

Historical Perspectives on the Science of Satellite Cells

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SATELLITE CELL OF SKELETAL MUSCLE FIBERS

ALEXANDER MAURO. From The Rockefeller Institute

In the course of an electron microscopic study of the peripheral region of the skeletal muscle fiber of the frog, the presence of certain cells, intimately associated with the muscle fiber, have been observed which we have chosen to call *satellite cells*. Since these cells have not been reported previously and indeed might be of interest to students of muscle histology and furthermore, as we shall suggest, might be pertinent to the vexing problem of skeletal muscle regeneration, a brief communication describing this finding is warranted prior to a more detailed study.

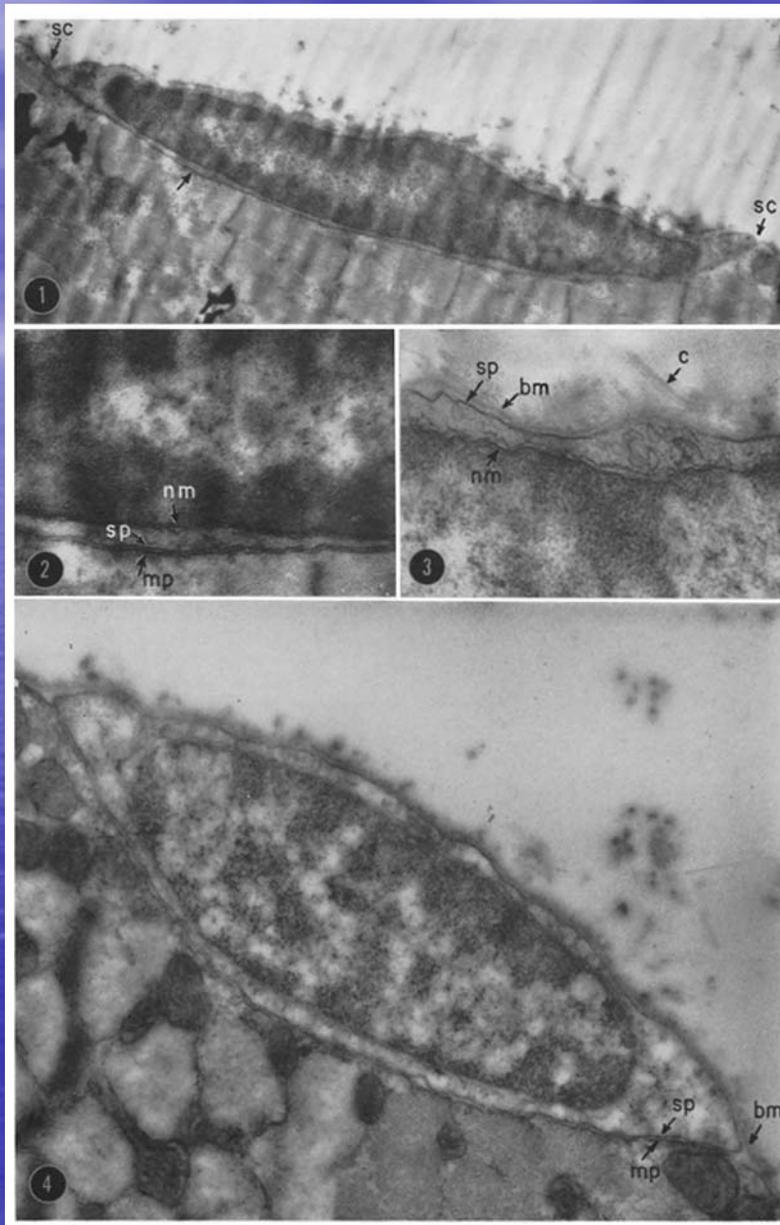
The observations reported here have been made on bundles of fibers dissected from the tibialis anticus muscle of the frog. The material

is that the peripheral muscle nuclei proper occur much more frequently than the satellite cells.

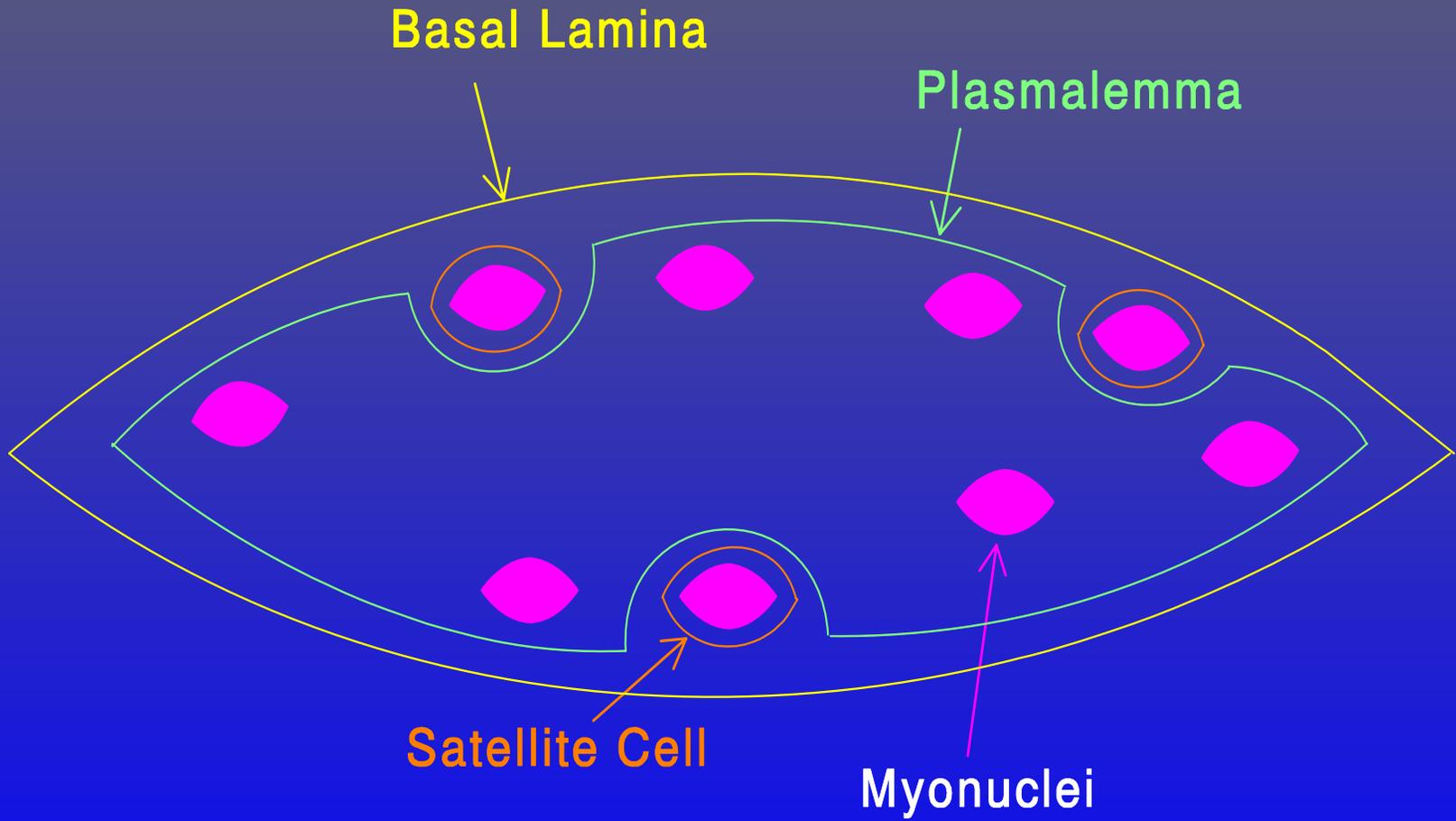
It is interesting that upon alerting other investigators to these findings, similar cells have been found in electron micrographs of two other muscles of the frog, namely sartorius (2) and ileofibularis (3), and of the sartorius and tongue muscle of the white rat (4). (Though the direct evidence is restricted to these two vertebrates, it seems reasonable to hazard a guess that skeletal muscle fibers of vertebrates in general contain satellite cells.)

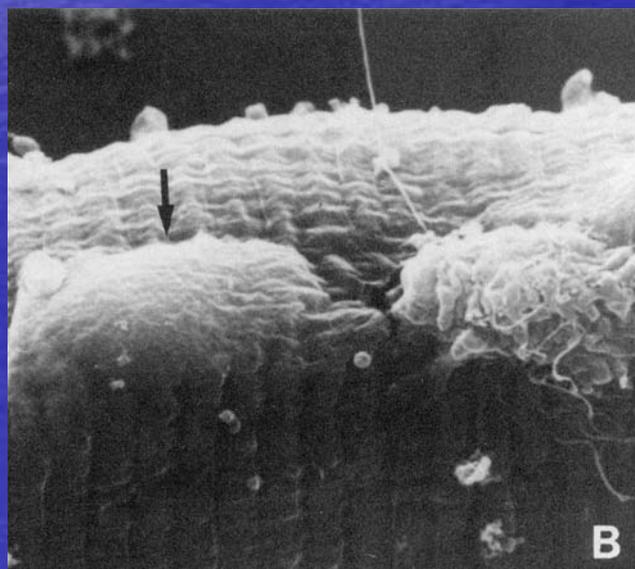
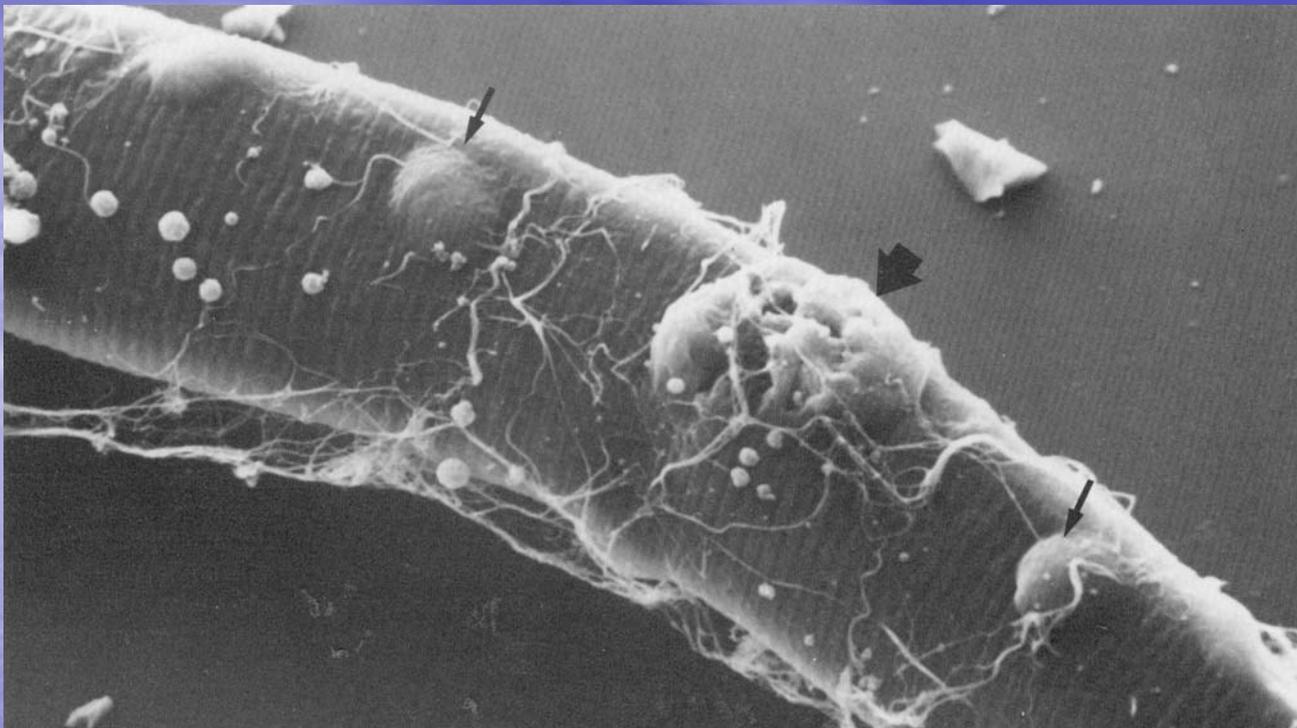
It is tempting to speculate about the origin and the role of the satellite cells. Before stating the several possible hypotheses that have figured in

Journal of Cell Biology 9:493-495 (1961)



A. Mauro, Journal of Cell Biology 9:493-495 (1961)





Function?

Regeneration of traumatized muscle?

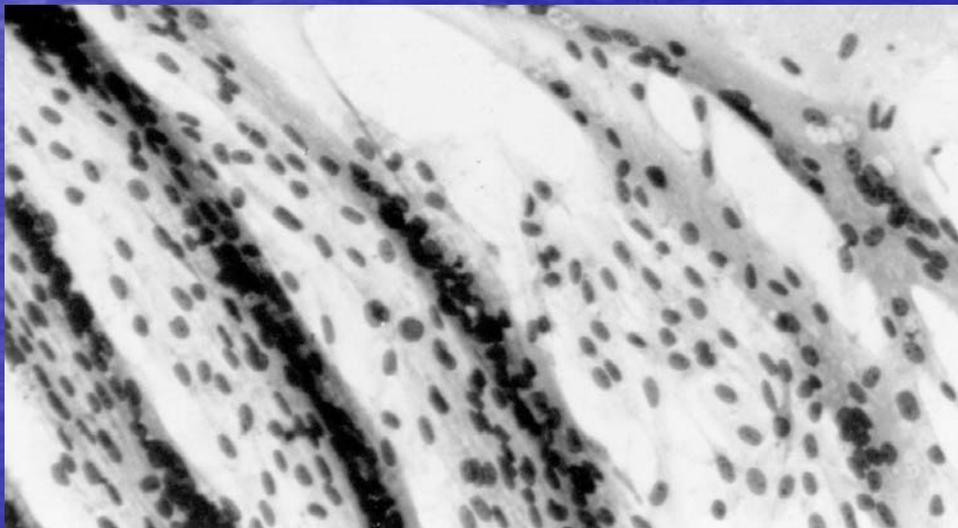
Increased proliferation due to trauma?

Stockdale F E; Holtzer H. 1961. DNA Synthesis and Myogenesis. *Exper. Cell Res.* 24:508-520.

Are nuclei within the fiber capable of DNA synthesis?

Incorporation of ^3H -thymidine into proliferating cells, but not myonuclei

Only myotubes synthesized myosin, meromyosins, actin



Smith (1963)

Cell (fiber) numbers increase prior to hatch

Cell numbers fixed following hatch

∴ Post-hatch development is due to ↑ cell size

At hatch, meat breed has ↑ number + slightly smaller fiber diameter compared to layer breed

At 10 wks ↑ fiber diameter in meat breed

Cell size/diameter has greatest influence on muscle size

Moss (1968a)

~ Constant ratio of fiber xs area and DNA content
∴ During growth fiber diameter ↑ in proportion to cell division

Moss et al. (1964)

Linear relationship between log of muscle wt and nuclei number

Moss (1968b)

Starvation causes ↓ muscle wt. and xs area of fibers with no loss of nuclei

Moss and Leblond (1971)

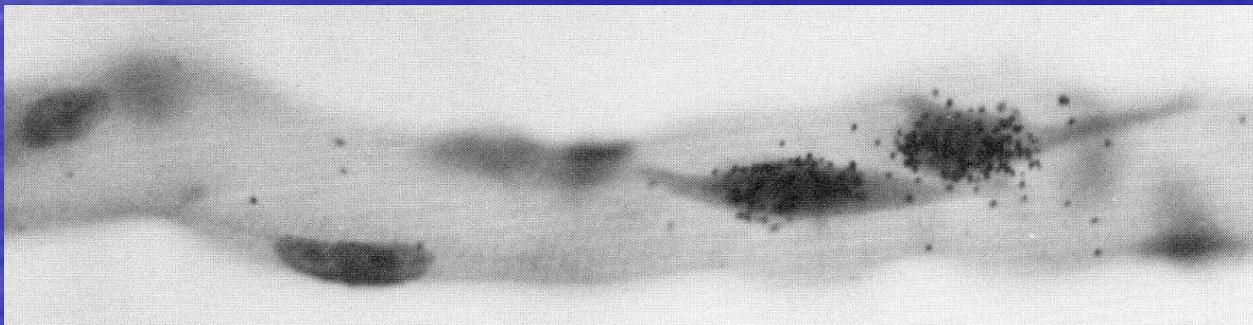
^3H -thymidine first incorporated into satellite cells,
none in myonuclei

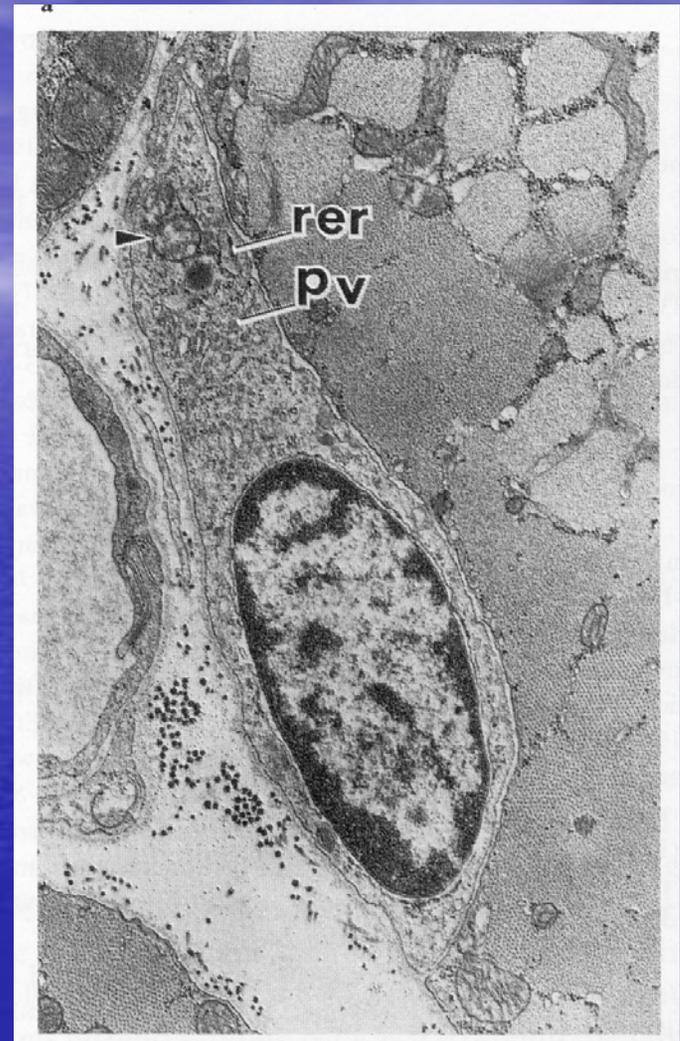
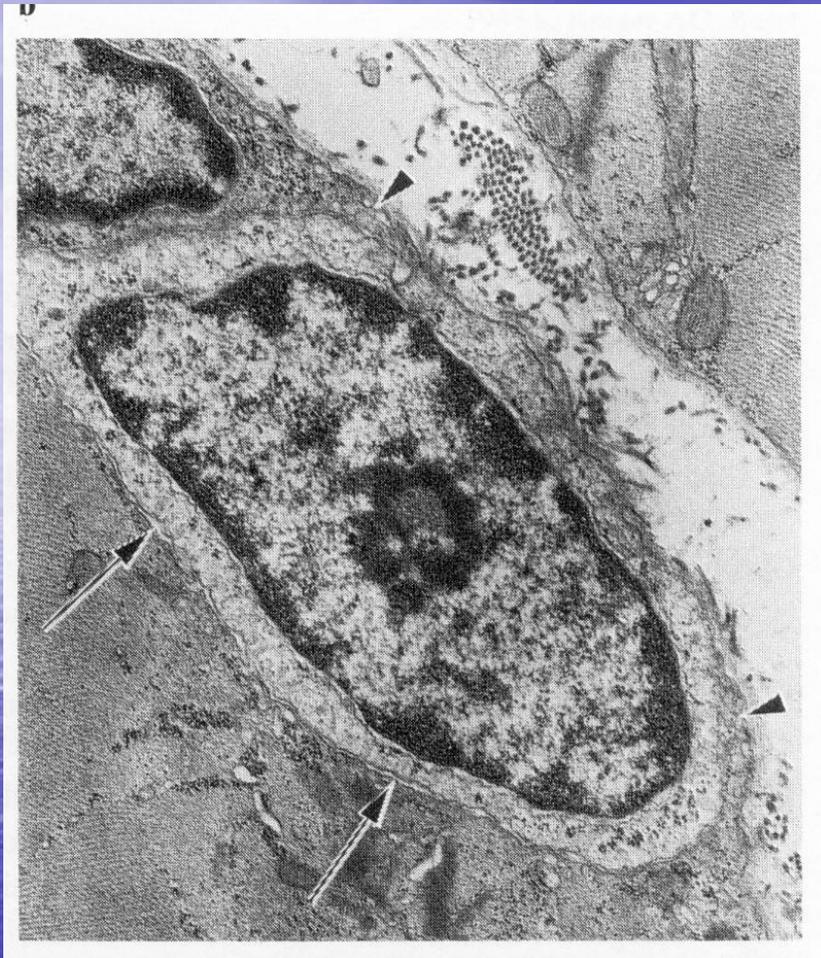
24 hr later: 2X the number of satellite cells labeled

$\frac{1}{2}$ the labeled nuclei incorporated into fibers

repeated

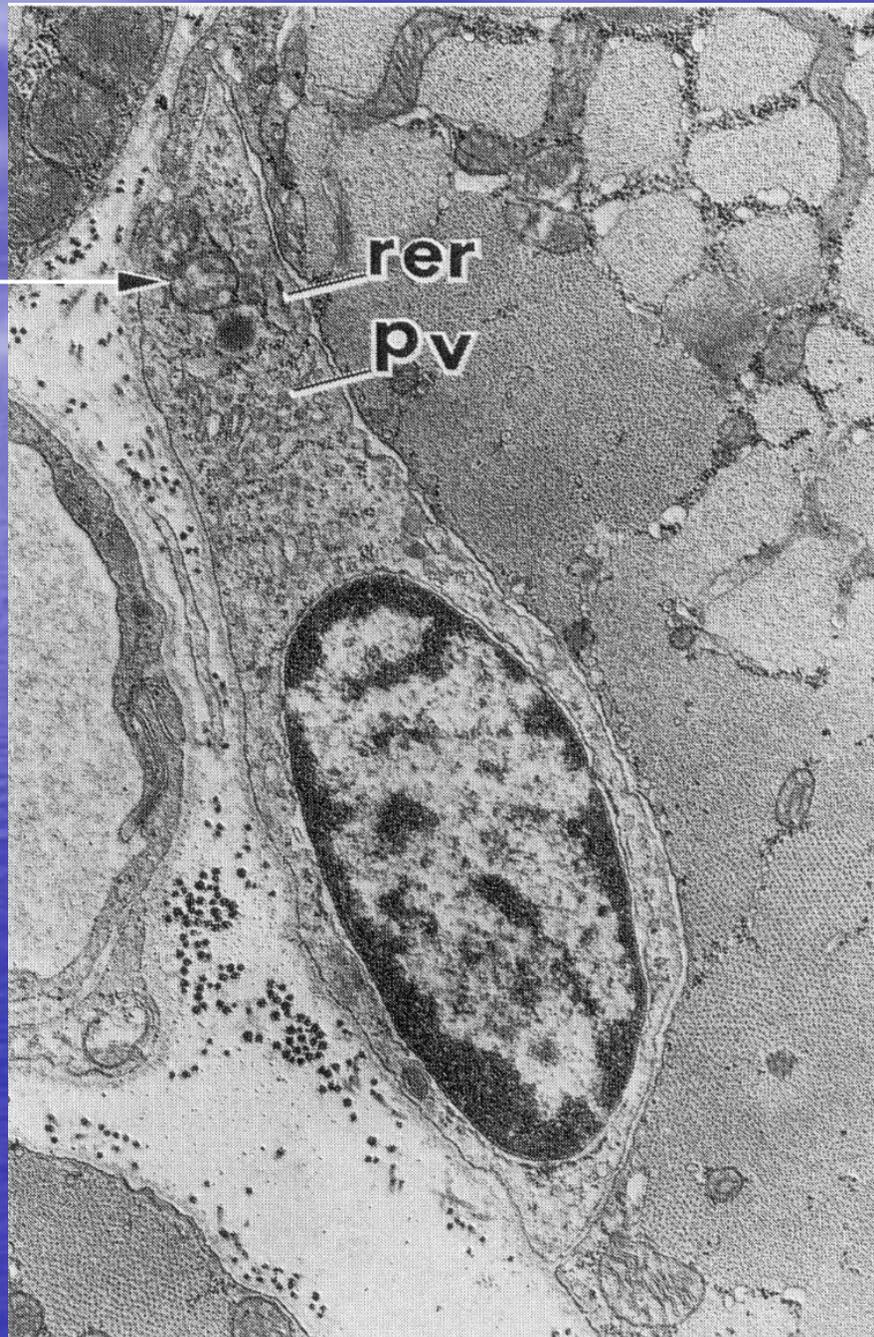
\therefore satellite cells primary source of postnatal muscle
nuclei





Campion, McCusker, Richardson. 1987. *Acta anatomica* 128:67-70

mitochondrion



Campion et al., 1987.
Acta anat. 128:67-70

Higher proportion active satellite cells during growth vs. adult

Adult satellite cells are mostly quiescent, but may be induced to divide and differentiate

Satellite cells from old animals have reduced proliferative potential

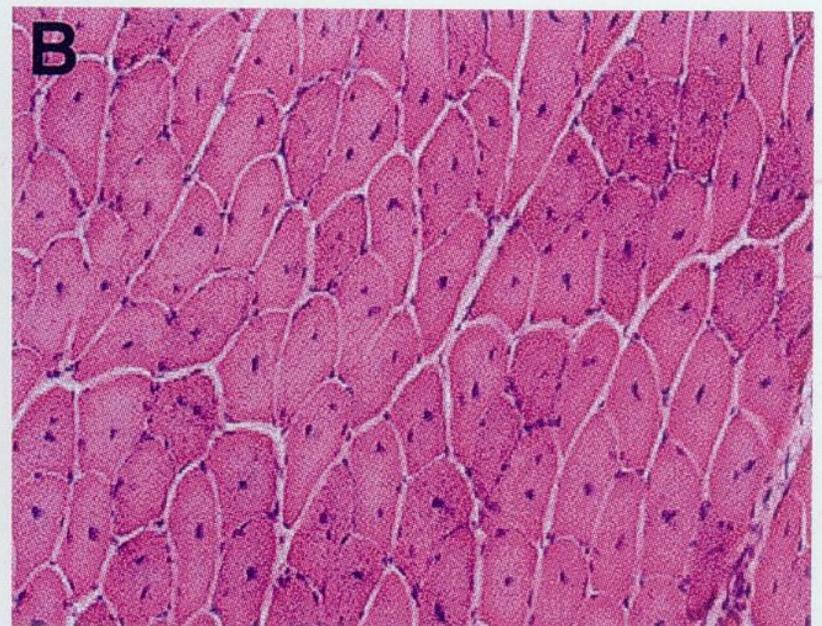
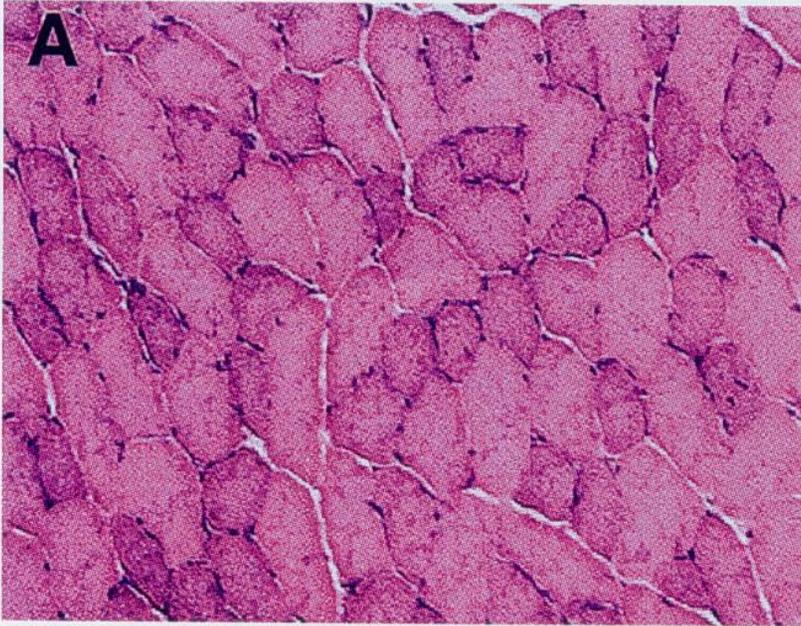
Repair following trauma



3 days following fiber death



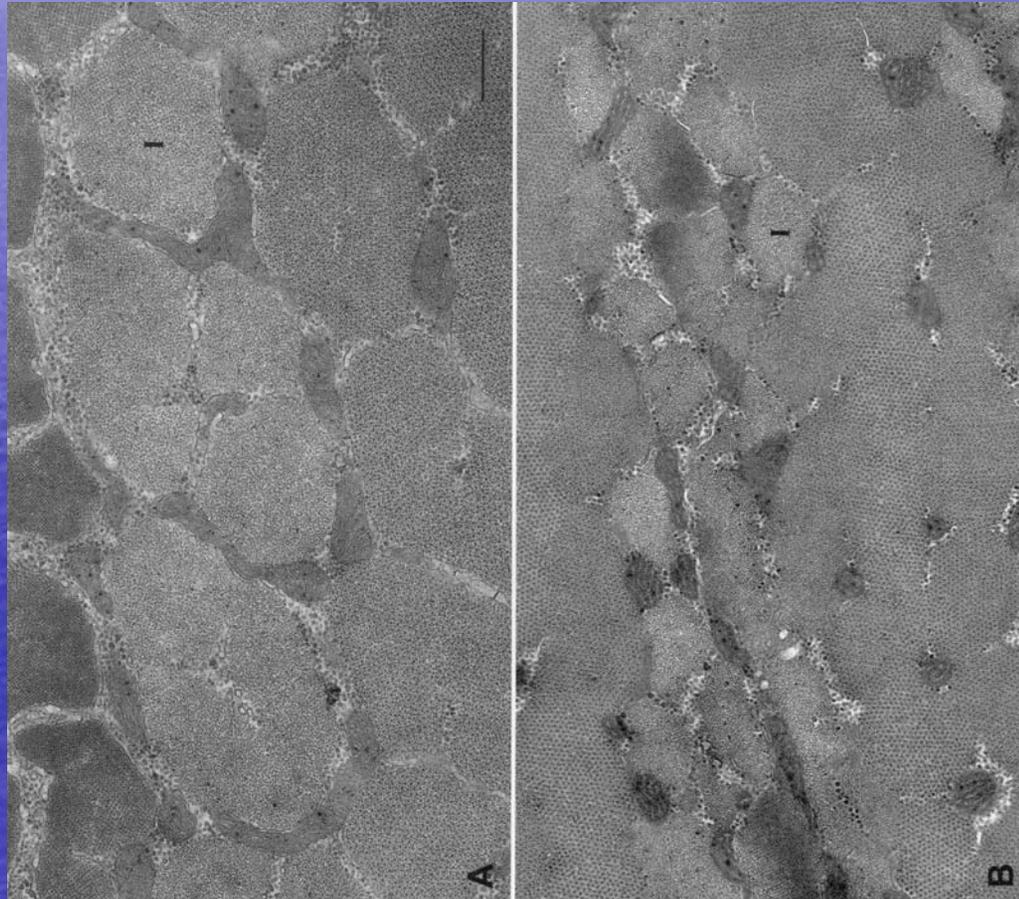
6 days following fiber death



G. Pavlath et al. *Developmental Dynamics* 212:495-508 (1998)

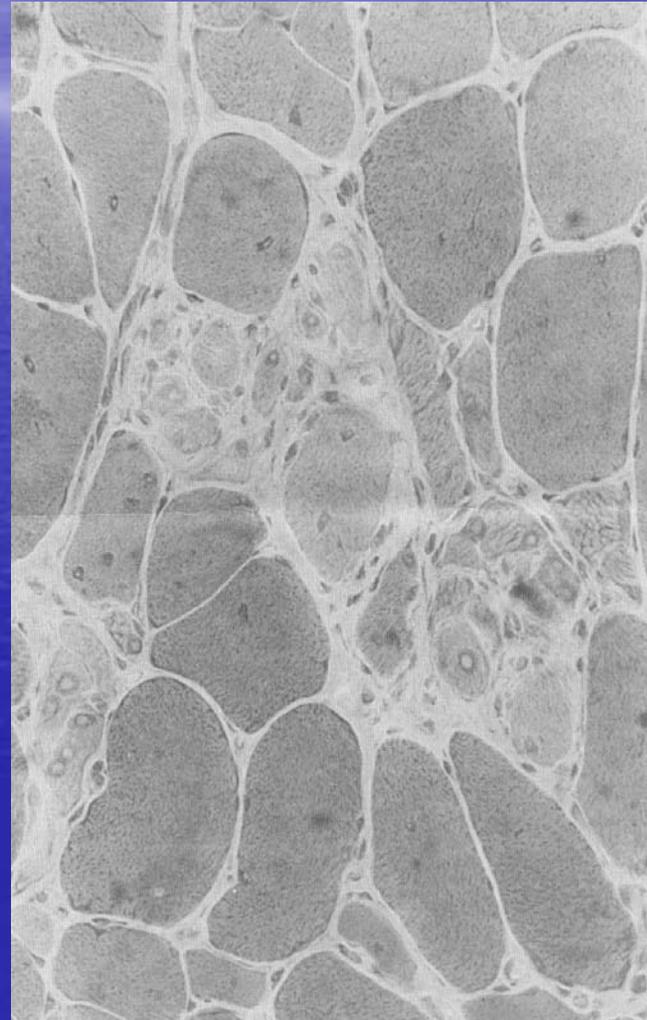
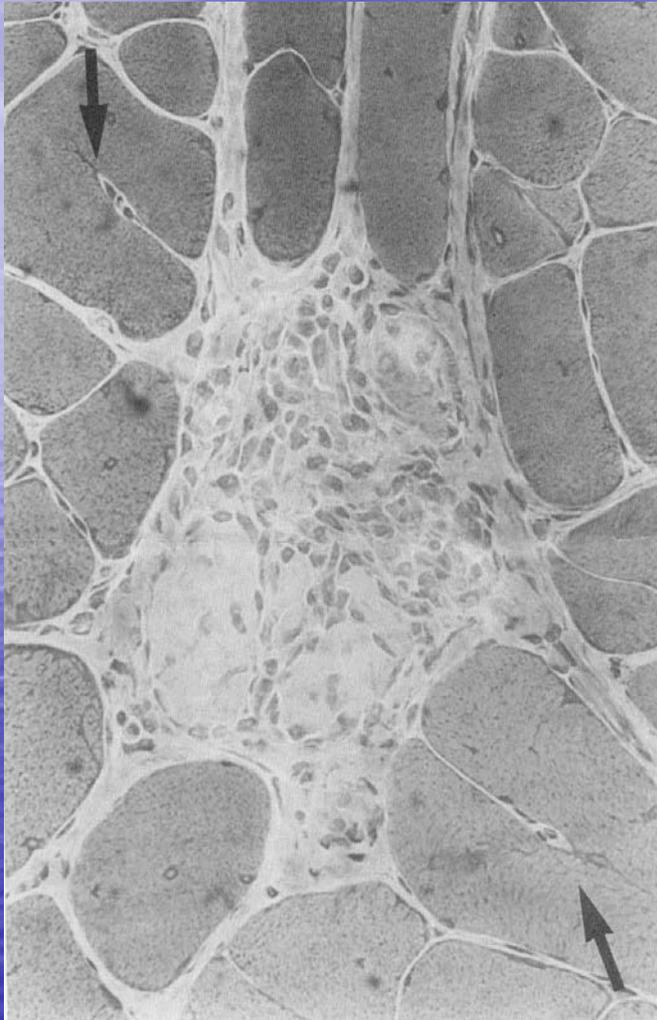
Recovery from atrophy

(bed rest, unweighting, spaceflight)
marked drop in satellite cell and myonuclei
numbers



Muscular dystrophy

Repeated bouts of degradation and repair



J. L. Carpenter et al., Amer. J. Pathol. 135:909-919 (1989)

Nutrition

Satellite cells from malnourished children are fewer in number and largely quiescent

Exercise

Peak ^3H -thymidine incorporation 72 hr following acute exercise

Repair fiber damage during normal exercise

Muscle cells in culture function similarly to muscle cells in the whole animal.

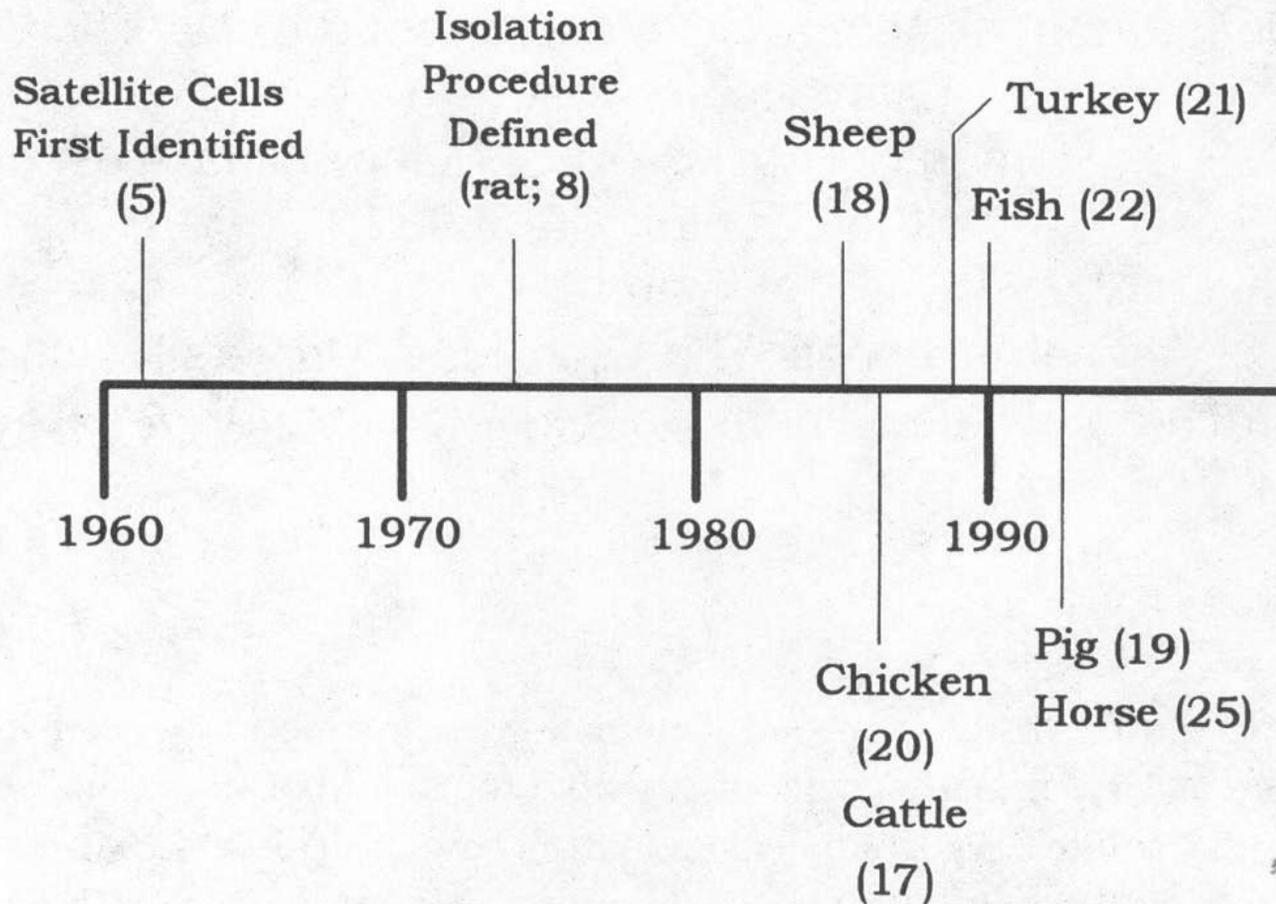
1. Divide
2. Operate biochemical pathways
3. Migrate
4. Fuse to form muscle fibers
5. Synthesize contractile proteins

Isolation and Culture

R. Bischoff. 1974. Enzymatic liberation of myogenic cells from adult rat muscle. *Anat. Rec.* 180:645-662.



R. Bischoff. *Develop. Biol.* 115:129-136 (1986)



M. Dodson et al., Domestic Animal Endocrinology 13:107-126 (1996)

Satellite Cell Isolation

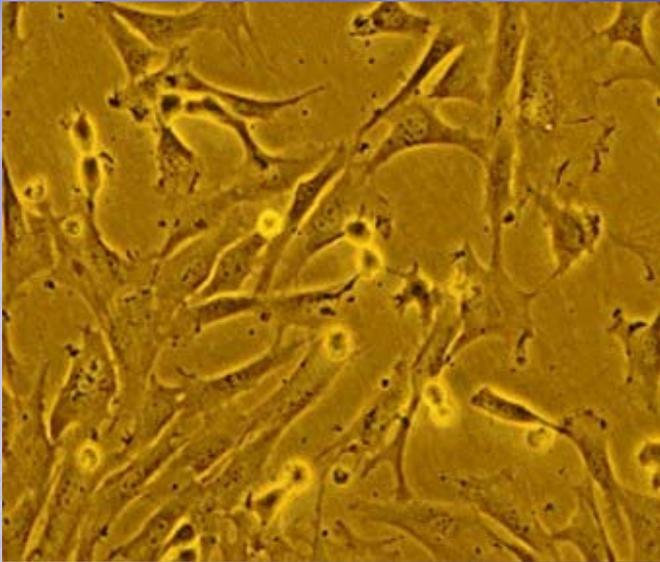
Muscle removal and preparation

- Protease liberation of cells
- Differential centrifugations
- Filtrations
- Plating or freezing

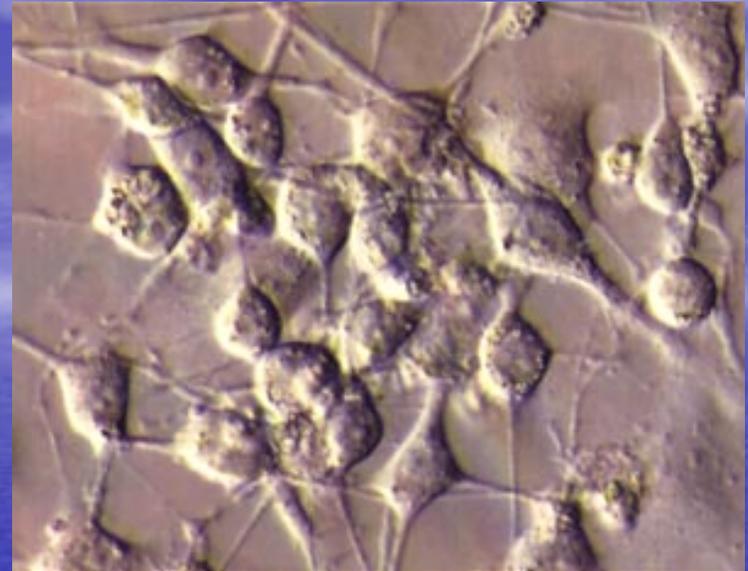
Cell Requirements

- a. Temperature
- b. pH
- c. osmotic pressure
- d. O_2
- e. CO_2 removed
- h. nutrients
- i. hormones, growth factors

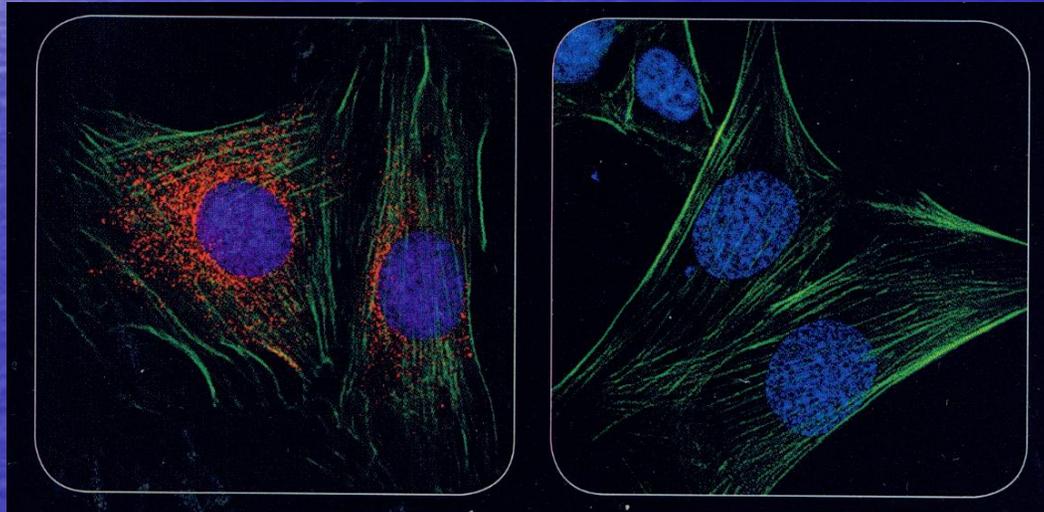




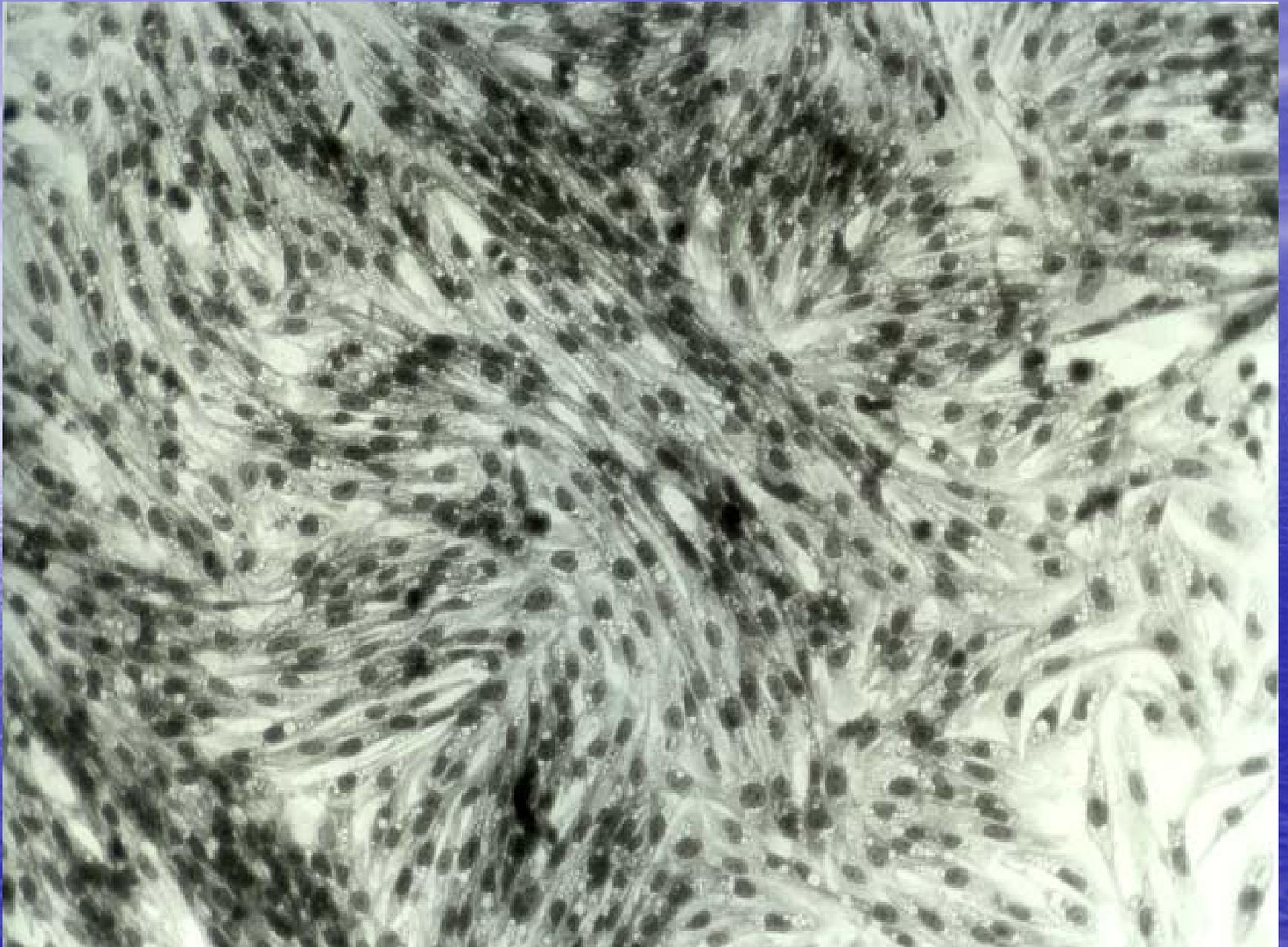
J. S. Choinski, Jr. Univ. Central Ark.

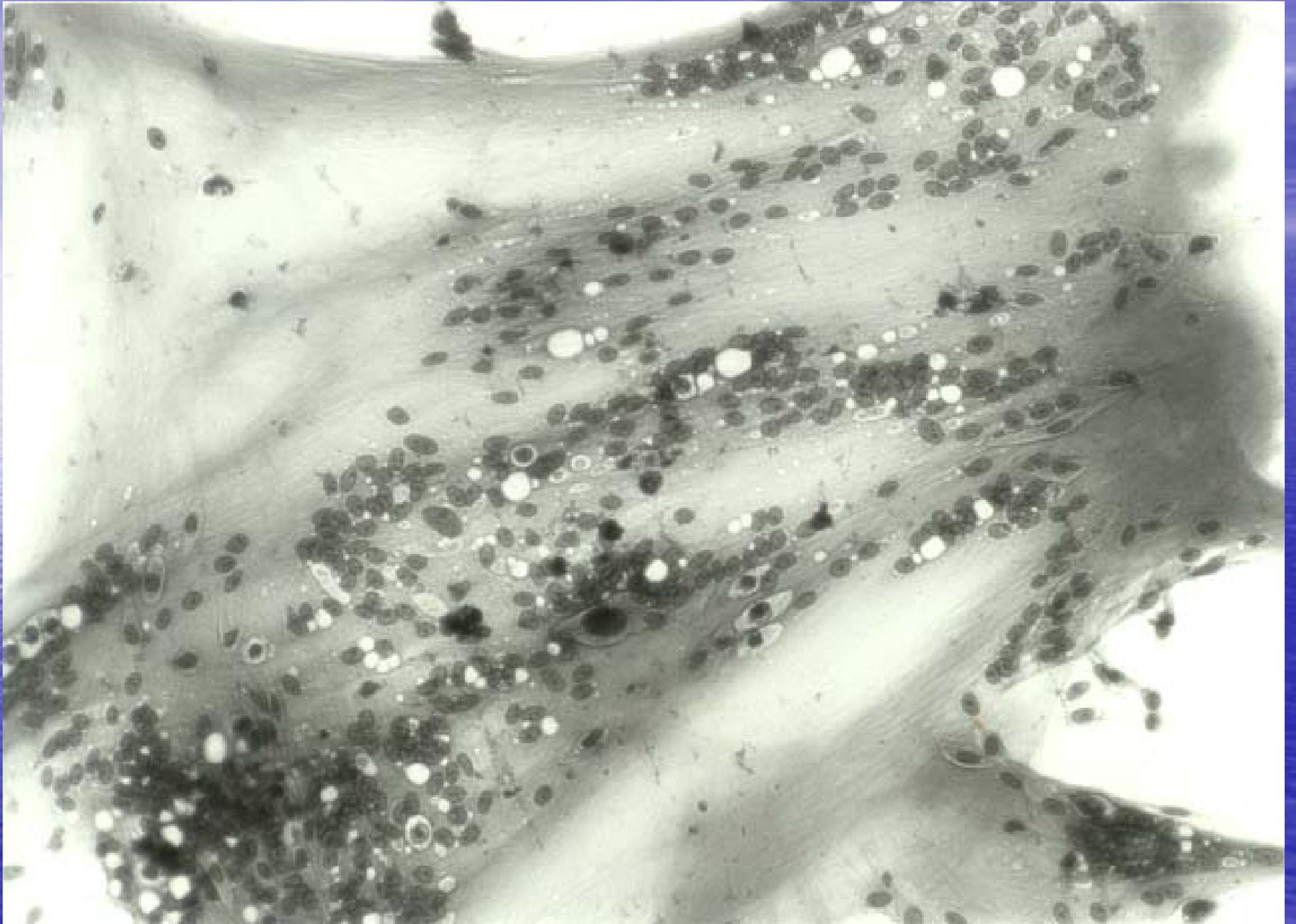


Univ. Rochester Med. Ctr



Cell Signaling Technology, Danvers, MA





Defined or serum-free media

- to establish nutrient requirements of cells
- to study growth factor and hormone effects

Characterization of the culture

- problem with fibroblast overgrowth
- accurate cell enumeration
- biological responses influenced by physiology of contaminant

Cell Cloning

Fluorescence-activated cell sorting
glass rings

Quixell cell manipulator robotic system

Percoll density gradient centrifugation

Future Impacts

Identify genes responsible for enhanced growth
and carcass traits

heterogeneity of the satellite cell population

“side populations”

transdifferentiation

relieve muscle atrophy (aging, hospitalization,
space flight)

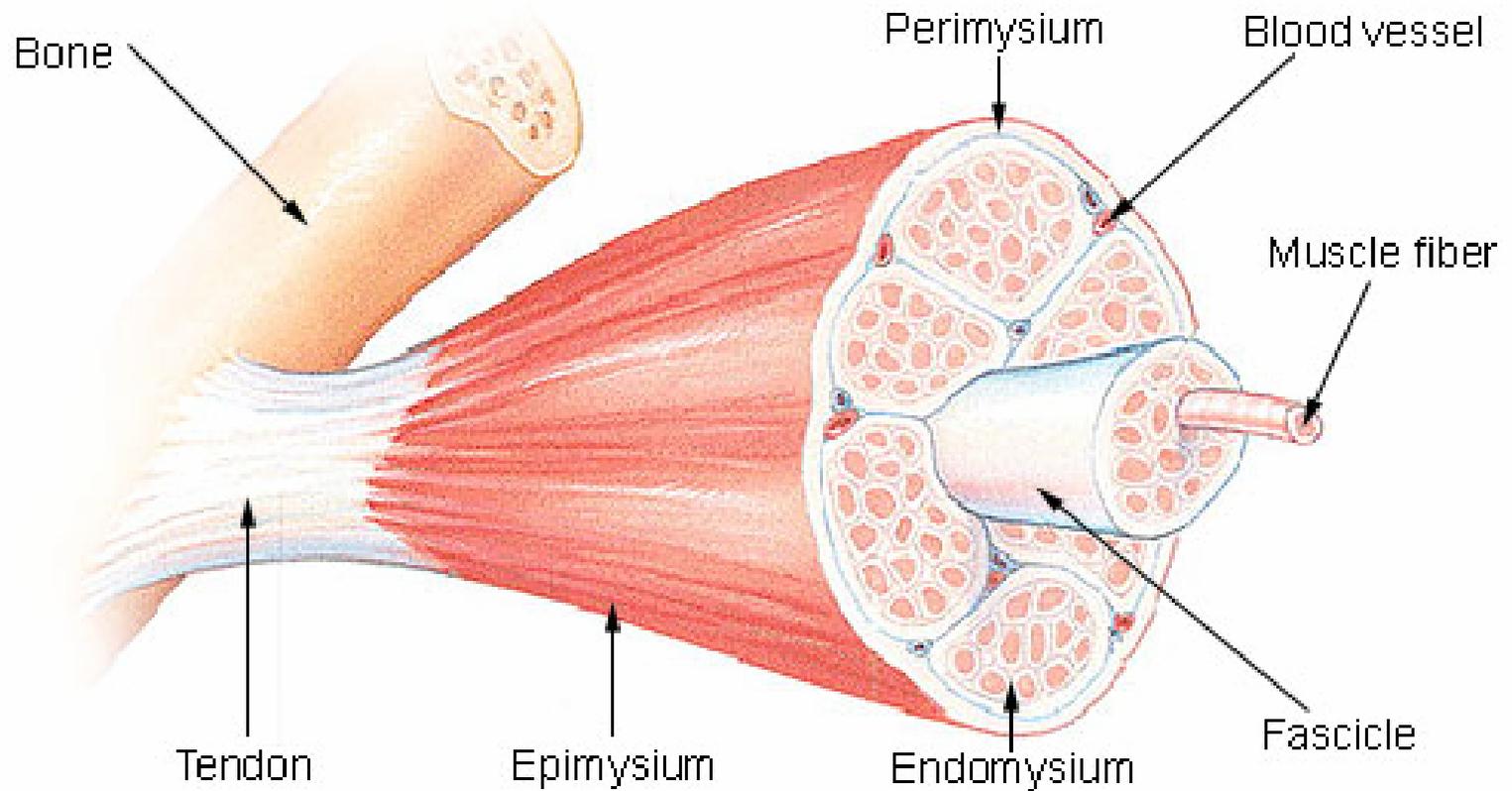
transplantation to relieve muscular dystrophy

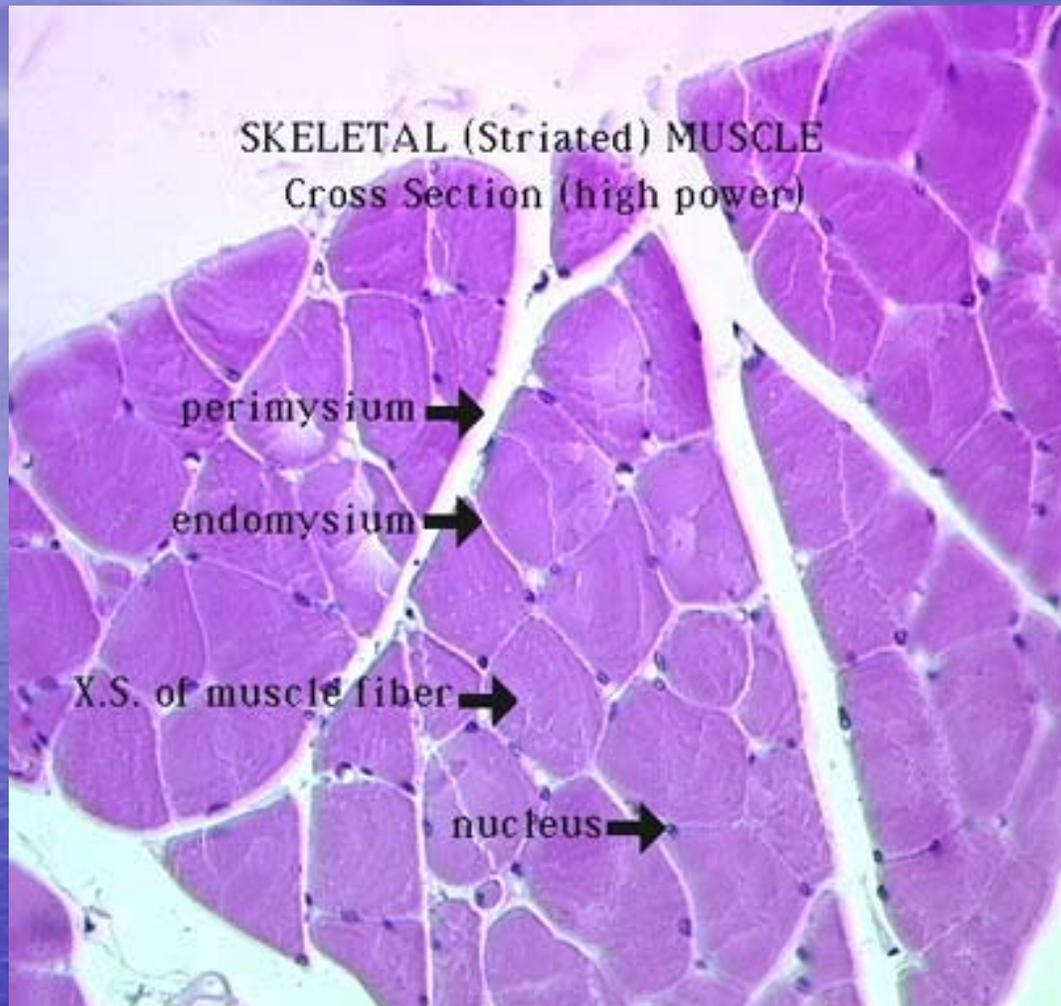
transplantation to improve cardiac function

muscle-mediated gene therapy



Structure of a Skeletal Muscle





S. Minckley, Mesa Community College