**ANSC/FSTC 607**
**Biochemistry and Physiology of Muscle as a Food**
**PRIMARY, SECONDARY, AND TERTIARY MYOTUBES**

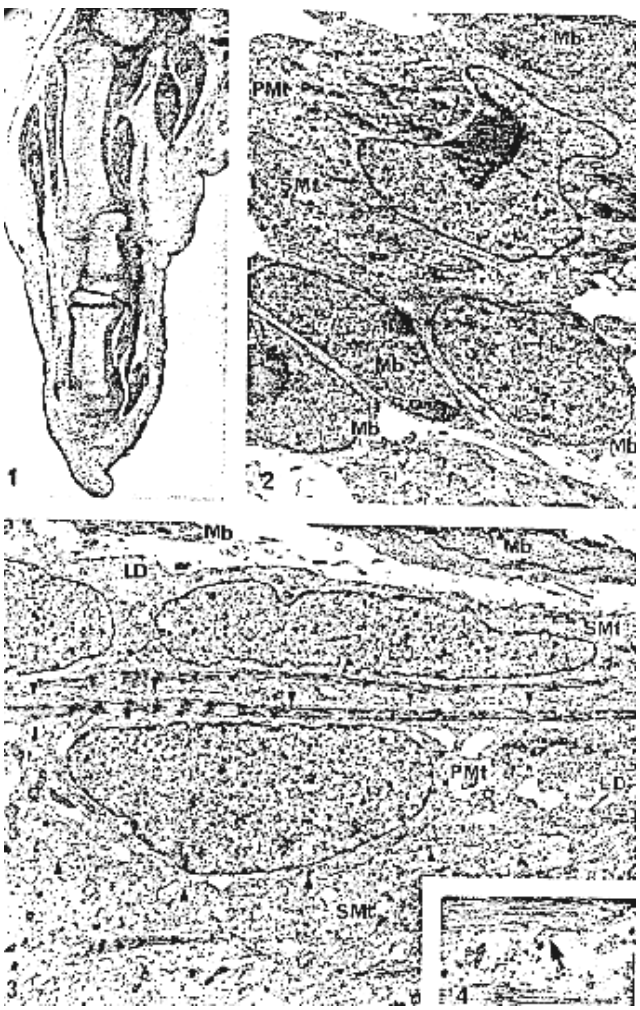
## I. Satellite Cells

A. Proliferative, myoblastic cells that lie in invaginations in the sarcolemma

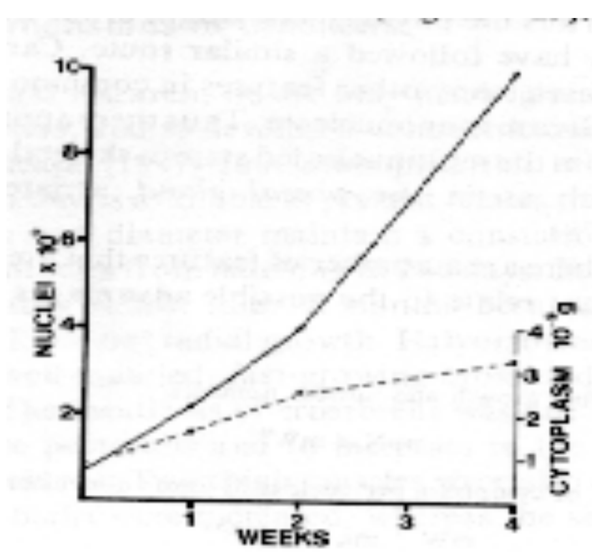
B. Can be stimulated to proliferate by muscle growth or damage

C. Can be isolated for cell culture

1. Proliferate like immortalized premyoblasts
2. Express myofibrillar proteins
3. Fuse to form new myotubes.




**Developing limb bud.** Satellite cells are involved in the formation of primary and secondary myotubes during fetal development. Premyoblasts from somites close to the point of limb formation migrate to a point just under the ectoderm. Myoblasts fuse to form myotubes, aligning



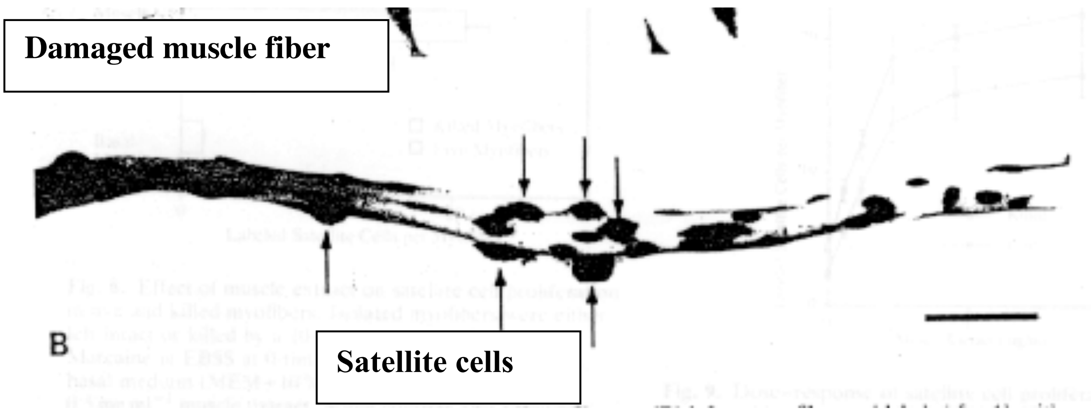

**Satellite cell hyperplasia.** The total number of muscle nuclei increases during postnatal growth. Nuclei increase at a faster rate than total cytoplasm (sarcoplasm), indicating that satellite cell hyperplasia exceeds myofiber hypertrophy.

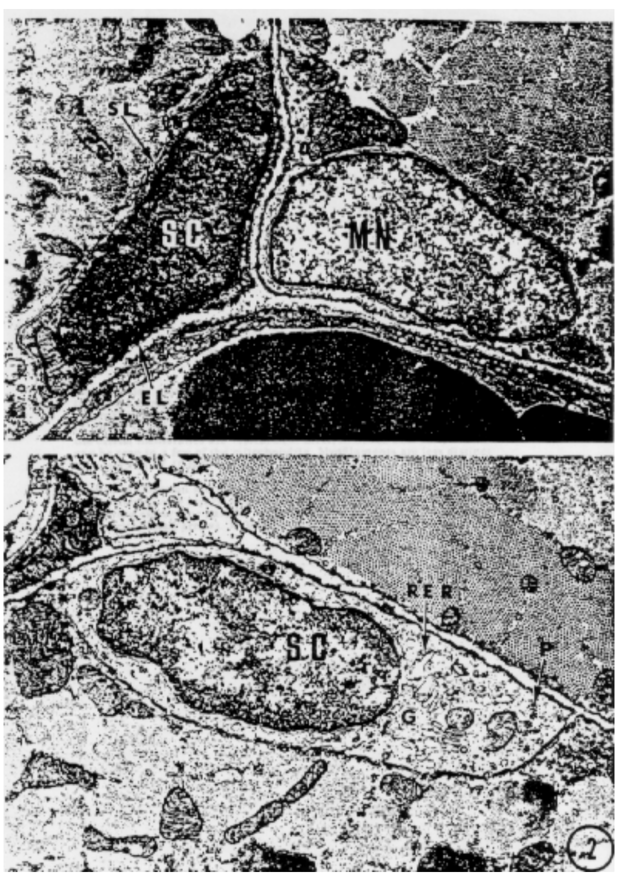
with developing limb bones.

## II. Satellite cells and muscle fiber repair

A. Proliferation increases greatly when the muscle is damaged.

1. Satellite cells migrate to damaged area.
2. Secretion of mitogenic factors by damaged muscle stimulates migration.
3. Satellite cells (now called "myoblasts" by some authors) fuse to form new myotubes.




**Skeletal muscle fibers from rat soleus muscle**. A satellite cell (**SC**) is shown between the external lamina (**EL**) and sarcolemma (**SL**). Note the paler myonucleus (**MN**) in the top micrograph.


**Regenerating myotube (MT).** A myotube formed after the muscle was damaged. The myotube with a central nucleus is shown adjacent to three myoblasts (MB). The external lamina (EL) from an originally minced muscle fiber appears to be completely surrounding the myotube and myoblasts.

## III. Changes in fiber number

A. Species-specific

1. Virtually no increase in myofiber number in animals born relatively developed.
    a. Cattle
    b. Hares
2. Measureable conversion of myotubes to myofibers early postnatally in animals born relatively undeveloped.
    a. Pigs
    b. Rabbits (domesticated)

B. Mechanism

1. In all species, primary myotubes develop prenatally (late embryo and early fetal periods).
2. Secondary myotubes develop primarily prenatally (late gestation) and early postnatally in some species.
    a. Use primary myotube as template.
    b. Split away from primary myotube because of contraction.
    c. Are innervated by the same motoneuron as the primary myotube.

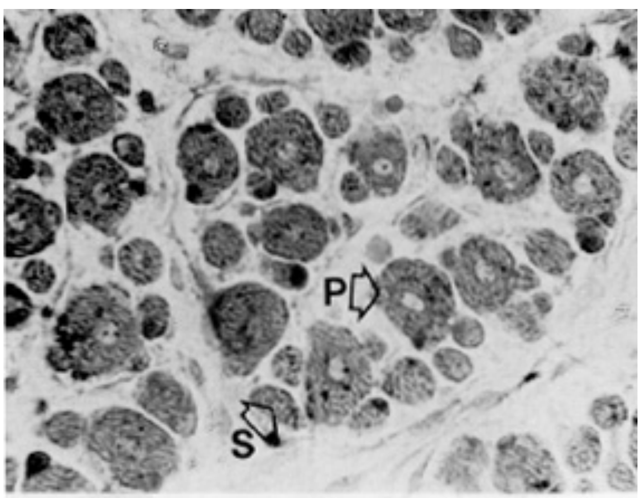
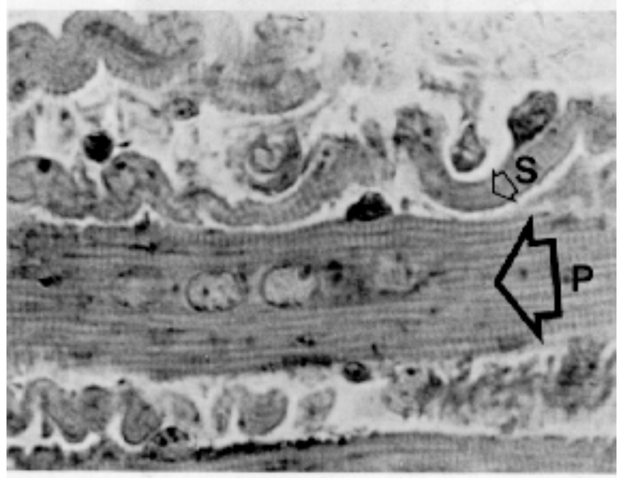
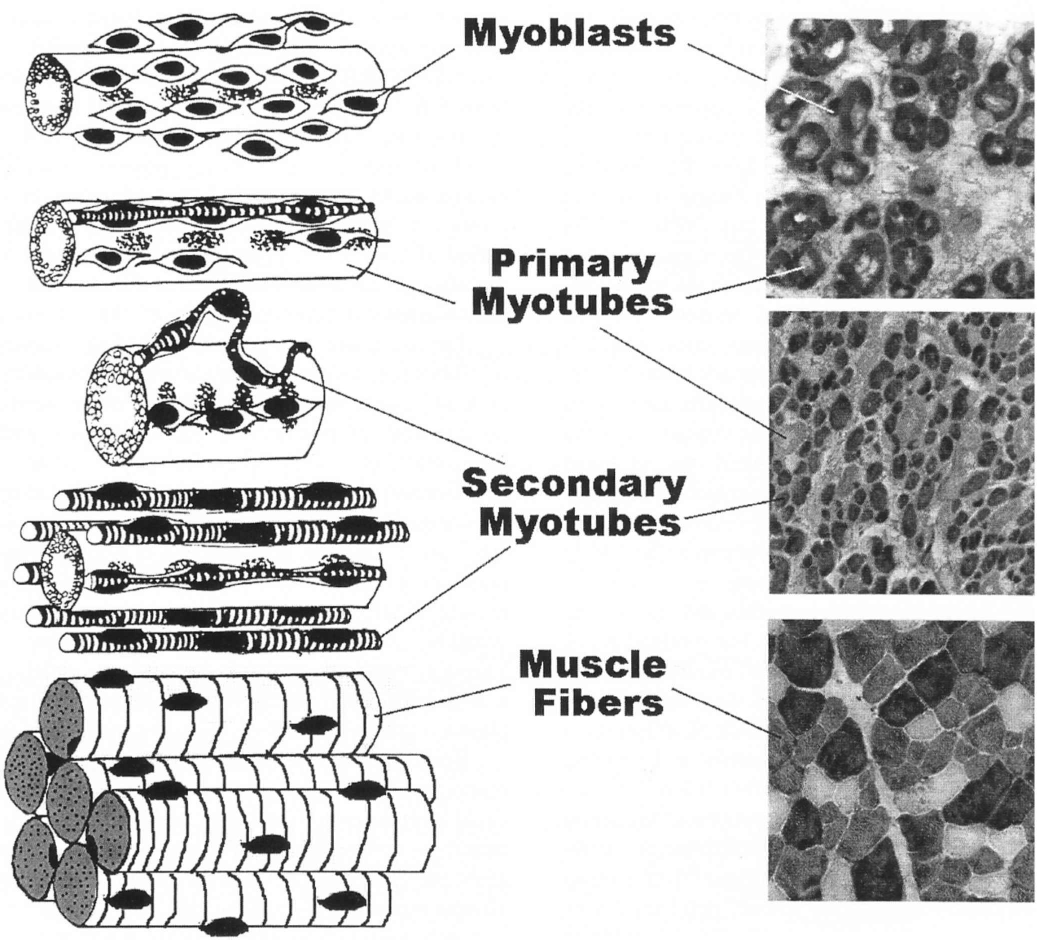



**Plate 13** Transverse section of muscle from a fetal pig: (P) primary fiber or classical myotube; (S) secondary fiber.

**Plate 14** Longitudinal section of muscle from a fetal pig: (P) primary fiber with axial nuclei; (S) secondary fiber being detached from the surface of the primary fiber.





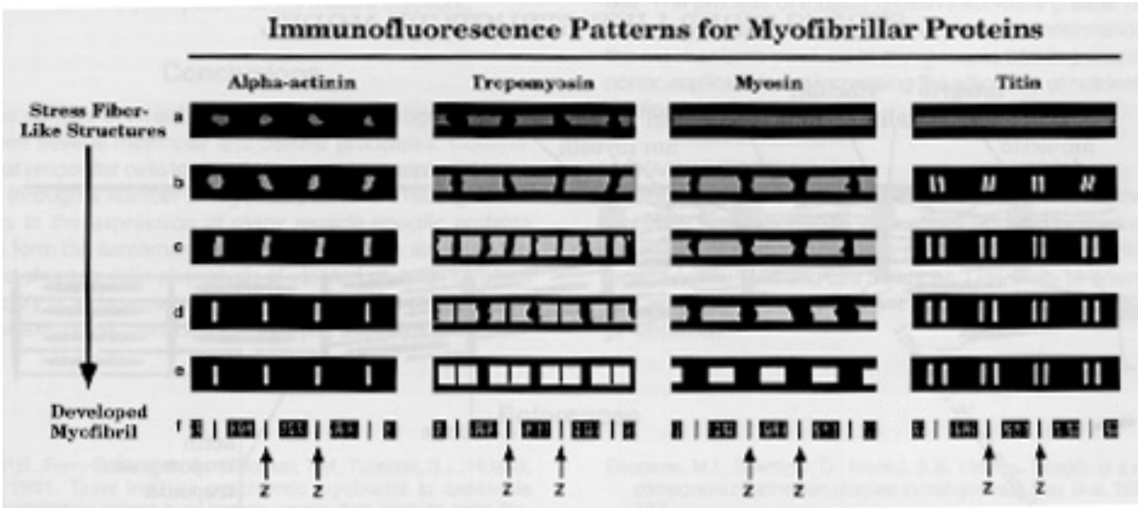

**IV. Primary and secondary myotubes**

A. Primary myotubes: progenitors of 10% of myofibers in adults.

1. From CMRI and CMRII myoblasts.
2. These myoblasts disappear once secondary myotube formation begins.

B. Secondary myotubes

1. Formed with primary myotubes as templates.
2. Formed with secondary myotubes as templates ("tertiary").
3. From CMRIII myoblasts.
    a. Require functional innervation for proliferation.
    b. Disappear in denervated muscle.




## V. Myofibril assembly

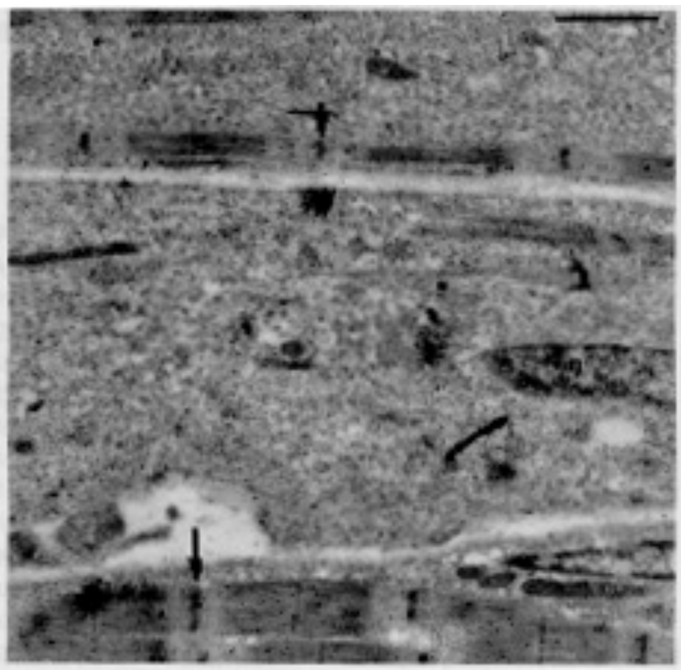
### A. Stress fiber model

1. A combination of nonmuscle (nm) and muscle-specific myofibrillar proteins aggregate immediately under the sarcolemma of the developing myofiber.

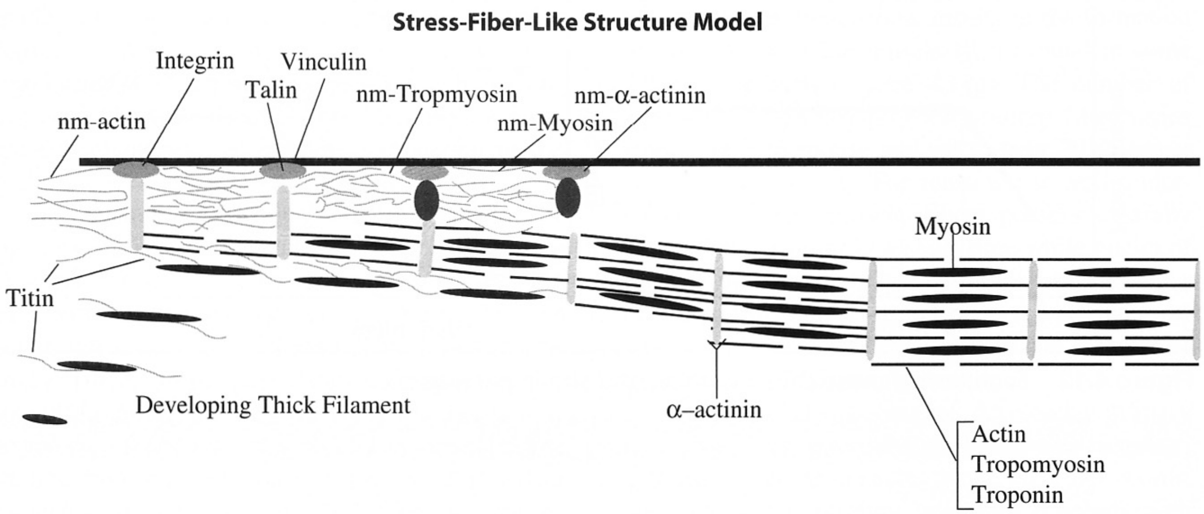
2. Muscle-type myofibrillar proteins and thick filaments are added adjacent to the stress fiber structure, using the original structure as a template.

3. The myofibril separates from the sarcolemma, and is added to the pool of myofibrils.

4. Sarcomere length *does not* increase in length as the myofibril develops.

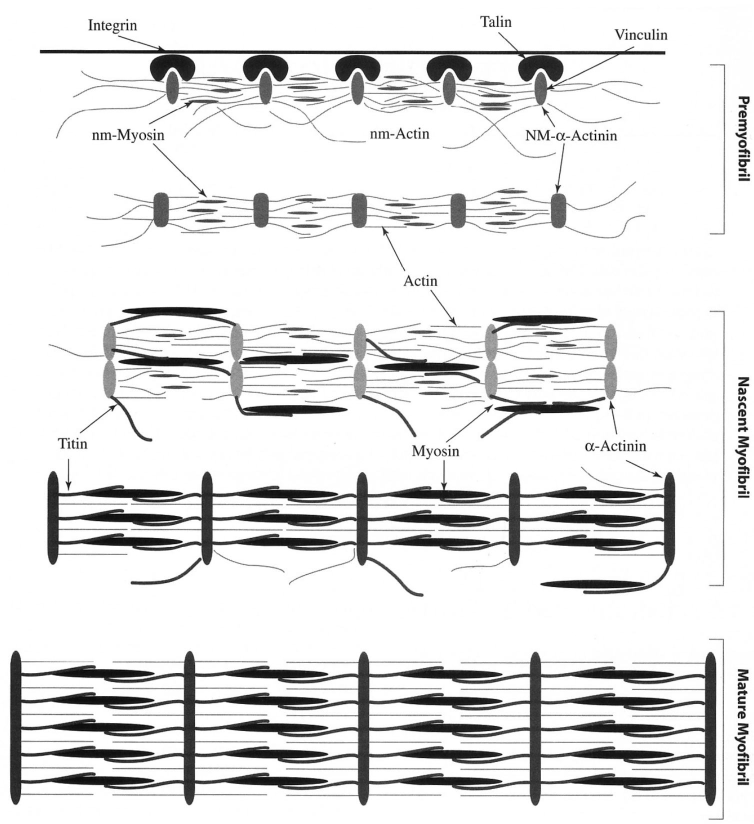


Subsarcolemmal myofibril formation in post-natal muscle. The square area marked in Figure 4 was enlarged to better illustrate the close apposition of the immature myofibril (arrow head at Z-line) to the sarcolemma in a poorly-developed myotube. This can be contrasted with the well-developed myotube in the lower part of the micrograph (arrow at Z-line). Scale is 1 micron and n = nuclei.




**B. Premyofibril model**

1. A premyofibril containing only nonmuscle proteins forms under the sarcolemma.
2. This detaches from sarcolemma and serves as the template for the developing myofibril.
3. Nonmuscle proteins are gradually replaced with muscle-type myofibrillar proteins.
4. There is a *lengthening* of the sarcomere, which does not occur in the stress fiber model.



## VI. Acquisition of fiber type-specific myofibrillar proteins

A. Type I

1. From primary myotubes (type $I_{emb}$).
2. From secondary myotubes if they are surrounded by type I myofibers.
3. Denervation of a slow-twitch muscle:
    a. Primary myotubes remain as type I.
    b. Secondary myotubes convert to type II.

B. Type II

1. From type $II_{emb}$ myotubes.
2. From secondary myotubes?

| | Muscle type | |
|---|---|---|
| Gene family | Slow | Fast |
| Myosin heavy chain | S | $F_{2A}$, $F_{2B}$, $F_{2X}$, $F2_{EO}$, $F_{SF}$ |
| Alkaline myosin light chain | $1_{SA}$, $1_{SB}$ | $1_F$, $3_F$ |
| Regulatory myosin light chain | $2_S$, $2_{S'}$ | $2_F$ |
| **Actin (not fiber-specific)** | **$\alpha_{SK}$** | **$\alpha_{SK}$** |
| Tropomyosin | S | F |
| Troponin C | S | F |
| Troponin I | S | F |
| Troponin T | S | F |

C. Acquisition of MHC isoforms during embryonic, fetal, and postnatal growth

1. Embryonic and fetal isoforms are expressed during the development of early myofibrils.
    a. Primary myotubes begin as type I myotubes, and later some primary myotubes differentiate into type II myotubes.
    b. Secondary myotubes are programmed to develop into type II myofibers.
2. The embryonic MHC isoforms are replaced by fetal isoforms.
3. Fetal MHC isoforms are replaced by adult isoforms as more myofibrils are added to the growing myofibers.

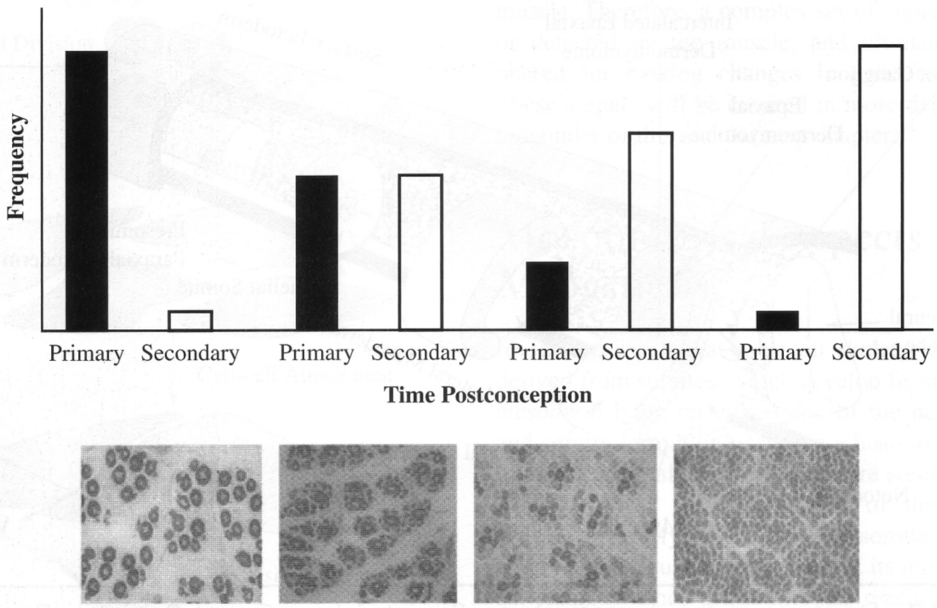



**Figure 4.9** Change in the relative size and frequency of primary and secondary muscle fibers during fetal development.

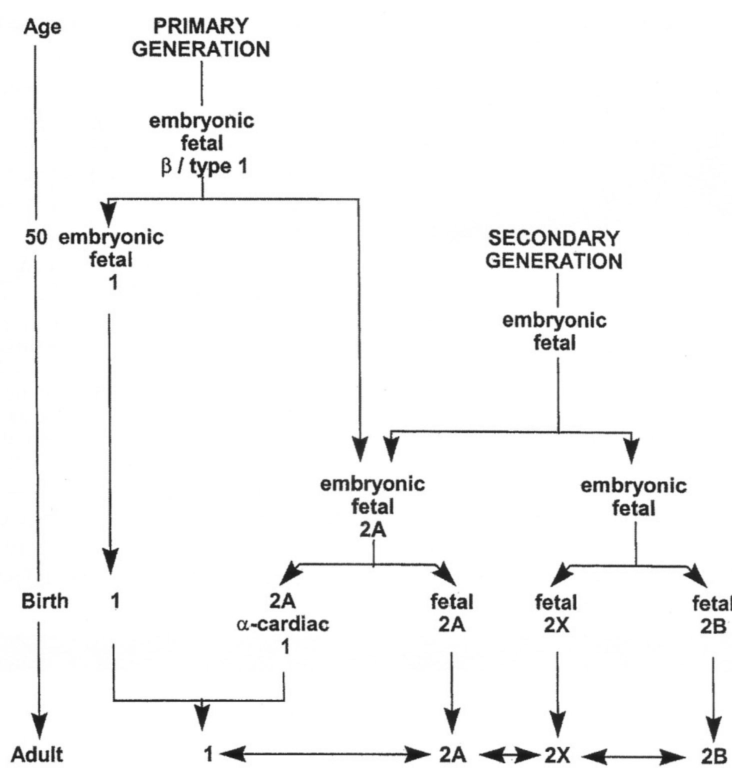
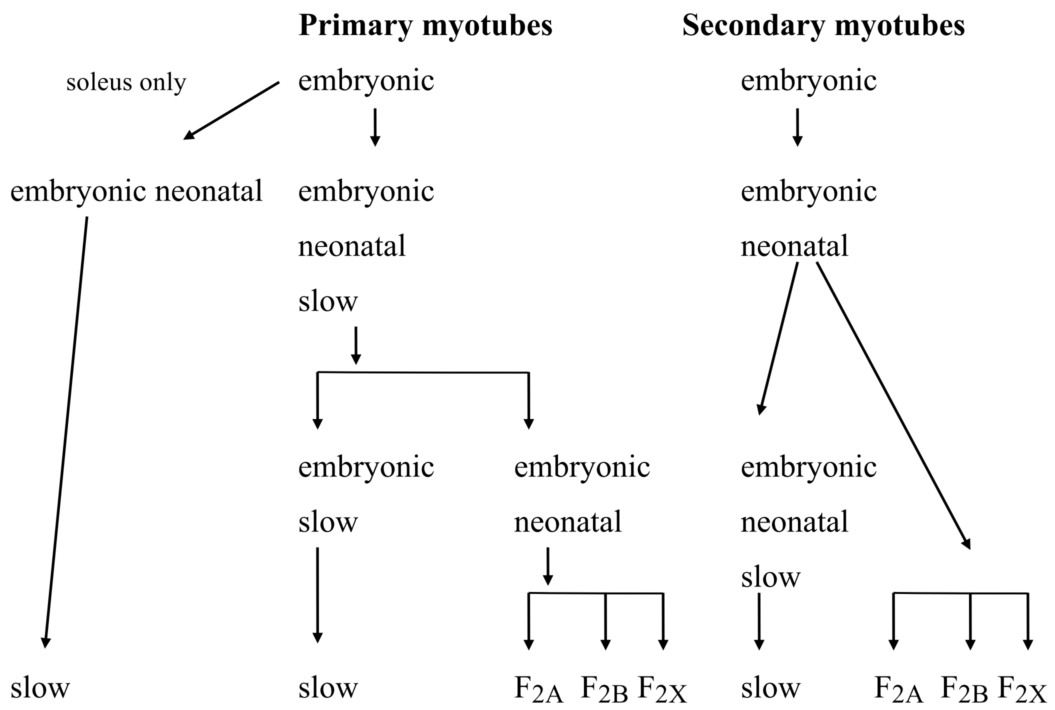



**Figure 6.11** Evolution of muscle fiber types in pigs. From L. Lefaucheur and D. E. Gerrard, Muscle fiber plasticity in farm mammals, *Journal of Animal Science,* Savoy, Illinois.


Primary myotubes
Secondary myotubes
soleus only
embryonic
embryonic
embryonic neonatal
embryonic
neonatal
slow
embryonic
neonatal
embryonic
slow
embryonic
neonatal
embryonic
neonatal
slow
slow
slow
F2A F2B F2X
slow
F2A F2B F2X