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Perspective

An introduction to Tensional Homeostasis

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ABOUT THE STUDY

Mechanical forces in the environment, such as gravity, shear stress, osmotic pressure, and tension, are known to affect the morphological and physical aspects of tissues and organs. Organ homoeostasis is reliant on the Extracellular Matrix (ECM) and the traction-force equilibrium in cells, both of which are controlled by the Extracellular Matrix (ECM). Tensional homoeostasis is the balance between extracellular forces applied on cells by the ECM or neighbouring cells and traction forces generated by cells themselves. Mechano-transducers like Focal Adhesion Kinase (FAK), Yes-Associated Protein (YAP)/ Transcriptional coactivator with PDZ-binding motif (TAZ), and myocardin-related transcription factor A sense the physical presence of tension from the surrounding environment *via* adhesion molecules and the actin cytoskeleton, and they respond to mechanical biological stimuli *via* mechano-transducers like FAK, YAP, and TAZ (MRTF-A).

YAP-controlled actomyosin-mediated tissue tension is required for organ shape creation and organ system alignment during embryogenesis, which is required for the right three-dimensional (3D) body shape.

Tissue stiffness and catenin activation are regulated by actomyosin-mediated cellular tensional homoeostasis, which causes epidermal hyperplasia and tumour growth. As a result, these spatiotemporal mechano-transduction processes and tensional homoeostasis play important roles in the regulation of cell functions in organ and tissue morphogenesis, such as myosin-based cell contraction, ECM production, cell migration, proliferation, and differentiation, and contribute to the performance of their specific functions.

The Integumentary Organ System (IOS), which includes skin and skin appendages such as hair, sebaceous glands, sweat glands, feathers, and nails, is responsible for waterproofing, cushioning, safeguarding deeper tissues, excreting waste, and maintaining homeostasis.

Internal tension-distribution patterns known as Langer's cleavage lines regulate the alignment of components of the IOS, such as appendages, cells, dermal ECM such as collagen, and elastic fibres, and they help to form strong and flexible physical structures for the maintenance of their integrity and flexibility. In the IOS morphogenesis process, tissue-scale tensions are known to be mediated by mechano-sensors and mechano-transducers like glycocalyx, lipid rafts/caveolin-1, cell adhesion (mediated by integrin, hemidesmosomes), and focal adhesion.

Calcium-sensing receptors, transient receptor potential channels, linkages and Piezo channels, intercellular complexes of desmosomes or cadherin, and the actin cytoskeleton are hypothesised to regulate the alignment of numerous cells and structures.

Tension is reduced due to the degradation of dermal ECM components such as collagen and elastic fibres, which affects the progression of cellular dysfunction, including decreased ECM production and increased tissue protease production, as a result of defects in tensional homoeostasis and mechanical stress signaling in skin ageing, wound healing, and disease. In scleroderma, dermal fibroblasts activate MRTF-A, a major regulator of tissue fibrosis that connects mechanical stimuli and ECM remodeling. Tensional homoeostasis is expected to play a key role in sustaining skin organ homoeostasis by transmitting mechanical stress signals.

3D Human Skin Equivalents (HSEs) are thought to be more useful models for drug discovery, clinical diagnostics, and basic skin research than two-dimensional monolayer cell cultures because they can partially reproduce physiological skin functions like proliferative capacity, ECM synthesis, cellular signalling, and responses to various stimuli. The use of HSE models as an alternative to animal trials for safety evaluation has recently gained popularity in skin research and medication development. Various investigations on cell kinds, substrates, culture conditions, 3D bio printing, and the Skin-on-Chip technology have been recorded in terms of improving the HSE structures and activities. Our latest research demonstrated the feasibility of fully functional regeneration of tissues and organs that replicate the embryonic processes of organogenesis, such as teeth, hair follicles, secretory glands, and the IOS.

However, given the current restricted availability of skin functions as an alternative animal experiment to mimic the 3D

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architecture of the IOS, it is projected that a more functioning HSE will be developed.

It was designed an HSE that reproduces tensional homoeostasis by keeping the ECM and cellular alignment in accordance with tension. Tensional homoeostasis also increases HSE's physiological activities, such as fibroblast ECM synthesis, epidermal keratinocyte proliferation, and cell response to a wide range of functional components. The obeservations were tensional homoeostasis reproduction results in alterations in cell adhesion *via* integrin 2 and mechanical stress signalling activation *via* nuclear translocation of MRTF-A. This study tells us that the Skin tension balance, as per our researches, regulates skin functionality *via* mechanical stress signals *via* epithelial–mesenchyme interactions.