The keratin cytoskeleton as a regulator of keratinocyte mechano-sensing

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Background

- Keratin cytoskeleton is an important cell shape and integrity regulator within the epidermis¹.
- When these filaments fail to assemble properly, keratinocytes become more fragile, which can lead to several skin blistering diseases².
- It is still not clear how keratins can act as mediators for mechanotransduction.
- Polyacrylamide hydrogels can be used as an in vitro model to control matrix stiffness and further study cell-ECM interactions.

Aim: Dissecting the role of keratin cytoskeleton in cell mechanotransduction

I. Substrate stiffening promotes cell spreading

II. Substrate stiffening influences keratin 14 organisation

III. F-actin and Src affect stiffness-dependent cell spreading

IV. Plectin modulates stiffness-dependent cell spreading

V. Substrate stiffness and plectin regulate EGFR signalling

VI. Substrate stiffness and keratins regulate Lamin A levels

VII. Conclusion & Future work

- Substrate stiffness regulates cell spreading.
- Cell contractility elements have different roles in cellular mechanotransduction.
- Keratin 14 bundles spacing and intensity changes in response to substrate stiffness.
- Substrate stiffness can regulate EGFR phosphorylation.
- The cytolinker protein Plectin has an active role in cell spreading and EGFR phosphorylation
- Substrate stiffness regulates Lamin A/C expression and depends on type I keratins