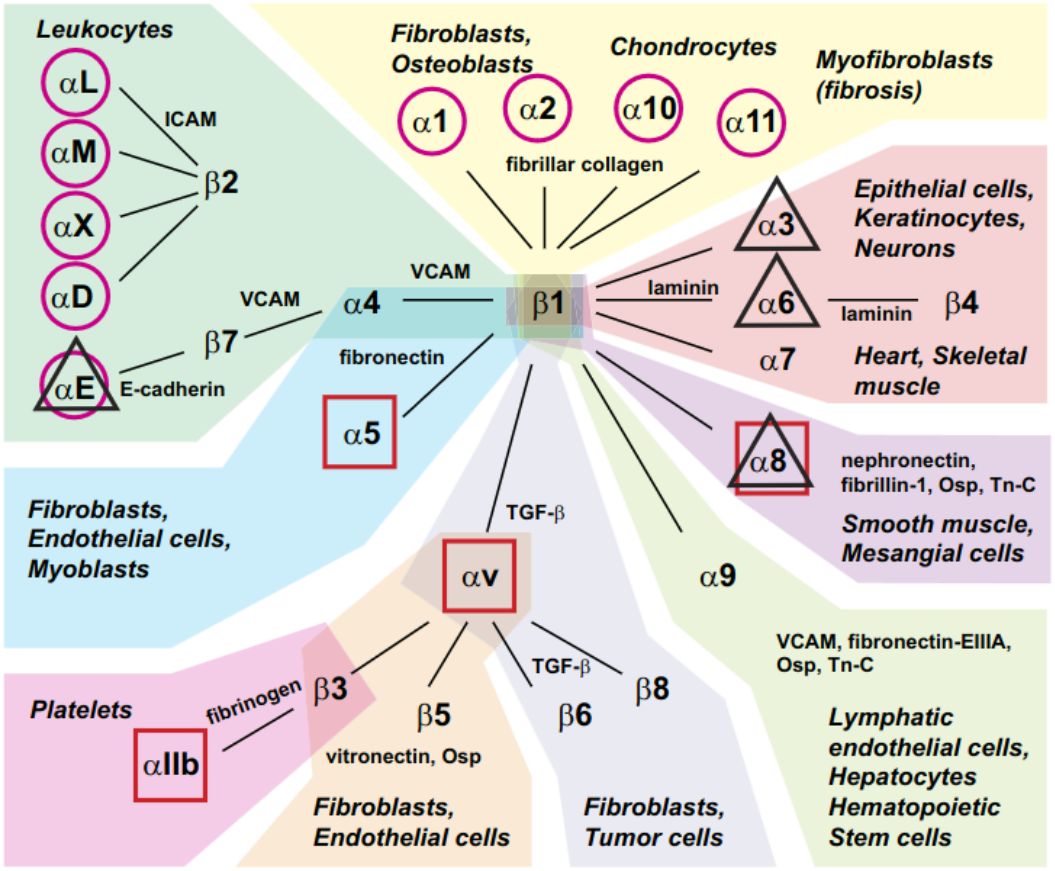
Parsons et al 2010 Nat. Rev.

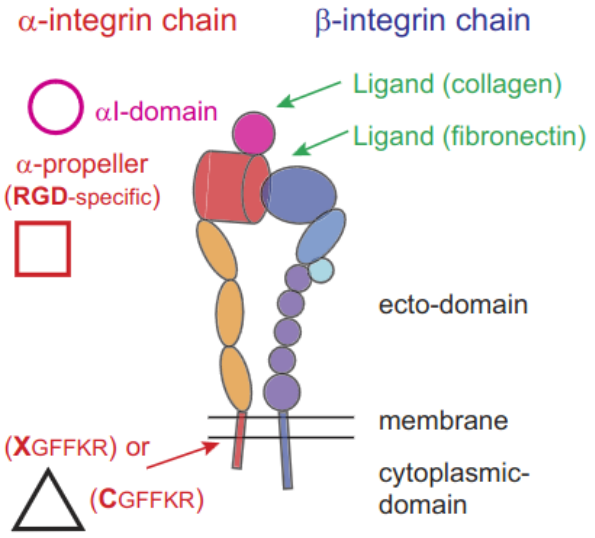
Focal adhesions

- Two sets of protein modules
  - ***strucutral module*** - proteins connecting the integrins to the actin cytoskeleton - talin, vinculin, and tensin etc. - their turnover was found to depend on the stiffness of the extracellular matrix
  - ***signaling module*** - FAK and paxillin etc. - high turnover rates and their mobilities were largely unaffected by extracellular matrix stiffness



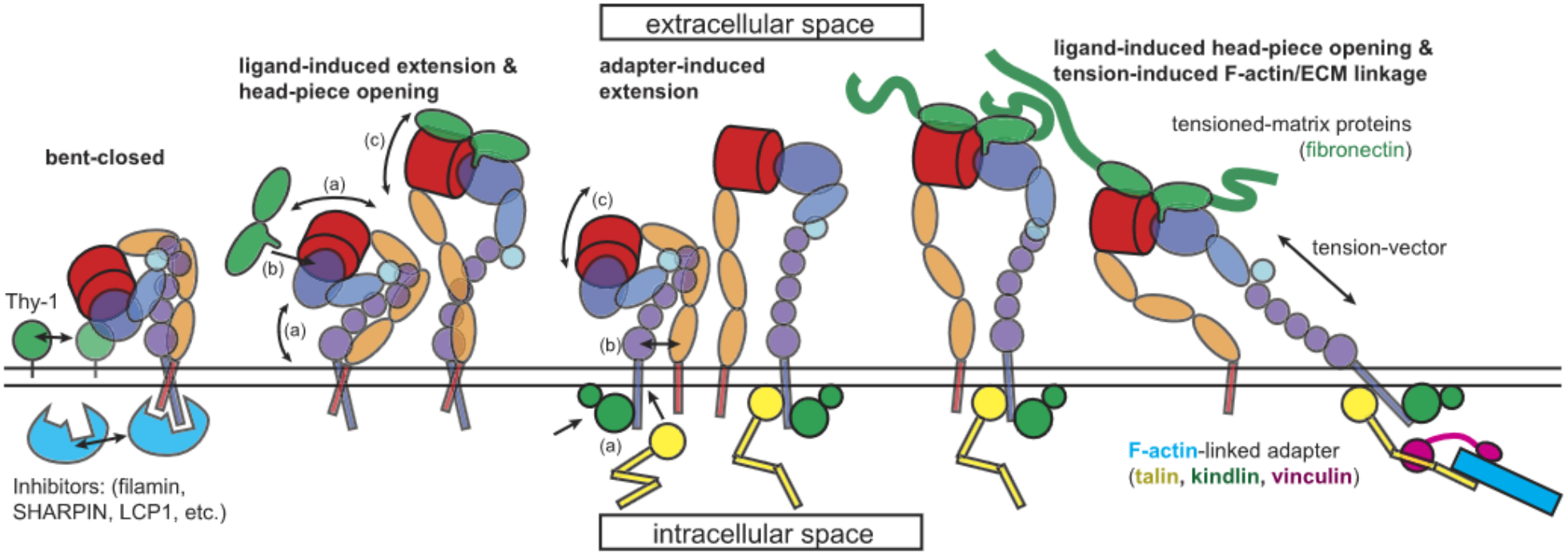
Integrin





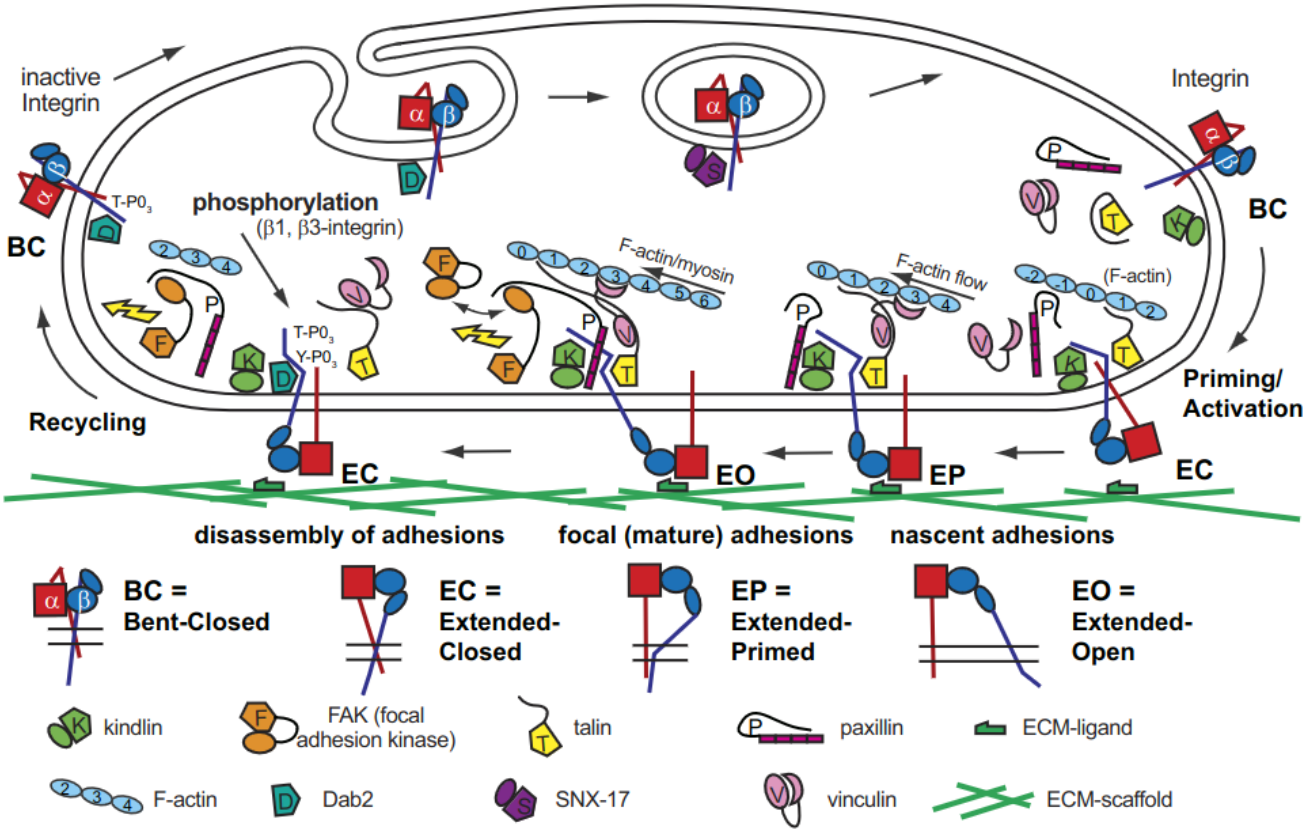
Bachman et al 2019 Phys. Rev.

Integrin activation



Bachman et al 2019 Phys. Rev.

Integrin activation

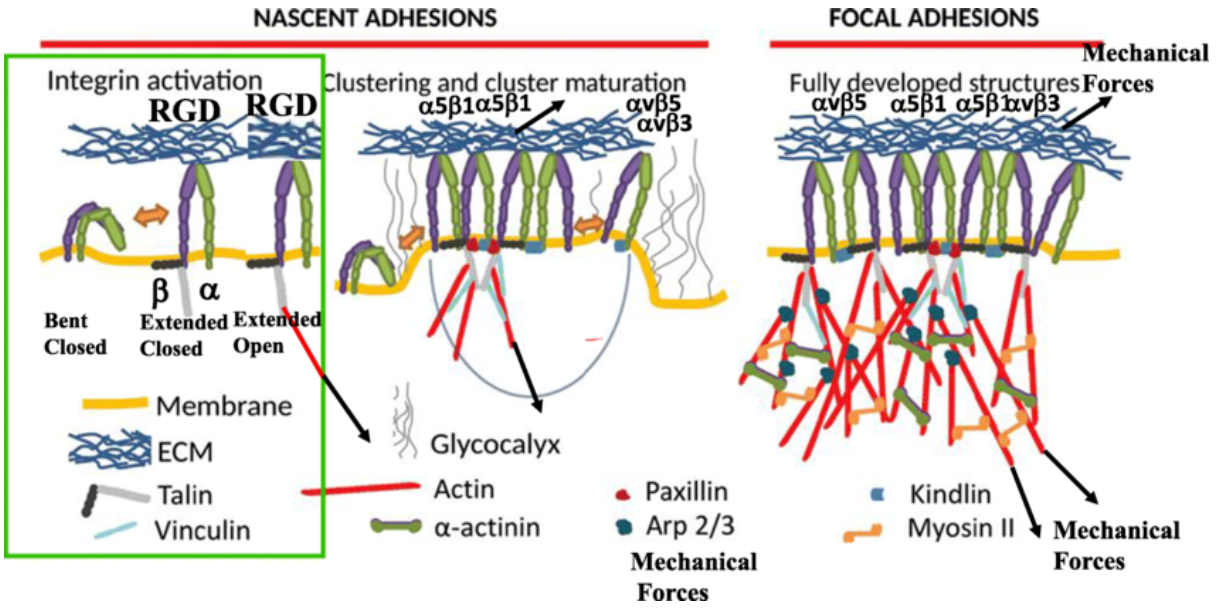


Bachman et al 2019 Phys. Rev.

Integrin clustering

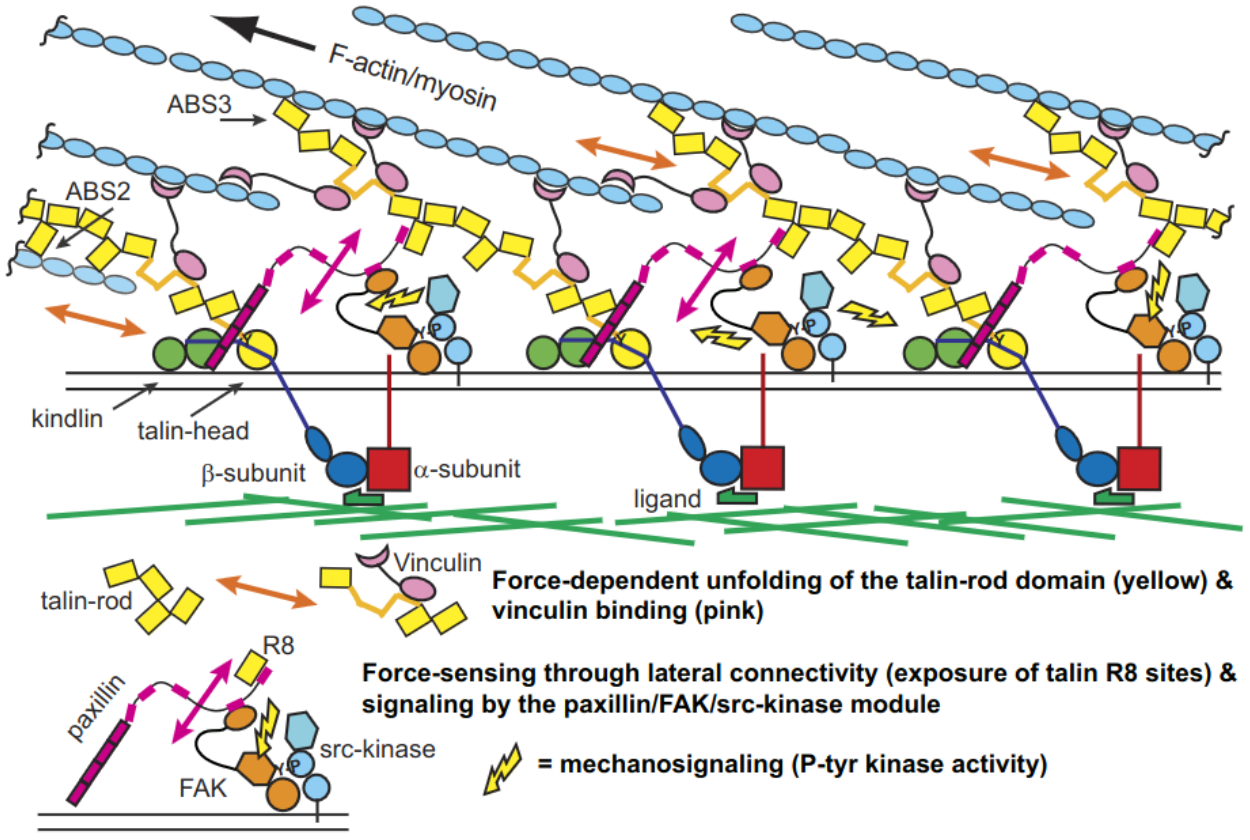
On integrin-ligand binding and activation

- they start to form clusters
- further assemble into larger integrin clusters to enable cell adhesion



Schussler et al 2021 JCTR

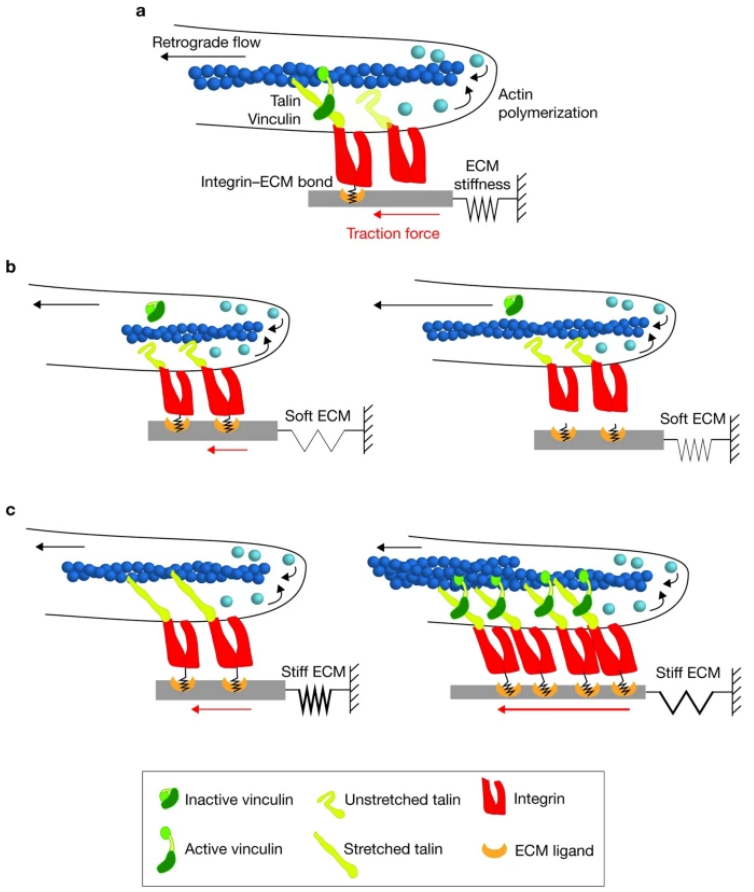
Protein interactions



Bachman et al 2019 Phys. Rev.

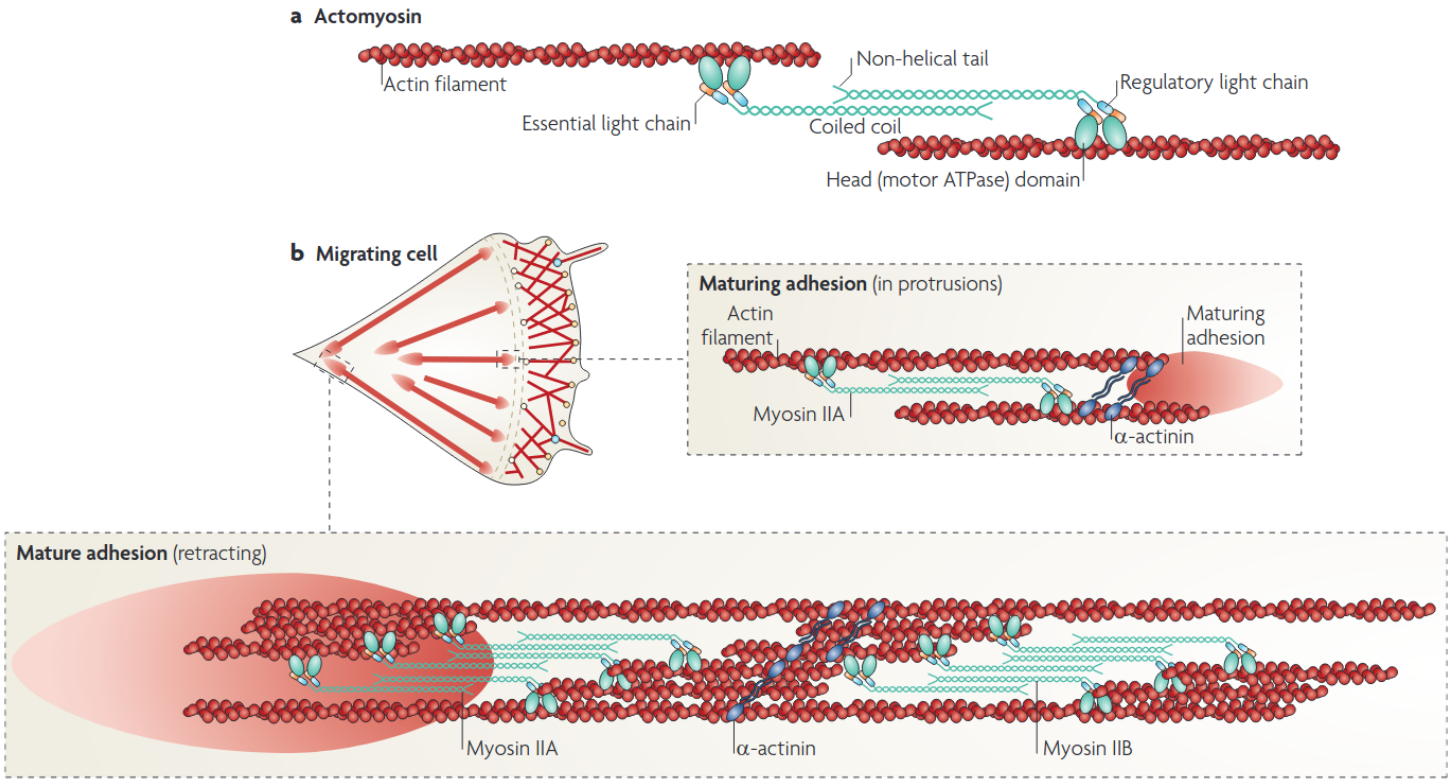
Molecular clutch

- Actin polymerization leads to formation of protrusions
- Actin polymerization can push membrane forward if it is anchored
- In the absence of anchoring – actin is pushed back --> **retrograde flow**
- Anchoring is provided by FA proteins between integrins and actin --> **clutch**



Swaminathan and Waterman 2016 Nat Cell Bio

Role of myosin

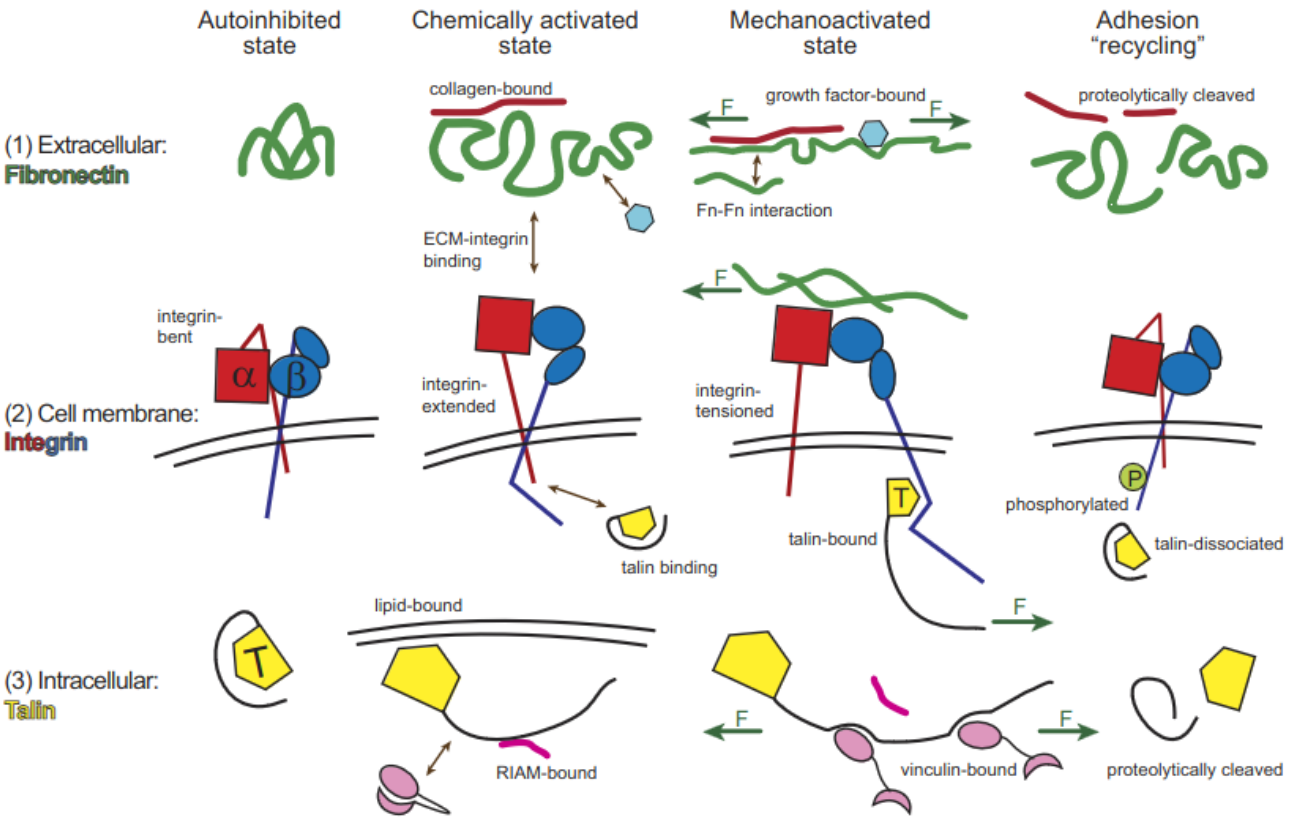


Parsons et al 2010 Nat. Rev.

Mechanosensing

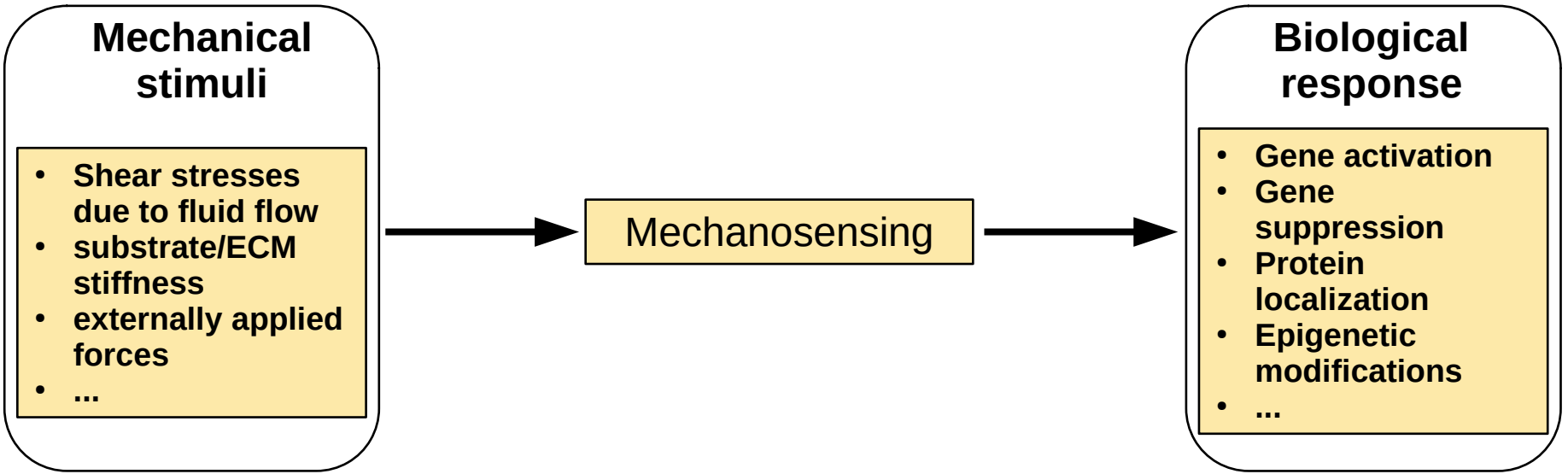
- Cell-matrix adhesions are considered **mechanosensitive**, as their size, composition, and signaling capacity are known to be affected by **mechanical load** and **substrate stiffness**
- In cellular mechanosensing, a mechanical signal is received by a mechanoreceptor, which is capable of translating the signal into a chemical cue
- Three levels of mechanosensing
  - The regulation of integrin conformation
  - the catch bond between fibronectin and integrins
  - intracellular adapter proteins

Mechanosensing

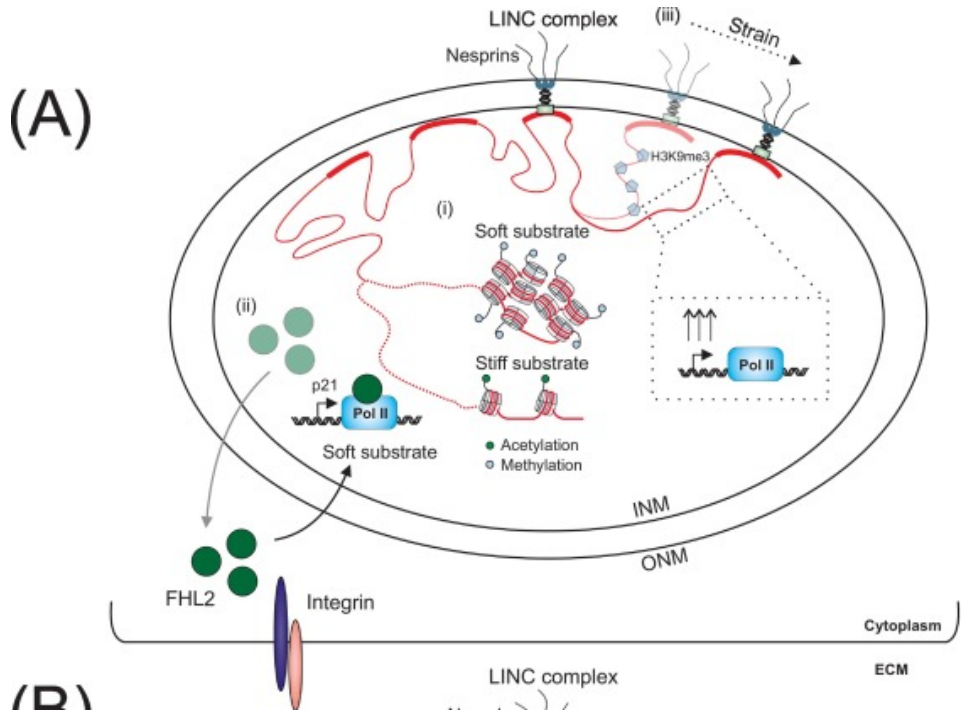


Bachman et al 2019 Phys. Rev.

Mechanotransduction



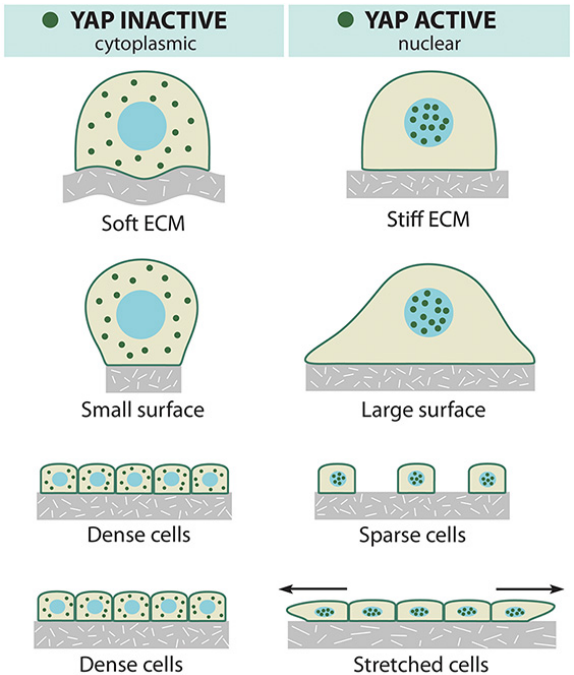
Mechanotransduction

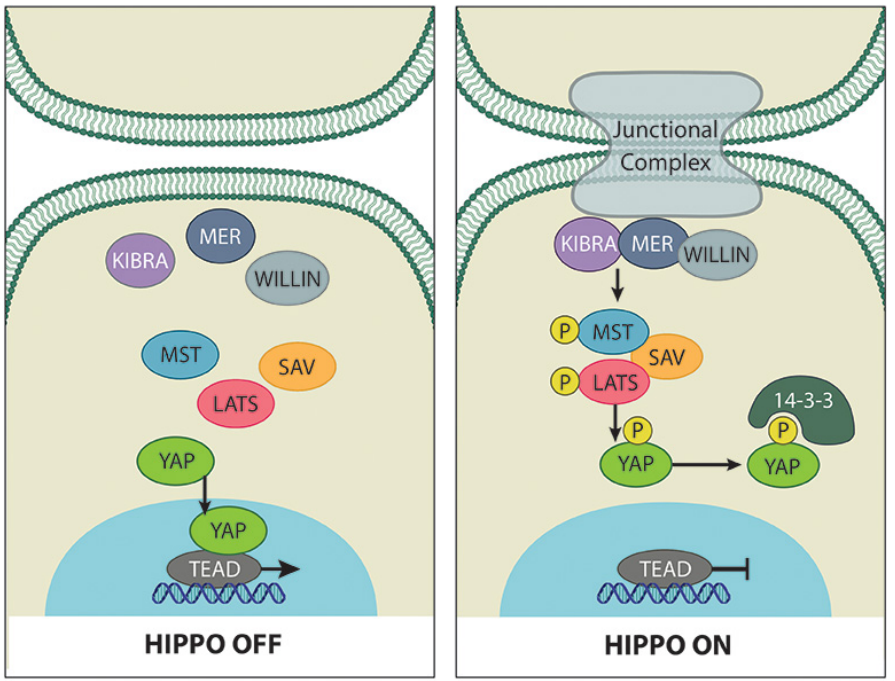


Wagh et al 2021 Tr. Cell Bio.

Hippo-YAP/TAZ pathway

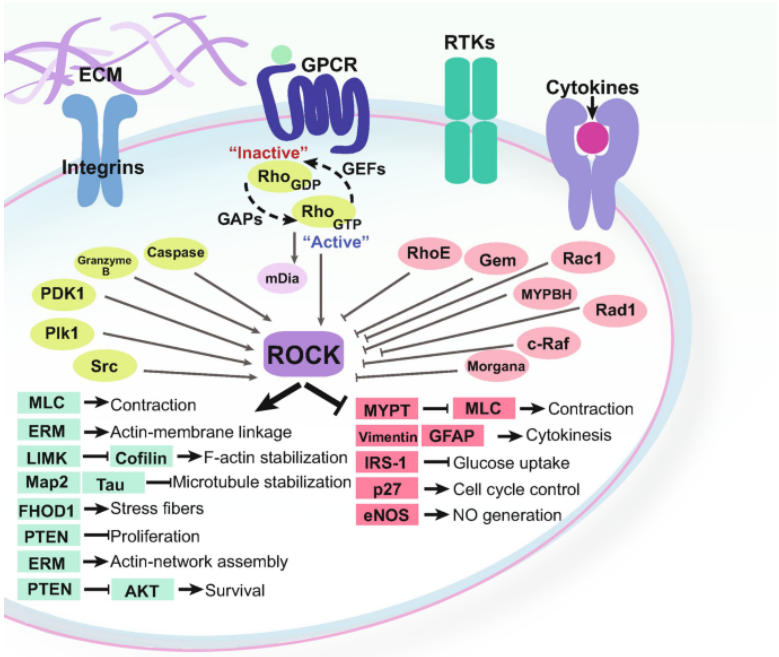
- The Hippo signaling pathway regulates organ size.
- The core of Hippo pathway is comprised of two highly conserved kinases – **YAP and TAZ**
- These two are transcriptional co-activators to drive gene transcription.





Rho/ROCK pathway

- The Rho GTPases are small GTPases
- They regulate
  - actin cytoskeleton remodeling
  - transcription
  - cell growth and proliferation
  - cell motility
  - morphology
  - cell cycle progression
  - ...
- activated by external signals
  - biochemical signals
  - mechanical signal



Porazinski et al 2020 Tumor Microenvironment

Model of YAP/TAZ activity

Biophysical *Journal*
Article

Biophysical Society

A Computational Model of YAP/TAZ Mechanosensing

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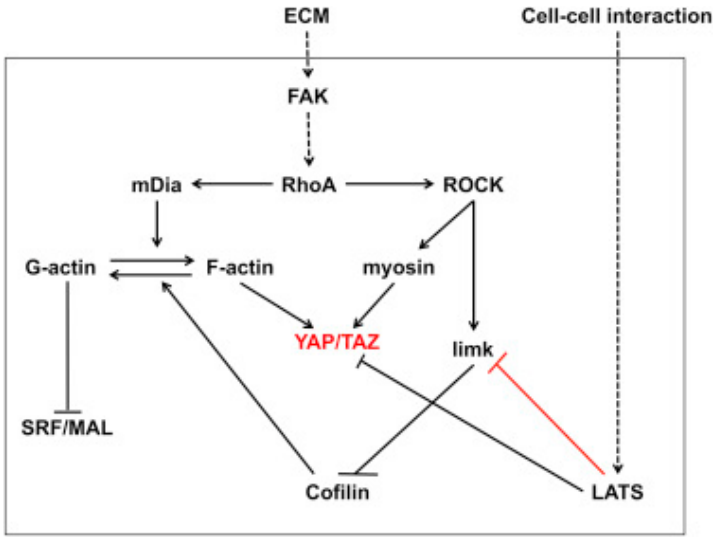

Sun et al 2016 Biophys J.