

## Mechanobiology and Diseases of Mechanotransduction

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KEY POINTS FROM DAN MURPHY

- 1) "Mechanical forces are critical regulators of cellular biochemistry and gene expression as well as tissue development."
- 2) Many "unrelated diseases share the common feature that their etiology or clinical presentation results from abnormal mechano-transduction."
- 3) There is an "undeniable *physical* basis of disease." **[Key Point]**
- 4) Abnormal cell and tissue responses to mechanical stress contribute to the etiology and clinical presentation of many important diseases.
- 5) There is a "strong mechanical basis for many generalized medical disabilities, such as lower back pain and irritable bowel syndrome, which are responsible for a major share of healthcare costs world-wide."
- 6) Physical interventions can influence cell and tissue function.
- 7) "Altered cell or tissue mechanics may contribute to disease development."
- 8) "Mechanical forces are critical regulators in biology." **[Key Point]**
- 9) Because of the recent advances in the molecular basis of disease, there has been a loss of interest in mechanics. **[Not in chiropractic]**
- 10) "Mechanical forces serve as important regulators at the cell and molecular levels, and they are equally potent as chemical cues."
- 11) Tissues are composed of groups of living cells held together by an extracellular matrix (ECM).
- 12) The surface membrane of cells is mechanically attached to all of the cell's organelles, to its nucleus and its chromosomes, and to its synaptic vesicles, by a "filamentous cytoskeleton." **["Filamentous Cytoskeleton"]**
- 13) Because our bodies are hierarchical structures, mechanical deformation of any tissues results in structural rearrangements in many tissues.
- 14) Mechanical loads anywhere in the body can affect many tissues and cells because they are physically interconnected.

- 15) "Forces that are applied to the entire organism (e.g., due to gravity or movement) or to individual tissues would be distributed to individual cells via their adhesions to the ECM support scaffolds that link cells and tissues throughout the body." **[This is consistent with chiropractic perspectives on the subluxation]**
- 16) If the ECM is less flexible, then stresses will be transmitted to and through the cell. **[Again, this is consistent with chiropractic perspectives on the subluxation]**
- 17) Living cells contain a cytoskeleton that generate and transfer tensional forces, known as "tensegrity." **[Tensegrinous Matrix]**
- 18) Changes in the cytoskeletal force balance alter tissue homeostasis.
- 19) "The physicality of the ECM substrate and degree of cell distortion govern cell behavior regardless of the presence of hormones, cytokines or other soluble regulatory factors." **[Again, this is consistent with chiropractic perspectives on the subluxation]**
- 20) "Cell-generated tensional forces appear to play a central role in the development of virtually all living tissues and organs, even in neural tissues."
- 21) "Mechanical forces directly regulate the shape and function of essentially all cell types."
- 22) Many of the enzymes and substrates that mediate cellular metabolism (e.g., protein synthesis, glycolysis, RNA processing, DNA replication) are physically immobilized on the cytoskeleton and nuclear nucleoskeleton matrix. Consequently, mechanical stresses through the cytoskeletal and nucleoskeletal matrix can alter physiology by physically altering biophysical properties, which in turn alter chemical reaction rates.
- 23) Mechanical stress stimulates rapid calcium influx in the neuromuscular synapse, again altering function.
- 24) "All cells also contain 'stress-sensitive' (mechanically-gated) ion channels that either increase or decrease ion influx when their membranes are mechanically stressed."
- 25) "The global shape of the cell dictates its behavior (e.g., growth versus differentiation or apoptosis), and these effects are mediated through tension-dependent changes in cytoskeletal structure and mechanics." **[Important]**
- 26) "These new insights into mechanobiology suggest that many ostensibly unrelated diseases may share a common dependence on abnormal mechanotransduction."

- 27) Local mechanical changes in tissue structure may explain why genetic diseases, including cancer, often present focally.
- 28) Physical therapy, massage, and muscle stimulation have well known therapeutic value because they alter mechanotransduction. **[Chiropractic adjustments and postural corrections should have been included here.]**
- 29) Most of the clinical problems that bring a patient to the doctor's office result from changes in tissue structure and mechanics.
- 30) Abnormal cell and tissue responses to mechanical stress may actively contribute to the development of many diseases and ailments. Consequently it may be wise to look for a physical cause for disease.
- 31) Mechanics must be reintegrated into our understanding of the molecular basis of disease.

### **CONCEPTS SUPPORTED BY THIS STUDY, FROM DAN MURPHY**

#### **THE CHIROPRACTIC CONNECTION**

The entire body is mechanically integrated through an extracellular matrix which attaches to cell membranes; cell membranes are attached to cell organelles through a filamentous cytoskeleton, including attachments to the nuclear membrane; the nuclear membrane is attached to the chromosomes through a nucleoskeleton. This is known as tensegrity or the Tensegrogenous matrix.

Altered alignment in gravity or altered movement patterns (both are aspects of the subluxation) adversely affect this tensegrogenous matrix, altering the function of cell membranes, cellular organelles, and genetic expression.

#### **THE TRANS FATTY ACID CONNECTION**

Trans fatty acids are human-made fat molecules that have an abnormal molecular configuration. Trans fat consumption will incorporate the abnormal molecules into the cell and organelle membranes, altering the membranes biophysical properties. This would also adversely affect the tensegrogenous matrix, altering the function of cell membranes, cellular organelles, and genetic expression.

#### **THE OMEGA-3 CONNECTION**

Having the innate balance of omega-3 to omega-6 fatty acids ensures optimal membrane fluidity, which would improve the tensegrity of the extracellular matrix / cell membrane interface, as well as the cell membrane cytoskeleton interface.