Myofibroblasts and Mechanical Signal Transduction

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Disclaimer

I am a fundamental scientist – I do not make money with what I am doing. I would love to have a financial conflict of interest, but unfortunately don’t. If you can change that embarrassing situation, please contact me after my talk.

References


Controlling Myofibroblast Formation and Function

Stress Controls the Myofibroblast Phenotype

Myofibroblasts Activate TGFβ1
Myofibroblasts Activate TGFβ1 by Contraction

Pulling is Easy – on Paper

Pulling Recombinant LAP and SLC

What do we Unfold?

Flourescent LTBP-1

- The 17 aa latency lasso domain is only detected in the presence of TGFβ1.
- Pulling recombinant LAP or SLC does not open the straitjacket in one step.
Fluorescent SLC

Formation of the LLC for Pulling Experiments

Pulling LAP-TGFβ1 in the LLC

Pulling Liberates TGFβ1 – Who Needs Cells Anyhow?

Summary

• Anchoring of the SLC in the LLC favors the simultaneous straightening of domains that provide latency (α-helix and latency lasso).
• The forces required to unfold the SLC straitjacket in the LLC context are lower than those required for the individual domains in "unbound" SLC.
• Hence, association with LTBP-1 decreases the force threshold for TGFβ1 activation from LAP, with LTBP-1 acting as a leverage point.

Thanks

Collaborators:
Gabor Csucs
Christiane Diederich
Cyril Follonier-Castella
Giulio Gabbiani
Jost Lussi
Chris McCulloch
Jean-Jacques Meister
Stéphane Pilate
Giorgio Pietramaggiori
Daniel Rüegg
Dean Shappard
The Unfolding Profile of LTBP-1 is Distinct from SLC

- Unfolding LTBP-1 results in a combination of short stretch-resistant domains and long flexible domains, all of them distinct from those observed in SLC/LAP.