ISMST
The International Society for Medical Shockwave Treatment

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# Acoustic stimulation and tropism on skeletal muscles: Tissue resilience & regeneration in sports and ageing

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# Conflict of Interest Declaration

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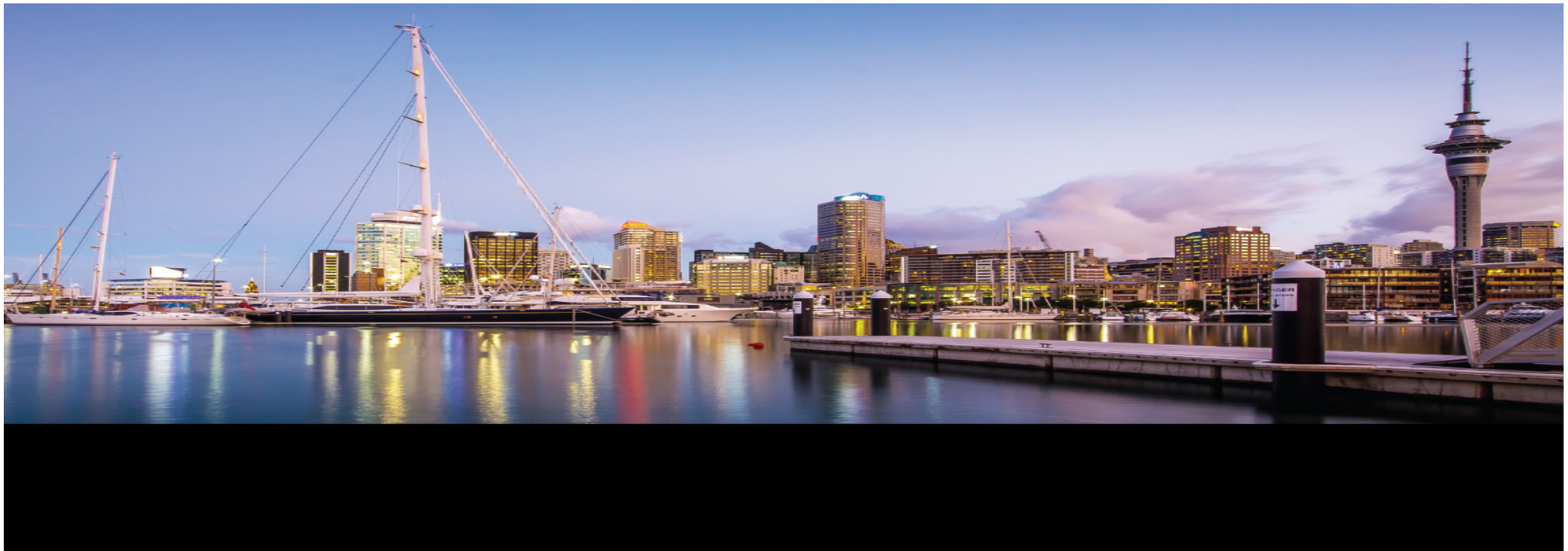
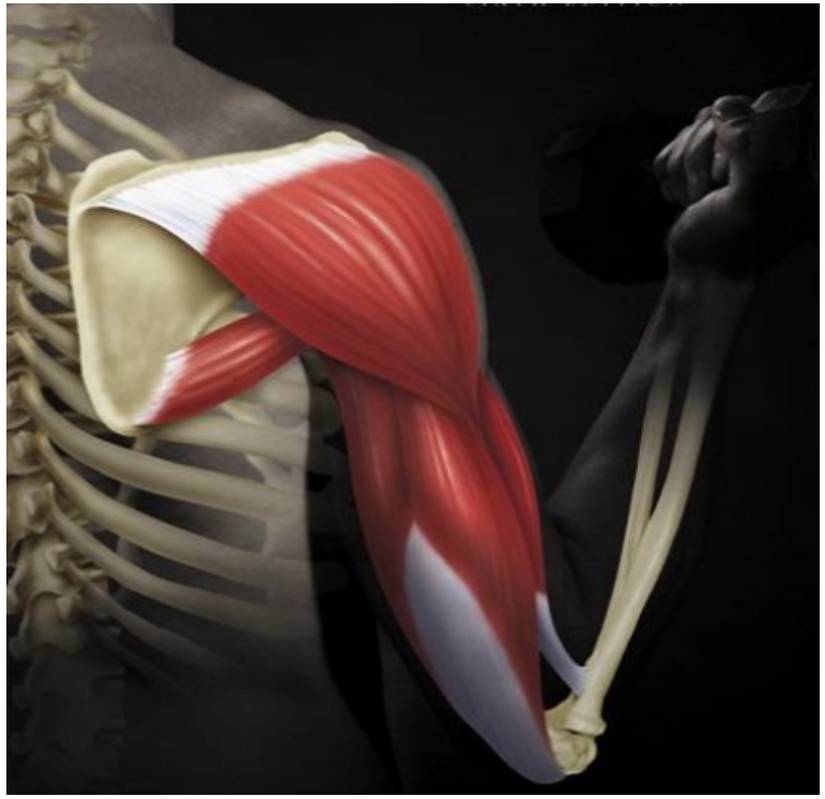


# AIM

## To promote investigation & collaboration in this area

# SM: Introduction

- Controlled via voluntary somatic muscle control
- Striated
- Approx. >400 SM in body
  - Muscle fibers, fascia, nerves & blood vessels
- 45% - 50% of body weight
- 70% - 75% water content
- Approx. 50% of total body protein content
- Multiplex functionality
  - Respiratory facilitation
  - Energy storage
  - Power generation
  - Thermoregulation
  - Posture & locomotion
  - Auto-para-endocrine networking
  - Metabolic regulation
  - High plasticity



# SM: Key Properties

1. **Excitability:** via peripheral & central nervous system

2. **Contractibility**: tensional & tractional; harnessed by fascia (connective tissue).

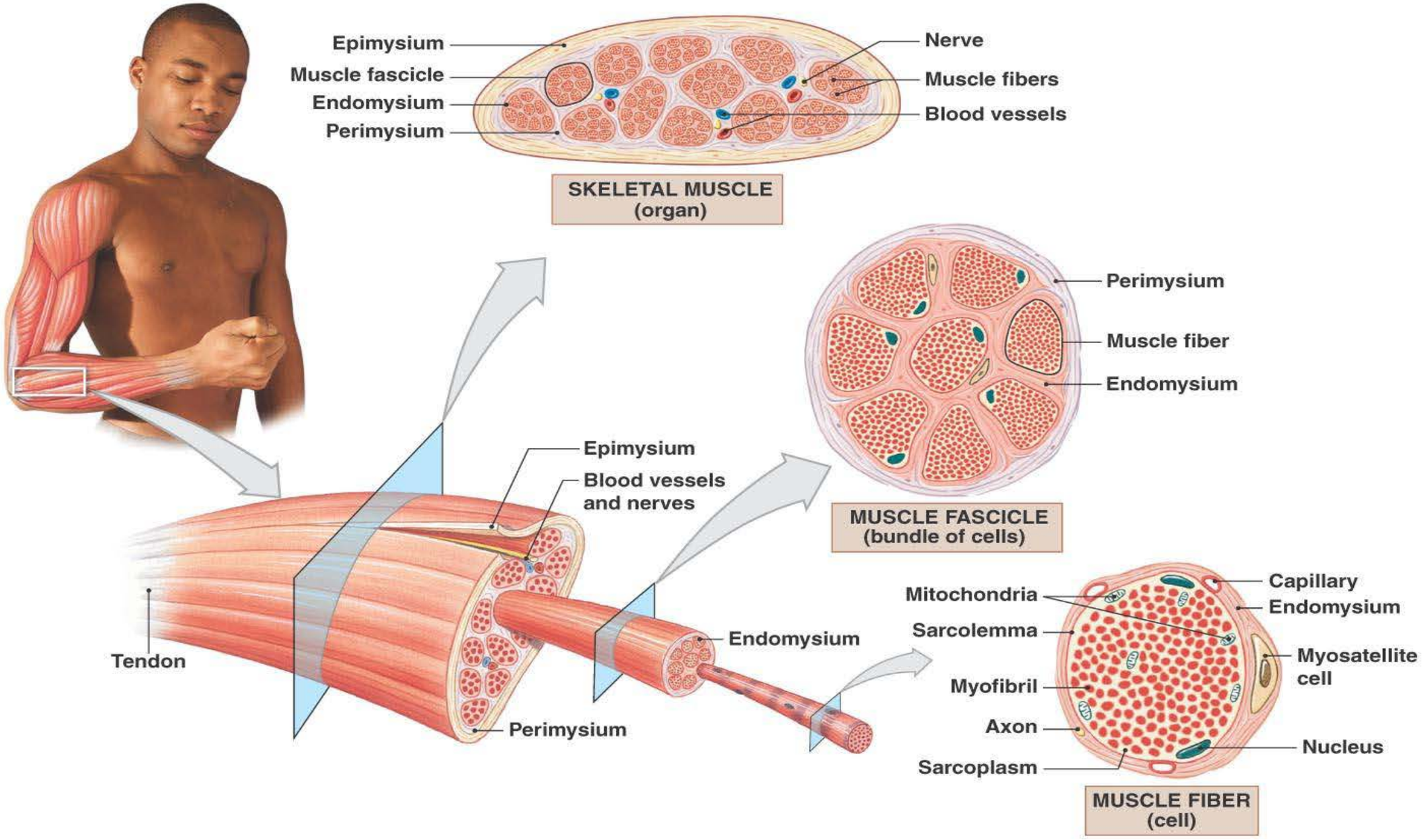
3. **Extensibility**: ability to continue contraction over a range of lengths.

4. **Elasticity:** ability to recoil toward original length.

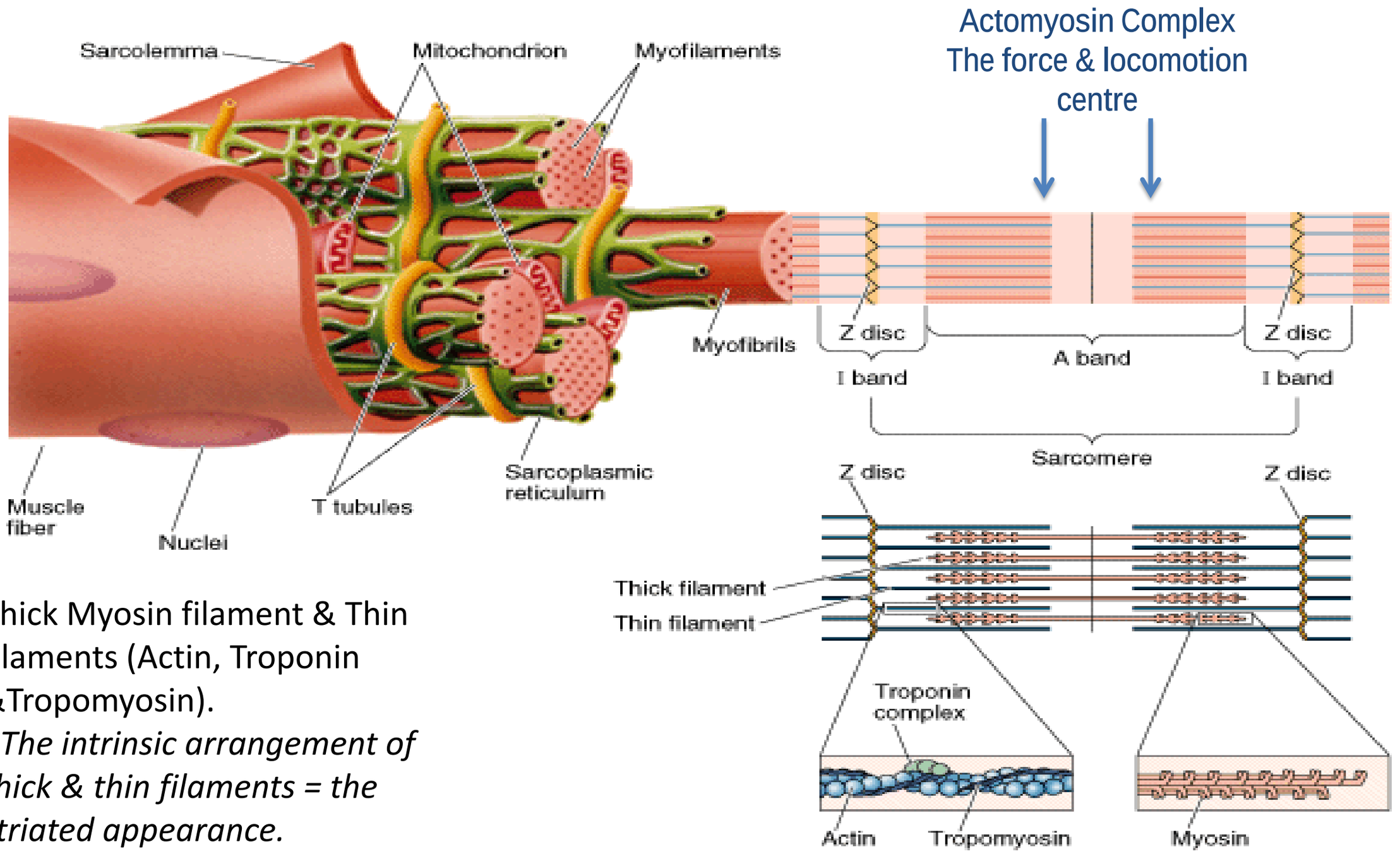
5. **Plasticity & regeneration:** ability to grow & adapt (cross-sectional fibre size increase / mitochondrial volume increase), and reconstruct.

6. **Energy biogenesis:** ie. $UPR^{MT/ER}$ / other metabolic pathways

# SM: Structural Organization



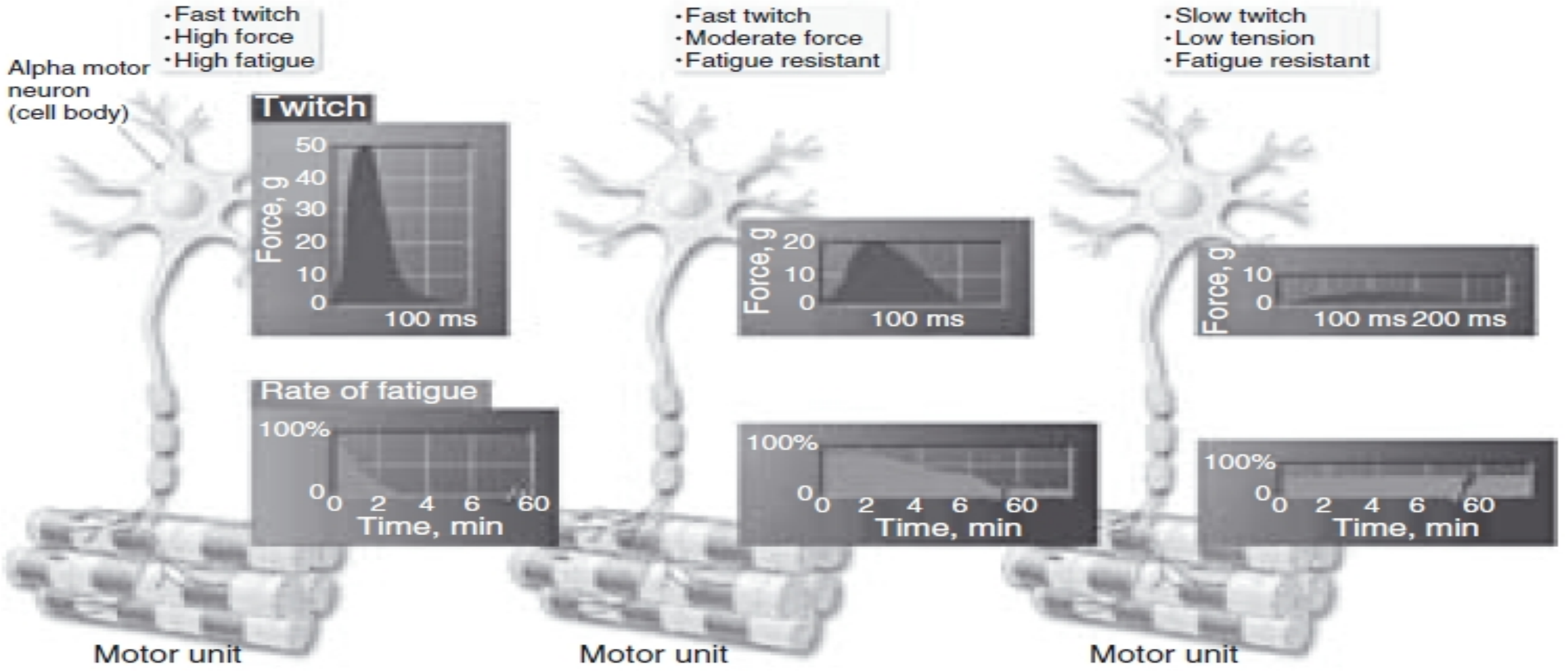
## ► Organization of a Muscle Fiber




Thick Myosin filament & Thin filaments (Actin, Troponin &Tropomyosin).

**The intrinsic arrangement of thick & thin filaments = the striated appearance.*

# SM Fibre Types: Contraction Velocity, Force & Fatigue




Contraction Speed: 40-90ms
V Large Motor Neuron
Low Mitochondria
High Glycolytic & ATPase

Contraction Speed: 50-100ms
Large Motor Neuron
Moderate Mitochondria
High Glycolytic & Int. ATPase

Contraction Speed: 90-140ms
Small Motor Neuron
High Mitochondria
Low Glycolytic & ATPase

# SM: Fibre Type

Muscle fibre type can be measured in 3 ways: myosin ATPase histochemistry, immunohistochemistry & metabolic enzymes (less commonly utilised).

1. Myosin ATPase staining
   - Staining intensities differ in pH sensitivity from each fibre type.
2. Immunohistochemistry
   - Variations exist between the fibre types on the basis of the different myosin heavy chain isoforms.
   - The MHC isoforms serves as ATPase conversion sites with varying ATP hydrolysis speed.
   - The main 3 isoforms are: MHCI; MHCIIa & MHCIIx
3. Metabolic enzyme
   - Provides information into metabolic pathways, describing muscle fibres as being aerobic / oxidative, fast-twitch oxidative, and slow-twitch oxidative.

# SM: Fibre Type of Different Muscles

Hip Extensors

- hamstrings & G max. mixture of type I & II fibres (slightly > TI)

Plantarflexors

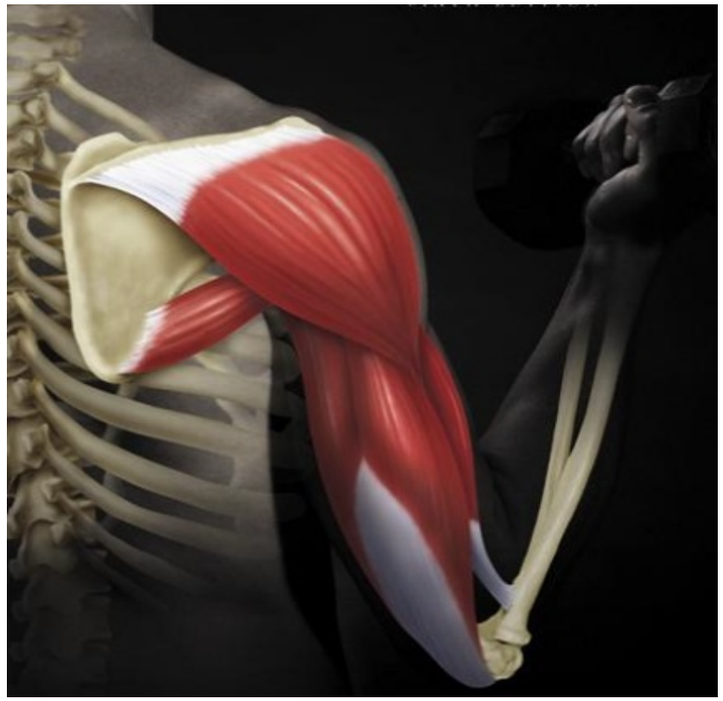
- soleus markedly TI.
- Gastrocs: mixture of TI & II

Knee extensors

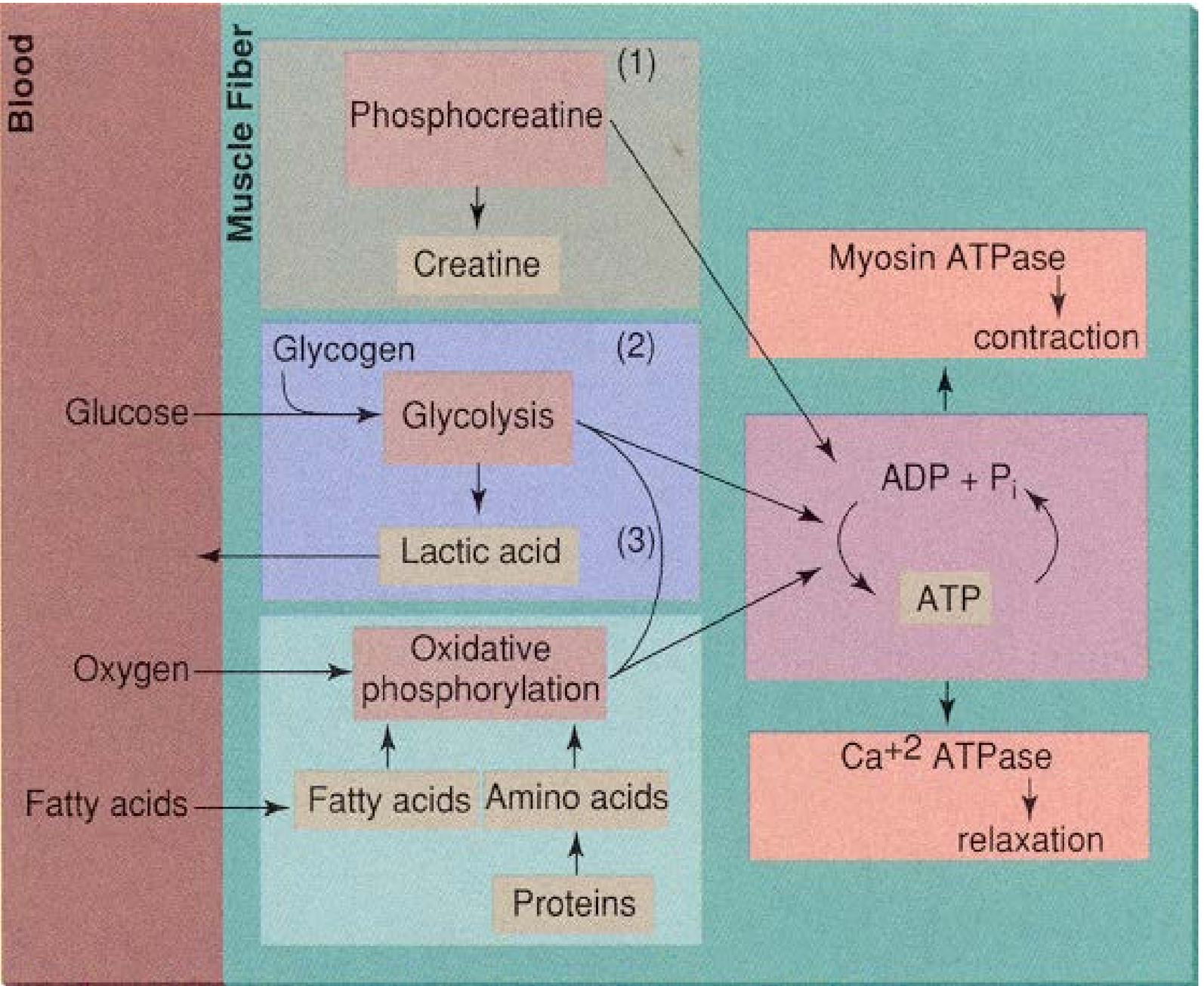
- rectus fem mixture (TI & TII; >II ).

Shoulders:

- biceps, triceps & pectoralis (TII)
- Lat Dorsi (balanced TI & TII)



# Sources of ATP




ATP Generation occurs in:

- Muscles
  - muscular contraction
- Cytoplasm
  - glycolysis
- Predominantly Mitochondria
  - oxidative phosphorylation (OXPHOS)

# SM: Regeneration

**Fundamentally 3 sequential overlapping stages:**

- Inflammatory response
- Activation, differentiation & fusion of satellite cells
- Maturation and remodelling of new myofibres

# SM: Functional Return

**Muscle cells need:**

1. Intracellular energy reserves (glycogen, creatine phosphokinase)
2. Optimal circulation (nutrient in; tissue waste disposal)
3. Normal $O^2$ levels
4. Normal pH
5. Lactic acid disposal & conversion (glucose)
6. Proteostasis / biogenesis (cellular folding; transcription; degradation & transport).
7. Satellite cell: functional niche signalling & activation

# SM: Remodelling

## Muscle fibre protein transcription, a complex process:

- Transcriptional catabolic & anabolic signalling (ie. miRNA; FOXO; mTOR; MYOG; Pax activity)
- Autophagy (eg. elimination of defective organelles for energy prod.)
- Hormonal signalling (ie. IGF1; SMAD's; Leptin)
- ATP conversion into cAMP (GPCRs; SM-Dopamine receptor 1 & 5 activation)
- Mechanical transcription & regulation
  - sacromeric-hubs ie Z-disk & M-lines
  - stretch / strain biomechanical responses onto matrix (satellite nice / zone)
- Circulation
- Tissue age / plasticity
- Satellite cell activation  (a pivotal function of SM regeneration)

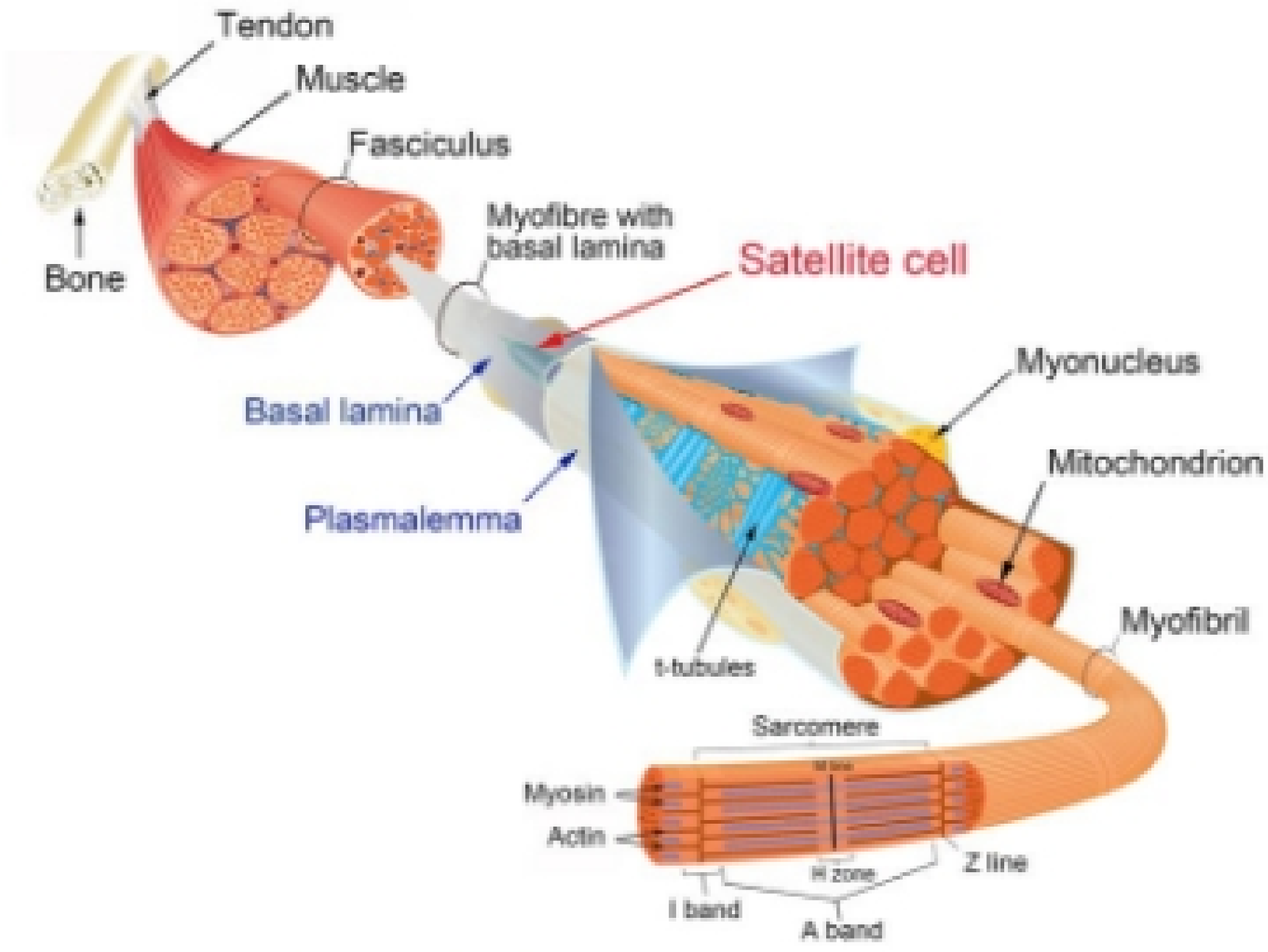
# SM Satellite Cells

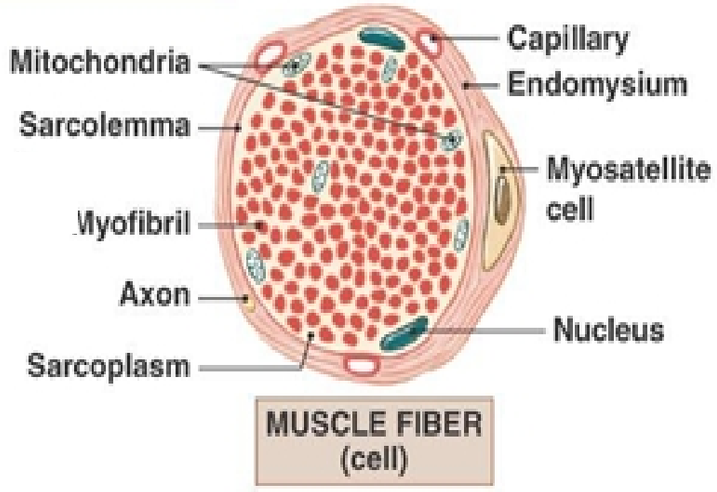
- Discovered by Alexander Mauro (over half century ago), and named as such due to their sublaminar location & intimate association with plasma membrane myofibers
- Quiescent state SC are activated by a mitogen  due to injury.
- Proliferation & differentiation of SC during regeneration influenced by:
  - Innervation**
  - Vasculature
  - Hormones
  - Nutrition
  - Extent of injury
- Adult SMSC's self replicate & differentiate (into functional progeny), a bona fide stem cell. The process of self replication is governed by the structure and signalling in their niche / zone (ie Wnt signalling).

# SM SC's: Identification markers

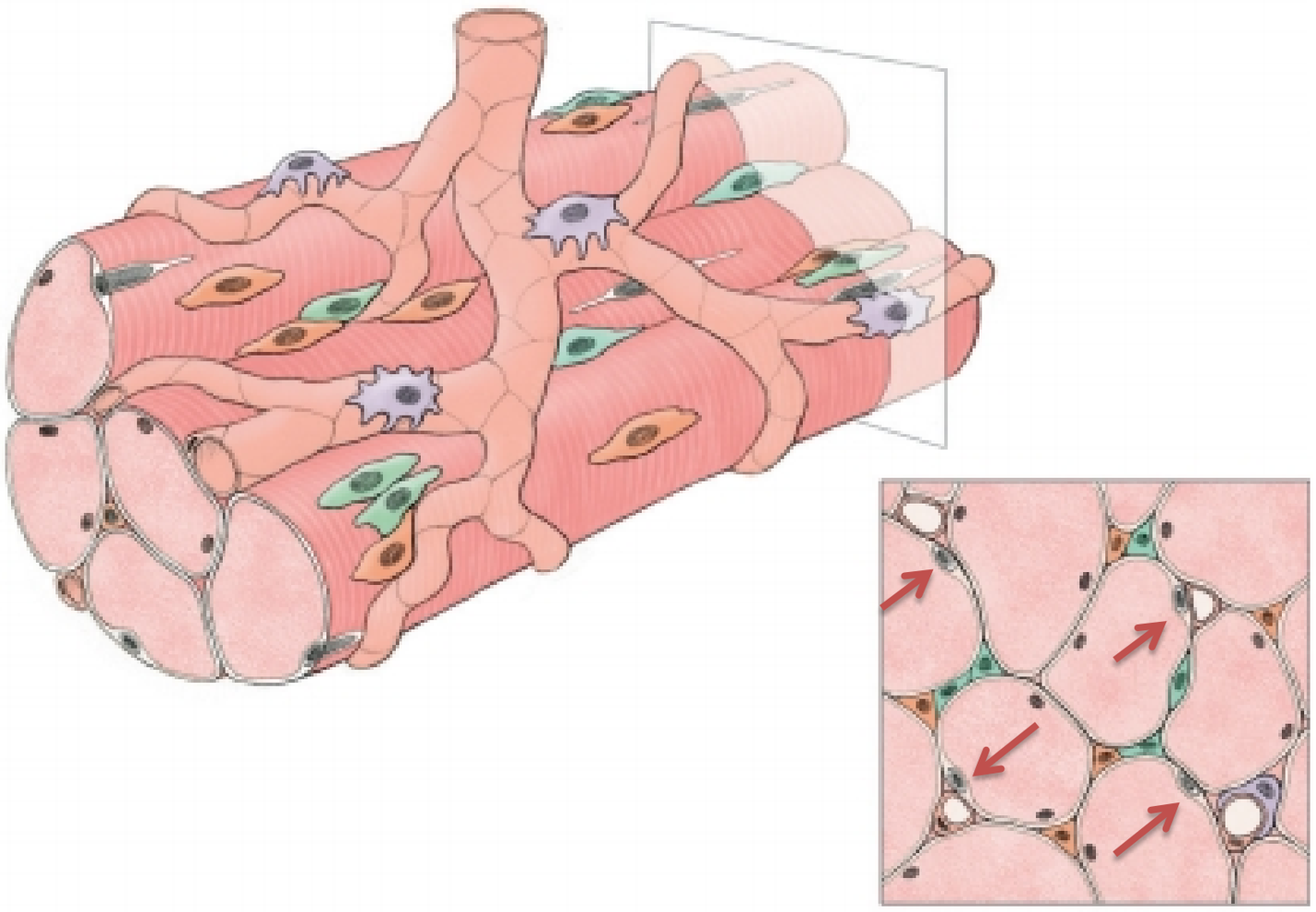
- SMSC's are classically identified based on anatomical location: just beneath the basal lamina, and outside the myofiber plasma membrane
- Most adult SMSC's express Pax7 (considered the canonical biomarker)
- Myogenic RF Myf5
- Homeobox TF Barx2
- Protein Cell adhesion molecule M-cadherin
- TRK c-Met
- Cell surface attachment receptor α7-integrin
- Transmembrane HSP sydecan-3 & 4
- Chemokine receptor CXCR4
- Caveolin-1
- Calcitonin receptor
- NEP lamin A/C
- Emerin

# SM SC's: anatomical location

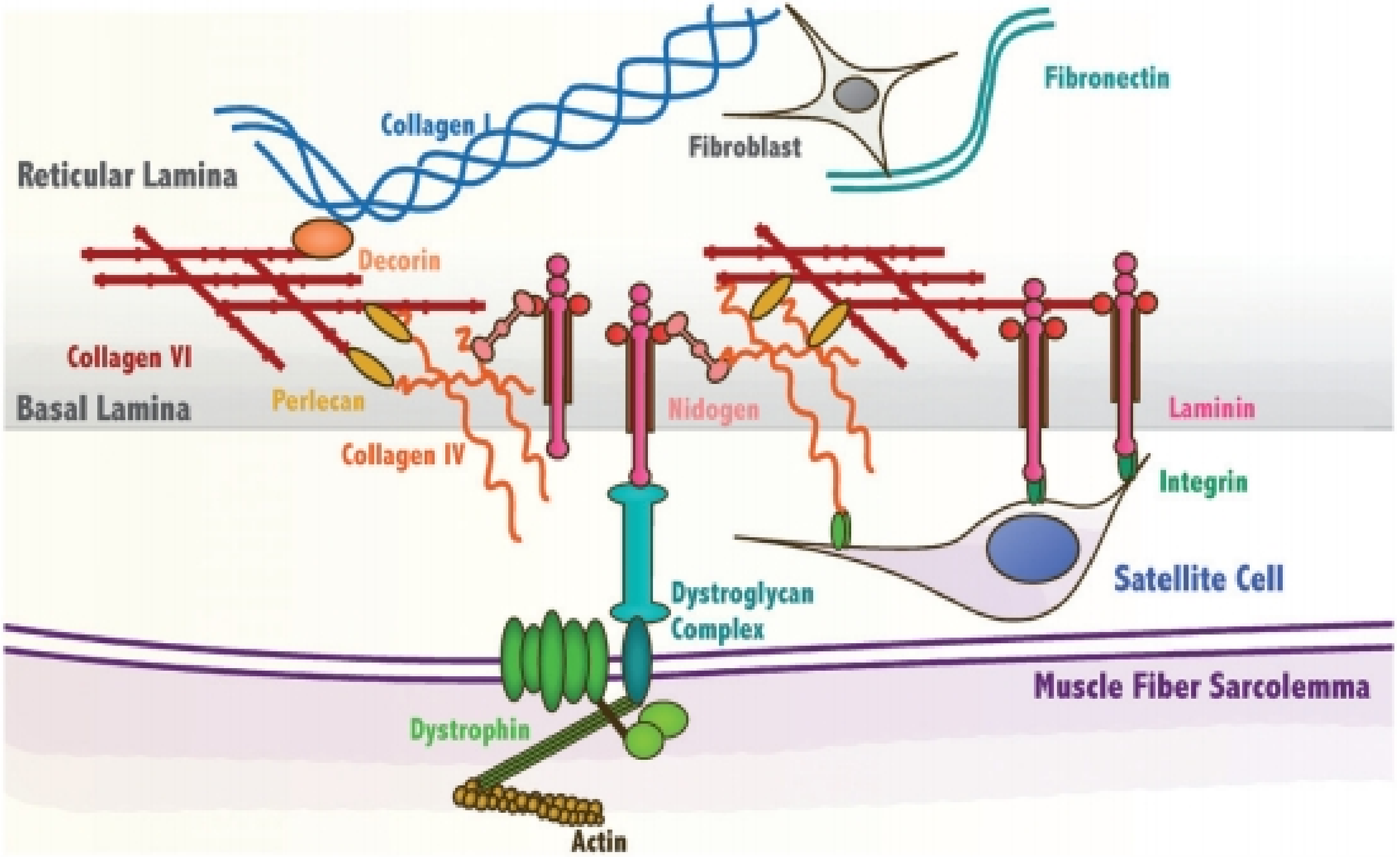


# SM SC's: anatomical location



# SM SC's: The Niche / Zone



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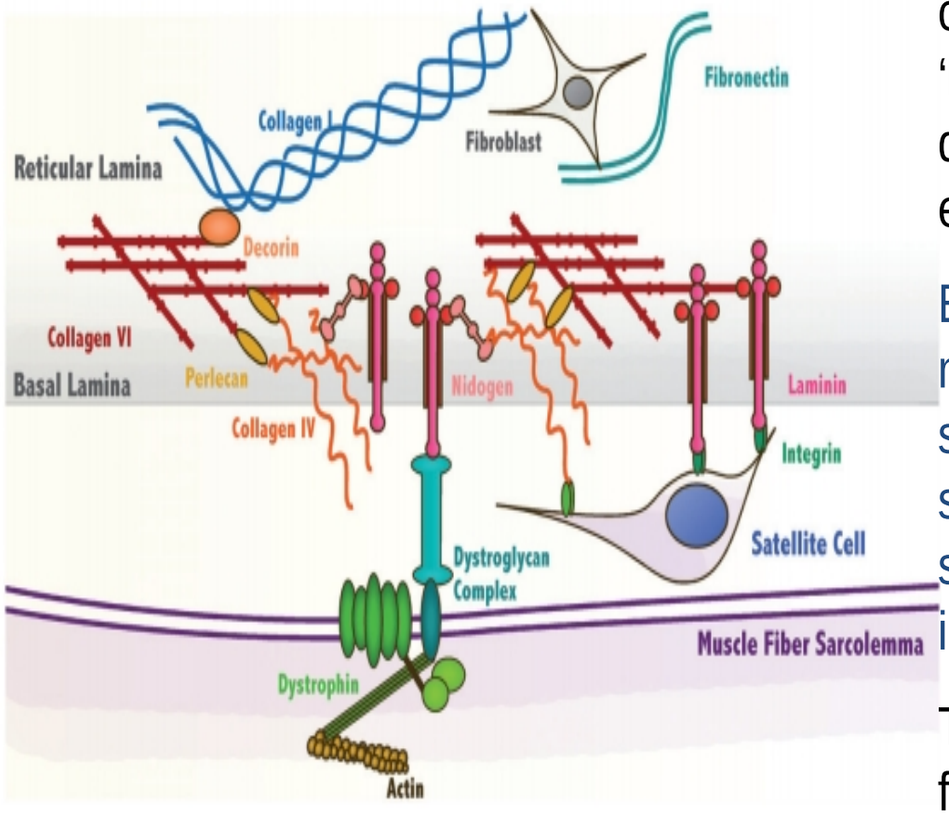
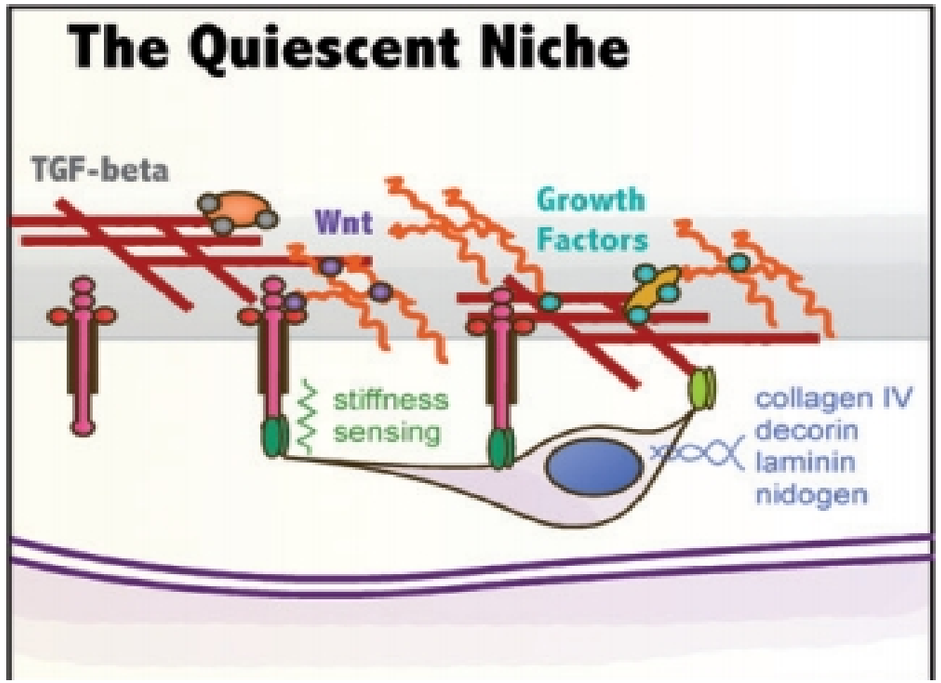



The 'Niche' is not merely an anatomical grid, but rather a dynamic communications conduit, sensing & transmitting signals (ie. biomechanical, chemical etc.) relaying the status & requirements of the tissue to its 'Regenerative Cell' source the Satellite Cells. Negative alterations or disruptions to the niche often result in defective regenerations in nearly every stem cell compartment of the region or body.

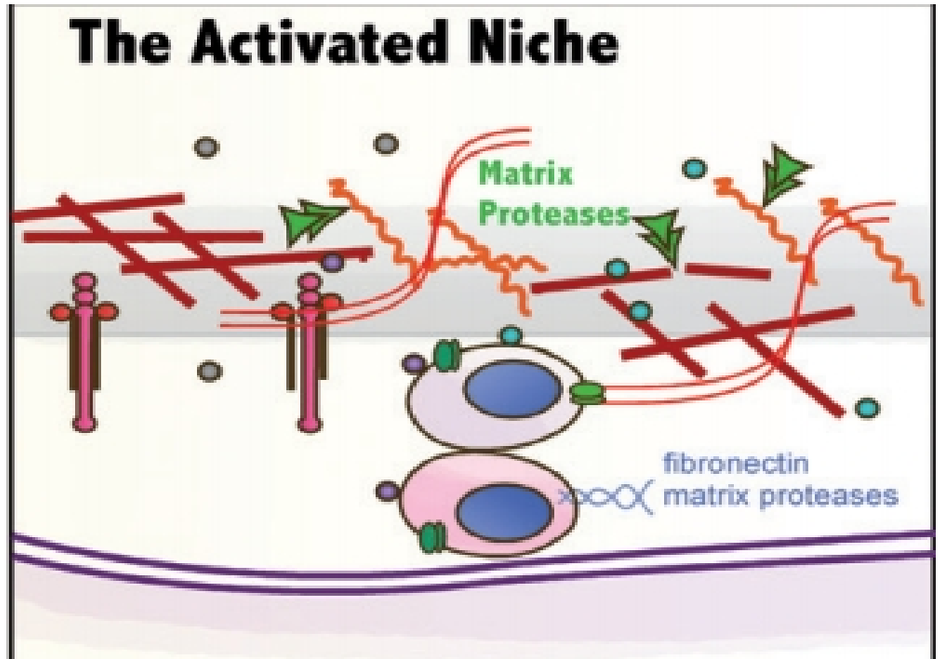
ECM components are considered essential mediators in the niche for the maintenance of stem cell identity, expression, and activation. It simultaneously provides the niche structural integrity, and physically separates the stem cell pool from other tissue resident cells. Stem cells sense & respond to the composition, porosity & stiffness of the ECM directly interacting with it via integrin focal adhesions.

The ECM surrounding muscle fibres comprise: collagens, laminins, fibronectin, glycosaminoglycans, short polysaccharide chains bound to core protein forming proteoglycans. This matrix termed 'Basement Membrane' is dual layered with the reticular lamina (superiorly) & basal laminar (inferiorly).

# SM SC's: The Niche / Zone

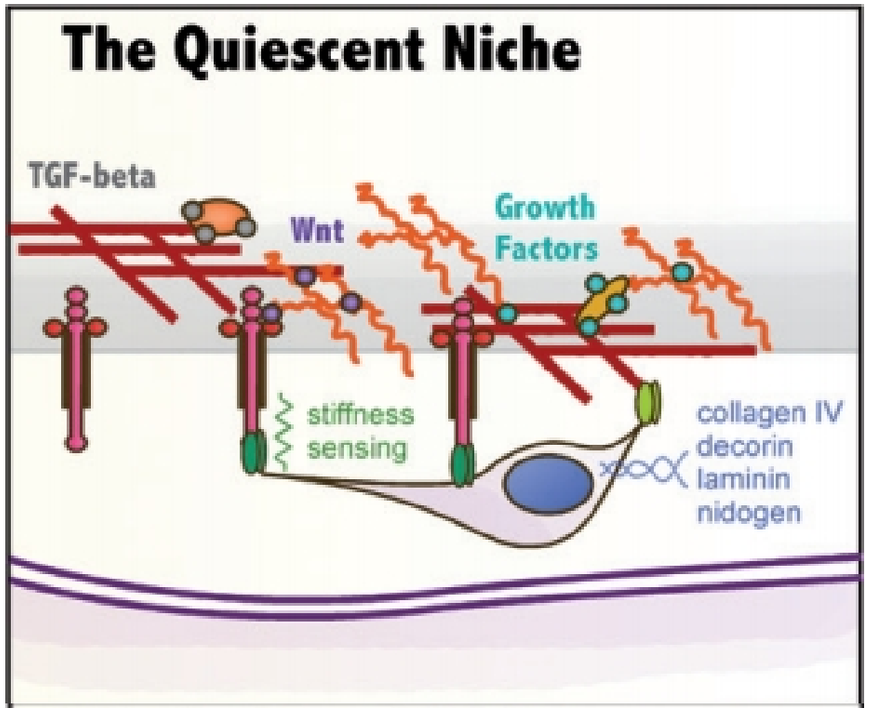


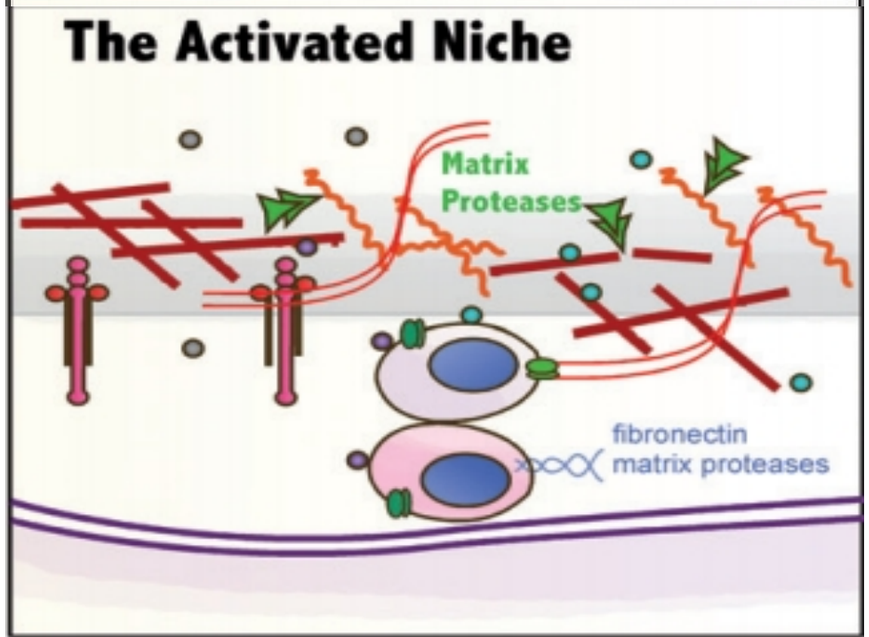

The quiescent SC senses the stiffness of its niche through integrins and expresses various matrix proteins to maintain its extracellular matrix (ECM). Within this matrix, growth factors and signalling molecules such as Wnts and TGF-b are sequestered, maintaining the ‘‘quiet’’ state.

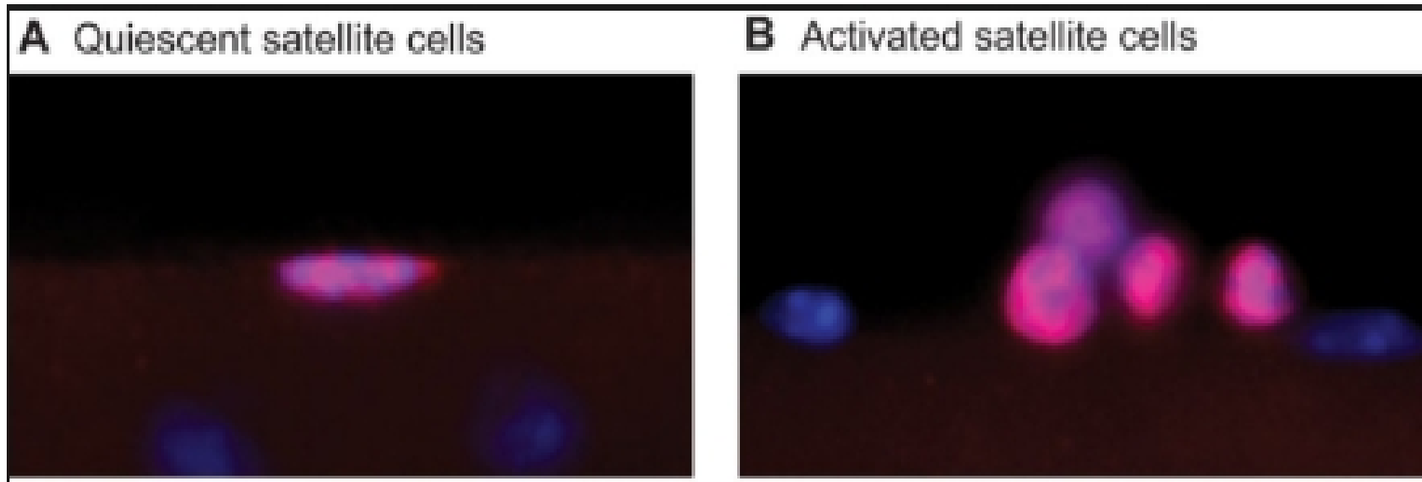


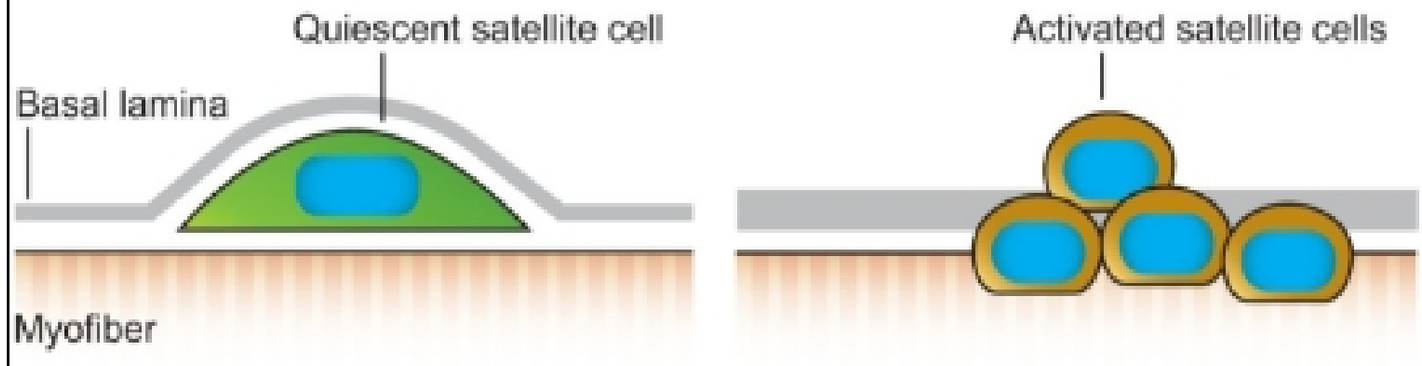

In response to injury or stimulus, components of the basal lamina are degraded by matrix proteases which results in the release of signalling molecules that play a role in activation and proliferation of the SC. The activated SC divides and some daughter cells begin to differentiate.

# SM SC's: Expression & Activation Markers



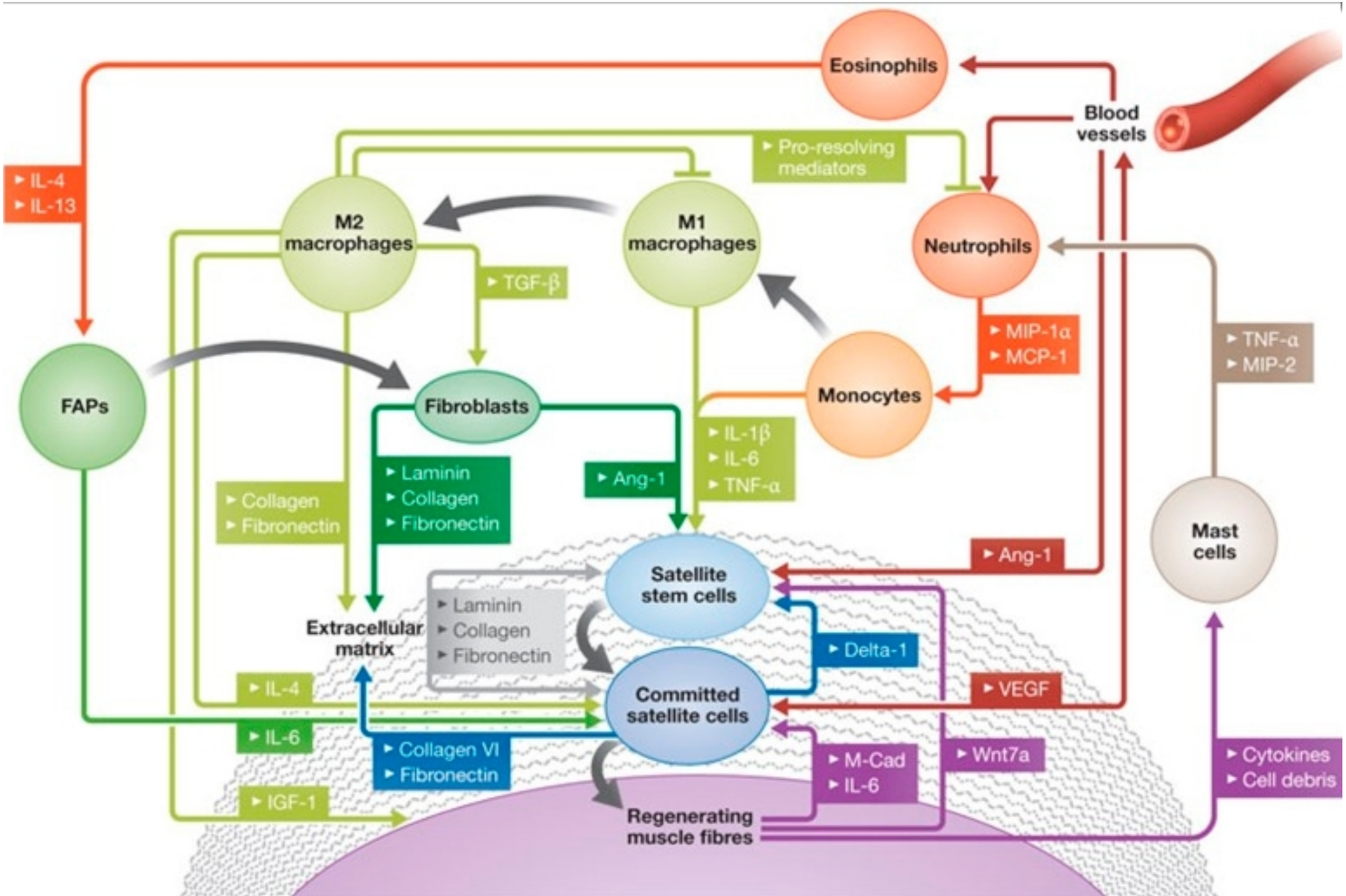

Quiescent satellite cell markers

| Nuclear | Surface | |
|---|---|---|
| Pax7 | α7-integrin | N-CAM |
| emerin | caveolin 1 | M-cadherin |
| lamin A/C | Calr | syndecan 3/4 |
| p57 | CD34 | V-CAM |
| | Cxcr4 | |

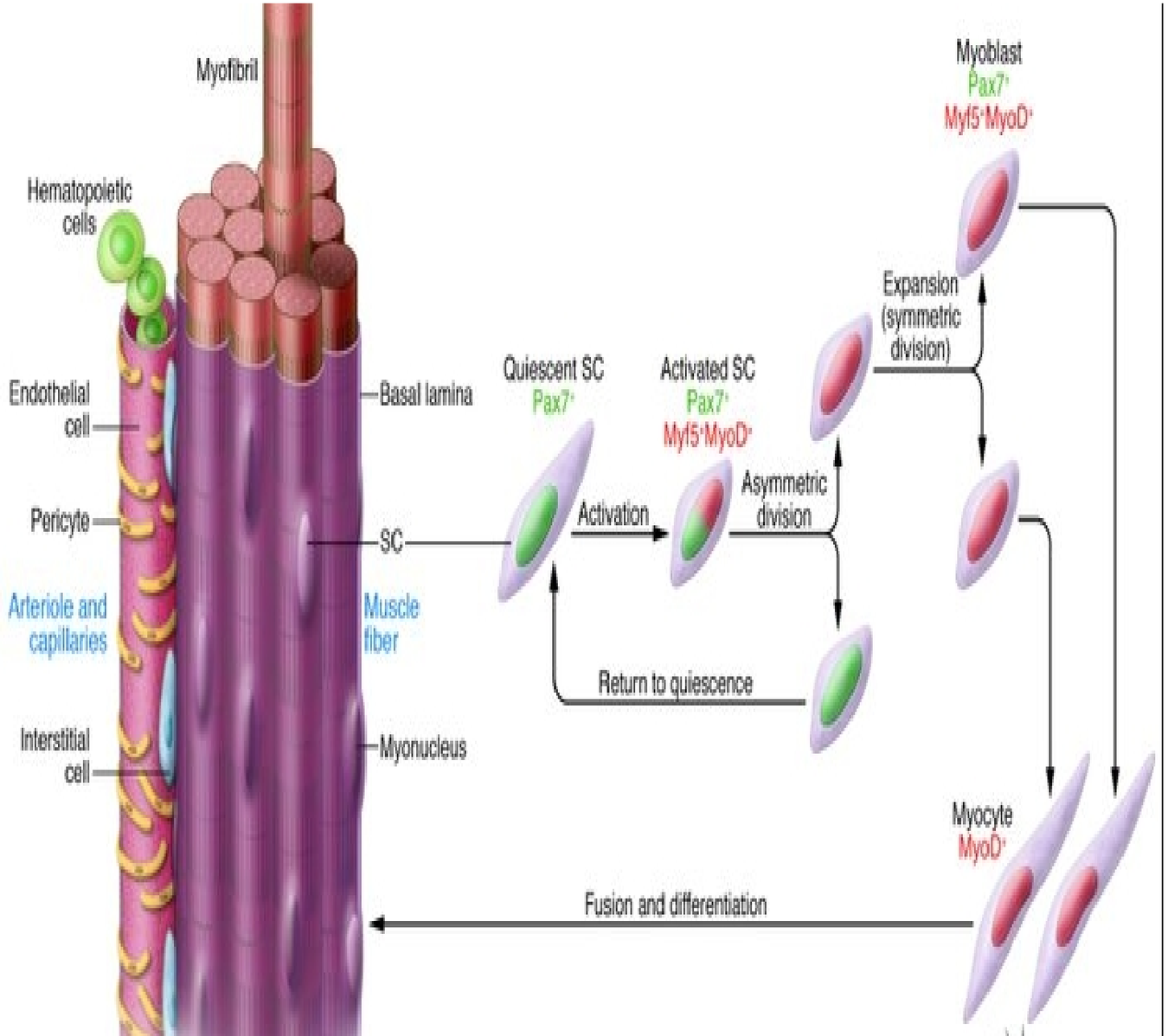
Activated satellite cell markers

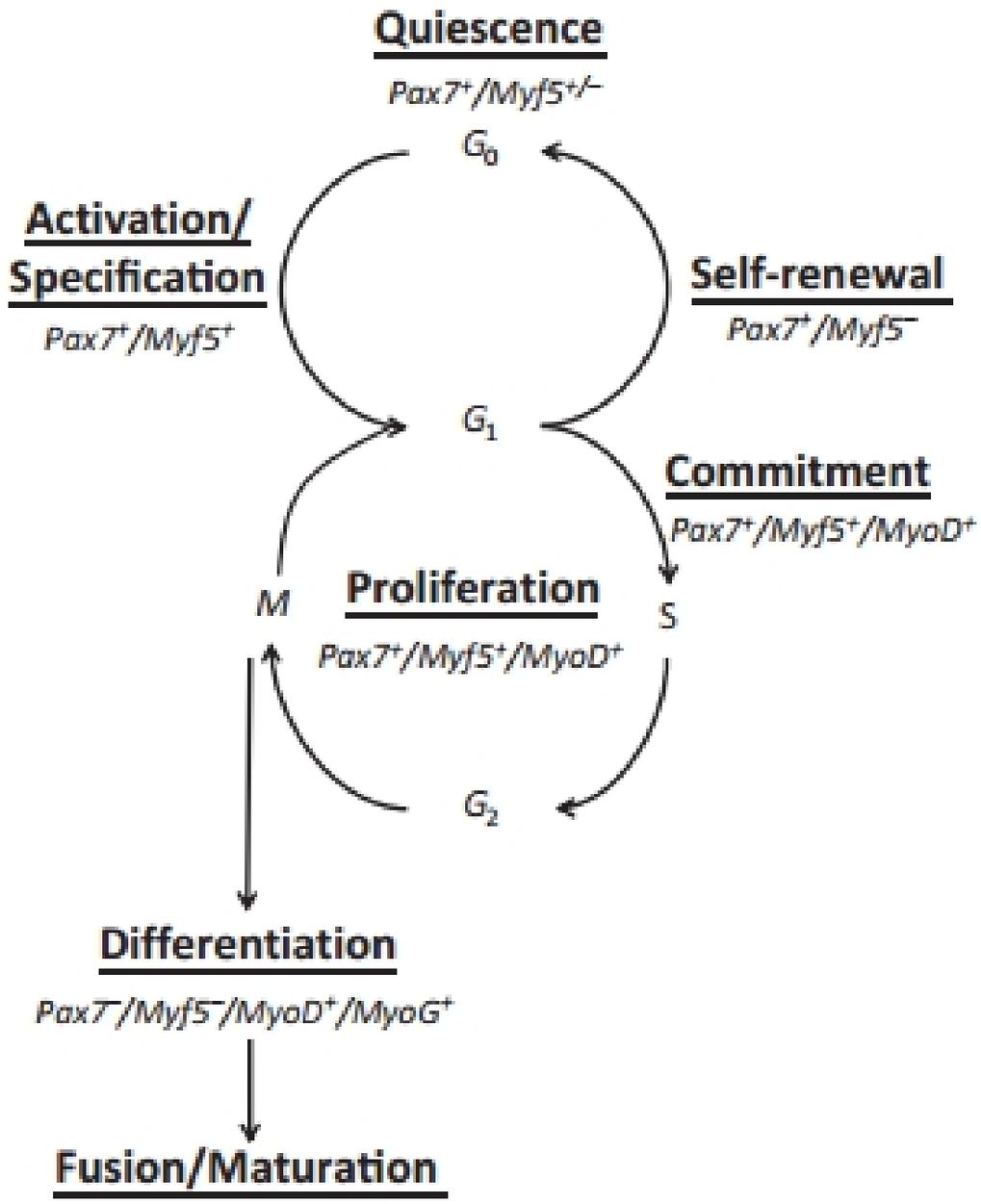
| Nuclear | Surface | |
|---|---|---|
| Pax7 | α7-integrin | M-cadherin |
| MyoD | caveolin 1 | syndecan 3/4 |
| emerin | Cxcr4 | V-CAM |
| lamin A/C | desmin | N-CAM |
| Ki67 | | |

# SM SC's: Paracrine & Cytokine Activation Markers

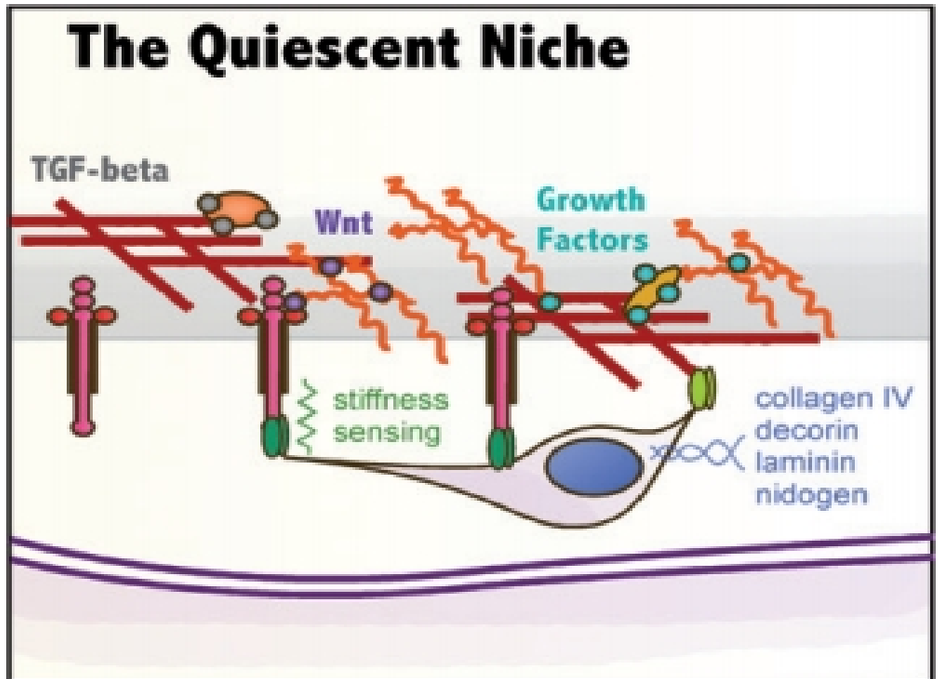


# SM: Satellite Cell Activation Cycle



# SM SC's: The Niche / Zone in Ageing & disease

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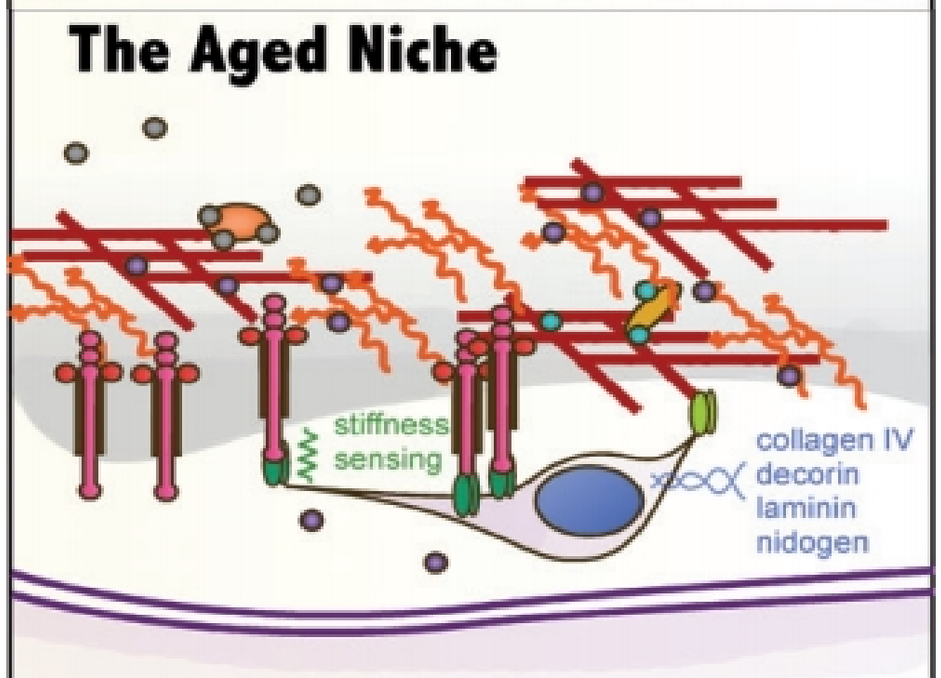
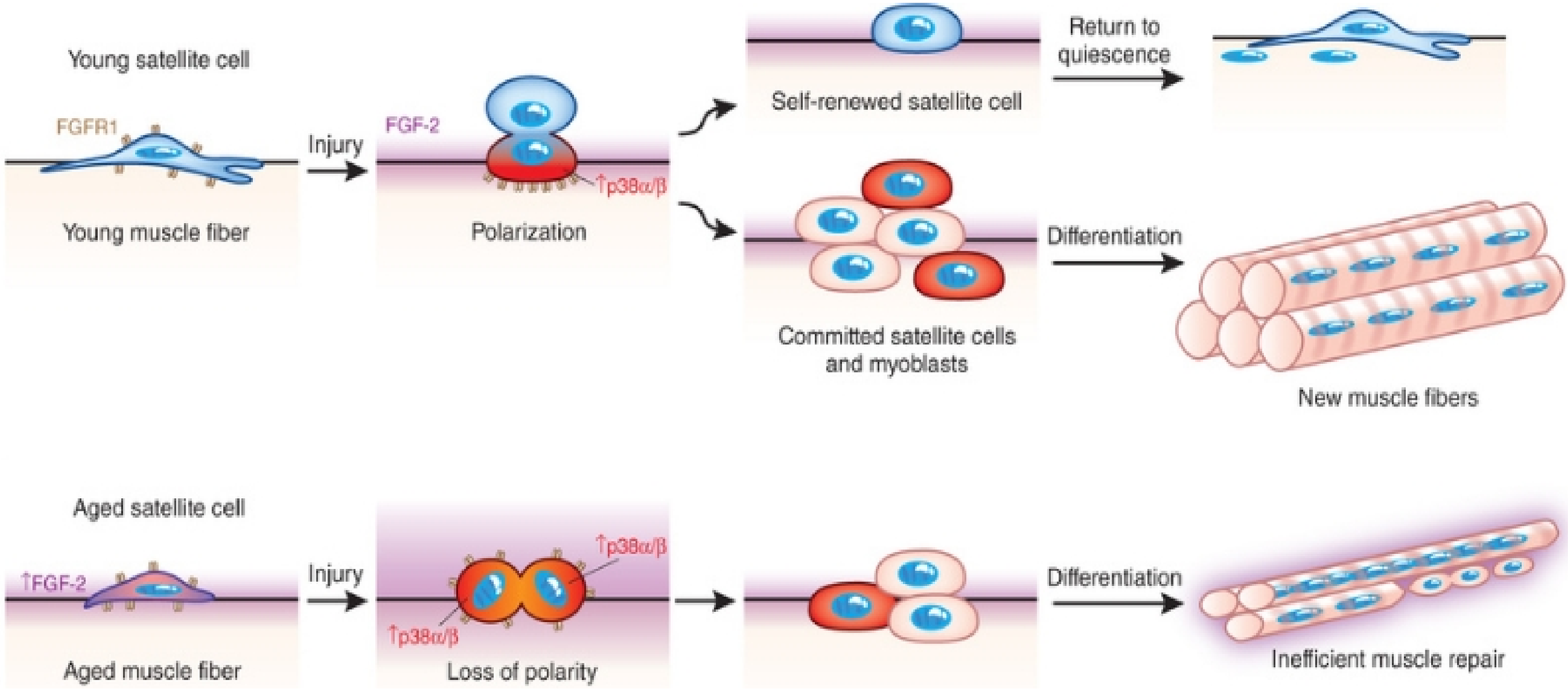
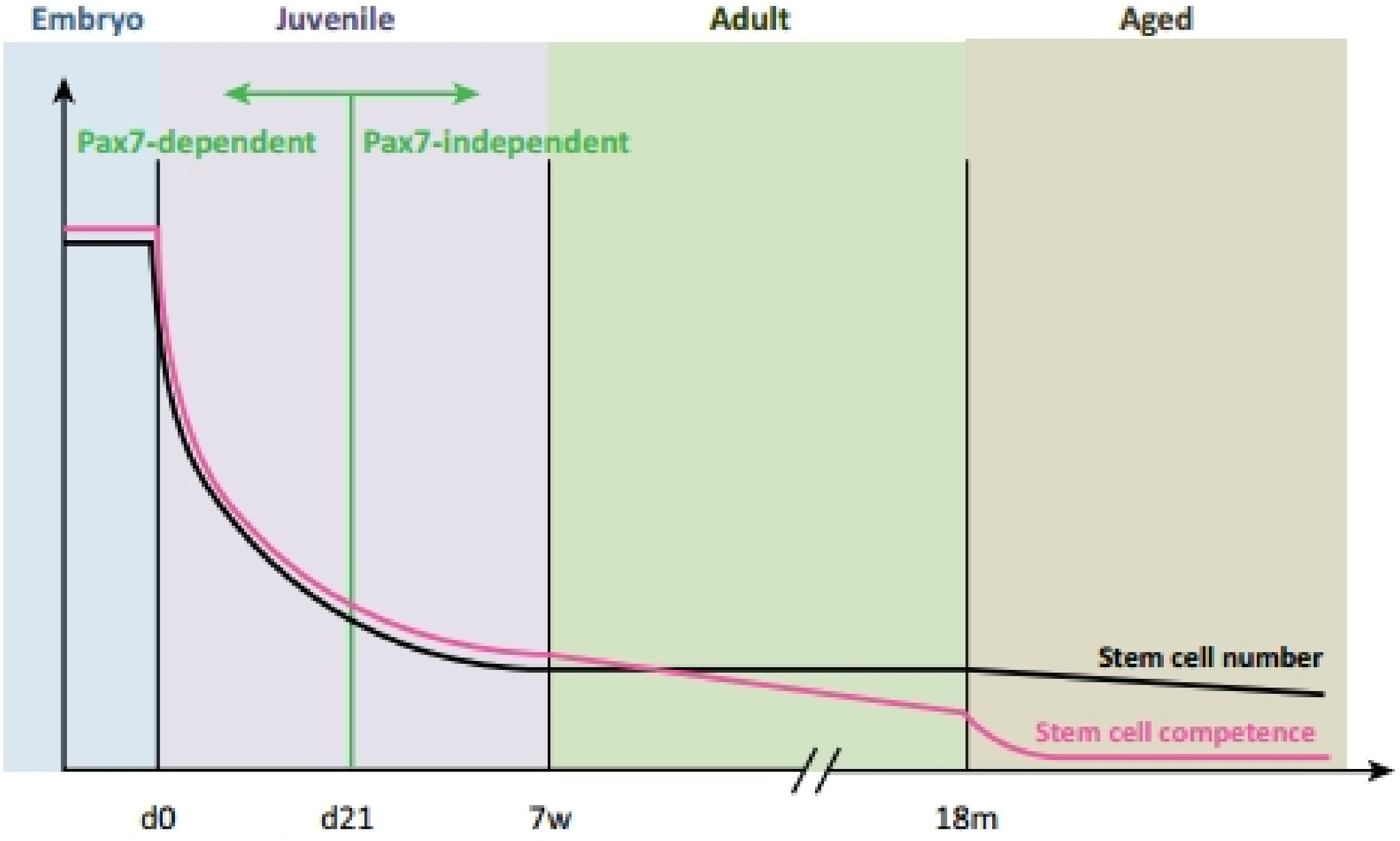



In the aged niche, matrix components accumulate to form a denser, thicker and amorphous basal lamina. The stiffness sensing and sequestration of signalling molecules may be affected by this change. The presence / storage of growth factors (ie. TGF-ß)and signalling molecules (ie. Wnt) are weakly expressed, augmenting the aberrant expression, proliferation, and activation of satellite cell.

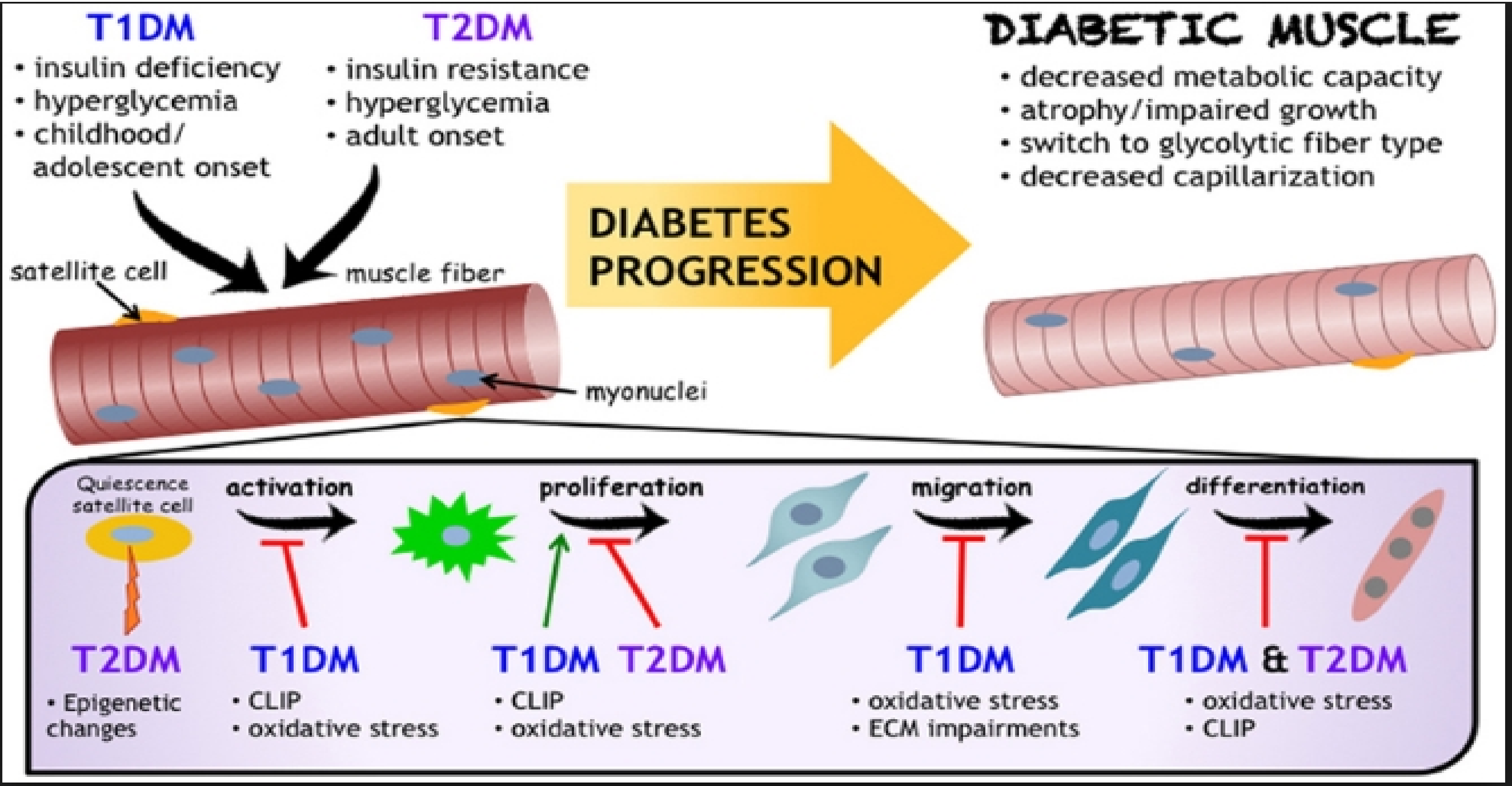
# SM SC's: In youth & ageing



# SM SC's: In youth & ageing



# SM SC's: In metabolic syndromes



# SM Injury & Issues In Sports

1. Commonly seen in sports (contusions – strains)
2. Repetitive training & competition – overuse
3. Sudden Increase in activity
4. Contact and non-contact injury
5. Psychological Stress
6. Prolonged Gluco-corticosteroid use (Type ll fiber syndrome)
7. Overuse of NSIAD's (delayed healing; pH disruptions)
8. Improper use of cyrotherapy (interferes with macrophages / IGF-1,.....)
9. Transcription signal mutation proteo & lysosome transcription pathology

# SM Issues In Ageing

## Sarcopenia

1. SM become smaller diameter
2. Less elasticity
3. Diminished satellite cell pool?
4. Niche environment compromised (structural irregularity ie. basal laminar thickening)
5. Strain tolerance diminishes
6. Recovery & regenerative capacity impaired
7. Muscle adiposity exchange
8. Metabolic aberrances

# SM: Disruptions to Remodelling

Leading to prolonged chronicity

Degeneration / sarcopenia

Disability

Depression

Socioeconomic stress

# Can we improve tissue resilience in sports & ageing?

# Sports Science & Medicine

| | Material & Method: Golf |
|---|---|
| Handed | Right (n=4) |
| Handicap Avg | 4.25 |
| Equipment | 6 iron |
| Baseline | 7 shots after 25 swing warm-up |
| Ball type | Actual match-play ball of individual preference |
| Measurement Inst. 1 | FlightScope™ (Golf Technologies) |
| Measurement Inst. 2 | Delsys wireless Trigno sEMG sensors (6 channel) |
| Muscles tested | Ant. delt.; pect. maj.; Upp. Trap (bilat); & lat dorsi (bilat) |


## Test Dates

March 3rd and May 5th 2015

## Flightscope Session Summary

### March 3rd

#### Summary

| | Distance (m) | | | Speed (mph) | | | Spin | | Ball Angle (°) | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Club | Carry | Total | Lateral | Club | Ball | Smash | (rpm) | Axis (°) | Launch Vert. | Launch Horz. | Descent | Height (m) | Flight (s) | Classification | Rating |
| 6-Iron | 101 | 113 | 0.9 R | 64.0 | 89.5 | 1.40 | 4863 | 7.7 L | 18.5 | 1.6 R | 36.1 | 14 | 4.2 | draw | |

Rated by total distance

### May 5th

#### Summary

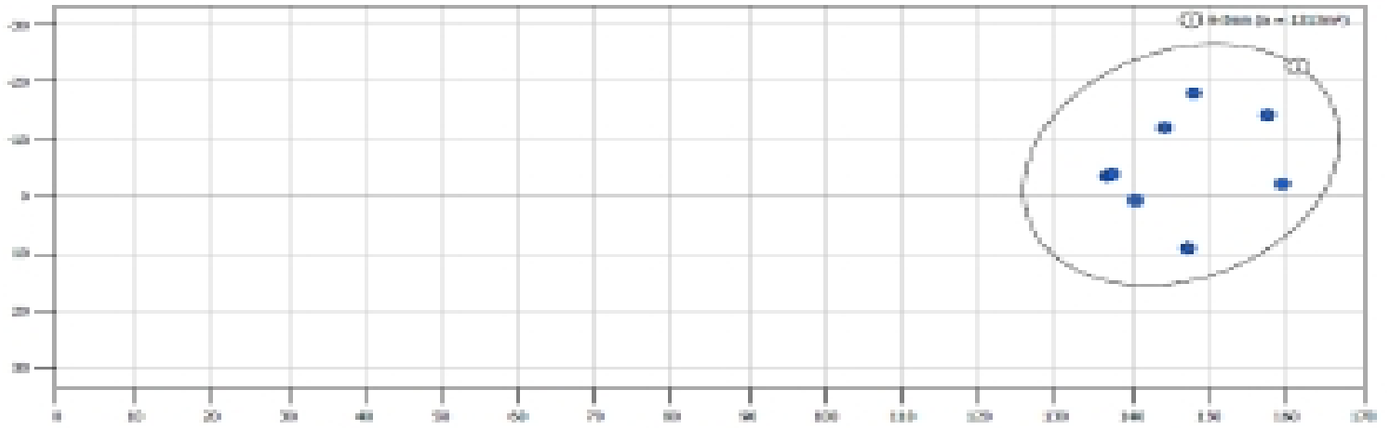
| | Distance (m) | | | Speed (mph) | | | Spin | | Ball Angle (°) | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Club | Carry | Total | Lateral | Club | Ball | Smash | (rpm) | Axis (°) | Launch Vert. | Launch Horz. | Descent | Height (m) | Flight (s) | Classification | Rating |
| 6-Iron | 104 | 126 | 3.7 L | 66.5 | 92.7 | 1.40 | 4047 | 11.0 L | 16.7 | 0.7 L | 31.5 | 12 | 3.9 | draw | |

Rated by total distance

## Grouping

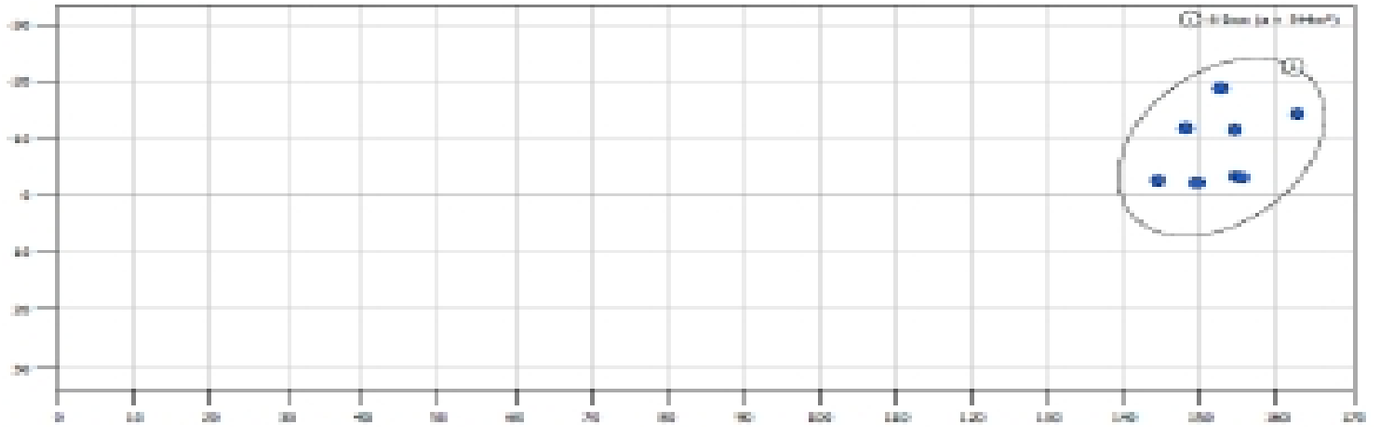
### March 3rd Grouping

Grouping



### May 5th

Grouping



From the grouping comparison, May the 5th appears better, the shots are consistently grouped on one side of the target line. When playing golf this would mean that you would know that you can aim at a certain point and not be right of that, potentially cutting out the risk of getting into trouble on the right. More shots are grouped along the target line.

# Overall Result: Golf Project

| Golf Data (mean avgs.) @ wk12 | Baseline | Post-ESWT | % of change |
|---|---|---|---|
| Swing speed | 140.21 km/h | 147.12 km/h | +10.49% |
| Club interface (Smash factor) | 1.32 m/sec | 1.46 m/sec | +11.06% |
| Ball distance | 143.25m | 167.40m | +11.6% |
| Muscle activation onset | 1.35 sec | 0.89 sec | |
| Energy output throughout the swing | 497.44üv/swing | 573.93üv/swing | +8.46% |

| | Material & Method: Weightlifting |
|---|---|
| Gender | Male (n=4) |
| Lift protocol | 120kg loaded back squat |
| # of Reps | 5 Loaded squats |
| Measurement Inst | Delsys wireless Trigno™ sEMG sensors |
| Measurement 2 | Current Personal Best lift |
| Tabulation Software | EMG Works version 4.1.7 |
| Muscles tested | Lats; bicep-fem; gastrocs |

# Overall Result: Weightlifting Project

| Weightlifting Data (mean avgs) @wk12 | Baseline | Post-ESWT | % of change |
|---|---|---|---|
| Muscle activation onset | 1.02 sec | 0.92 sec | |
| Energy output throughout the lift | 5394.36üv/squ | 4,043.03üv/squ** | 33.45% |
| Personal Best | 655kgs | 738kgs | +11.2% |

# Soccer Medicine Conference: Case Study

**Subject profile:**
16 yr old, Male: Right footed National U-17 level Centre Back
Weight:76kg;  Height: 180cm

**History & Nature of Complaint:** (Our 1st Consult – Week 14)
- Right proximal hamstring strain
- Symptomatic with running & kicking
- 15 week unresolved with progression of severity & disability
- Sidelined – unable to participate in training and match play

**Potential Consequence:**
Missing National U-17 selection in 5 weeks

Proximal Hamstring Injury:
- Commonly seen injury
- Lethargic healing
- Symptomatic persistence
- High recurrence
- Recurrence (often increased severity)

# Soccer Medicine Conference: Case Study

Baseline & Post-ESWT Assessment (Wk 3 & Wk 24):

Bilateral musculature circumference measurement: Mid thigh region

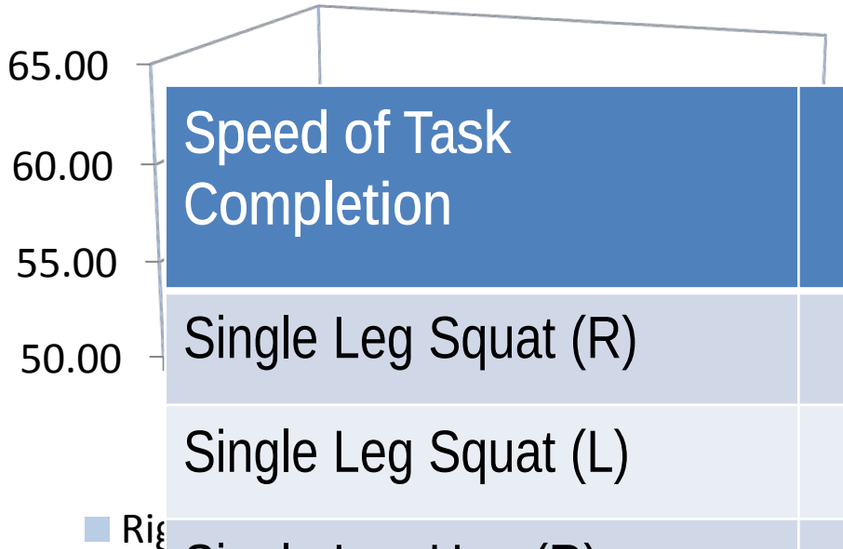
Hamstring range of motion

Subjective pain scale (VAS)

ViMove protocol measuring varus and valgus angles (Baseline & Wk. 24)

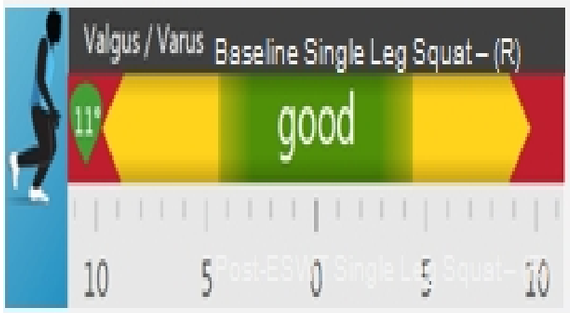
- 5 repetitions – bilateral single leg hops
- 5 repetitions – bilateral single leg squats

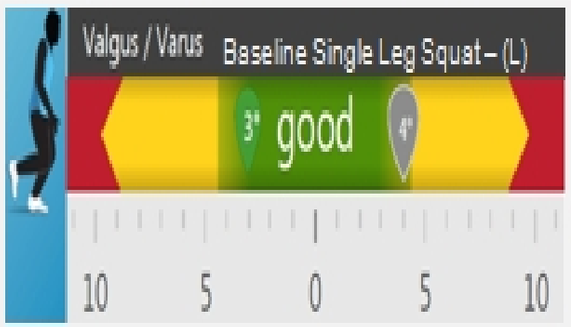
# Soccer Medicine Conference: Case Study Result

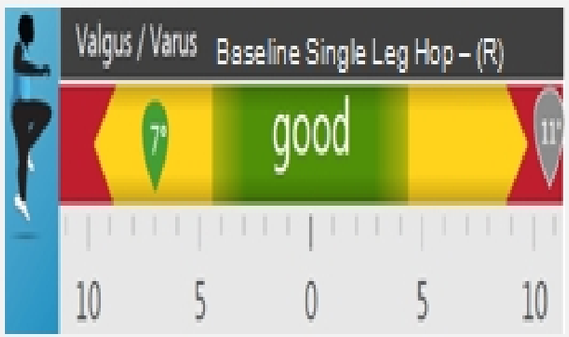


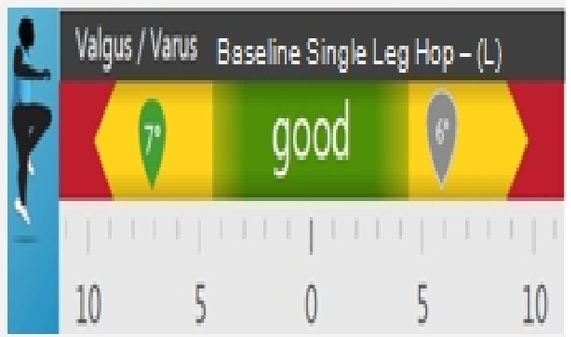

| Speed of Task Completion | Baseline | Week 24 |
|---|---|---|
| Single Leg Squat (R) | UC* | 14.02 sec |
| Single Leg Squat (L) | 16.47 sec. | 14.03 sec |
| Single Leg Hop (R) | UC* | 23.33 sec |
| Single Leg Hop (L) | 26.09 sec | 23.26 sec |

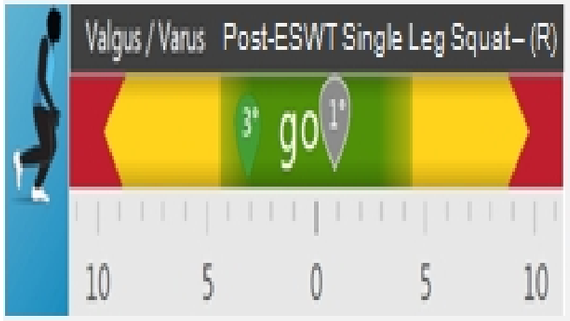
# Soccer Medicine Conference: Case Study Result

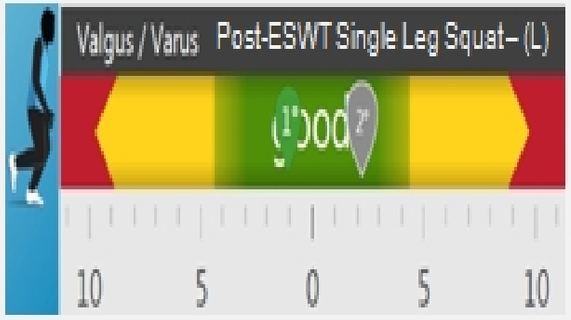


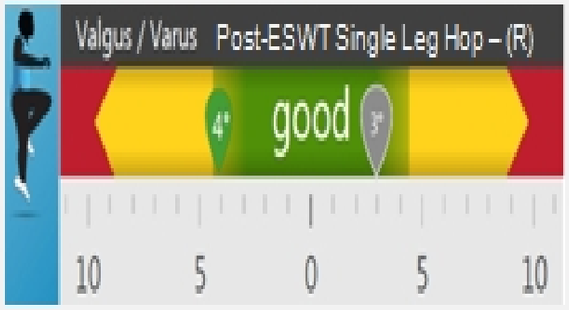



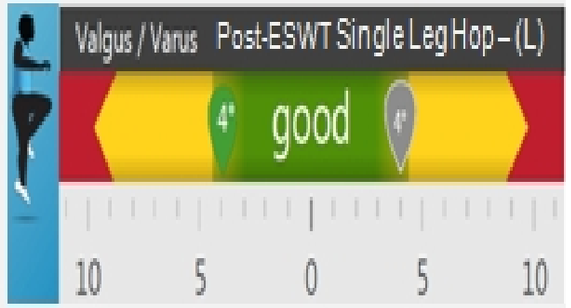



# Project in the Older Adult

| No. Of Subjects | Gender | Mean Age | General Health | Activity Level |
|---|---|---|---|---|
| 6 | Male n=3<br>Female n=3 | 61.62 (oldest 72 / youngest 58) | In general good health.<br>T2DMDiabetic (3)*<br>Hypertension (1)*<br><br>*on pharmacogenics | All active |

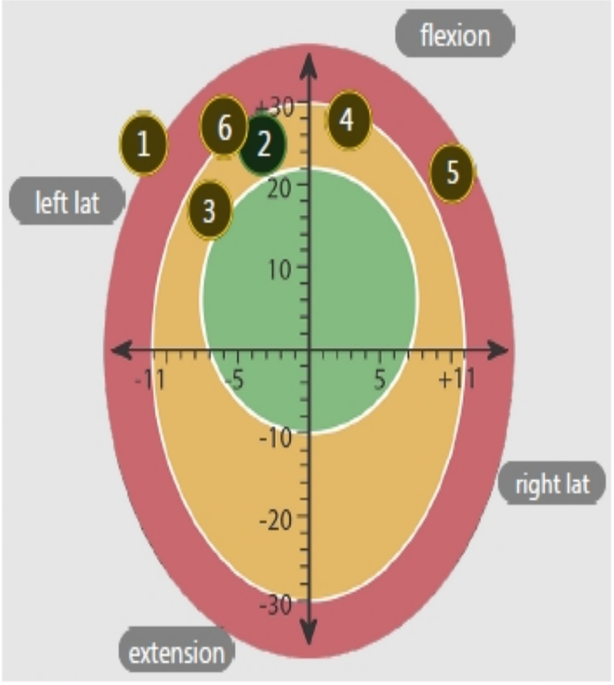
Aging / Sarcopenia Project Pre ESWT

ViMove
Kompass Health Associates

Assessment Date: NOV 11 2015

## Functional Live Assessment

Hurdle Step




**Score**

**86**

| Flexion | |
|---|---|
| L | R |
| 26° | 27° |

| Lateral | |
|---|---|
| L | R |
| -7° | 7° |

Rep Movement Patterns

Aging / Sarcopenia Project Post ESWT

ViMove
Kompass Health Associates

Assessment Date: Jan 14 2016

## Functional Live Assessment

Hurdle Step


**Score**

**53**

| Flexion | |
|---|---|
| L | R |
| 7° | 8° |

| Lateral | |
|---|---|
| L | R |
| -3° | 3° |

Rep Movement Patterns

ViMove

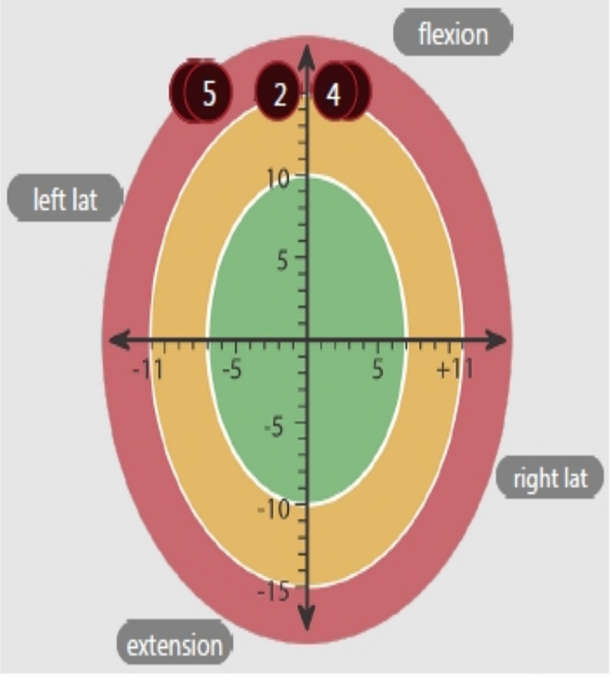
Aging / Sarcopenia Project Pre ESWT

Kompass Health Associates

Assessment Date: Nov 11 2015

## Functional Live Assessment

Inline Lunge




**Score**

**82**

| Flexion | |
|---|---|
| L | R |
| 27° | 29° |

| Lateral | |
|---|---|
| L | R |
| -5° | 4° |

Rep Movement Patterns

ViMove

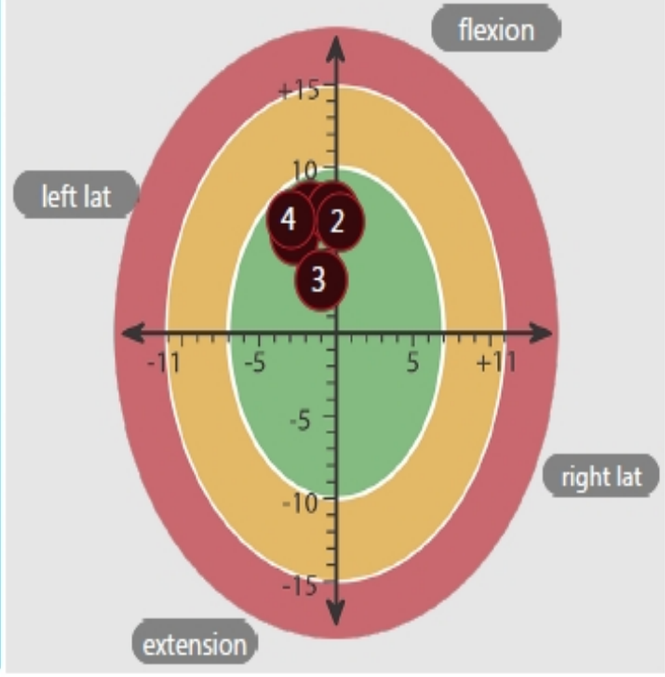
Aging / Sarcopenia Project Post ESWT

Kompass Health Associates

Assessment Date: Jan 14 2016

## Functional Live Assessment

Inline Lunge




**Score**

**46**

| Flexion | |
|---|---|
| L | R |
| 4° | 3° |

| Lateral | |
|---|---|
| L | R |
| 2° | 1° |

Rep Movement Patterns

| Test | Baseline | Post Intervention |
|---|---|---|
| DorsaVi Move | | |
| Hurdle Step | 86 | 53 |
| Inline Lunge | 82 | 46 |
| Stand from Sit | 1.08ec | 0.775sec |
| Weight | 424kgs | 433kgs |
| | | |
| Co-finding (Glycaemic Control) | | |
| Subject #1 67yr Male T2DM | Fast: 141dl / PostPara:195dl | Fast: 133dl / PostPara: 162dl |
| Subject #2 63yr Male T2DM | Fast: 144dl / Post Para: 198dl | Fast :136dl / PostPara: 170dl |
| Subject#3 69yr Male T2DM | Fast: 155dl / PostPara: 193dl | Fast:136dl / PostPara: 178dl |
| | | |
| *Note: T2DM Subjects on Metformin and insulin comb. | | **Lean muscle mass increases approx. 1.8 – 2.2kgs |

# Summary

Acoustic wave stimulus are seen to:

- Promote tissue regeneration (aberrance rectification)
- Increase tissue resilience – growth facilitation and fatigue resistance
- Improve muscle tone and postural stability
- Similar outcomes seen in both young athletic and older subjects
- In the athletic population, these outcome potentially increases career longevity
- To sports institutions, these outcomes could provide investment security against overuse injuries.
- In the ageing population, these outcomes suggest that they could hold a pertinent key to:
  - sarcopenia
  - falls prevention
  - improved quality of live

# Summary: Proposed Mechanism of Action

Contents lists available at ScienceDirect

International Journal of Surgery

journal homepage: www.journal-surgery.net

Review

## Shock wave as biological therapeutic tool: From mechanical stimulation to recovery and healing, through mechanotransduction

M.C. d'Agostino [a,*], K. Craig [b], E. Tibalt [a], S. Respizzi [a]

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[b] Kompass Health Associates, Auckland, New Zealand

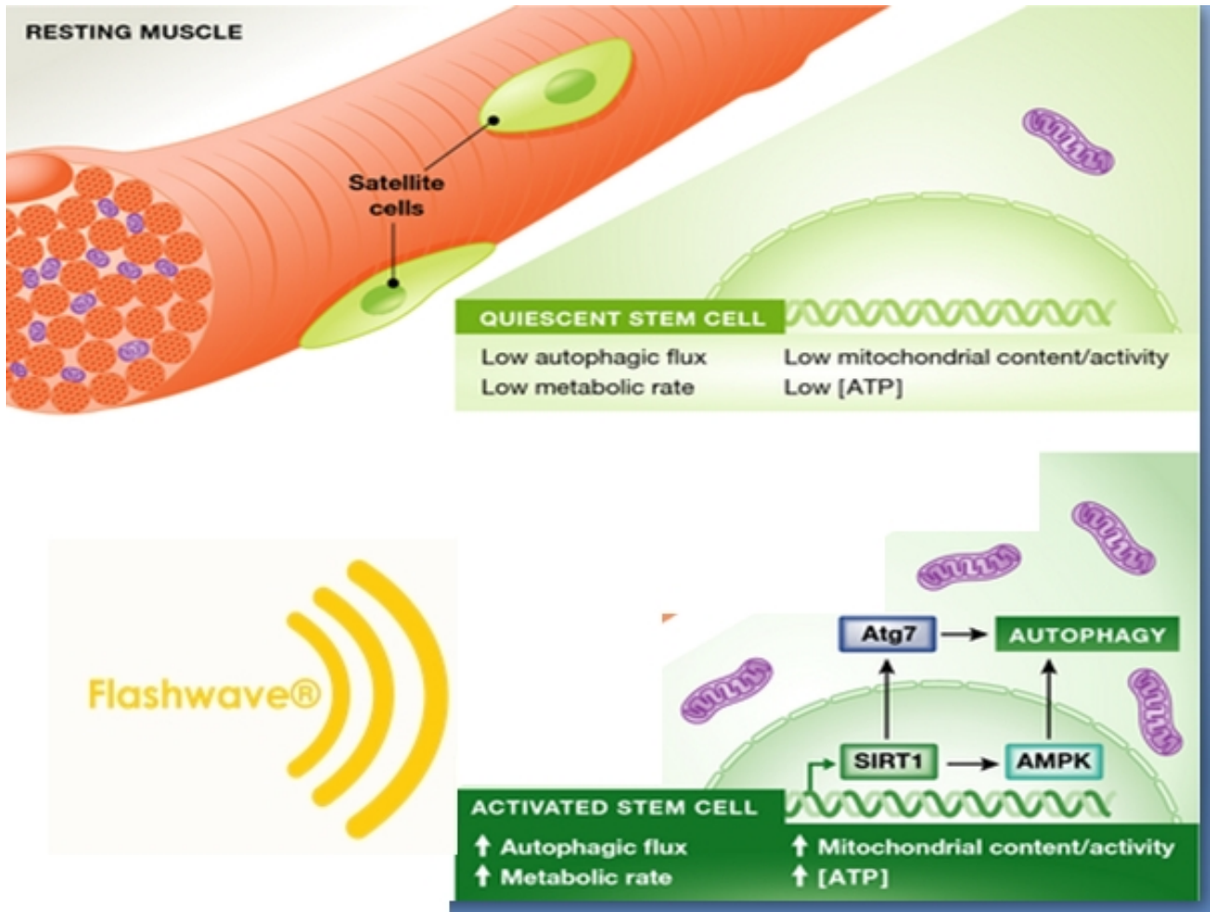
### HIGHLIGHTS

- SW represents a revolutionary form of mechanotherapy (acustic stimulation).
- Unlike urological lithotripsy (mechanical model), on living tissues, SW exert an anti-inflammatory action and pro-angiogenic and regenerative effects as well (biological model).
- Mechanotrasduction pathways sustain their clinical and experimental results.
- We present a summary of current knowledge of SW mechanisms of action, according to main recent data (mechanobiology).
- Better comprehension of SW mechanobiology could led to new therapeutical perspectives.

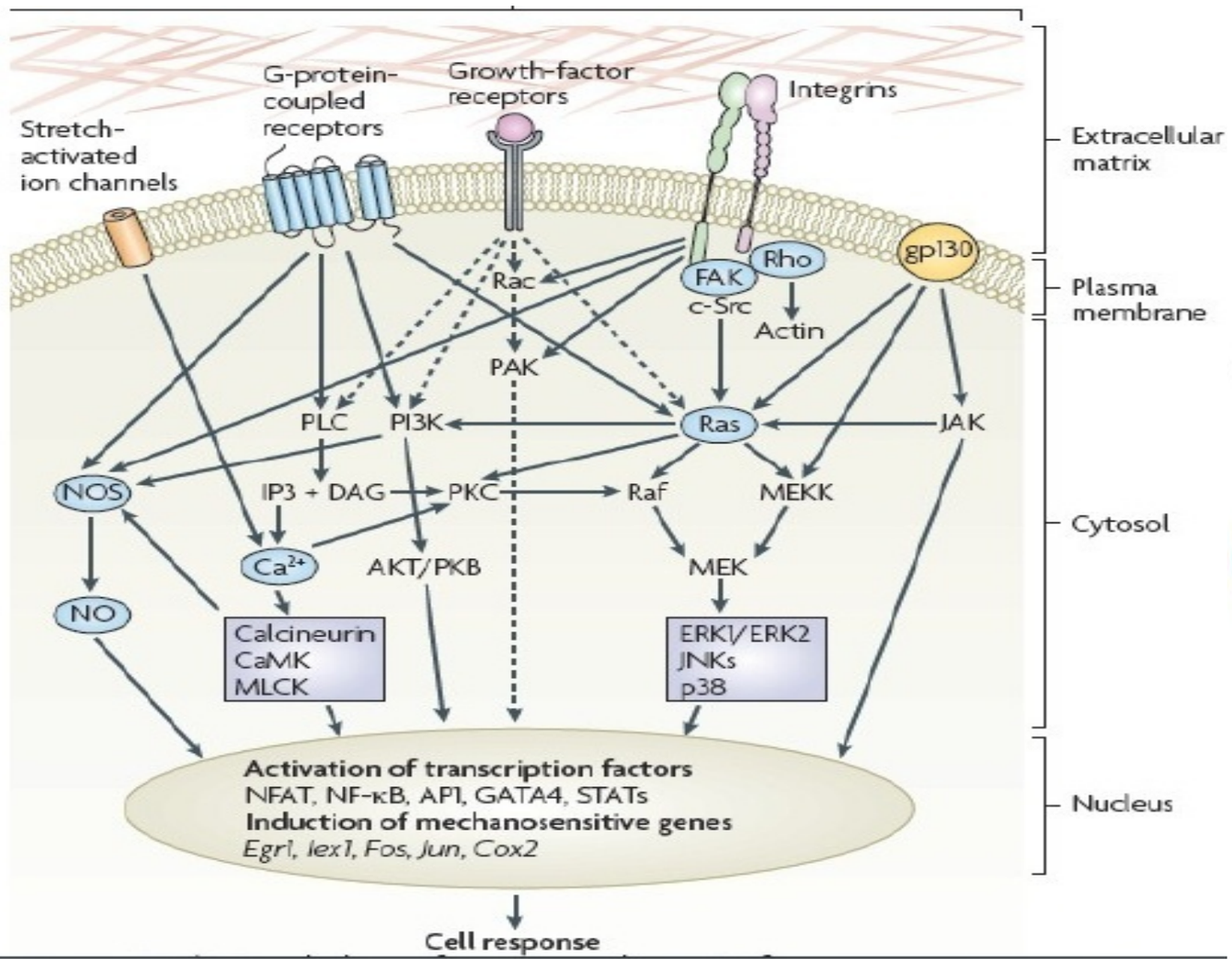
# Summary: Proposed Mechanism of Action

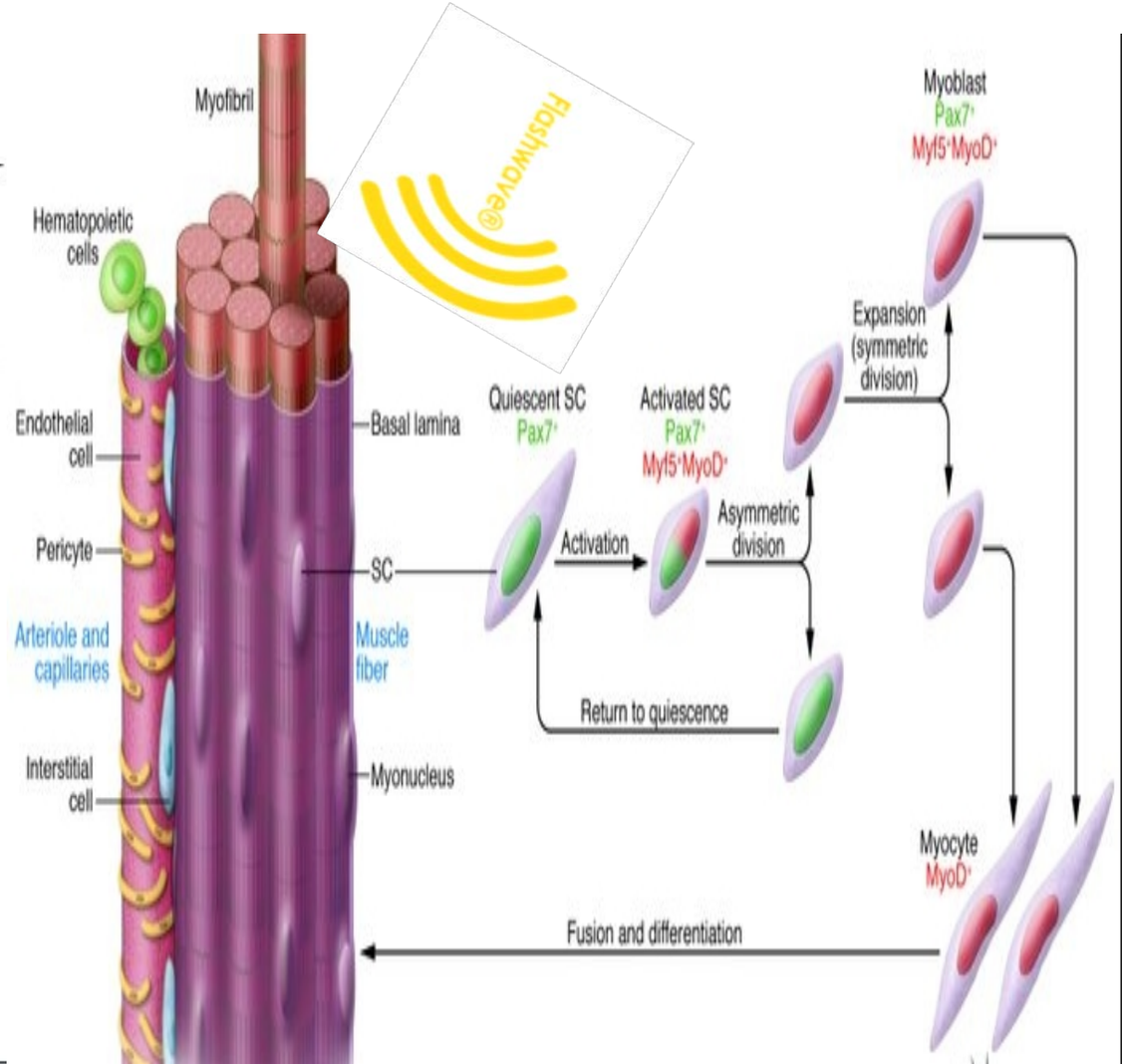
The acoustic stimulus is known to:

- Trigger a biocellular cascade in a process termed ‘bio cellular transduction’
- The cellular sensing occurs between the ECM & intra-cellular matrix; influencing
  - angiogenic factors
  - ion channels
  - integrins / cadherins
  - growth factor receptors
  - myosin motor
  - cytoskeleton filaments
  - improved micro and regional circulation
  - modulation of inflammation
  - regulation of immune factors
  - stem cell activation



# Summary: Proposed Mechanism of Action



# Summary: Proposed Mechanism of Action

The influence of Flashwave on tissue allows for:

- Tissue regeneration and repair
- Improved tissue resilience
- Functional recovery
- Functional optimisation


# Future Applications??

Muscular Dystrophies / myopathies?

- Duchenne’s
- Miyoshi’s
- TIDM Myotonic MD
- Pharyngeal MD
- Metabolic correction in T2DM

Wisdom’s Invitation: *Jer. 33:3*

“Call to Me, and I will answer you,
I will show you great and unsearchable things
that you do not yet know”

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# Thank you