

# *Medicinal Signaling Therapies For Injury, Pain and Healing*



**Kathleen O'Neil Smith M.D.**

**Treat Wellness LLC**



# Disclosure

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*I do not have any affiliations or financial arrangements with any commercial entities whose products, research or services are discussed in this presentation*



# Objectives

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- 1. Appreciate fascia as an organ system: functional anatomy and physiology**
- 2. Review fascia in pain and sports medicine**
- 3. Review current understanding of fascia and Medicinal Signaling Therapies (Nutrients, Hormones, Peptides, ESWT, PRP, Exosomes, MSC's)and sports medicine**
- 4. Case studies case studies using fortreat and pain**



# Goals of Regenerative Medicine

to address the patient's symptoms

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**Genetics/Epigenetics**

**Methylation/PPAR**

**Immune Dysregulation**

**Redox: Oxidative Stress**

**Inflammation**

**Cellular Health**

**Detoxification**

**Mitochondrial Health**



# Peak Wellness

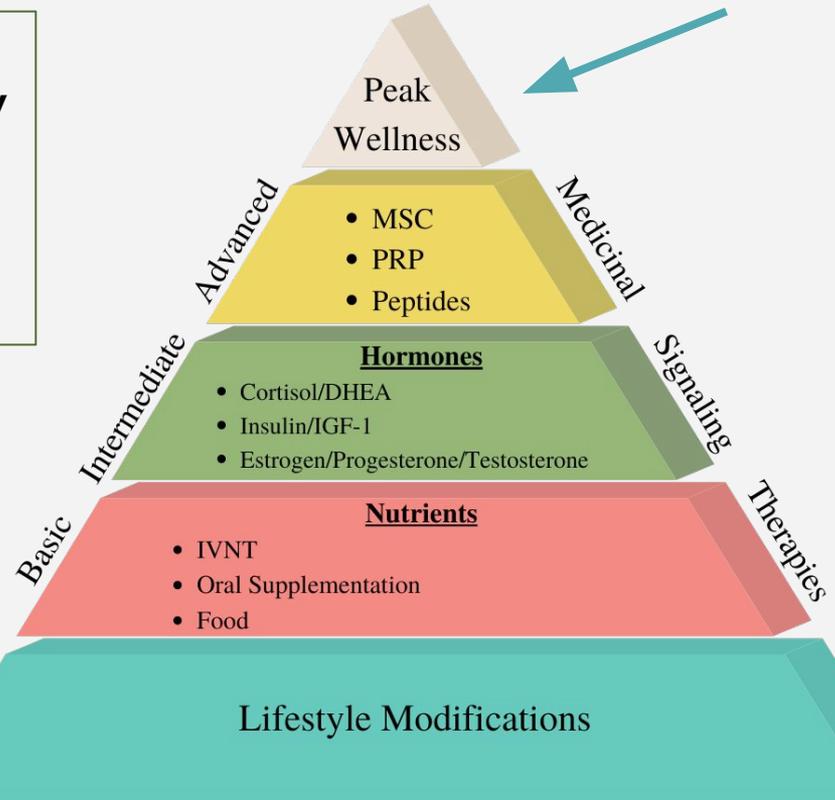
## Key

**MST = Medicinal Signaling Therapy**

**IVNT = Intravenous Nutritional  
Therapy**

**MSC = Medicinal Signaling Cells**

**PRP = Platelet Rich Plasma**



# Lifestyle Modifications

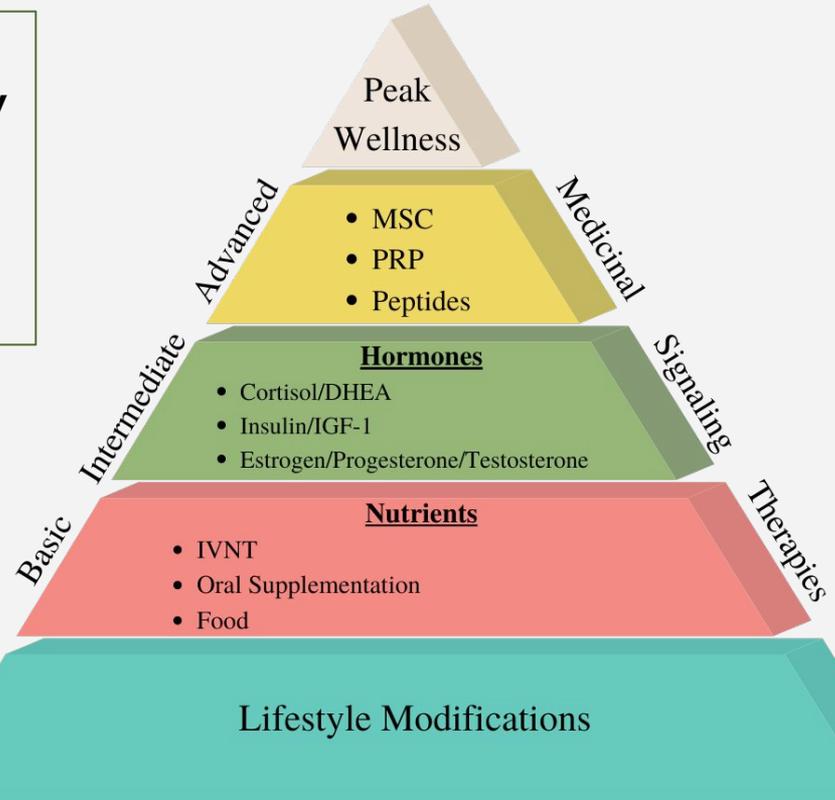
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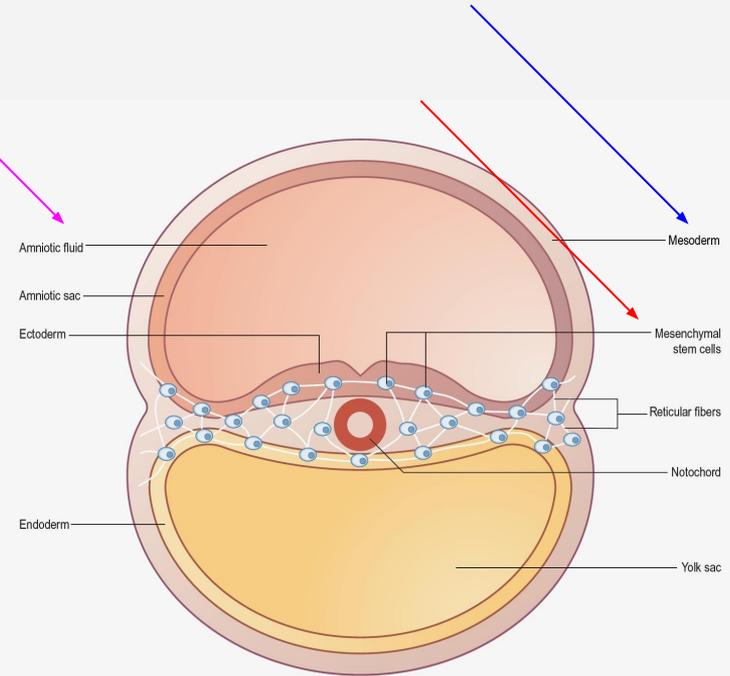
# Fascia:

*An Essential Bioactive Organ System*

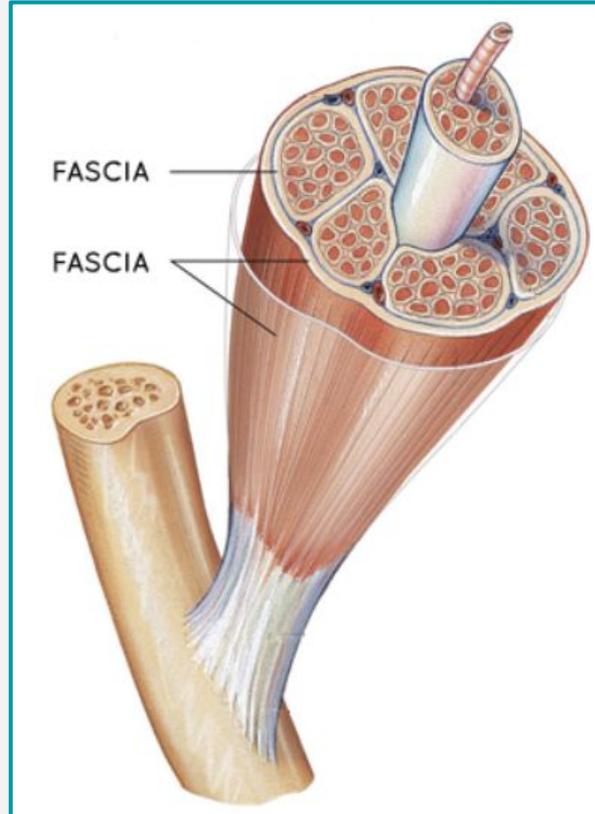
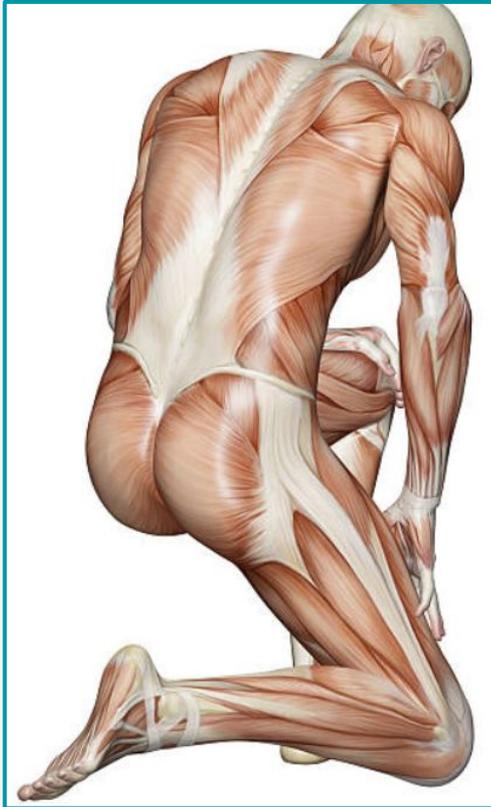


# Fascia from MESODERM (Middle Layer)

- **Week 2-3 , one cell layer blastula**
- *Somites arise here for specialization*
- **Form smooth, cardiac, skeletal muscle; mesentery; bone; cartilage; RBC; WBC; dura mater; notochord; and microglia**
- *Mesoderm is folded and refolded by “gastrulation”*



# Macro → Micro

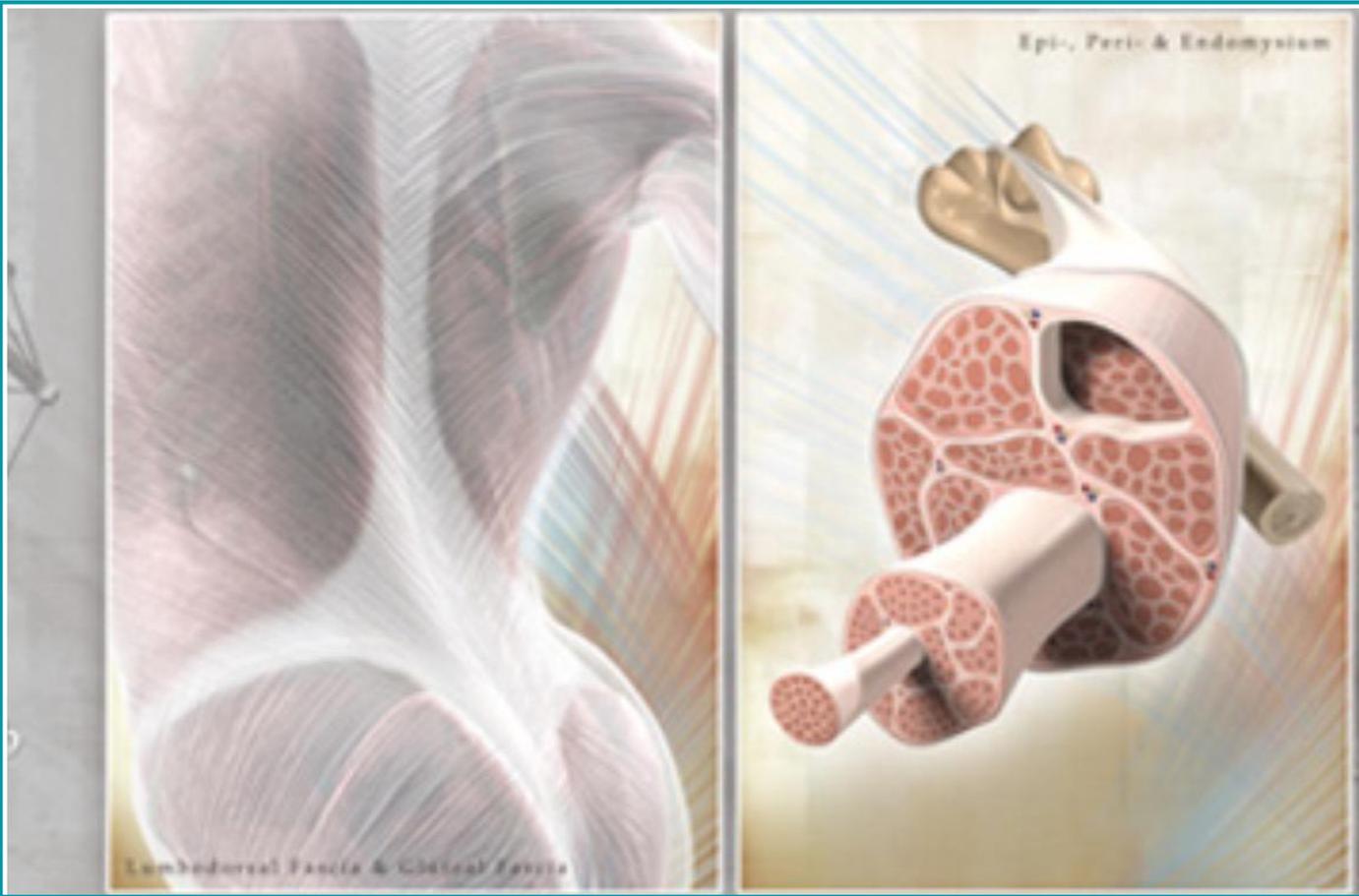


# Strolling Under the Skin

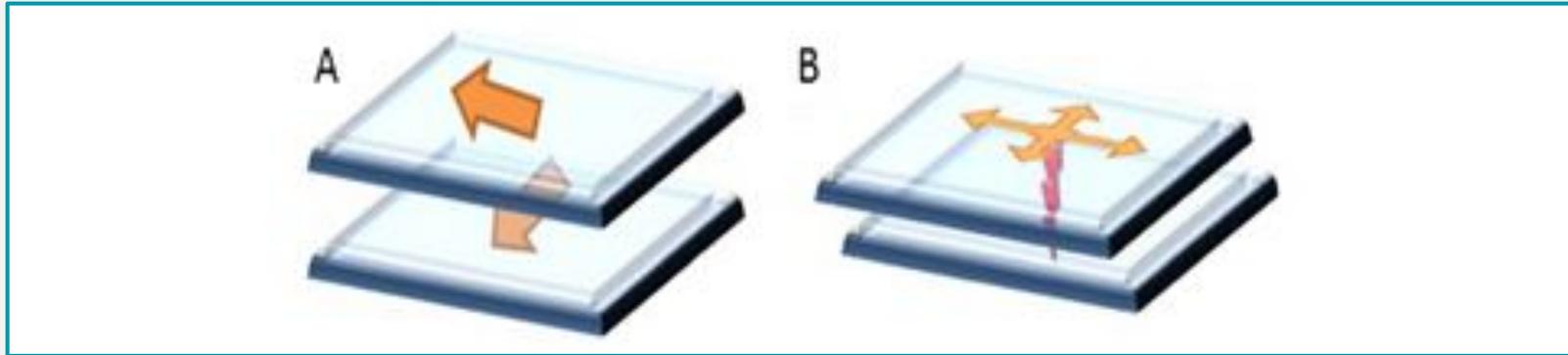


<https://www.youtube.com/watch?v=eW0lvOVKDxE&app=desktop>





# Three Dimensional Glide



Pavan, Piero G., Antonio Stecco, Robert Stern, and Carla Stecco. "Painful connections: densification versus fibrosis of fascia." *Current pain and headache reports* 18, no. 8 (2014): 441.





**YOUR LUNCH**

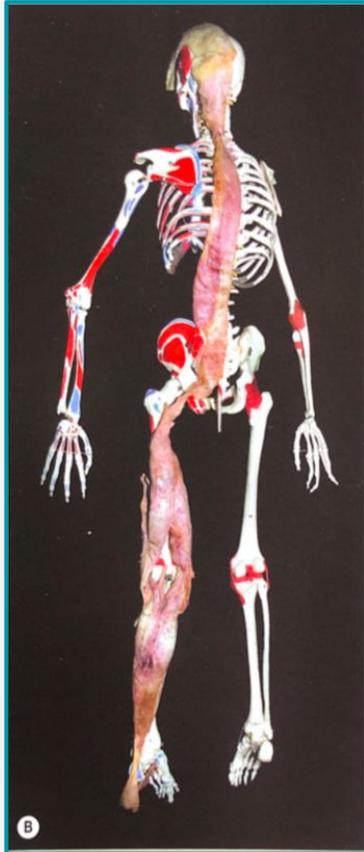
<https://tastykitchen.com/blog/>



**YOU**

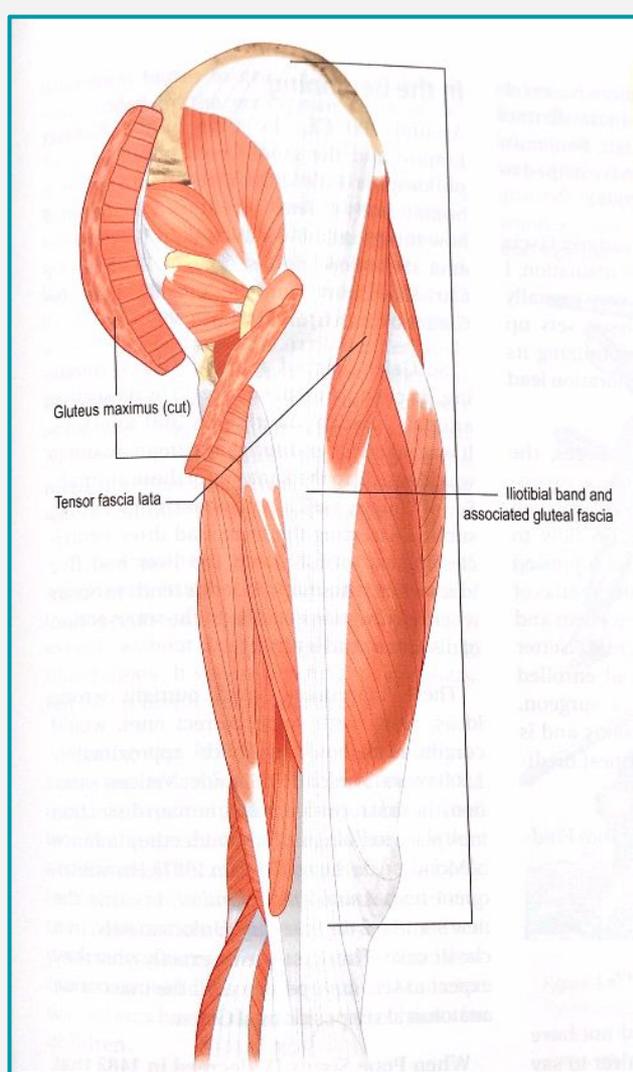
Used with permission from Thomas Myers, taken from Fascia: What it is and Why it Matters by David Lesondak, Handspring Publishing Ltd (2018).

# Fascia and Anatomy



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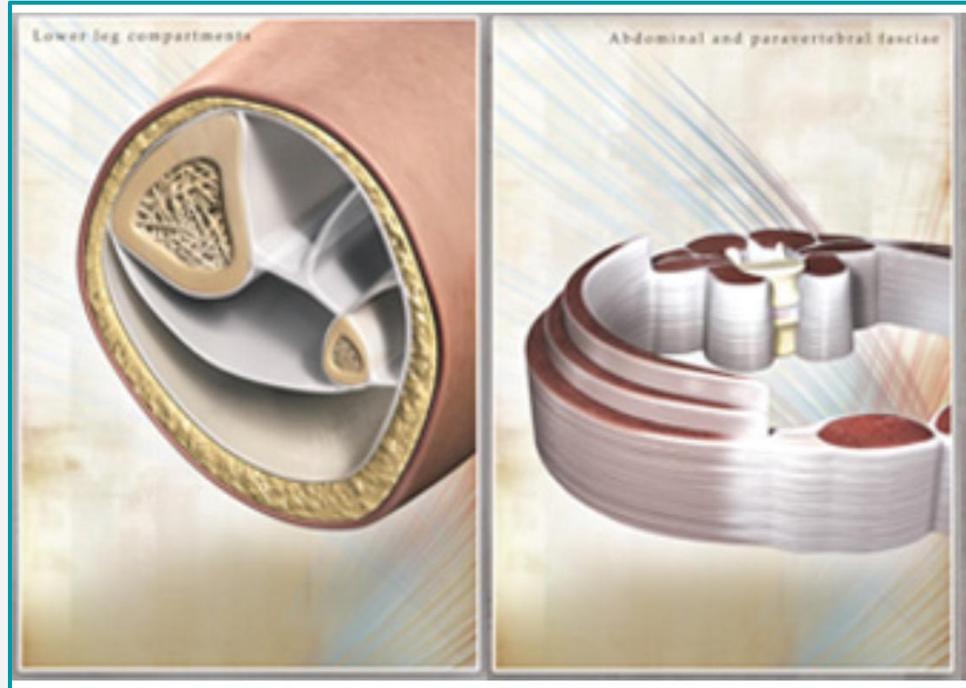




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# Fascia and Anatomy



# Fascia and Nerves



**Figure 4.1**

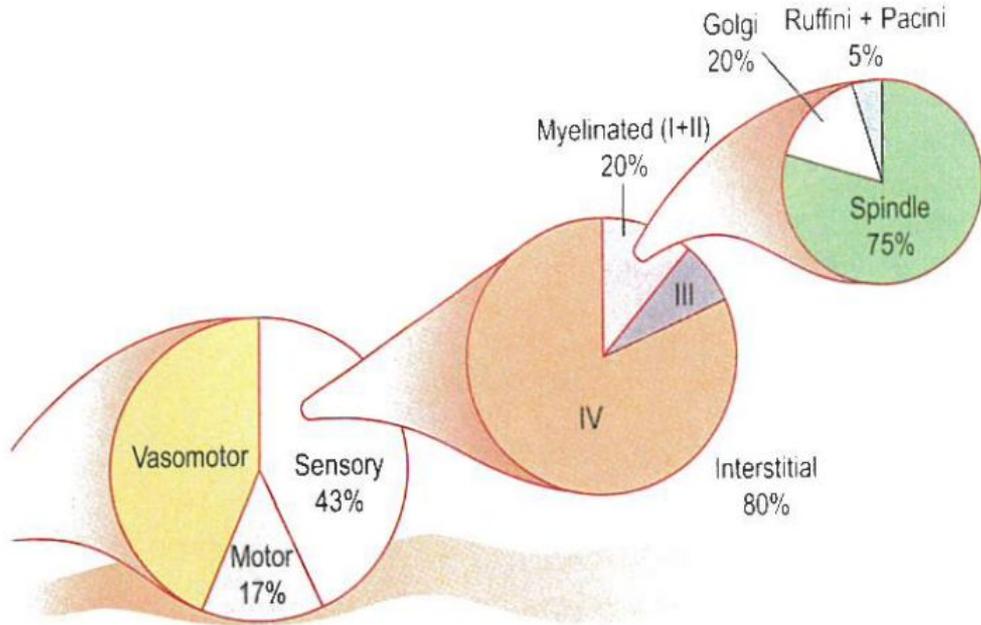
A dense network of nerve fibers in the thoracolumbar fascia of a rat. The surface area of the picture represents 0.5 mm (less than a tenth of an inch).

Reproduced with kind permission from Tesarz et al. 2011.

Used with permission from Thomas Myers, taken from *Fascia: What it is and Why it Matters* by David Lesondak, Handspring Publishing Ltd (2018).



# Fascia and Nerves

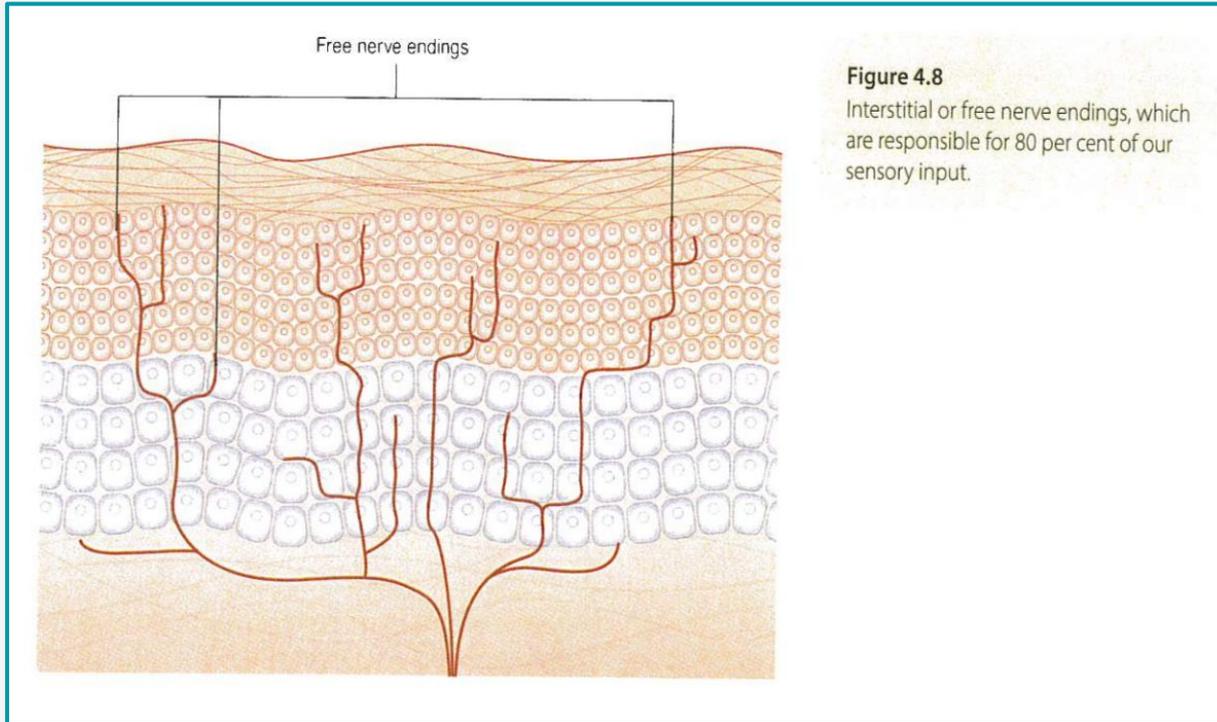


**Figure 4.3**

In the typical muscle nerve there are three times as many sensory nerves as there are motor nerves. Of those about 80 per cent of the sensory information comes from interstitial nerves.



# Fascia and Nerves



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# Fascia:

***Injury, Inflammation & Pain***



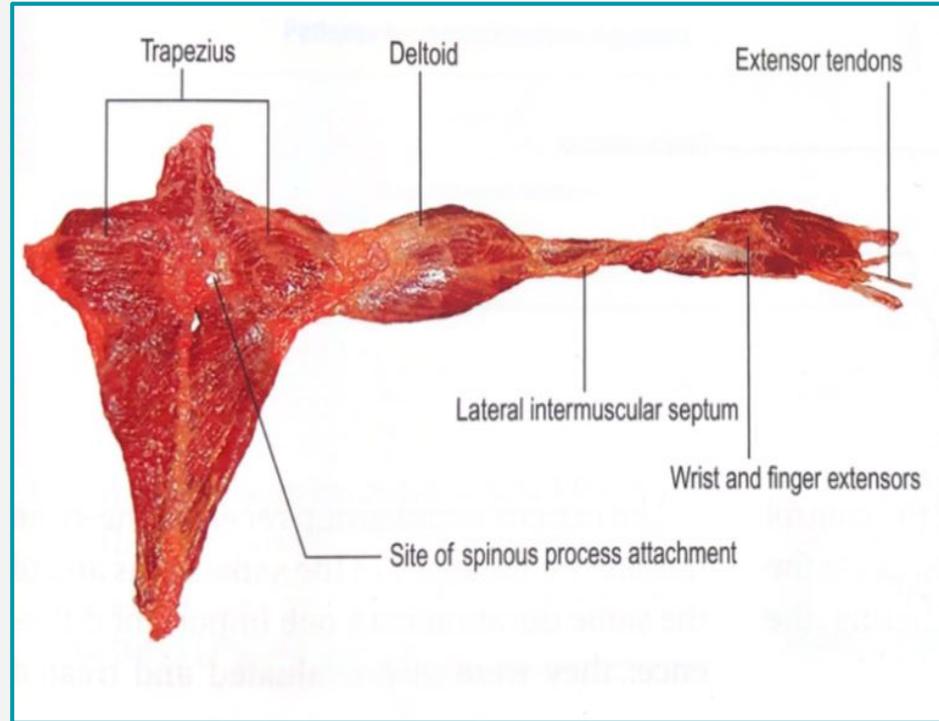
# FASCIAL ELASTICITY



<https://nflspinzone.com/2015/08/10/tom-bradys-38-best-games/>  
<https://time.com/4031023/tom-brady-shines-in-first-game-after-deflategate-ruling/>  
<https://www.stack.com/a/heres-why-its-really-really-hard-to-sack-tom-brady>



# Fascia and Anatomy



Lesondak, D. (2017). *Fascia: What it is and why it matters*. Edinburgh: Handspring Publishing.



# Fascial Elasticity



Source: Canva.com



# Fascial tissue research in sports medicine: from molecules to tissue adaptation, injury and diagnostics: consensus statement

PDF

Martina Zügel<sup>1</sup>, Constantinos N Maganaris<sup>2</sup>, Jan Wilke<sup>3</sup>, Karin Jurkat-Rott<sup>4</sup>, Werner Klingler<sup>5</sup>, Scott C Wearing<sup>6</sup>, Thomas Findley<sup>7</sup>, Mary F Barbe<sup>8</sup>, Jürgen Michael Steinacker<sup>1</sup>, Andry Vleeming<sup>9</sup>, Wilhelm Bloch<sup>10</sup>, Robert Schleip<sup>11</sup>, Paul William Hodges<sup>12</sup>

Author affiliations +

Abstract

*“The **fascial system** builds a three-dimensional **continuum** of soft, collagen-containing, loose and dense fibrous connective tissue that **permeates the body** and enables all body systems to operate in an integrated manner.”*

the *microlevel* (molecular and cellular responses) to the *macrolevel* (mechanical properties), (2) summarise the responses of the fascial system to altered loading (physical exercise), to injury and other physiological challenges including ageing, (3) outline the methods available to study the fascial system, and (4) highlight the contemporary view of interventions that target fascial tissue in sport and exercise medicine. Advancing this field will require a coordinated effort of researchers and clinicians combining mechanobiology, exercise physiology and improved assessment technologies.

Zügel M, et al. *Br J Sports Med* 2018;**52**:1497.  
doi:10.1136/bjsports-2018-099308



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Abstract

*“Injuries to the fascial system cause a significant loss of performance in recreational exercise as well as high-performance sports, and could have a potential role in the development and **perpetuation** of musculoskeletal disorders, including lower back pain.”*

and (4) highlight the contemporary view of interventions that target fascial tissue in sport and exercise medicine. Advancing this field will require a coordinated effort of researchers and clinicians combining mechanobiology, exercise physiology and improved assessment technologies.

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## Abstract

The fascial system builds a three-dimensional continuum of soft, collagen-containing, loose and dense

*Fascial tissues deserve more detailed attention in the field of sports medicine. A better understanding of their adaptation dynamics to mechanical loading as well as to biochemical conditions promises valuable improvements in terms of injury prevention, athletic performance and sports-related rehabilitation. This consensus statement reflects the state of knowledge regarding the role of fascial tissues in the discipline of sports medicine.*

summarise the responses of the fascial system to altered loading (physical exercise), to injury and other physiological challenges including ageing, (3) outline the methods available to study the fascial system, and (4) highlight the contemporary view of interventions that target fascial tissue in sport and exercise medicine. Advancing this field will require a coordinated effort of researchers and clinicians combining mechanobiology, exercise physiology and improved assessment technologies.



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The fascial system builds a three-dimensional continuum of soft, collagen-containing loose and dense

*“It aims to (1) provide an overview of the contemporary state of knowledge regarding the fascial system from the **microlevel (molecular and cellular responses)** to the **macro-level (mechanical properties)**, (2) summarize the responses of the fascial system to altered loading (physical exercise), to injury and other physiological challenges including aging, (3) outline the methods available to study the fascial system, and (4) highlight the contemporary view of interventions that target fascial tissue in sport and exercise medicine.”*

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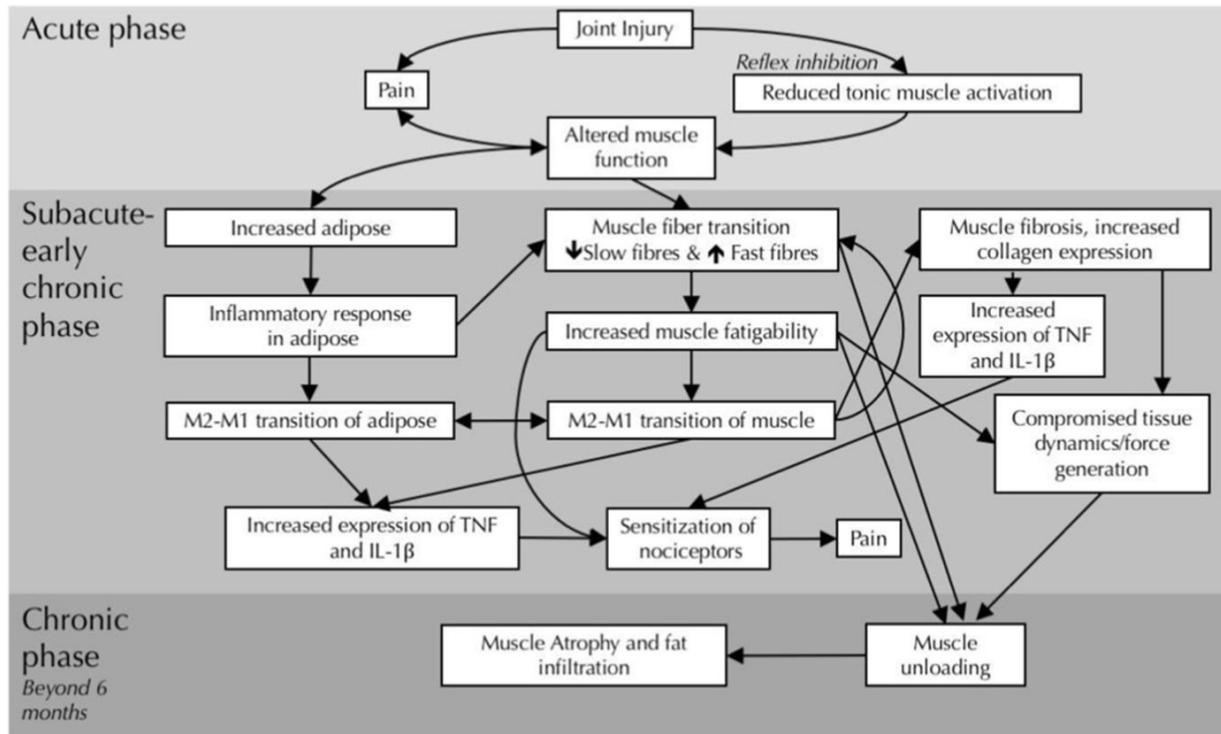
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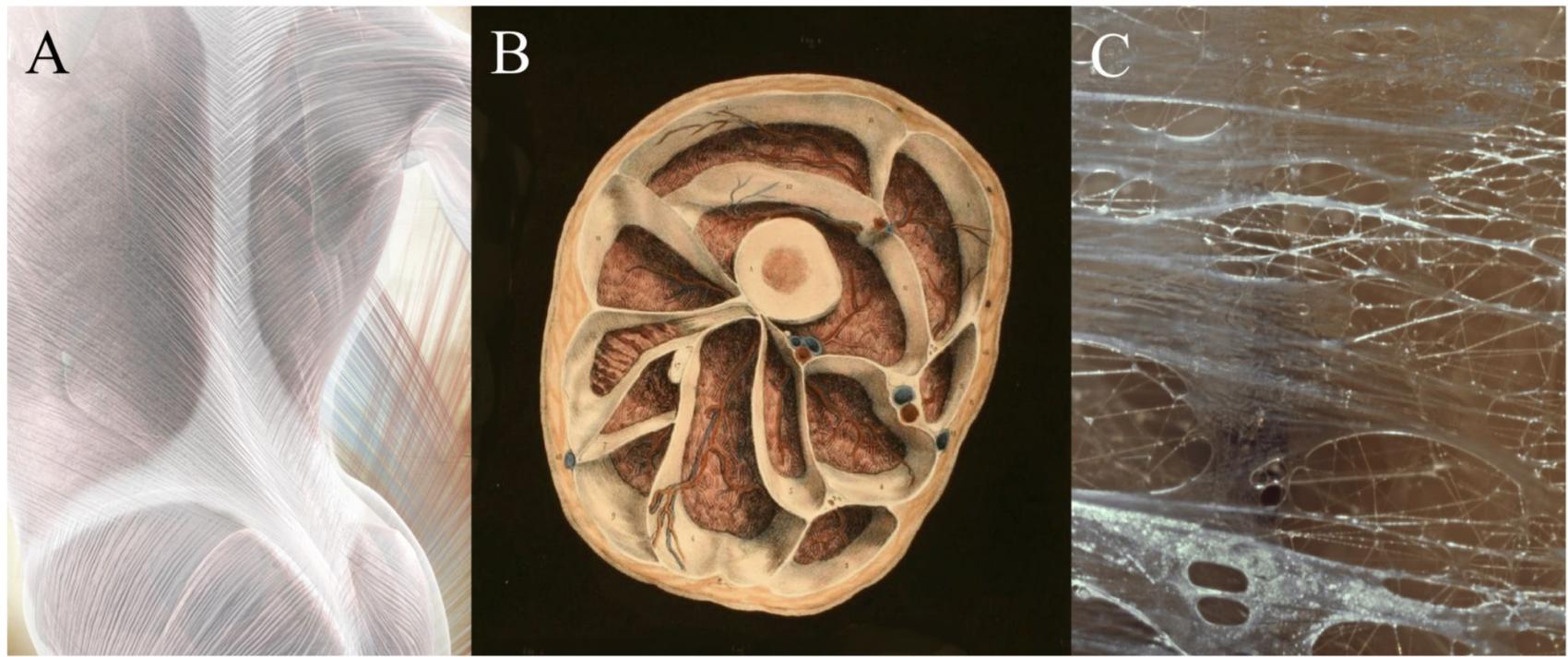
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**Figure 4** Proposed timeline and mechanisms for fascial, adipose and muscle changes in the multifidus muscle after intervertebral disc lesion. Three phases, acute (top), subacute-early chronic (middle) and chronic (bottom), are characterised by different structural and inflammatory changes. IL-1 $\beta$ , interleukin-1 $\beta$ ; TNF, tumour necrosis factor.

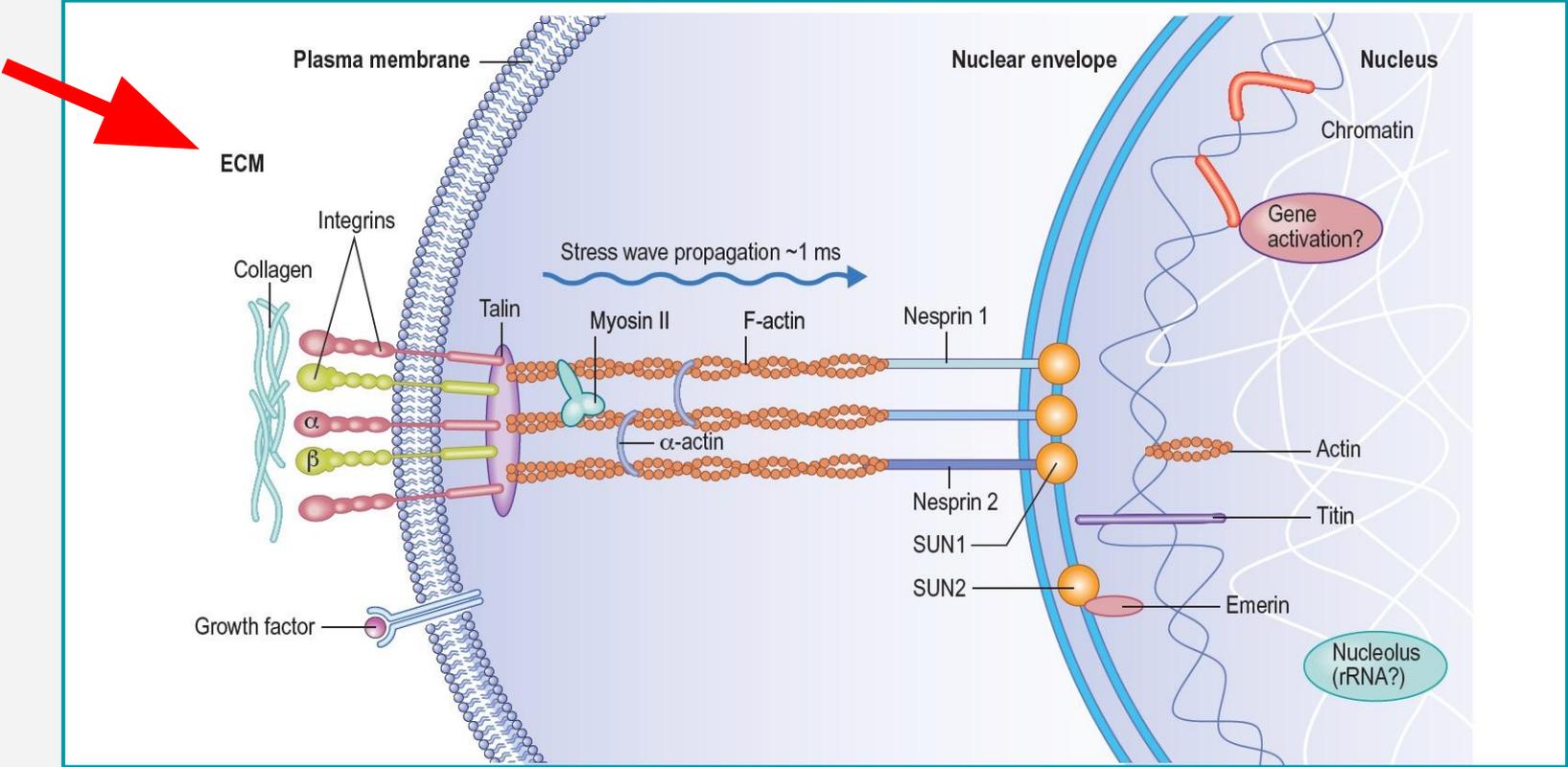




**Figure 1** Components of the fascial system. The fascial system includes large aponeuroses like the first layer of the thoracolumbar fascia (A), but also a myriad of enveloping containers around and within skeletal muscles (B) and most other organs of the body. The internal structure of fascial tissues is dominated by collagen fibres which are embedded in a semiliquid ground substance (C). Images with friendly permission from fascialnet.com (A) and thomas-stephan.com (C).



# Fascia and Influence of Exposome on Terrain



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# Terrain:

## *Internal Terrain*

### **Internal Environment:**

- ❑ Human genome: methylation
- ❑ Gut microbiome
- ❑ Dehydration
- ❑ Acidic milieu/toxicity
- ❑ Immune dysregulation
- ❑ Inflammation
- ❑ Oxidative stress
- ❑ Cellular health: FAB
- ❑ Mitochondrial dysfunction



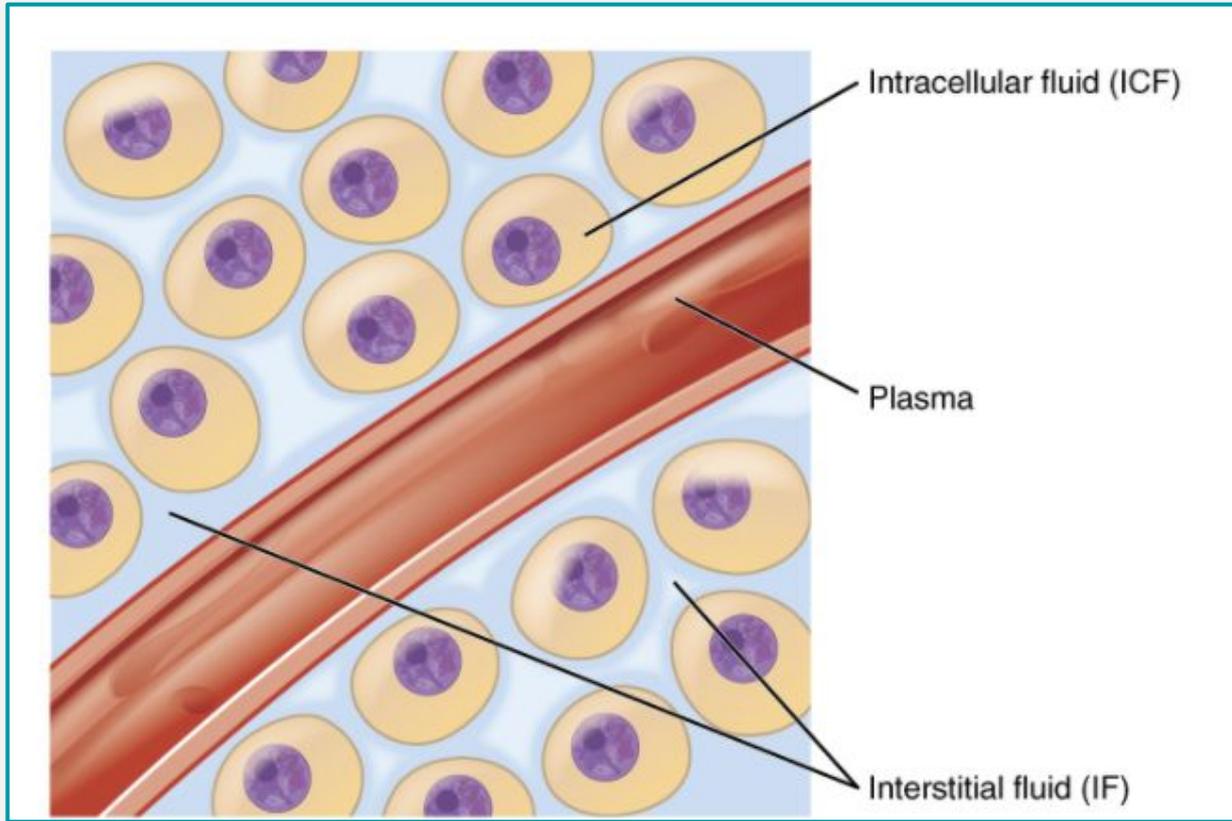
# Terrain:

***External Terrain=Exposome  
Lifestyle factors***

## External Environment: Examples

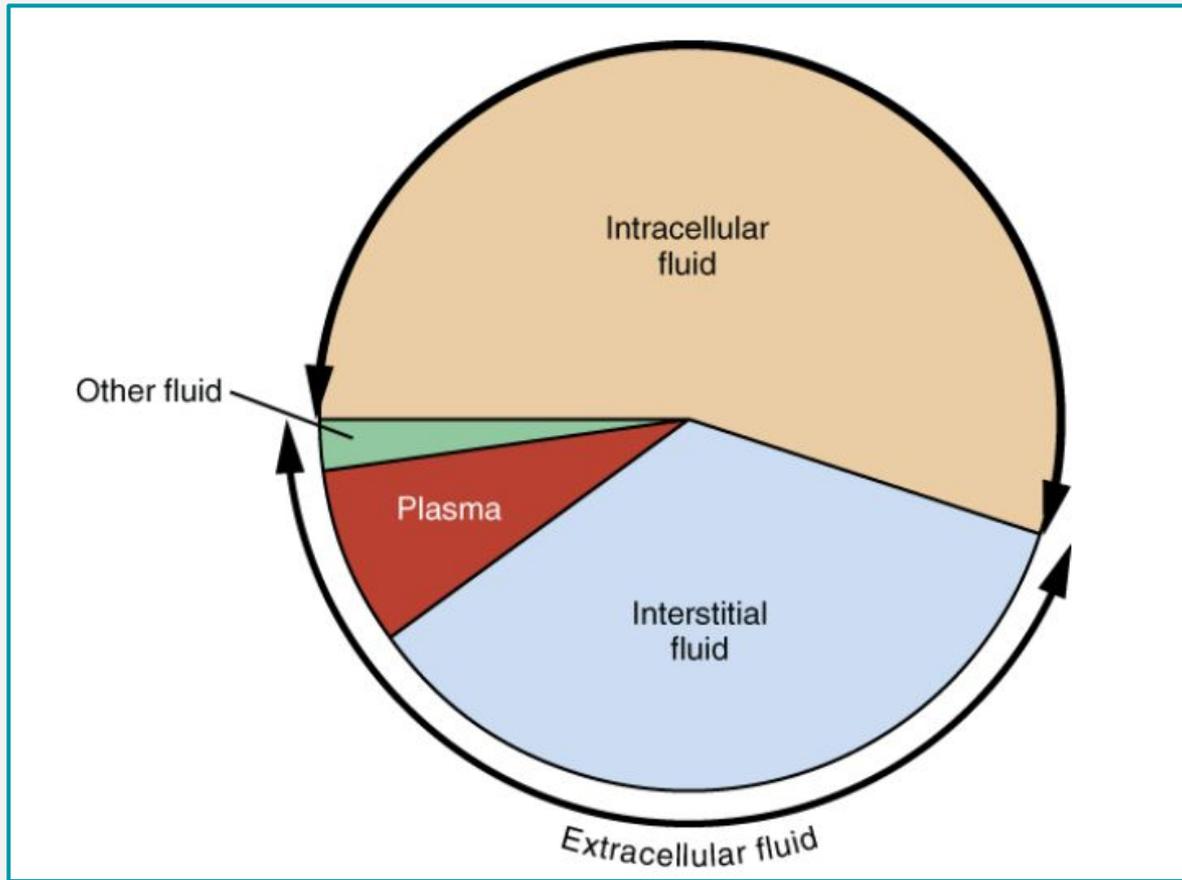
- ❑ Diet
  - ❑ Industrialized foods: novel food additives including nanoparticles & engineered foods
- ❑ Lifestyle
  - ❑ Excess stress
  - ❑ Lack of movement
  - ❑ Reduced vagal tone
- ❑ Radiation
- ❑ Meds / Vaccines
- ❑ Adjuvants
  - ❑ Metals: aluminum
  - ❑ Immune system disruptors
  - ❑ Endocrine disruptors
  - ❑ Squalene





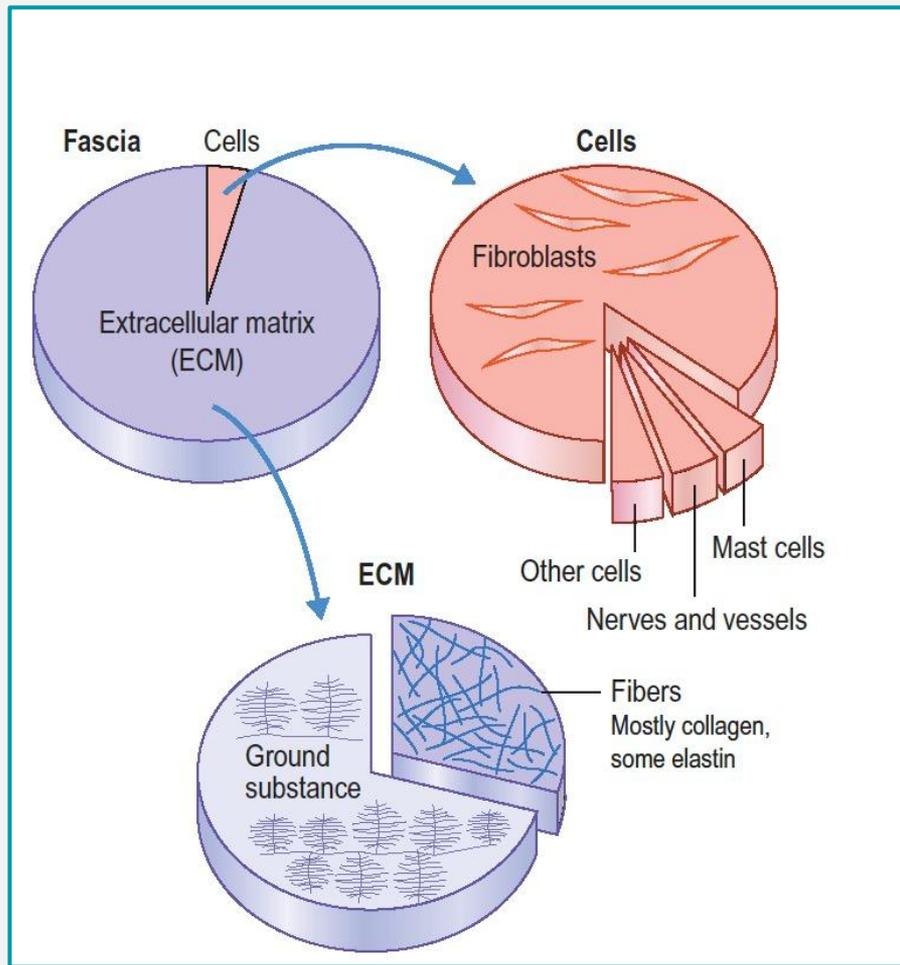
Source: <https://opentextbc.ca/anatomyandphysiology/chapter/26-1-body-fluids-and-fluid-compartments/>





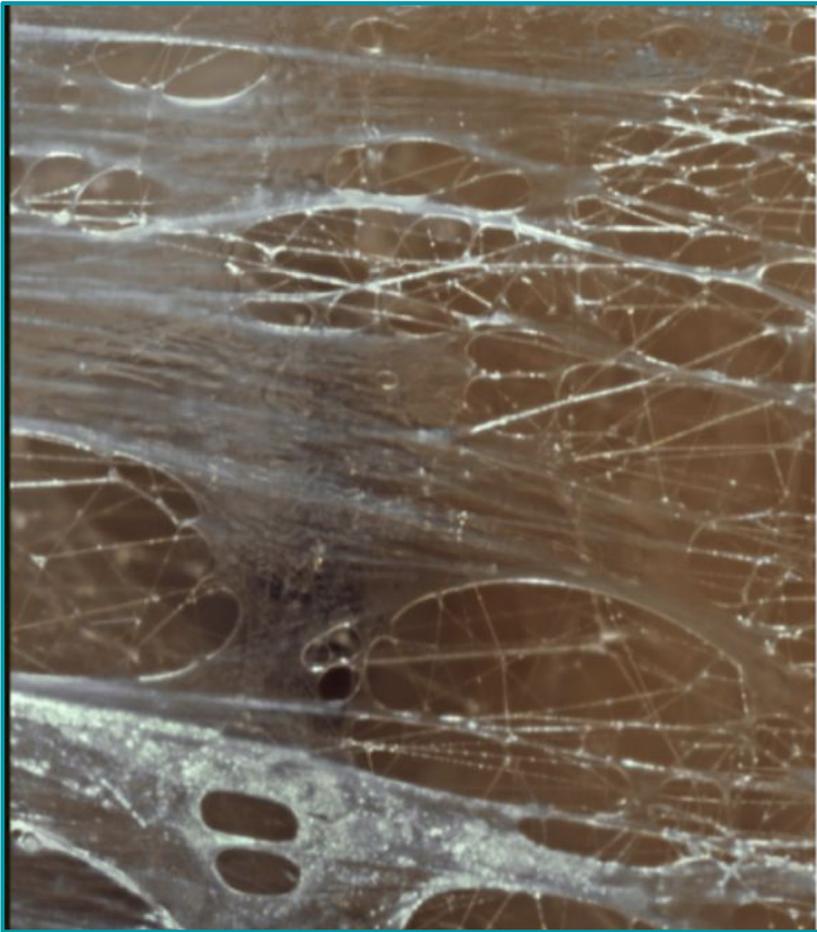
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**Figure 4.1**

A dense network of nerve fibers in the thoracolumbar fascia of a rat. The surface area of the picture represents 0.5 mm (less than a tenth of an inch).

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# ECM: Governs Cellular Functions

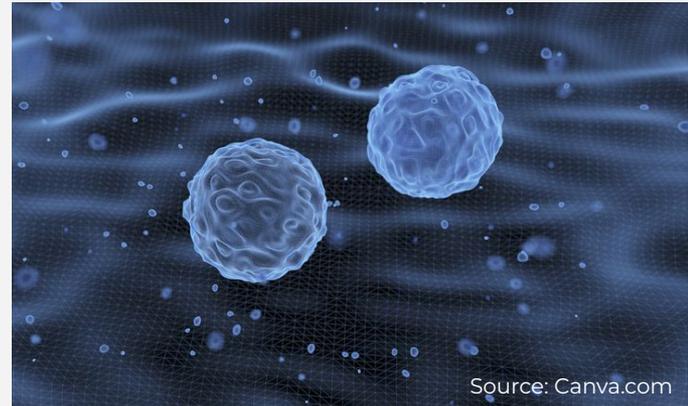
- Cocktail of proteins, signalling molecules, and chemicals that cells exude as they grow
- Cells use matrix to impart strength & shape to tissues like bone & brain
- ECM used to be dismissed as an inert garden trellis, now proven that ECM is critical for cell behavior
- Muscle stem cells self renew only on soft gels (not hard plastic plates)
- U. TORONTO 2017- certain receptor proteins on muscle stem cells respond differently to their binding partners depending on whether underlying growth substrate is soft or stiff

*Nature* 566, 563-565 (2019) doi:  
10.1038/d41586-019-00681-1



# ECM & Stem Cells

- ECM guides stem cells to repair damaged tissues, re-form blood vessels damaged by stroke & alter cellular responses to chemotherapy
- ECM serves as a reservoir of signaling molecules that serves as a highway between cells
- (25 yrs ago, ECM was just thought to be structural)
- Regen med is trying to improve engineered ECMs but can be tricky
- Each synthetic or naturally derived biomaterial has pros and cons

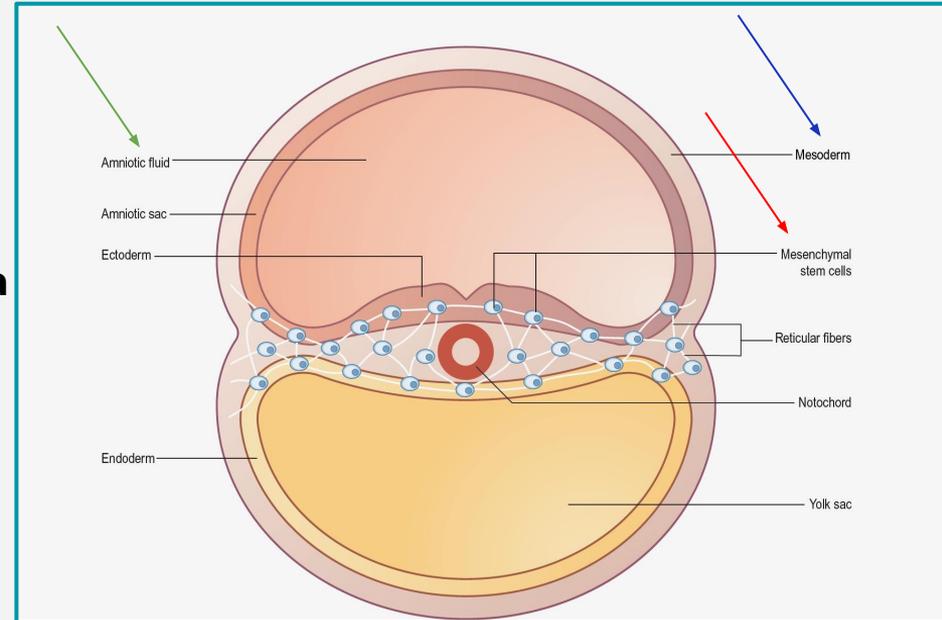


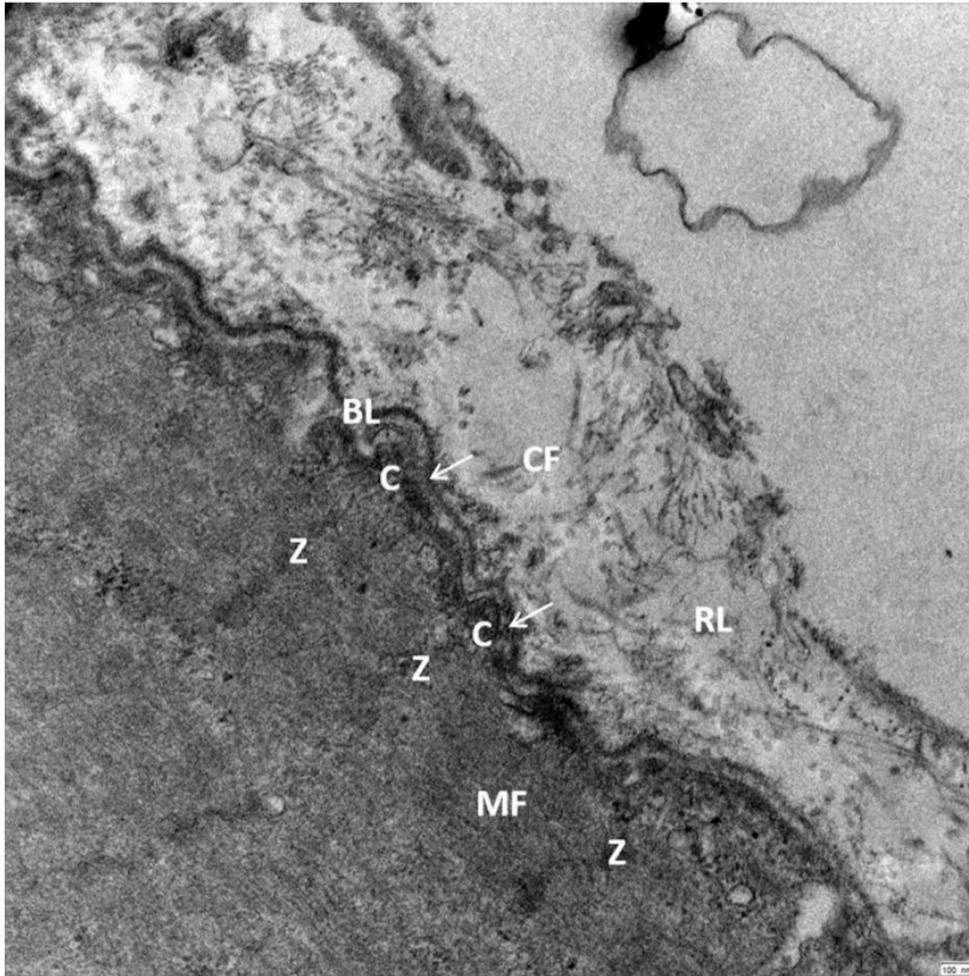
Source: Canva.com



# Fascia from MESODERM (Middle Layer)

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- *Somites arise here for specialization*
- **Form smooth, cardiac, skeletal muscle, mesentery, bone, cartilage, RBC, WBC, dura mater and notochord and microglia**
- *Mesoderm is folded and refolded by “gastrulation”*





**Figure 2** Transmission electron microscopy reveals the close cell–ECM interaction in human skeletal muscle (musculus vastus lateralis, 25 000× magnification) allowing a bidirectional cell–ECM interaction. Myofilaments (MF) are connected by Z-lines (Z) and costameres (C) to the adjacent basal lamina (BL) and the surrounding reticular lamina (RL). Crossbridging structures (arrows) connect the Z-lines and costameres to the dense part of the basal lamina. The reticular lamina is structured by a network of collagen fibrils (CF) and additional ECM molecules, which have a close connection to the basal lamina allowing bidirectional transmission of mechanical forces. ECM, extracellular matrix.

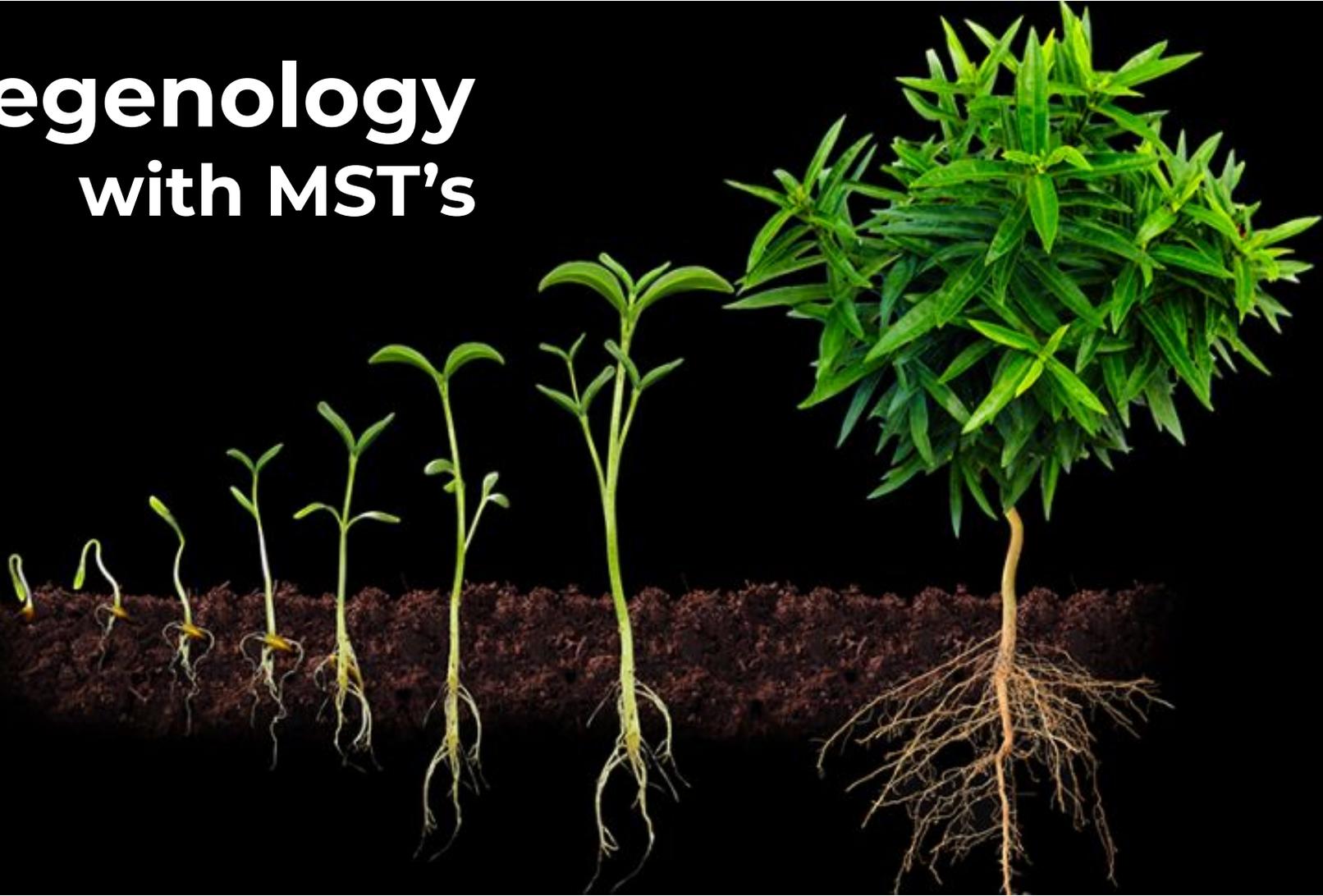


# Fascia

***Regenerative Potential***



# Regenology with MST's



# Peak Wellness

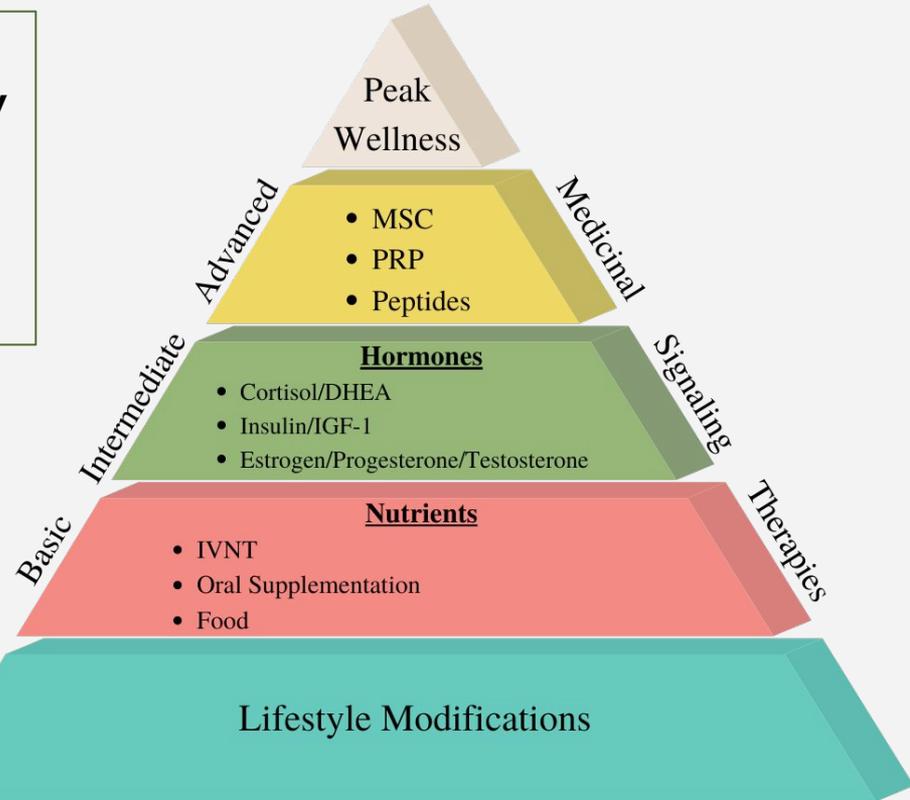
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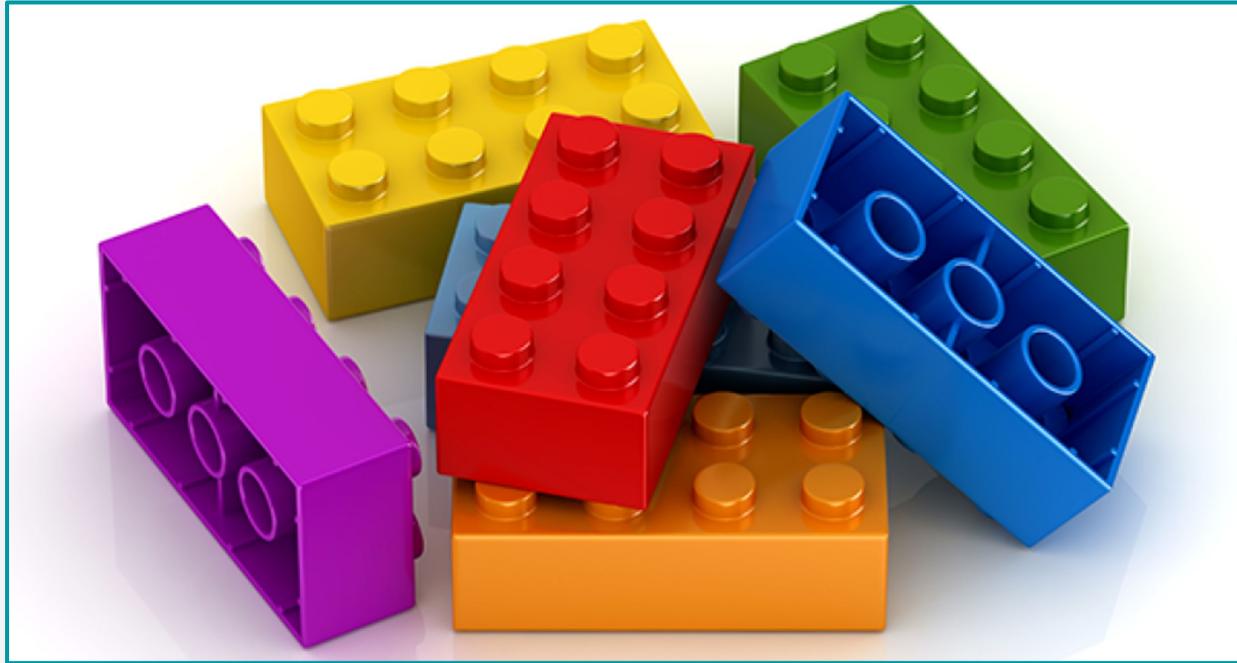


# Rx for Improving Fascia:

- **Lifestyle:**
  - Sleep, hydration, anti-inflammatory diet, movement
- **Supplements:**
  - Omega 3 fish oils, phosphatidylcholine, collagen & Vit C & Cu, glutathione , curcumin,
- **Hormonal Balance:**
  - E, P, T, Cortisol, DHEA, Insulin, IGF-1
- **PRP/PRF** (platelet-rich plasma)
- **Peptides:**
  - BPC-157, GHK-Cu
- **Miracle Wave** (ESWT: acoustic percussion)
- **Other MST's:**
  - Acupuncture, Needling, Structural Integration Therapy



# From Part to Whole



<http://mentalfloss.com/article/92127/how-many-combinations-are-possible-using-6-lego-bricks>



# From Part to Whole



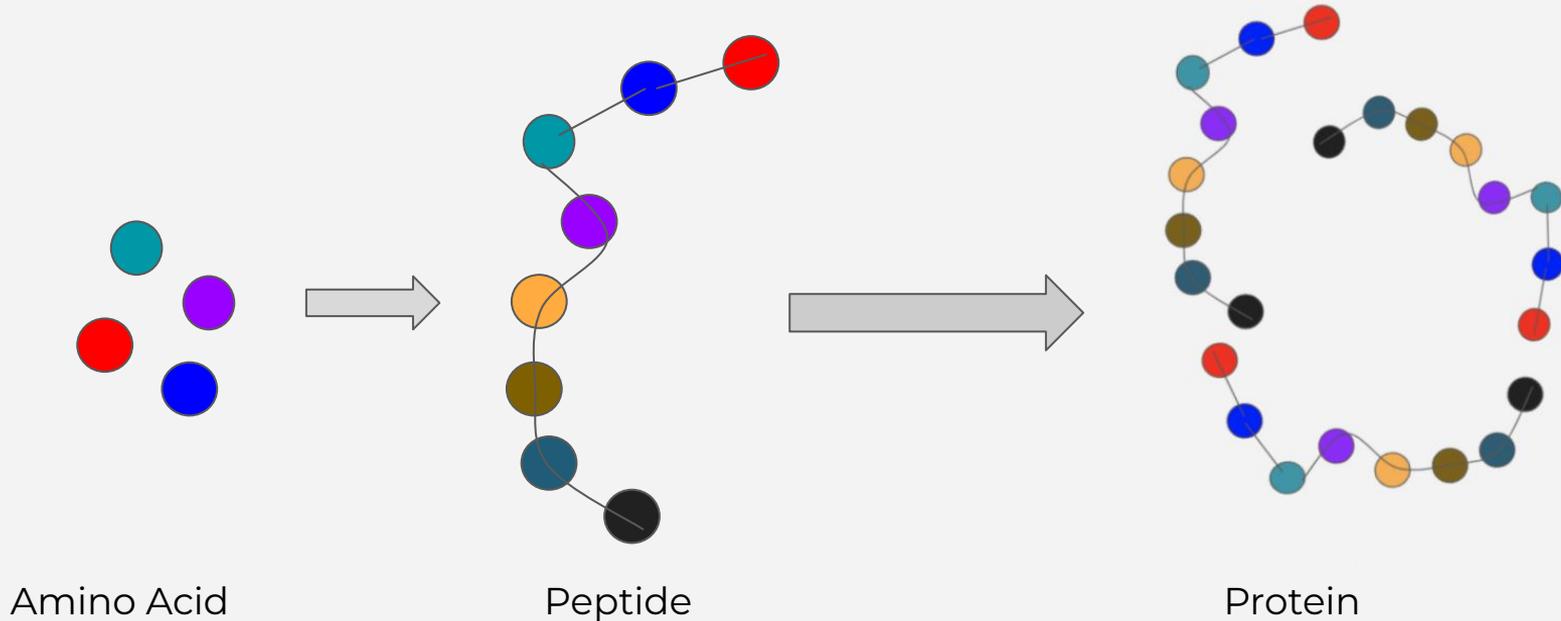
<https://www.blendswap.com/blends/view/86309>



<http://www.mp3.xyz/awesome-winter-soldier-minifigure-collection-lego-marvel-super-heroes-xYluVeCVY7q.html>



# Peptides for injury, pain & healing



**Table 1**

Thymosin proteins and their functions.

Name	Species	Role	References
PROTHYMOSIN $\alpha$ (ProT $\alpha$ )	mice, rat, human	chromatin remodeling, transcriptionally regulation, cell proliferation and survival	(Ueda et al., 2017; Samara et al., 2017; Samara et al., 2016; Ueda et al., 2012)
THYMOSIN- $\alpha$ 1 (T $\alpha$ -1)	rat, mice, humans	immunoregulation	(You et al., 2006; Romani et al., 2004; King and Tuthill, 2016; Liu et al., 2016a; Romani et al., 2017; Garaci et al., 2007)
THYMOSIN- $\beta$ 4 (T $\beta$ -4)	mice, rats, humans, cattle, chimpanzees	actin polymerization, angiogenesis, cell migration, collagen deposition, wound healing, fibrosis, neovascularogenesis, tissue repair and regeneration	(Chopp and Zhang, 2015; Kuzan, 2016; Goldstein and Kleinman, 2015)
THYMOSIN- $\beta$ 10 (T $\beta$ -10)	rat, mice, humans, cattle,	cytoskeleton organization and morphology, proliferation, motility, anti-inflammatory effects, insulin secretion	(Sribenja et al., 2009; Zhang et al., 2017b)
THYMOSIN- $\beta$ 15 (T $\beta$ -15)	rat, mice, human	motility, progression and metastasis of non-small cell lung cancer	(Banyard et al., 2007)

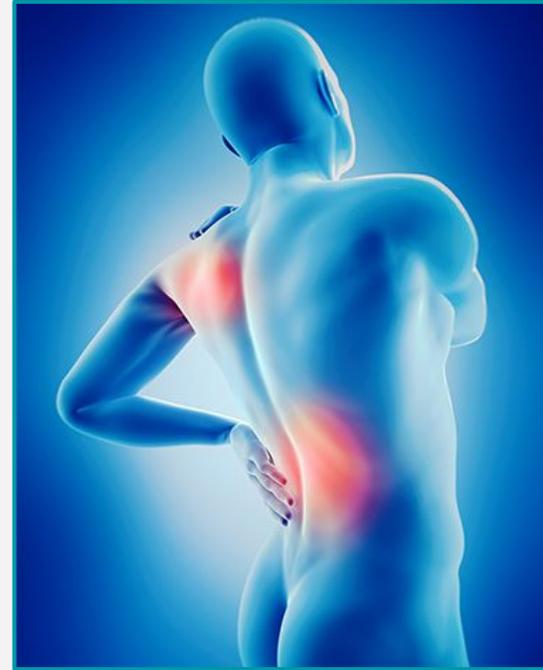


# BPC-157 for inflammation

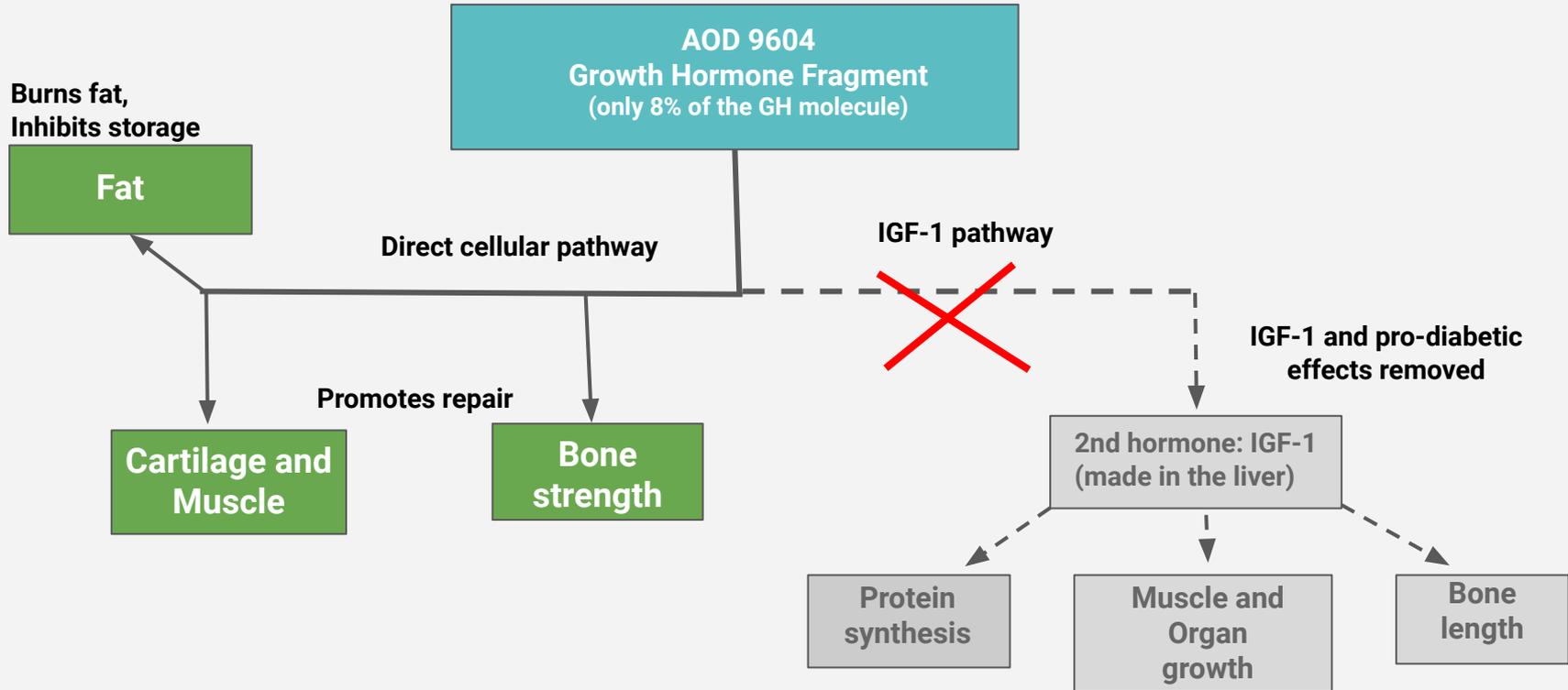
## **BPC Reduces:**

- # of inflammatory cells,
- Levels of leukotriene B4
- Thromboxane B2
- Myeloperoxidase

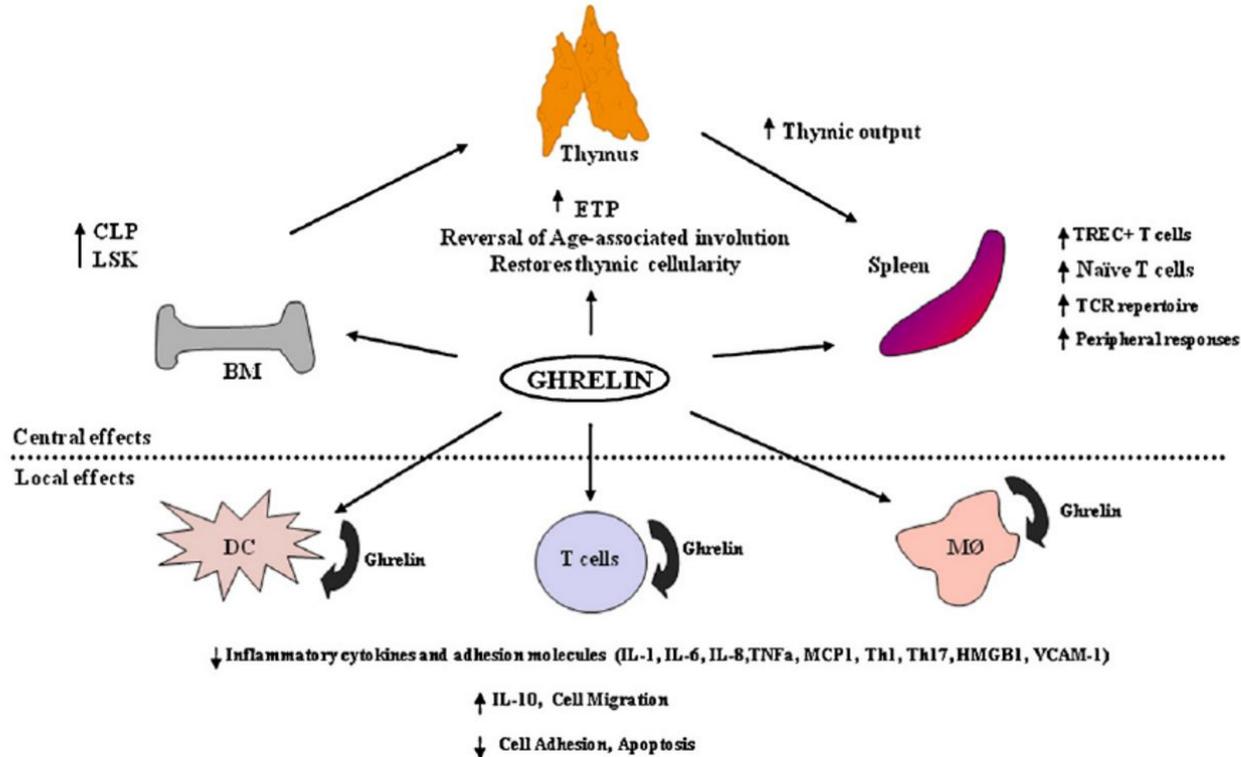
**in serum and inflamed tissues**



# AOD 9604 (+ HA)



# GHRP: Ipamorelin



Possible therapeutic effects on:

- Endotoxemia and Sepsis
- Colitis and Inflammatory Bowel Syndrome
- Cardiovascular, Hepatic, Respiratory and Renal Inflammation/Injury/Fibrosis
- Traumatic Brain Injury/Pain/Parkinson's disease
- Cachexia/Anorexia
- Ischemia/Reperfusion Injury
- Arthritis and Multiple Sclerosis
- Burn Injury
- Age-Associated Inflammation
- Thymic and bone marrow development and involution



# ESWT / Sound Waves

to treat

*injury*

*pain* and

*healing*

## got pain?

Try a new SOUND approach to help you heal.

### Healing Amplified™

If you are suffering from pain, ask your healthcare provider how **The Miracle Wave® Acoustic Wave Therapy** can help you!

**WRIST PAIN**  
Carpal Tunnel Syndrome  
De Quervain's  
Tenosynovitis

**MUSCLE SPRAINS & STRAIN**  
Calf Strain &  
Hamstring Strain

**NECK PAIN**  
Cervical Sprain & Strain  
Headaches  
TMJ

**SHOULDER PAIN**  
Rotator Cuff Strain  
Biceps Tendonitis

**ELBOW PAIN**  
Tennis &  
Golfer's Elbow  
Overuse/Repetitive  
Strain Injuries

**BACK & HIP PAIN**  
Osteoarthritis  
ITB Syndrome  
Bursitis  
Sciatica

**KNEE PAIN**  
Osteoarthritis  
Patellar Tendonitis  
Ligament Meniscal  
Injuries

**FOOT & ANKLE PAIN**  
Sprains/Strains  
Plantar Fasciitis  
Achilles Tendonitis

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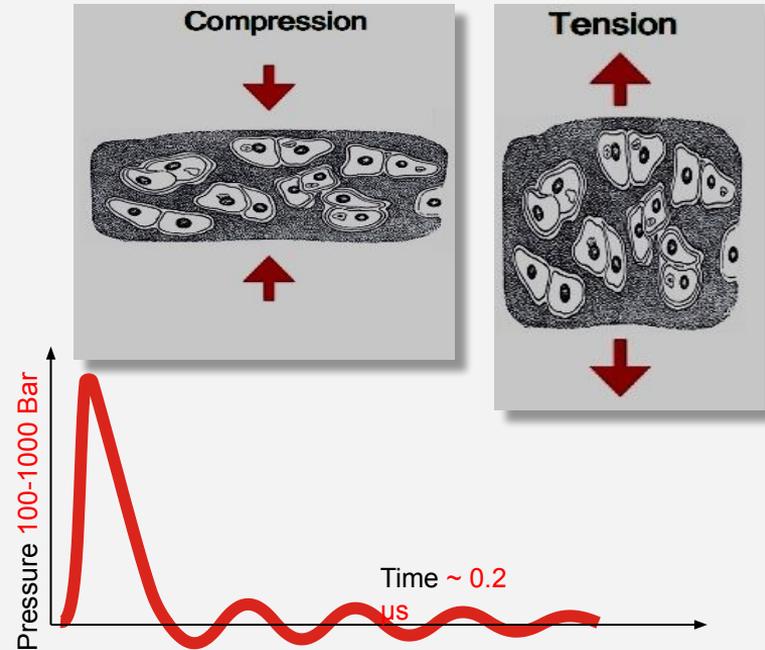


@KinasMedical



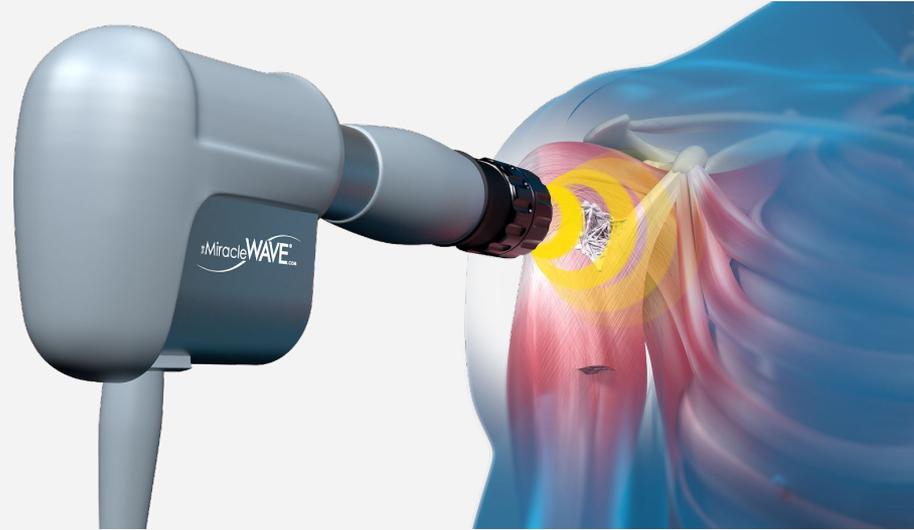
# How Do Shock Waves Work?

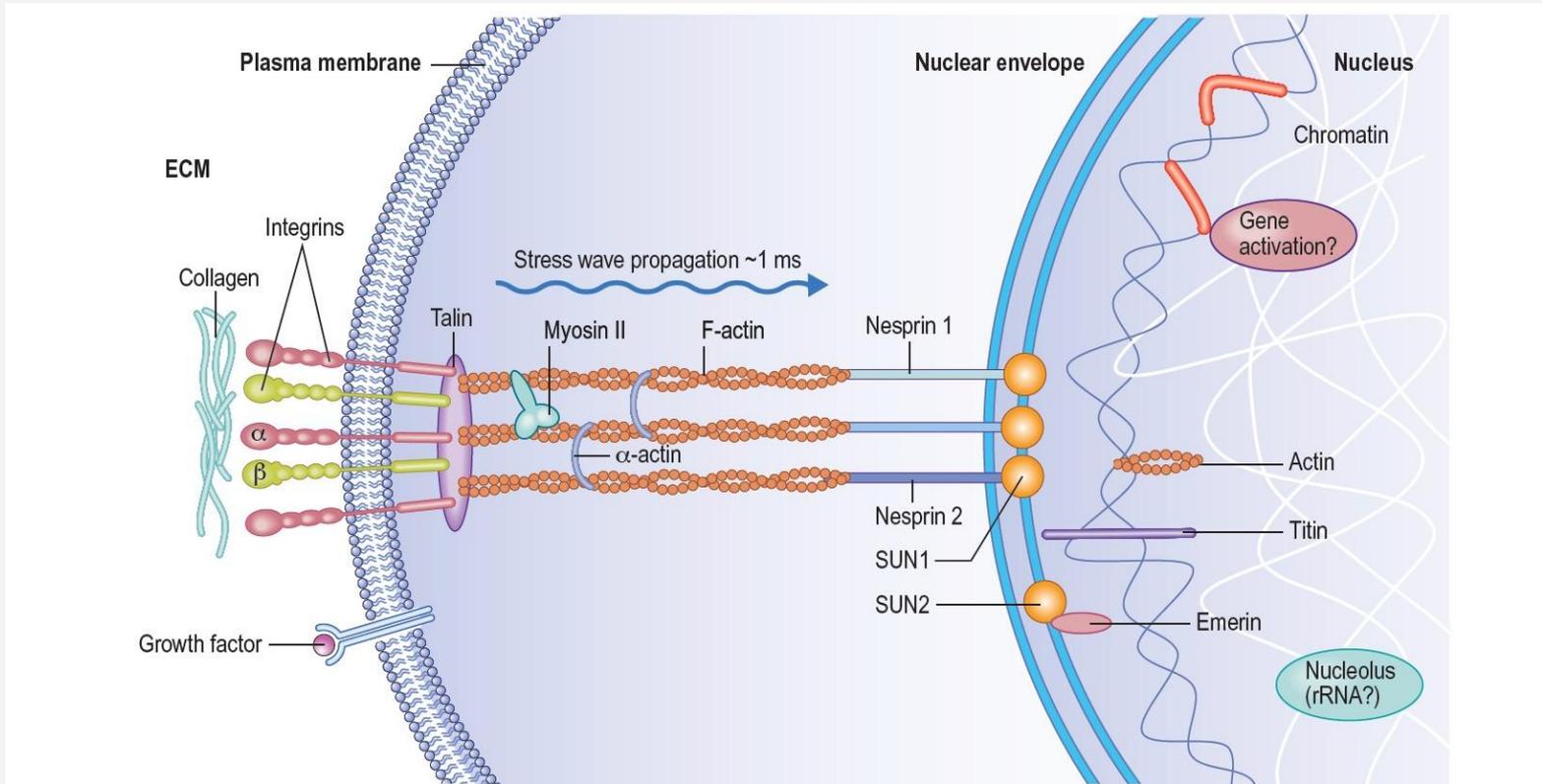
- Shock waves are transmitted to the point of pain and surrounding aliments.
  - Creating a physiological cascade that promotes tissue regeneration
- Due partly to mechano-transduction
  - cells convert mechanical stimulus into electrochemical activity
- Tension and compression create changes to cells and the surrounding tissues
  - Indirect effect
  - Direct Effect



# Biological Effects of Shockwave Therapy

- Increased microcirculation
- Vasodilation due to release of nitric oxide
- Cell matrix stimulation (Mechanotransduction)
- Release of Substance P
- Analgesia effect (pain-gating)
- Increase of cell wall permeability (Cell metabolism)
- Stimulation of growth factors (neovascularization, cell proliferation)
- Stimulation of stem cells (cell proliferation)





Reproduced with permission from Handspring Publishing Ltd, taken from Fascia: what it is and why it matters by David Lesondak (2017)"



# Case Studies:



# 61 year old female <sup>1/4</sup>

- A chef for 35 years: % mouth pain and neck pain
- 2 dental titanium implants bilaterally (2015)
- In 2019, on x-ray bone fragile→losing implants
- Aug '19 → exosomes, peptides (BPC 157) x 7 ( 4 on right, 3 on left)
  - BPC sq 4x/wk
  
- Severe neck pain that radiates down the left arm



# Rx: 61 year old F with oral implant frailty & pain

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- 2019 x 2 in right oral cavity: 8/1/19 & 10/18/19: growth factors, BPC, & AOD
- 2020 x 2 in right oral cavity: 2/25/20 & 8/18/20: growth factors, BPC, & AOD
- 2021 x 3 in left oral cavity: 2/12/21 & 5/27/21 & 11/18/21: growth factors, BPC, & AOD



# BPC-157: Healing an oral injury

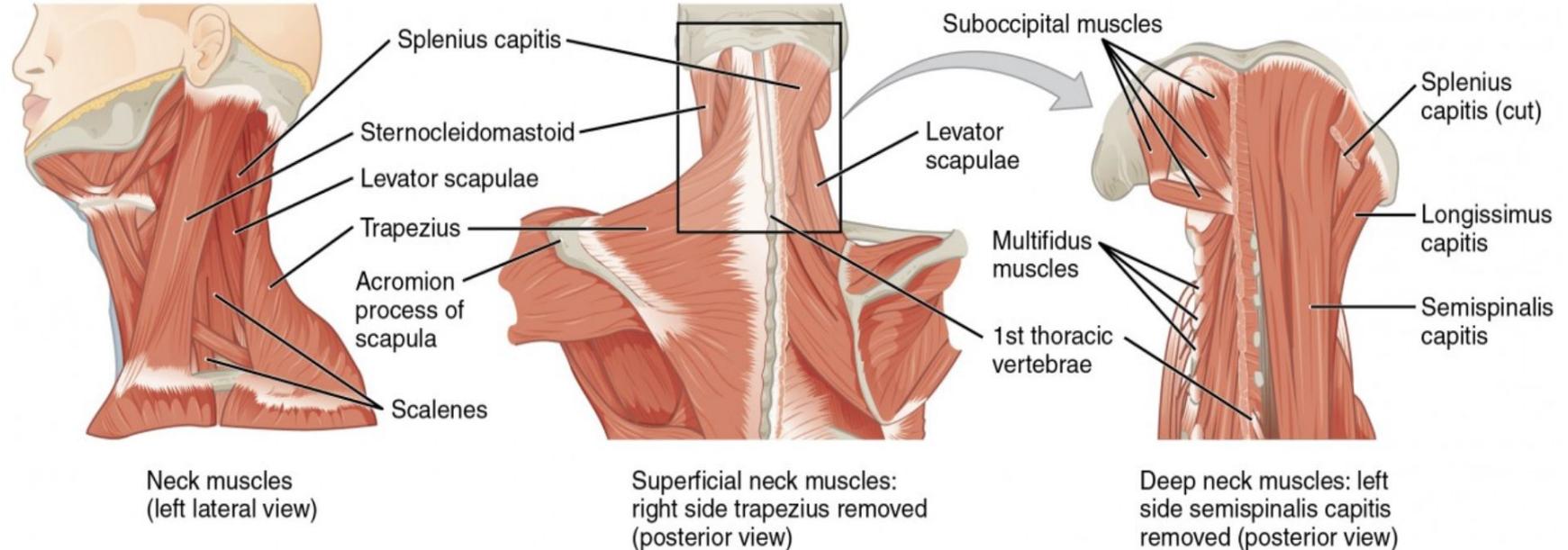
- BPC promotes tendon-to-bone healing and regeneration
- BPC increased type 1 collagen



Type of Collagen	Location
Type I	Tendons, legaments, bone, dentin, dermis of skin
Type II	Cartilage
Type III	Reticular fibers, dental pulp, lymph nodes, bone marrow
Type IV	Basement membrane



# ESWT posterior and lateral neck



**Figure 6. Posterior and Lateral Views of the Neck.** The superficial and deep muscles of the neck are responsible for moving the head, cervical vertebrae, and scapulas.



# Rx: 61 year old F with neck pain

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## Neck Pain

- ESWT & Structural Integration Therapy
- BPC 30 units sq + topical
- TB4 1cc sq



# Intra-articular Injection in Knee of D1 Athlete

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- Age: 18
- Gender: Male
- Chief Complaint: Right Knee Pain and post exercise effusion ; less and less able to train; now unable to run or squat
- Desired Outcome/Treatment Goals: Full ROM right knee with no pain and no post exercise knee effusion



# Surgical History f/b Intra-articular knee injection

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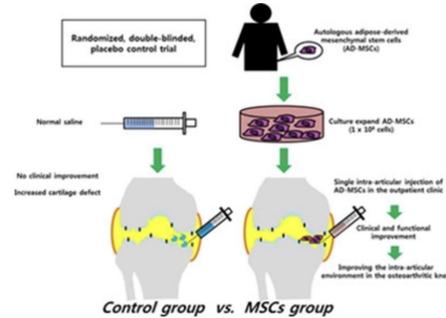
- March 2018 first surgery for a meniscus tear
- October 2018 second surgery to scrape (scar tissue?)
- February 2019 surgeon wanted to perform cadaveric tissue transplant
- Treatment #1: intra-articular injection in March of 2019 @ TWLLC



June 17, 2019

## Single MSC Injection Provides Functional improvements and Pain Relief for Knee Osteoarthritis Patients

Review of  
“Intra-  
Articular  
Injection  
of



Autologous Adipose tissue-derived Mesenchymal Stem Cells for the Treatment of Knee Osteoarthritis: a Phase 2b Randomized Placebo Controlled Clinical Trial” from STEM CELLS Translational Medicine by Stuart P. Atkinson The ability of mesenchymal stem cells (MSCs) to differentiate into cartilage tissue and their paracrine anti-inflammatory and immunomodulatory effects has led to their



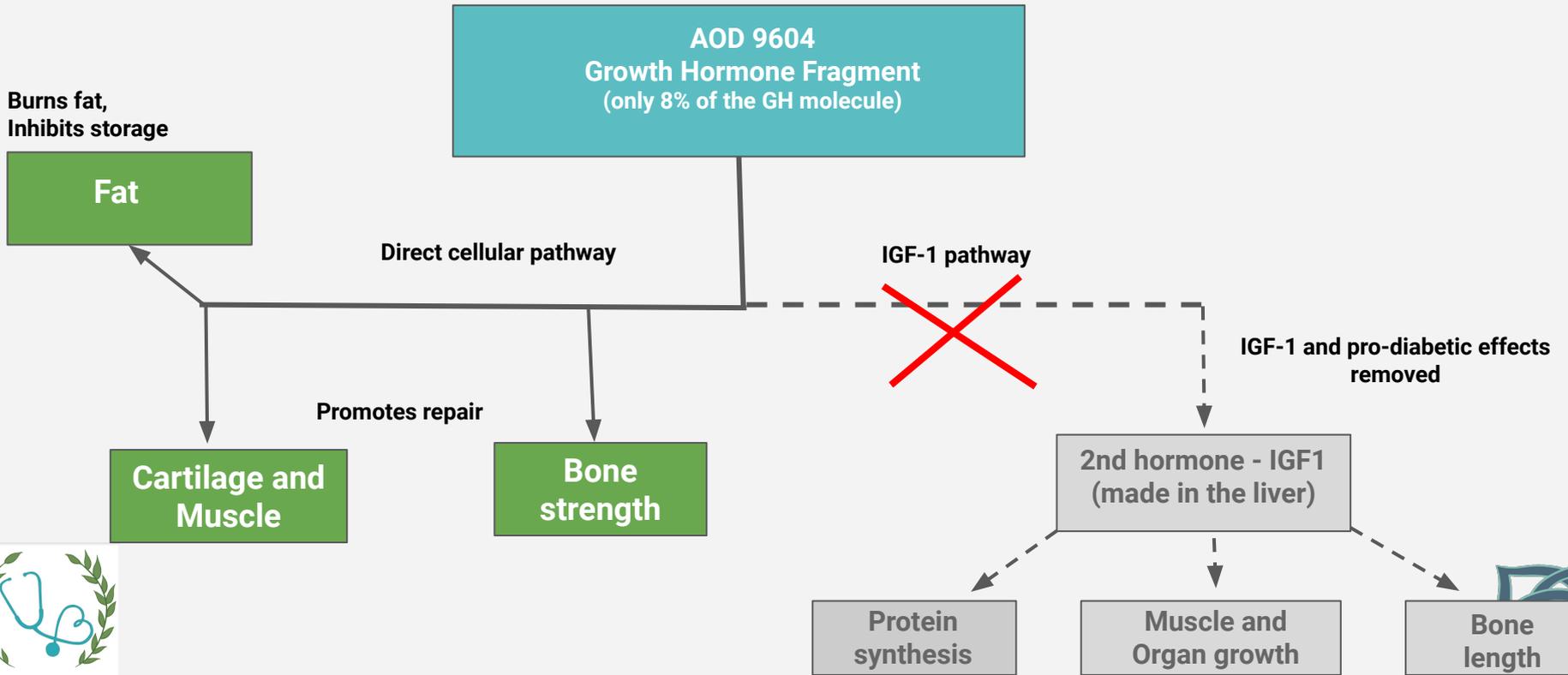
# Treatment

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- March 2019 right knee injection
  - MSC's
  - PRP
  - BPC-157
  - AOD+HA



# AOD 9604 (with HA)



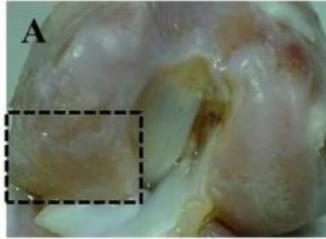
# AOD-HA

Group 1: 0.6 ml saline

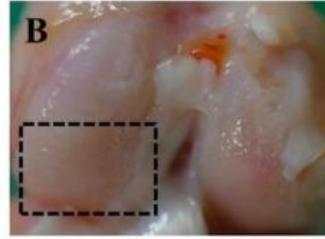
Group 2: 0.6 ml HA

Group 3: 0.6 ml AOD

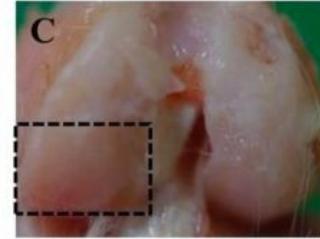
Group 4: 0.6 ml HA with 0.6 ml AOD



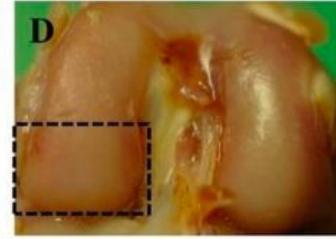
Ulceration



Fibrillation



Erosion



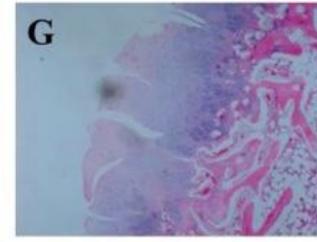
Softening



Disorganized



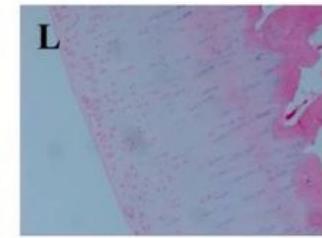
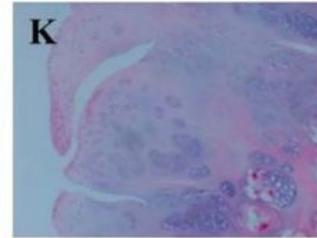
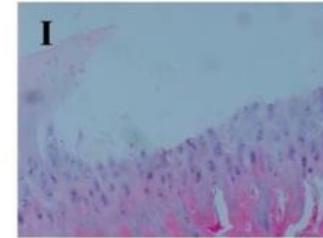
Cleft to transitional zone



Cleft to radial zone



Surface irregularity



Kwon, Dong Rak and Gi Young Park. 2015. "Effect of Intra-Articular Injection of AOD9604 with Or without Hyaluronic Acid in Rabbit Osteoarthritis Model." *Annals of Clinical and Laboratory Science* 45 (4): 426-432.



# 6 months Post Injections

- 08/30/2019
- Interview:



# Objectives

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1. **Fascia as an Organ System: *Functional* anatomy and physiology**
2. **Importance of Fascia in Pain and Sports Medicine**
3. **Current Understanding of Fascia and MST**
4. **Newer Regenerative Approaches to Healing fascia, including hormones and peptides.**





# *Thank You*

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