

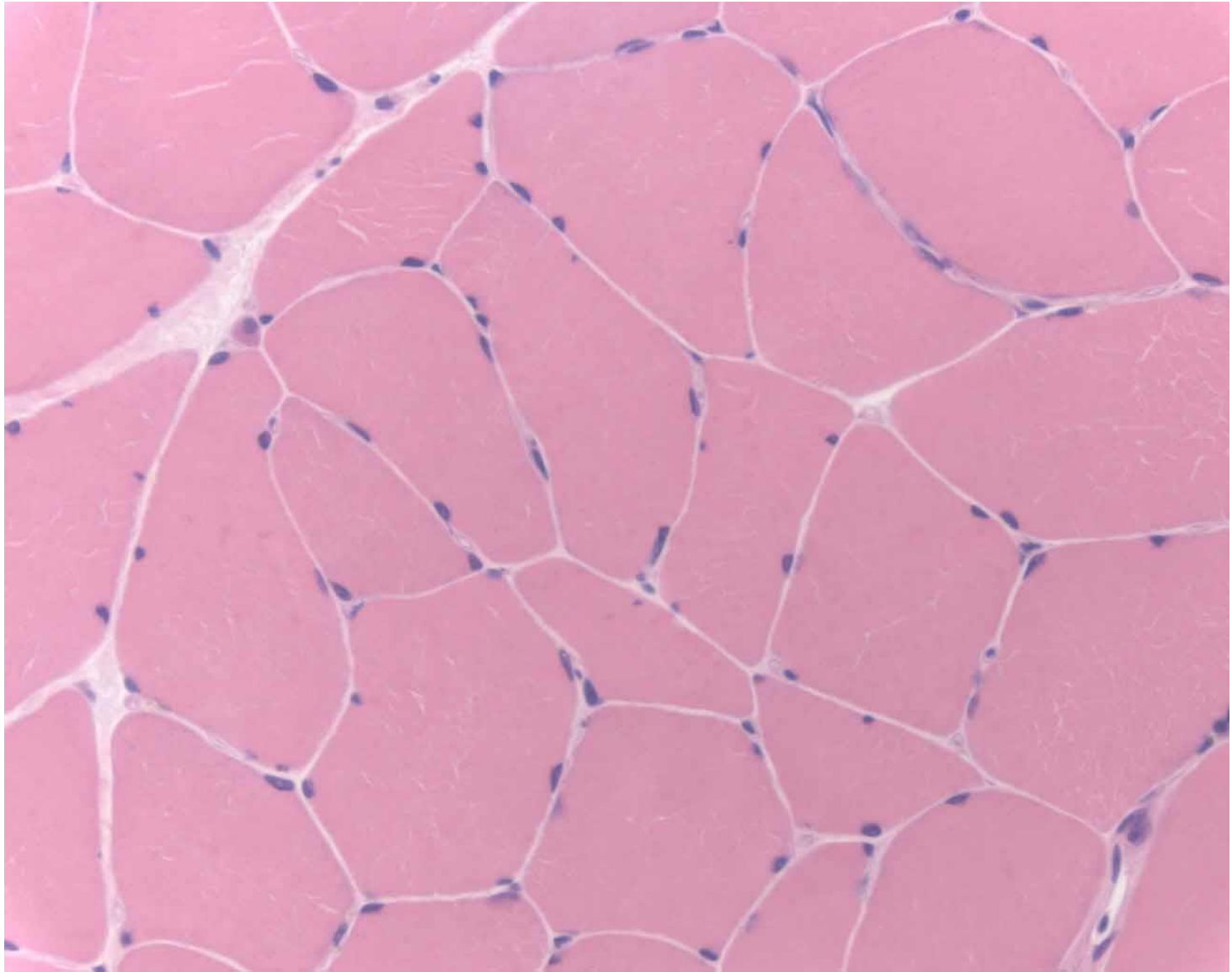
Electron microscopy in the investigation and diagnosis of muscle disease

Roy Weller

Clinical Neurosciences

University of Southampton School of Medicine

Normal Muscle



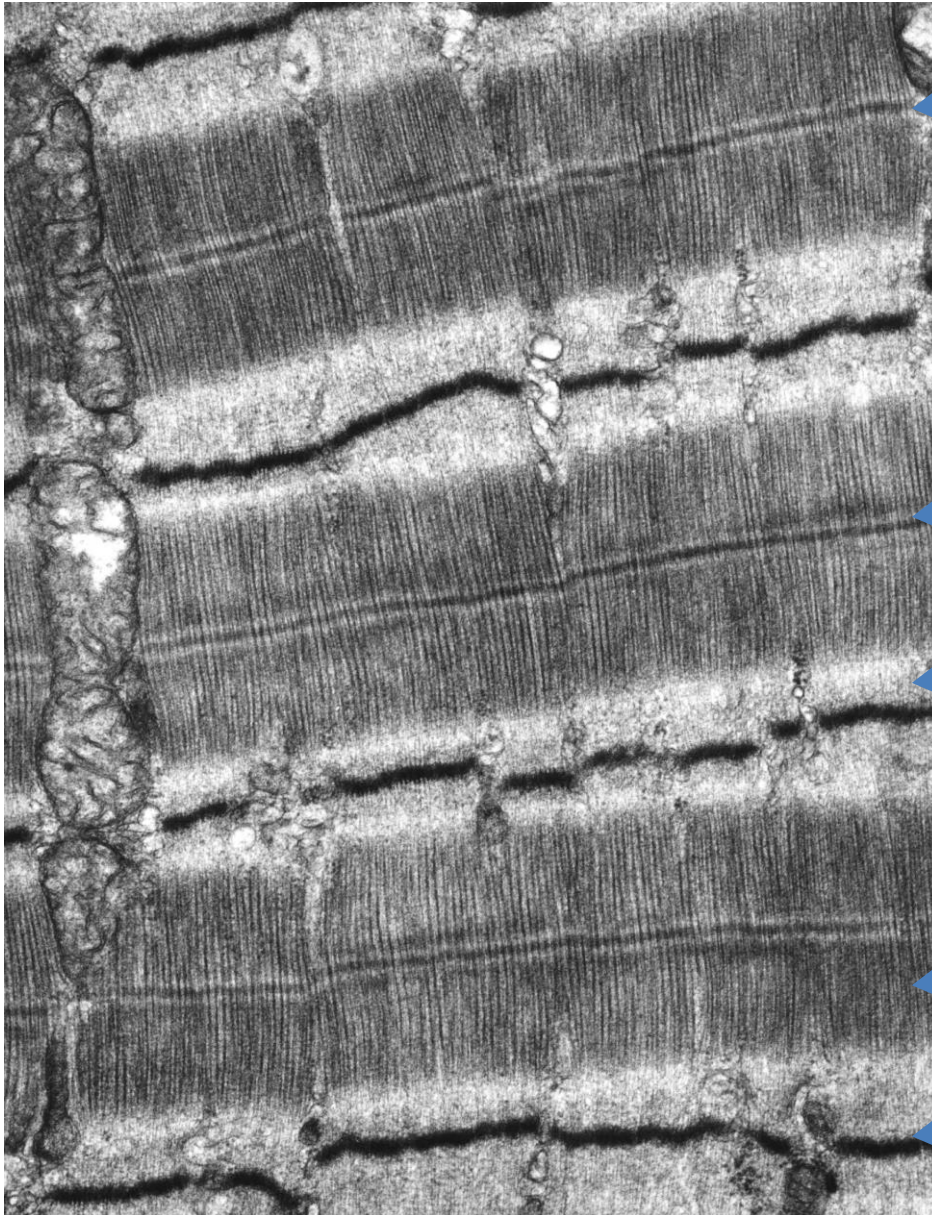
Normal Muscle



The Sarcomere

The names for the different parts are derived from German

The Sarcomere



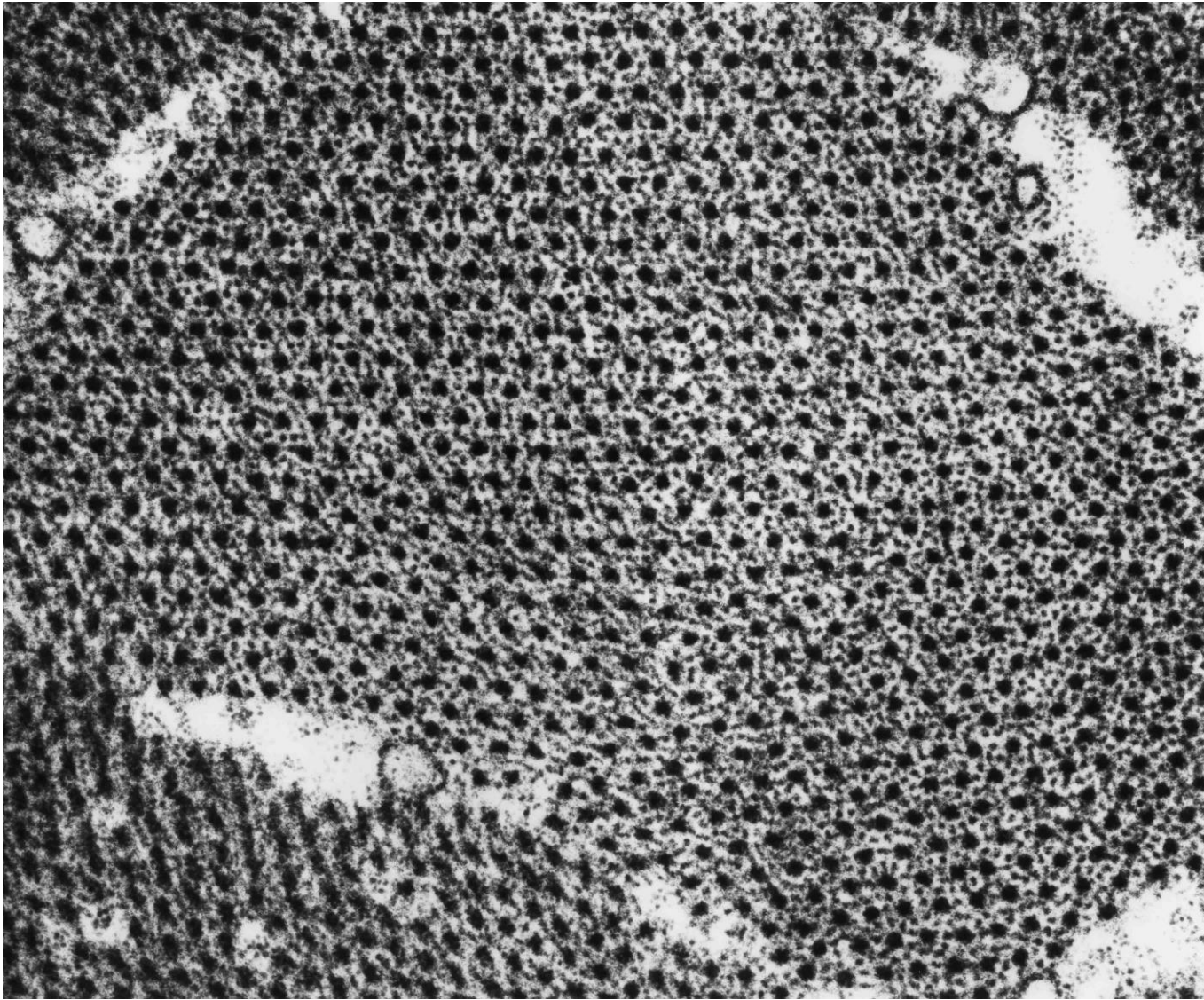
← **H-zone** (from the German “**h**eller”,
brighter)

← Inside the H-zone is a thin **M-line**
(from the German **M**ittelscheibe, the
disc in the *middle* of the sarcomere)
formed of cross-connecting elements
of the cytoskeleton

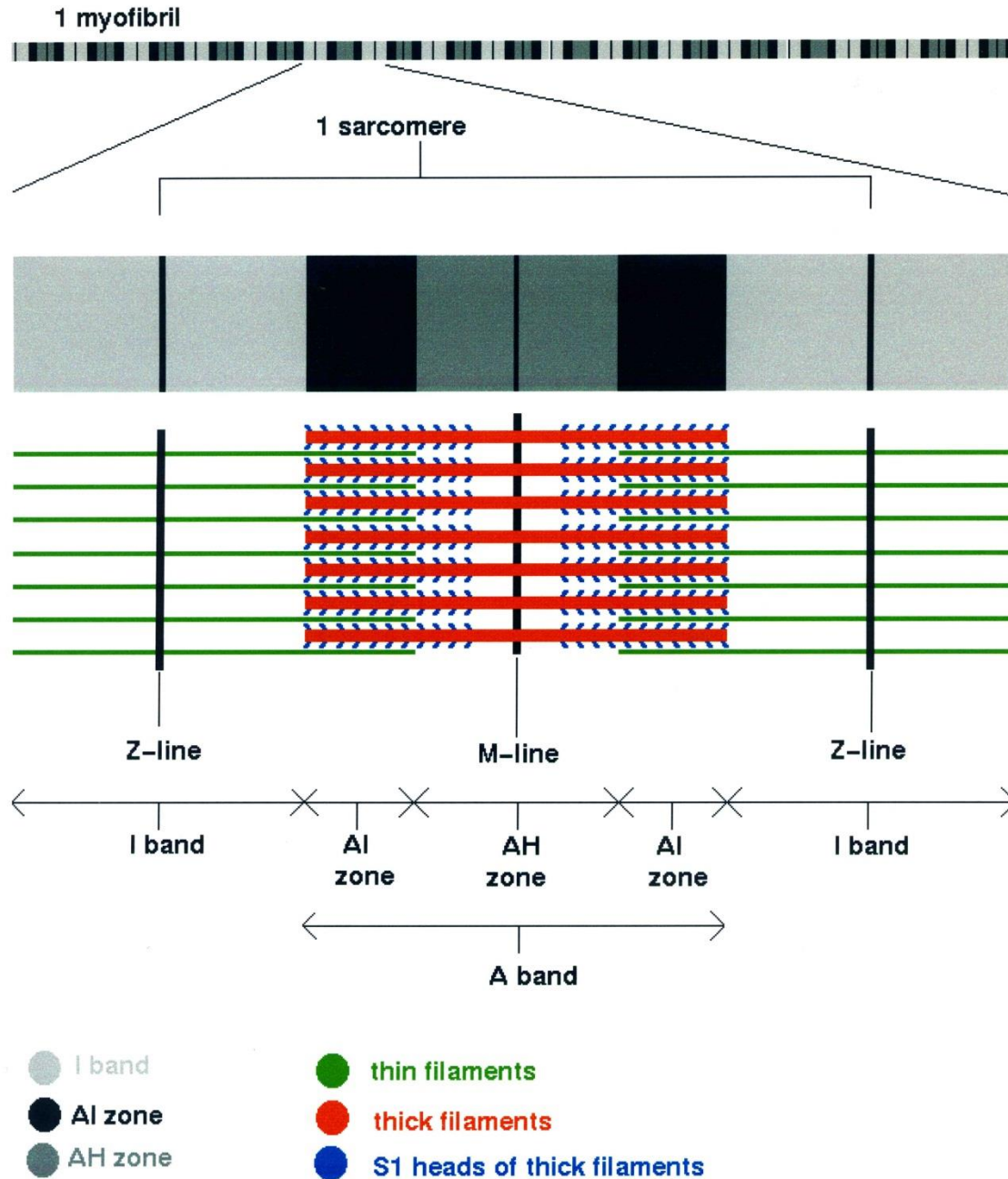
← **I-band** = Isotropic in polarised light
as the actin filaments are thin and do
not interfere with the light

← **A-band** = Anisotropic in polarised
light as the myosin filaments are
thicker and do interfere with the light

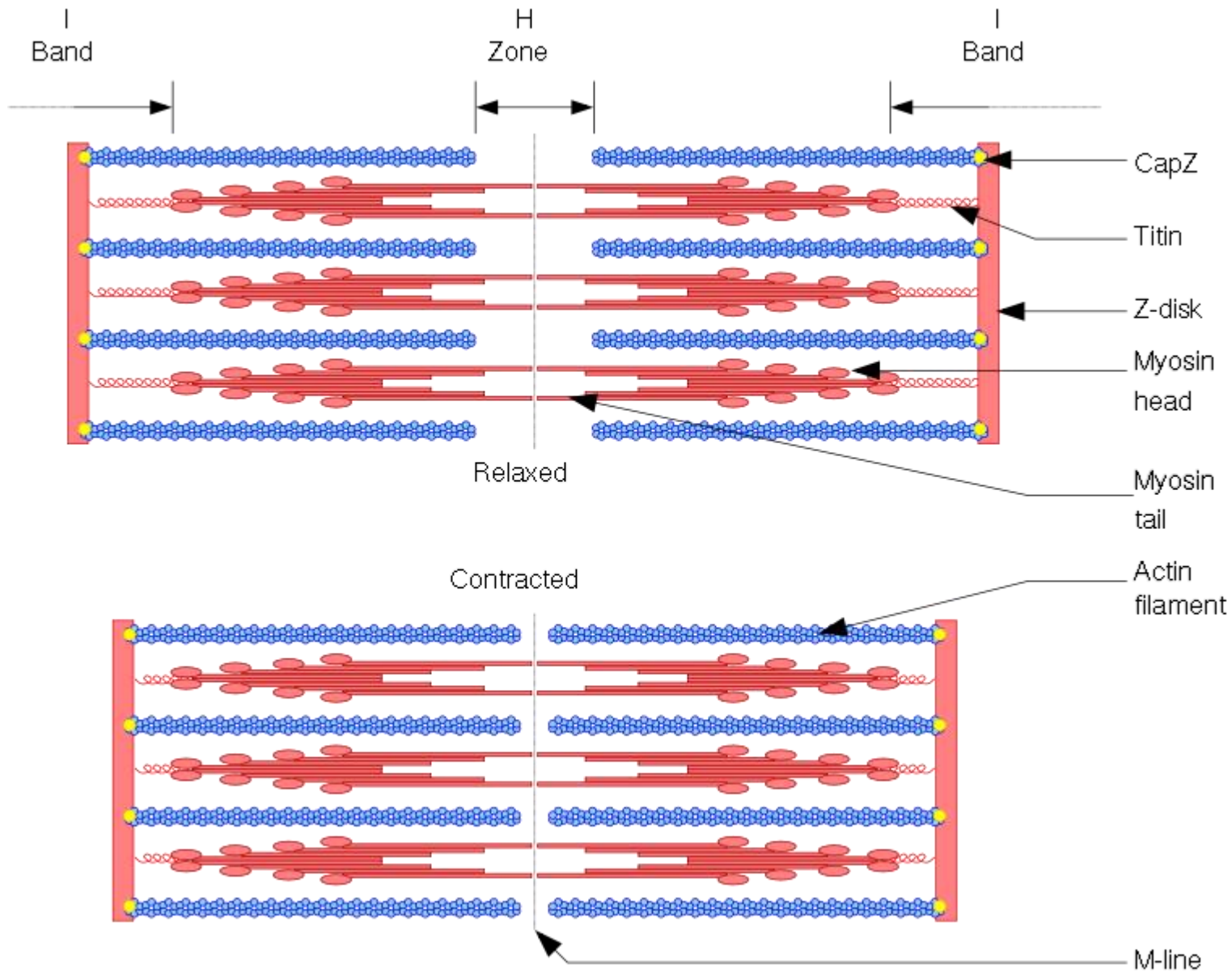
← **Z-line** = **Z**wischenscheibe *the disc in
between* the I bands

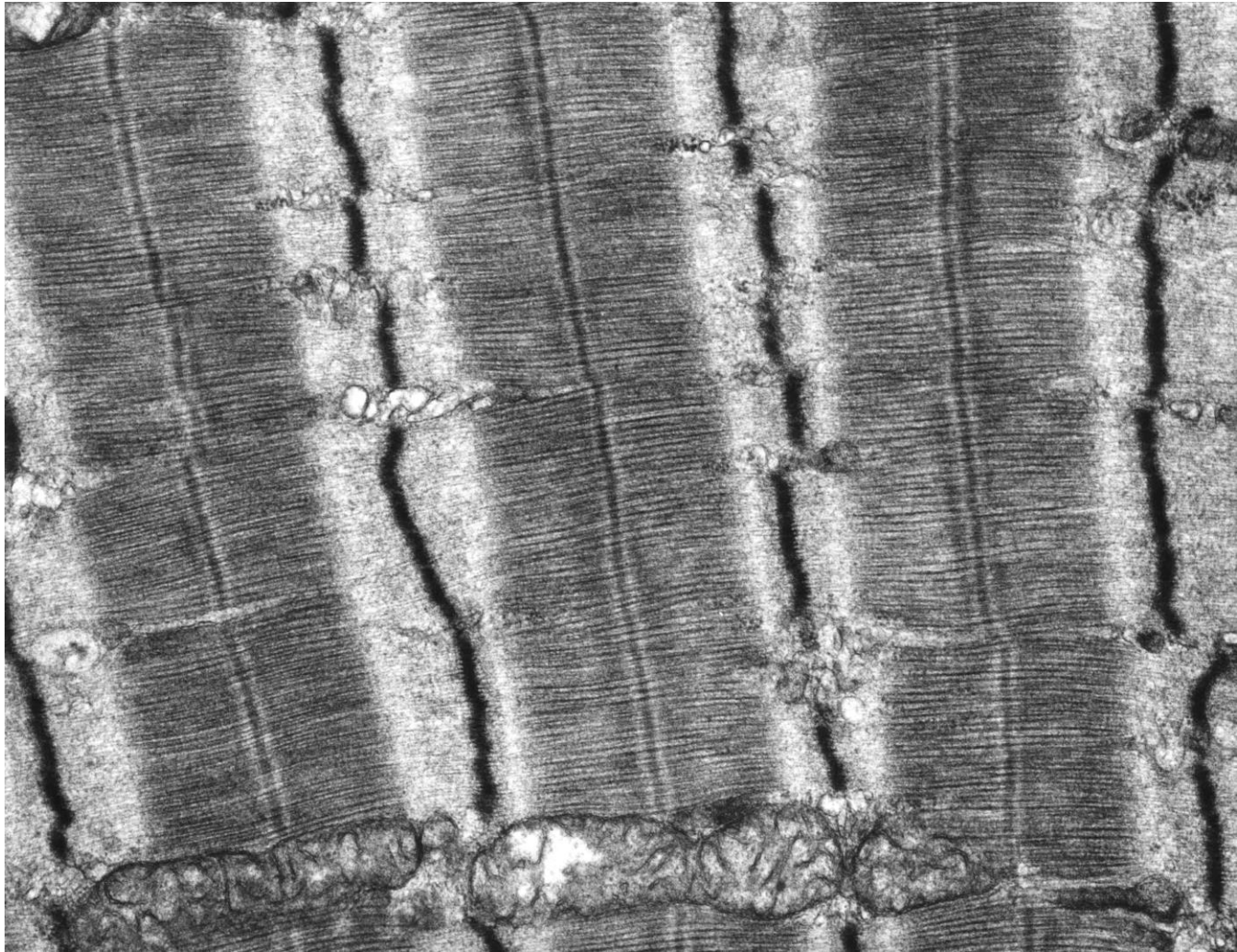


TS through an A-band

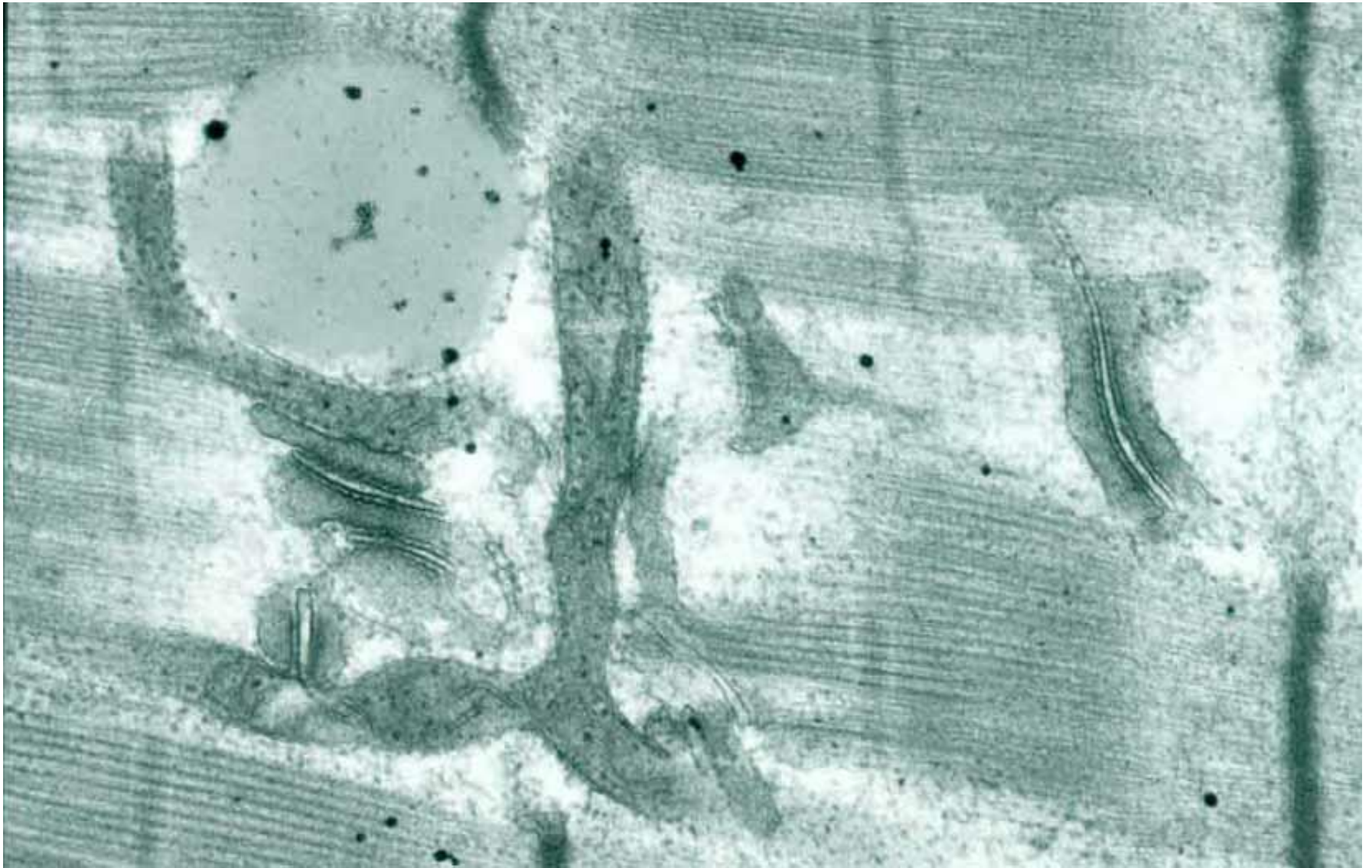


The appearance of the sarcomere in longitudinal section





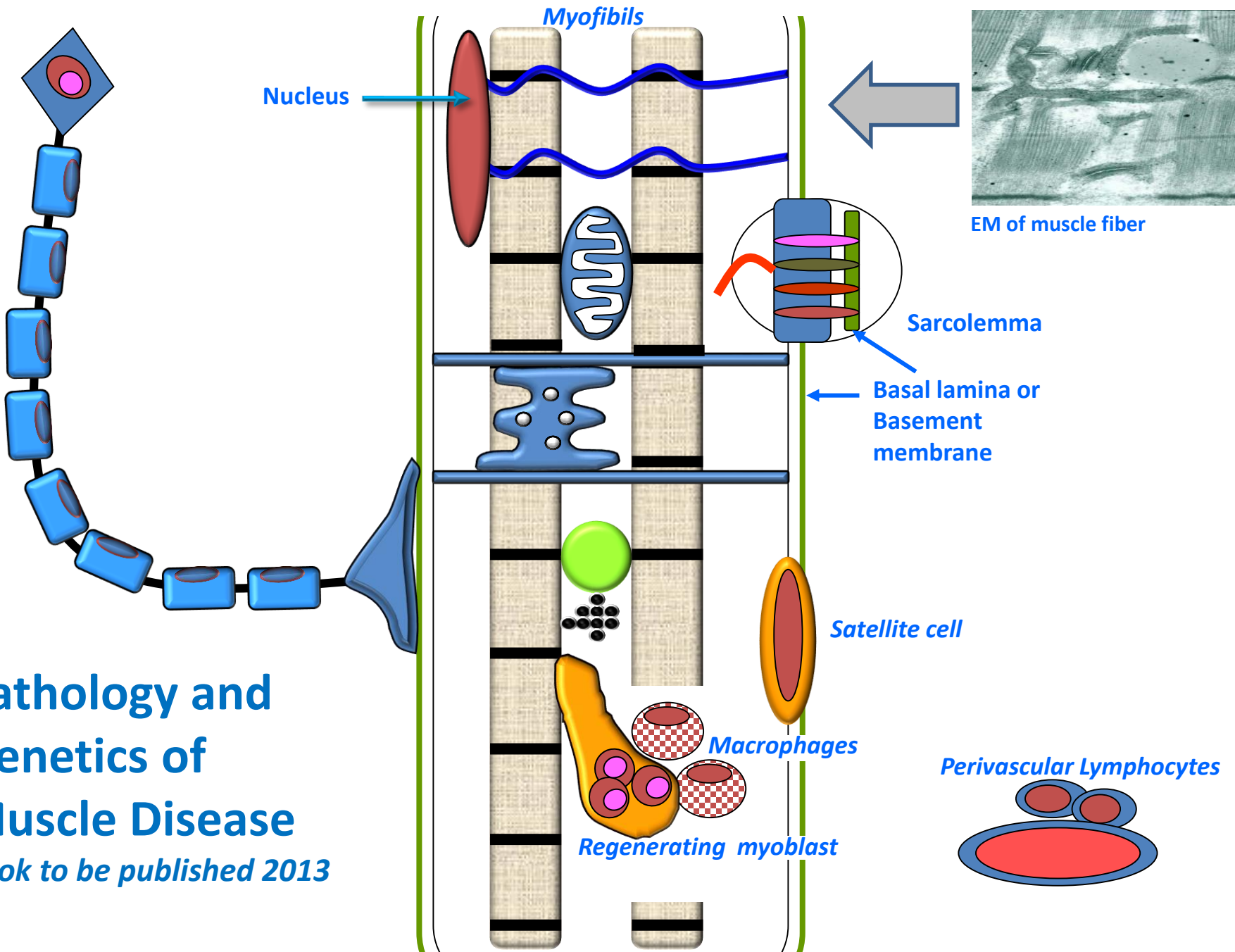
Sarcomeres



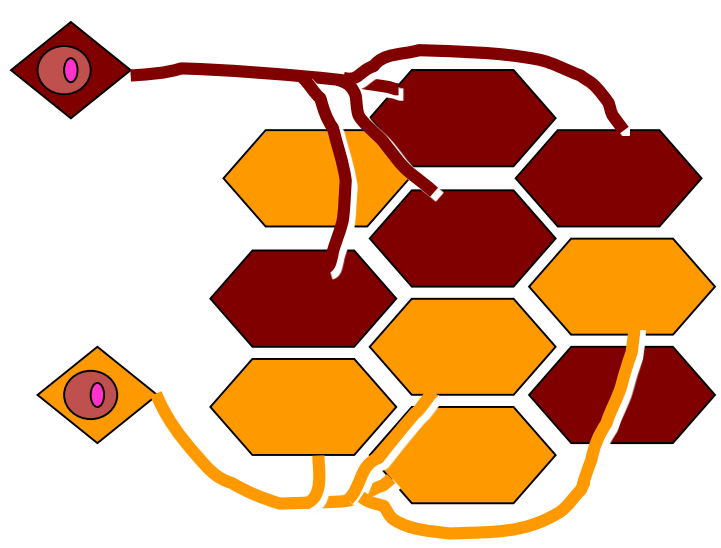
T-tubes and Lateral Sacs

Pathology and Genetics of Muscle Disease

Book to be published 2013



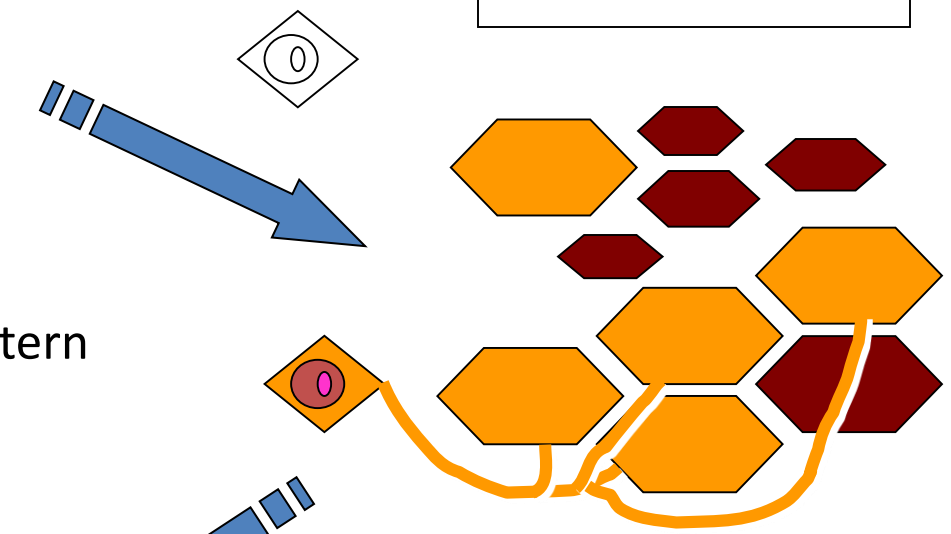
Neurogenic muscle disease



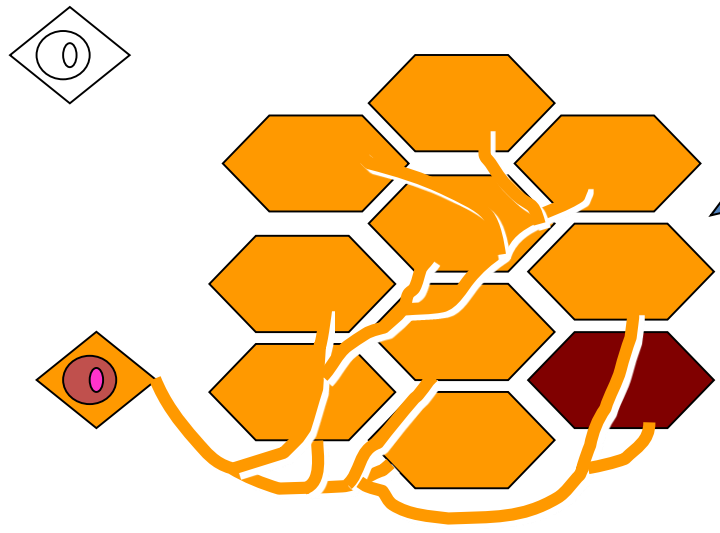
Normal – Chequer-board Pattern

Neurogenic Muscle Disease

ATPase stain



Denervation – small group atrophy

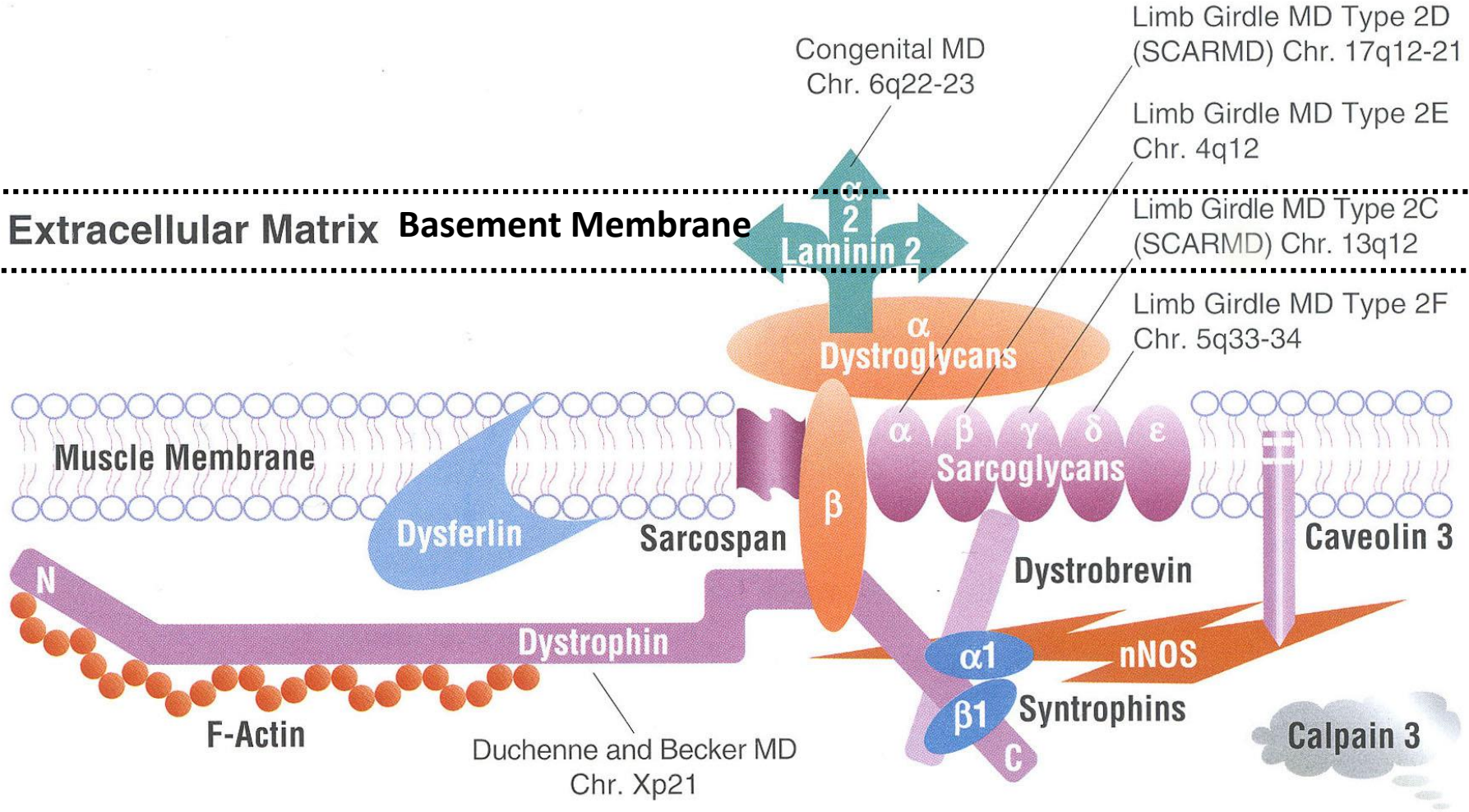


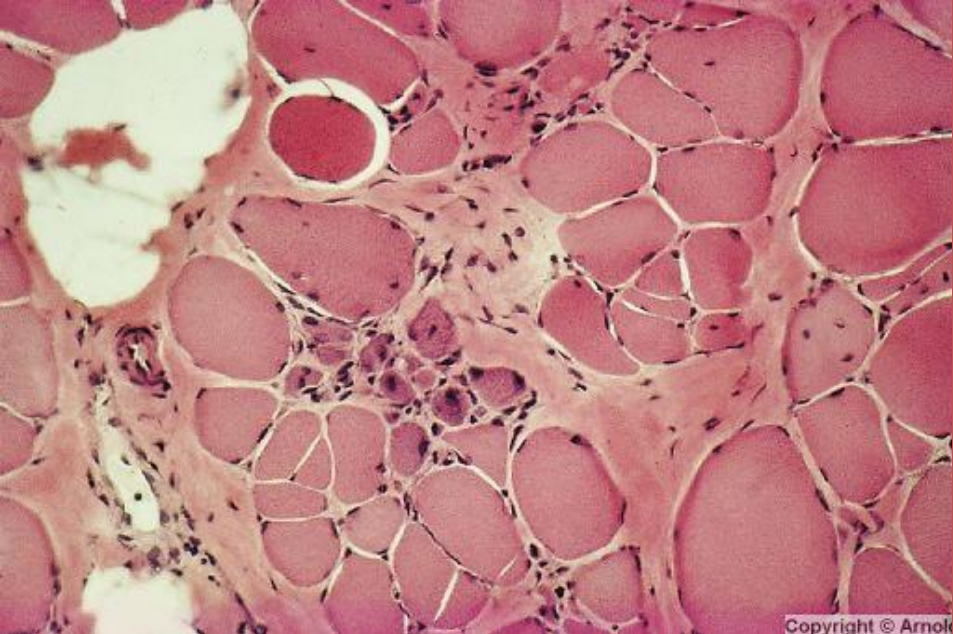
Reinnervation and fibre type grouping

**Sarcolemmal disorders
including Duchenne
muscular dystrophy**

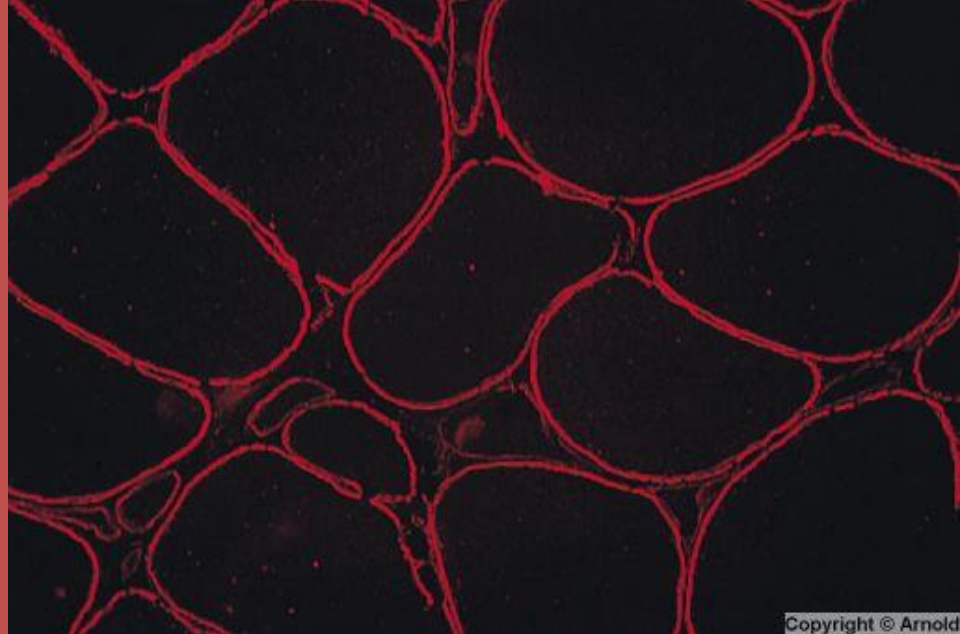
Muscular Dystrophies associated with the lack of Sarcolemmal proteins

Extracellular Matrix Basement Membrane

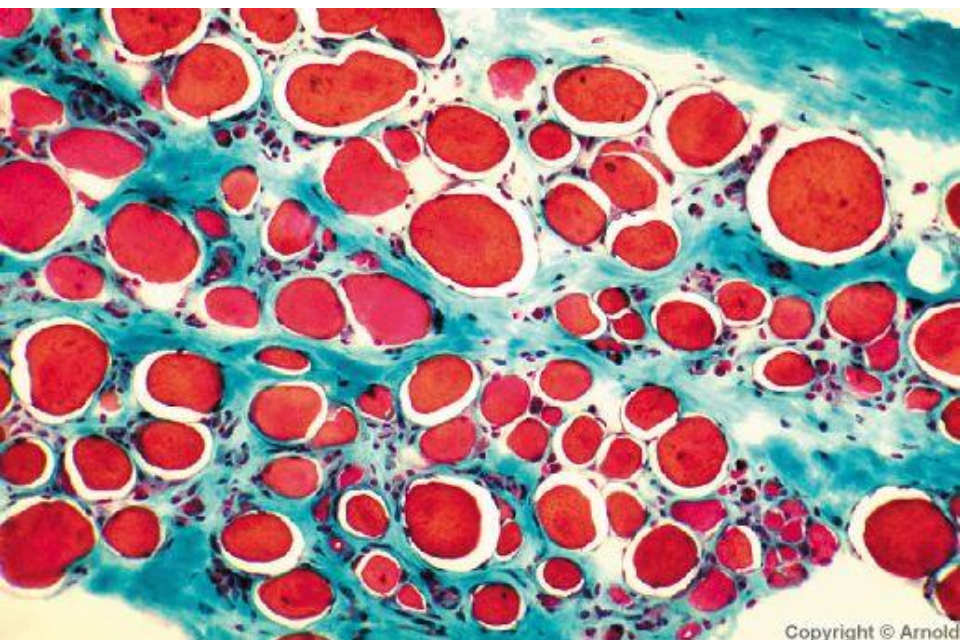




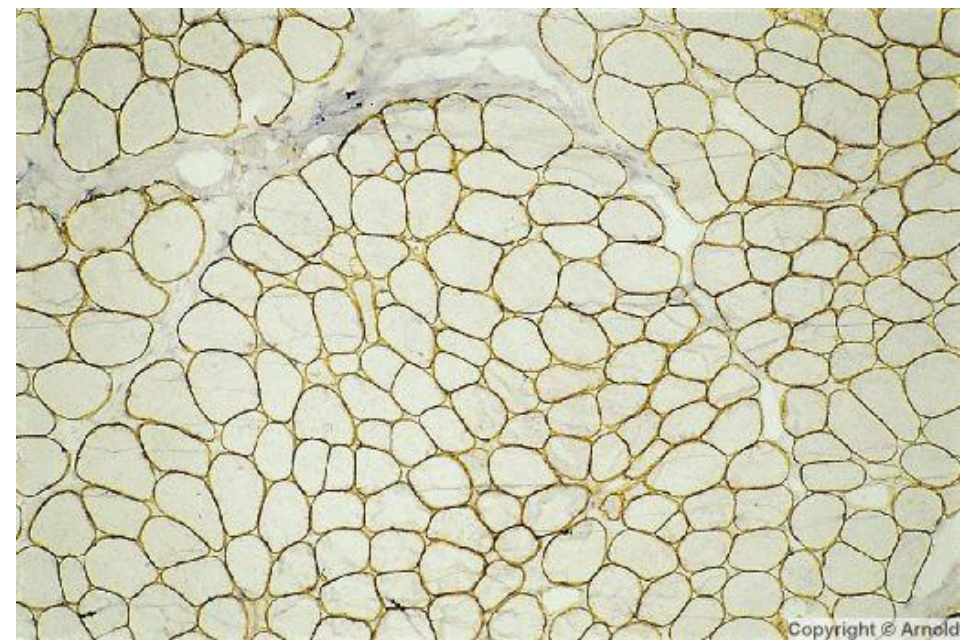
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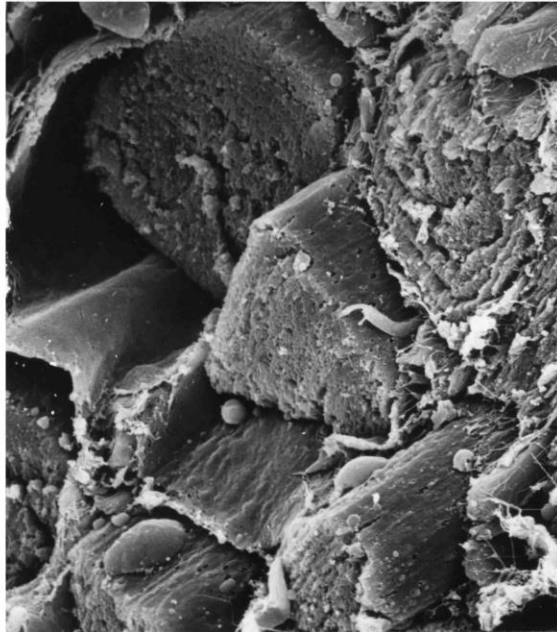
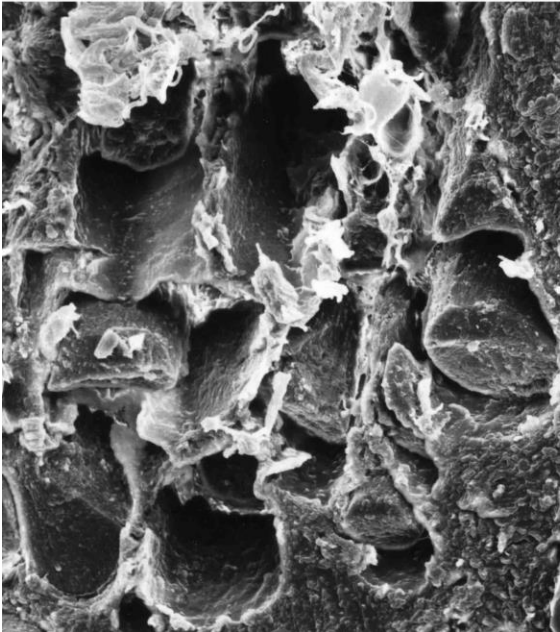
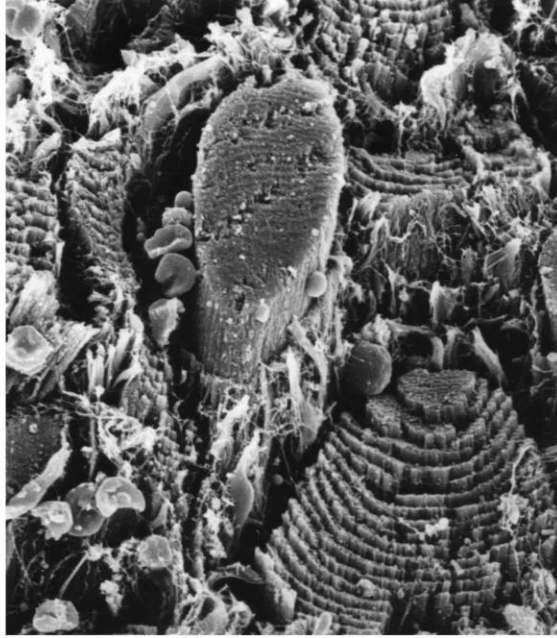
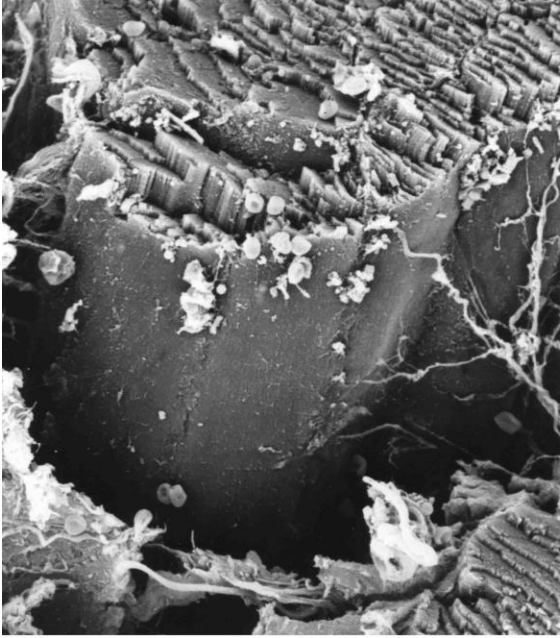


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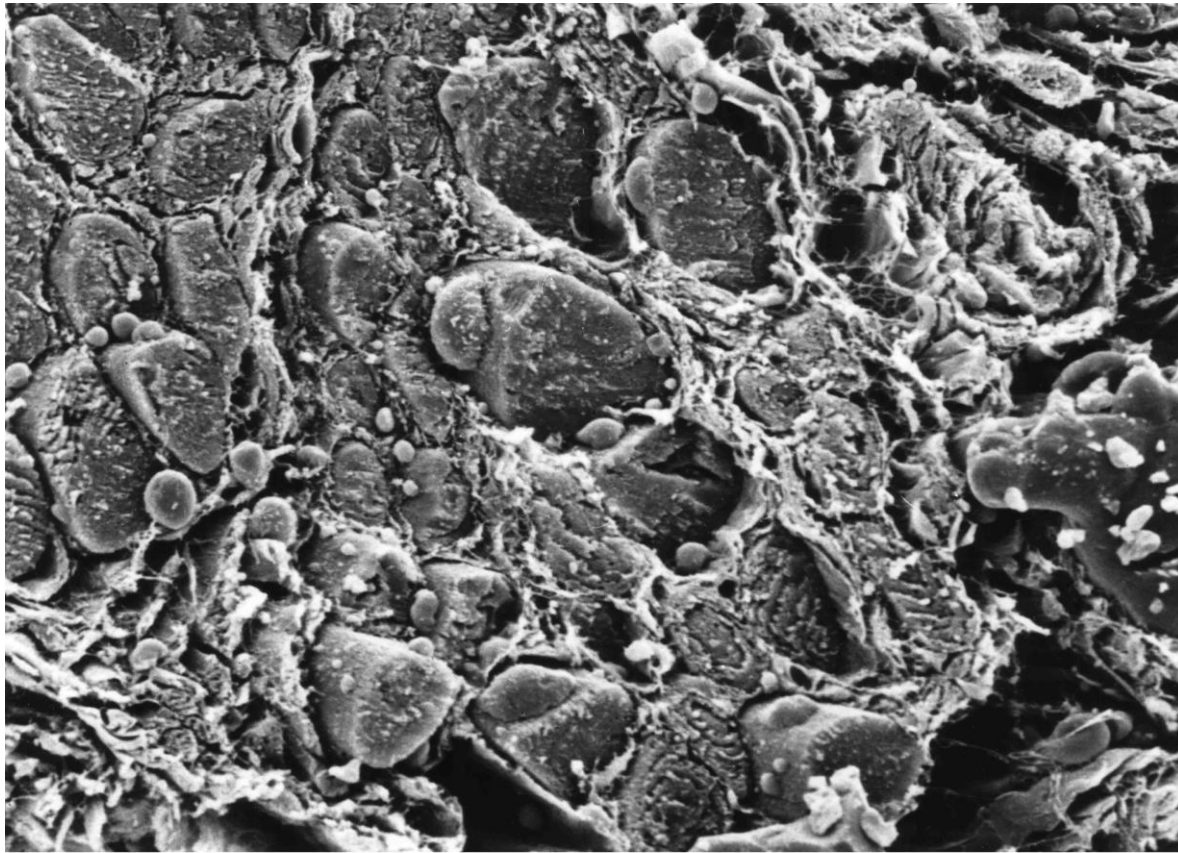
Duchenne Muscular Dystrophy

Dystrophin Immunocytochemistry- Normal

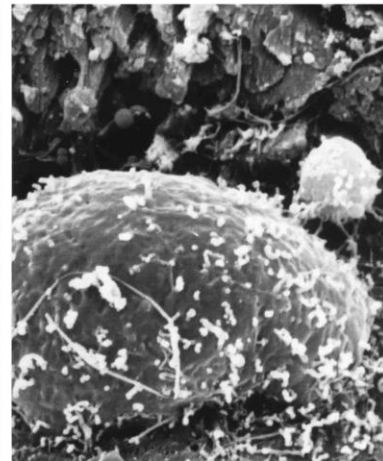
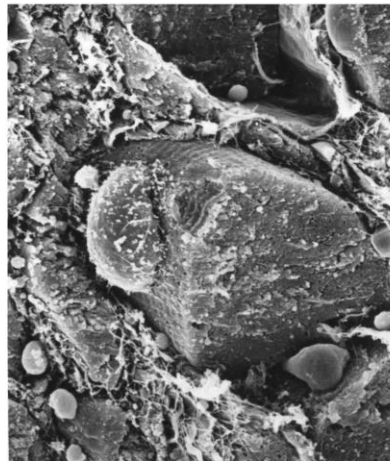
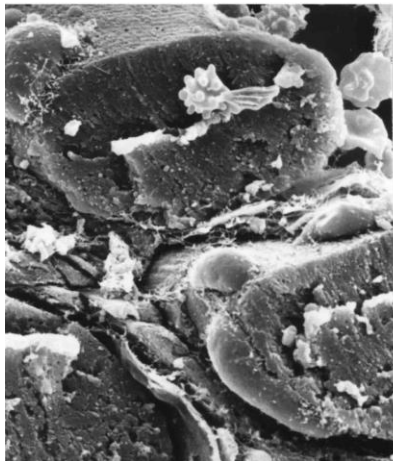
Normal



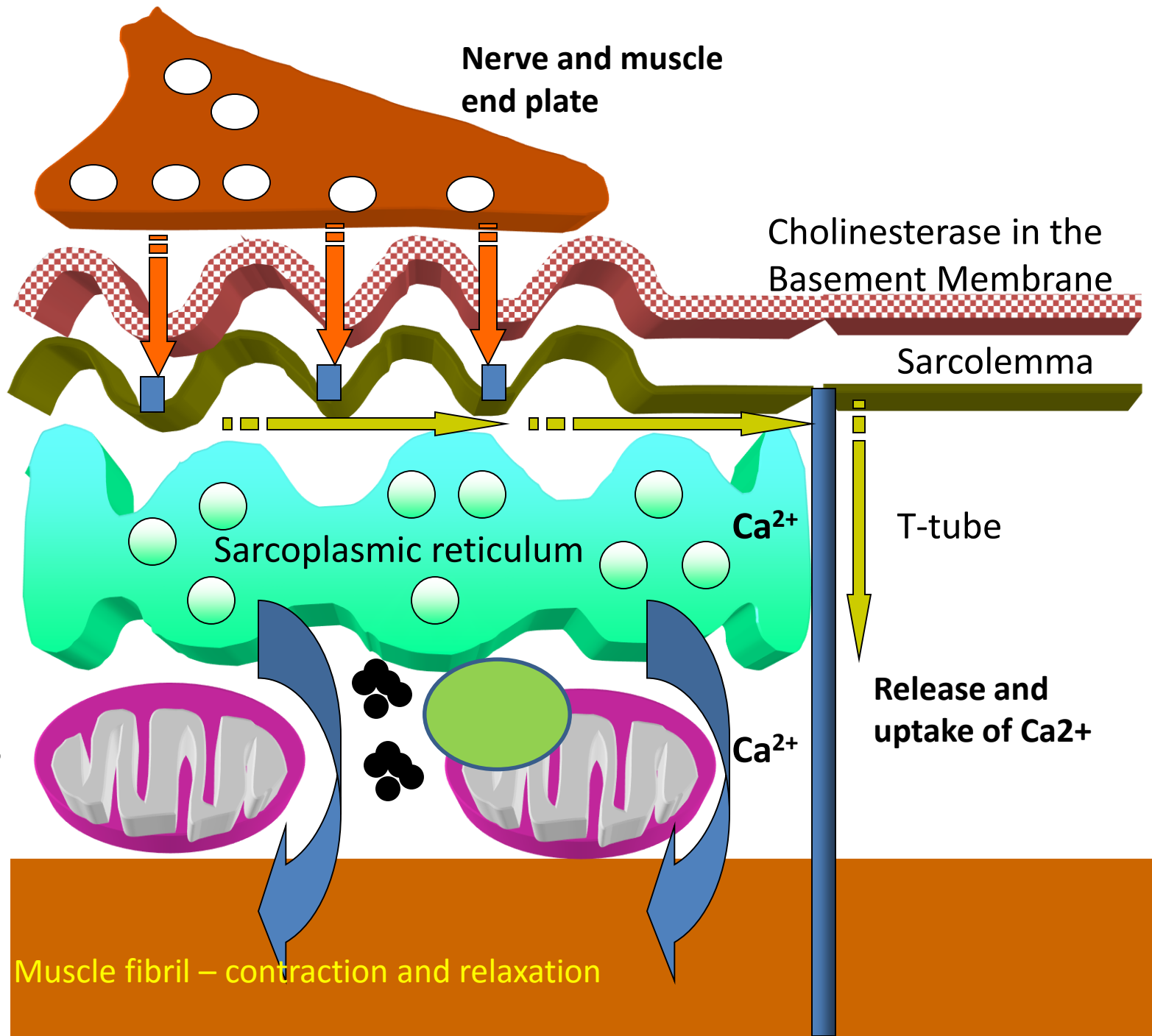
Duchenne Muscular dystrophy: separation of basement membrane from the muscle fibre



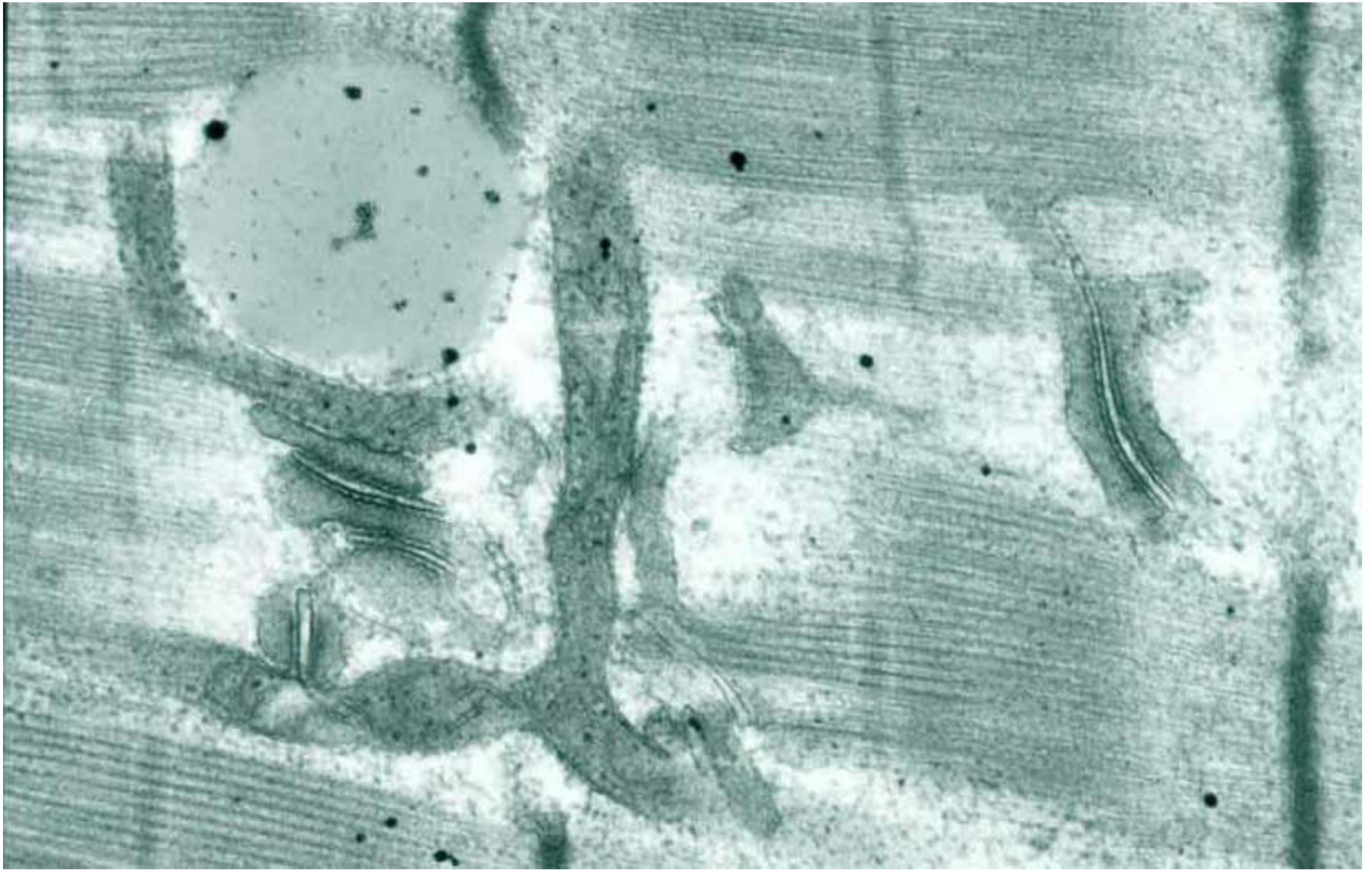
Duchenne Muscular dystrophy: separation of basement membrane from the muscle fibre



Ion Channel disorders

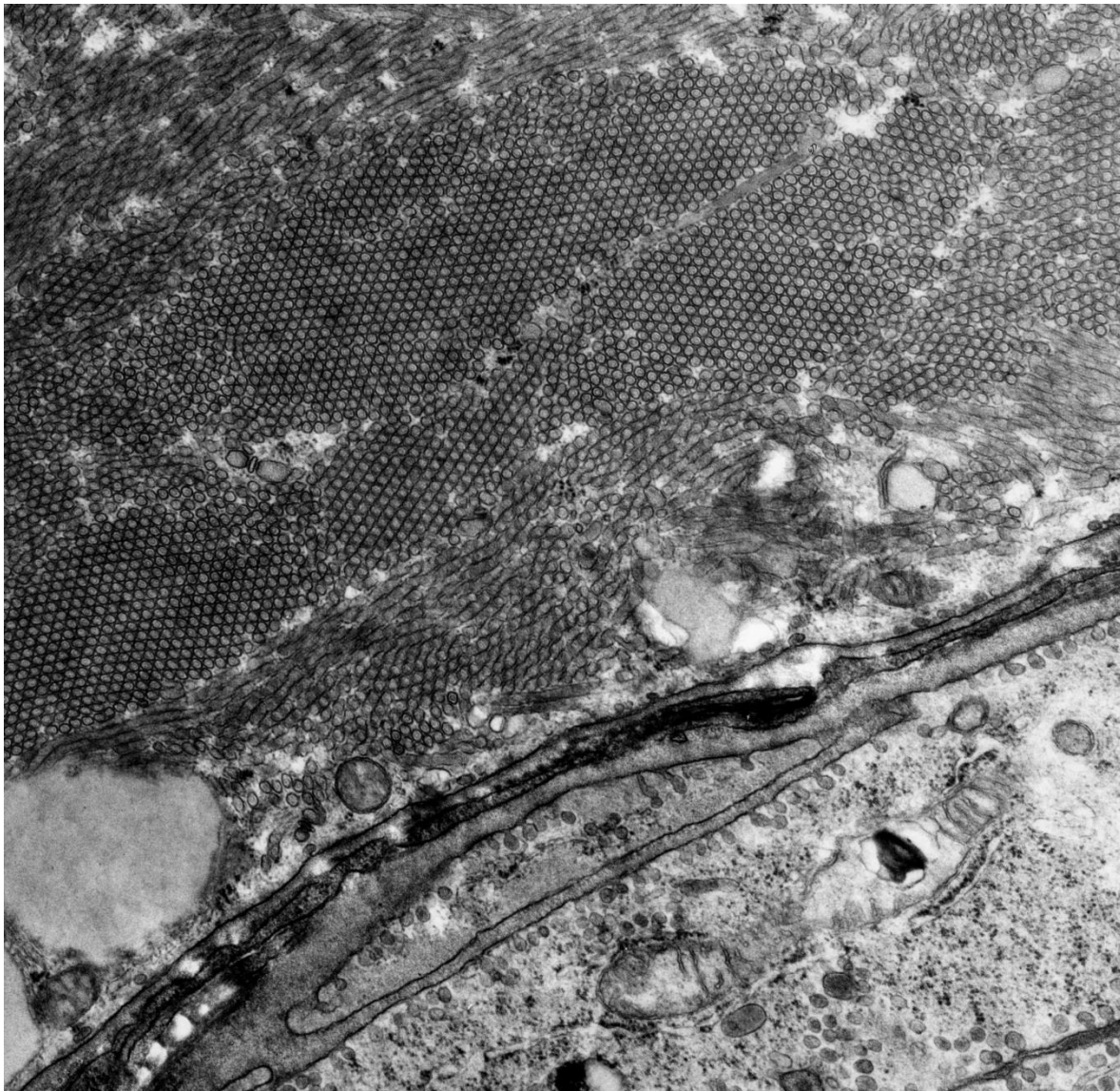


Genetic Disorders of
Ion Channels
Mitochondria
Glycogen and lipid

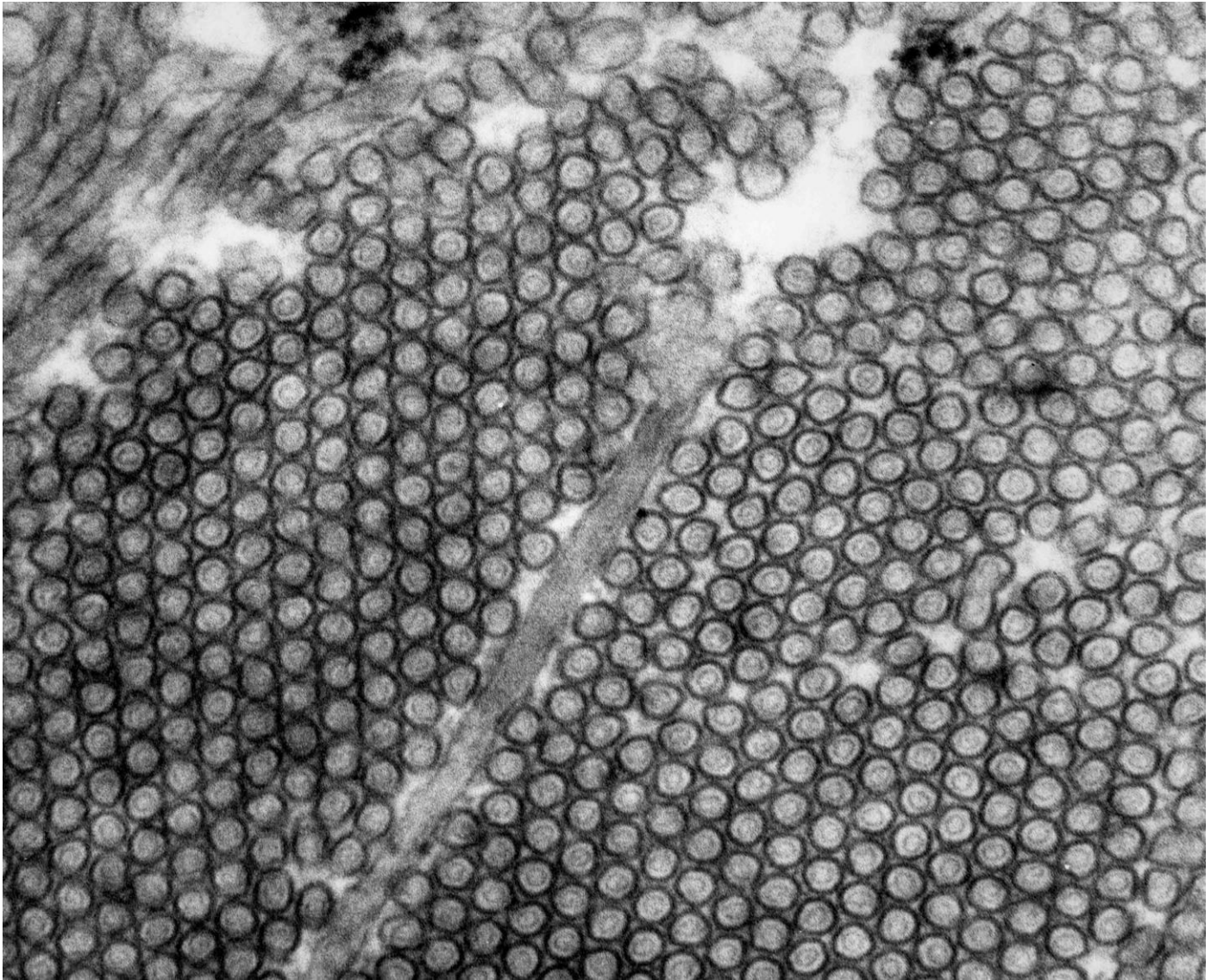


T-tubules and Lateral Sacs

D



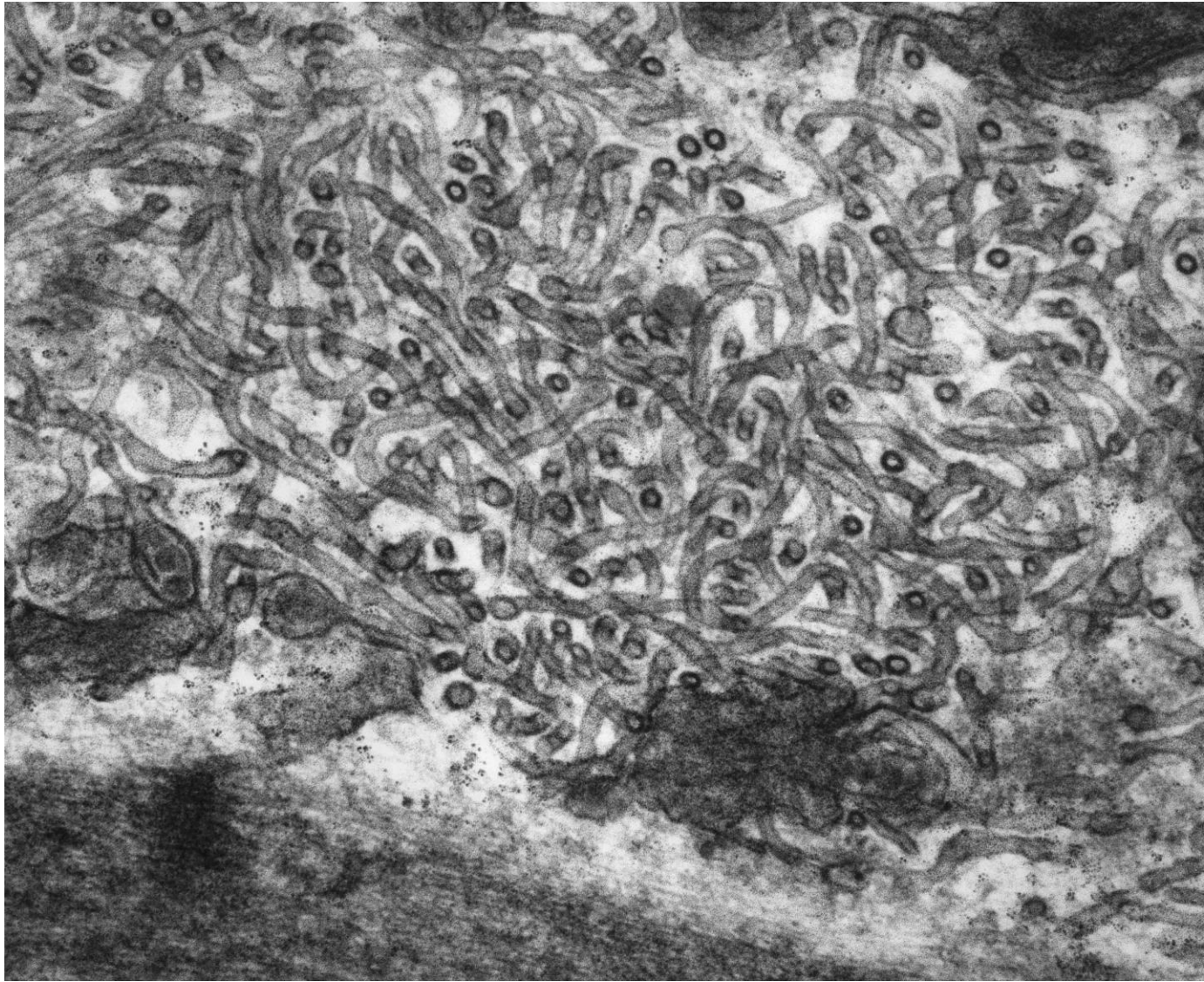
Myopathy with Tubular Aggregates



Tubular Aggregates

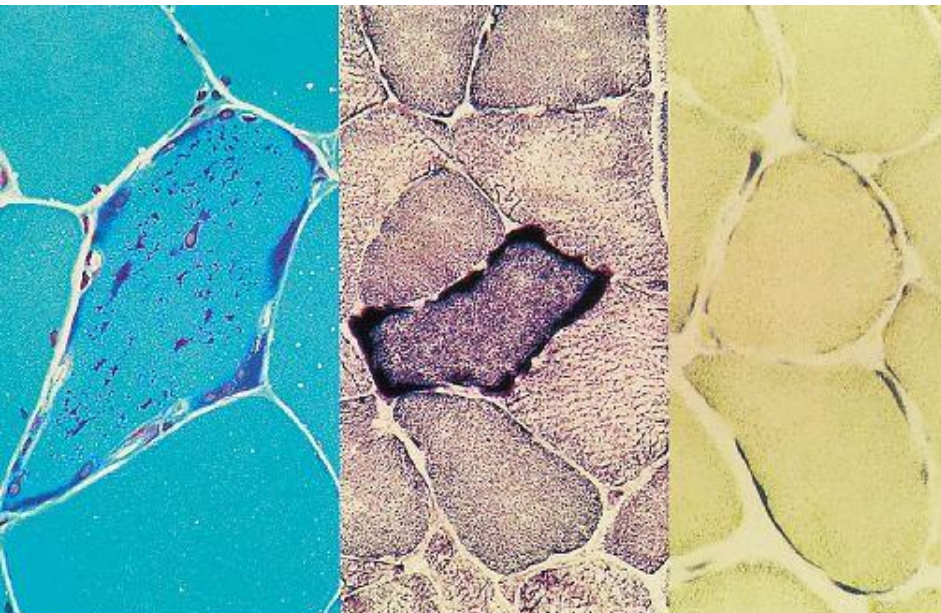
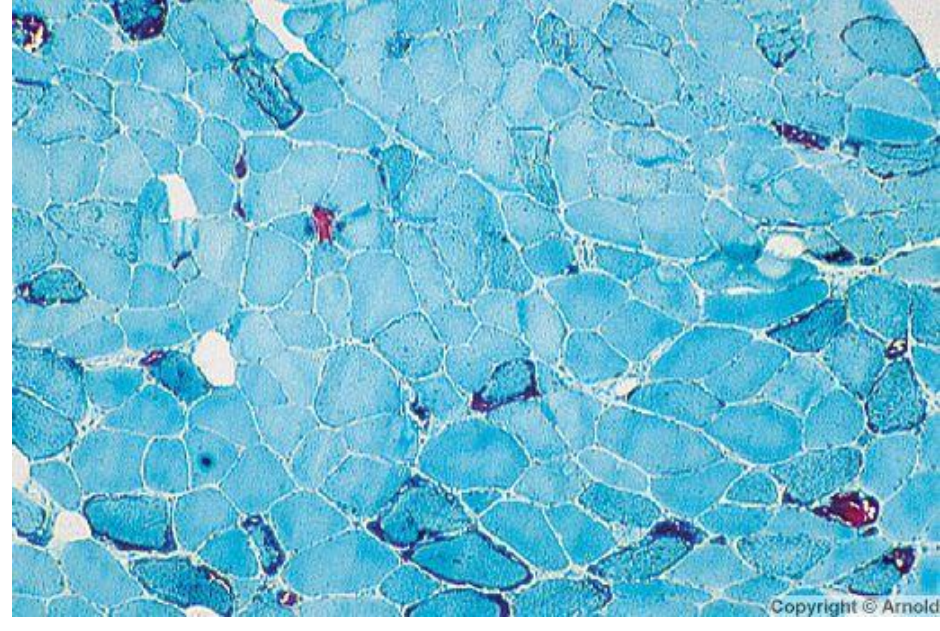
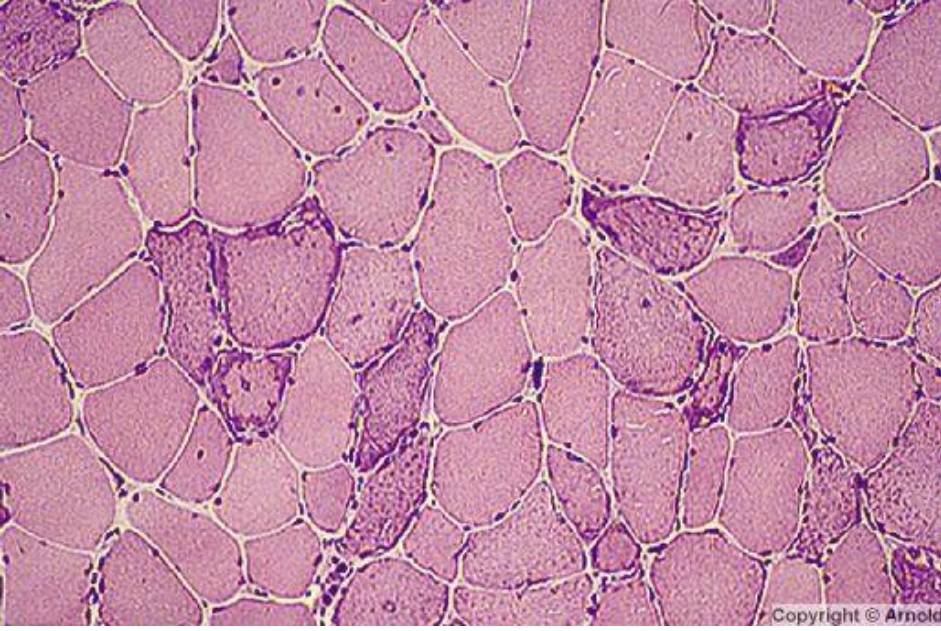


Tubular Aggregates

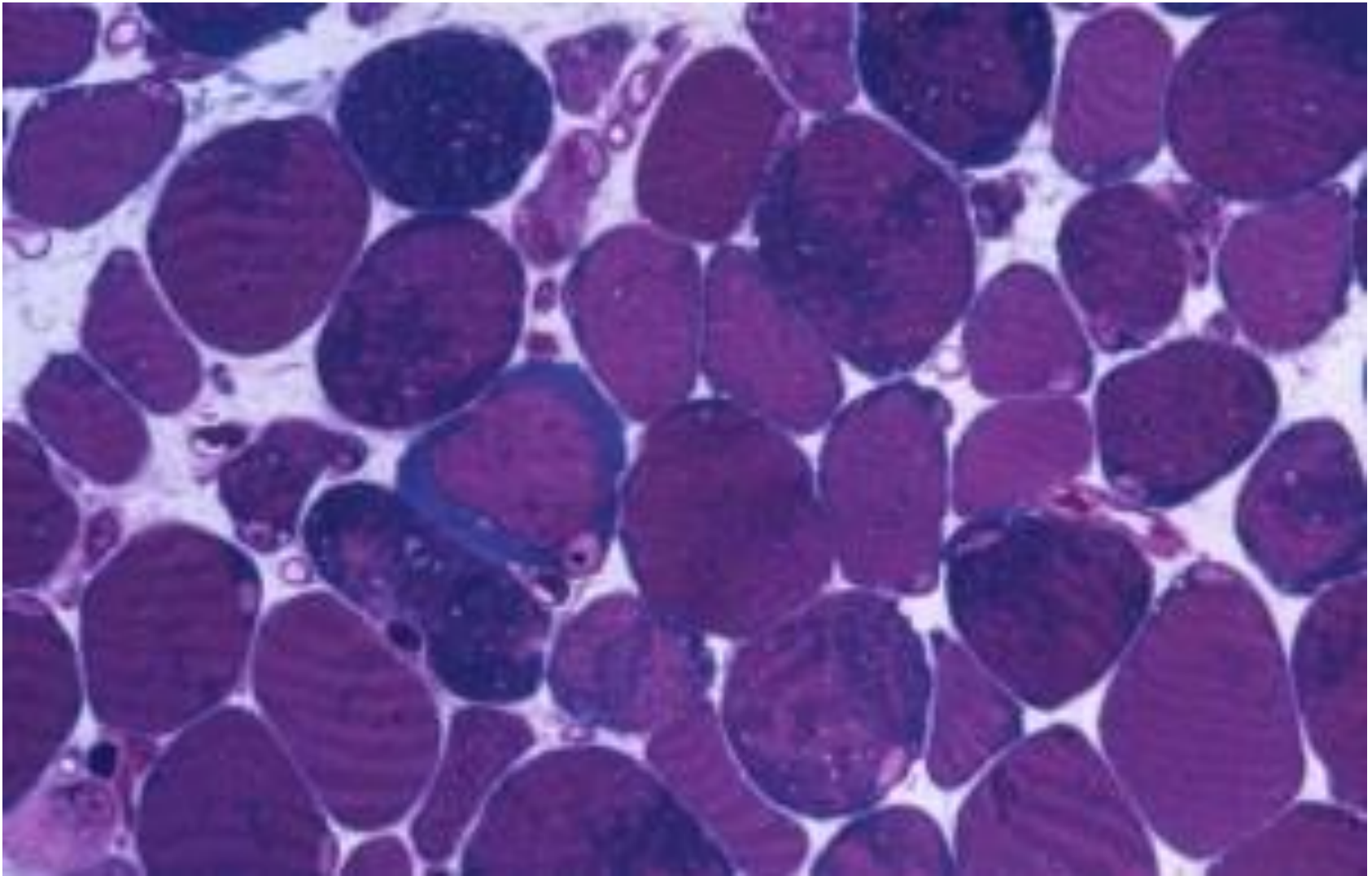


Tubular Aggregates

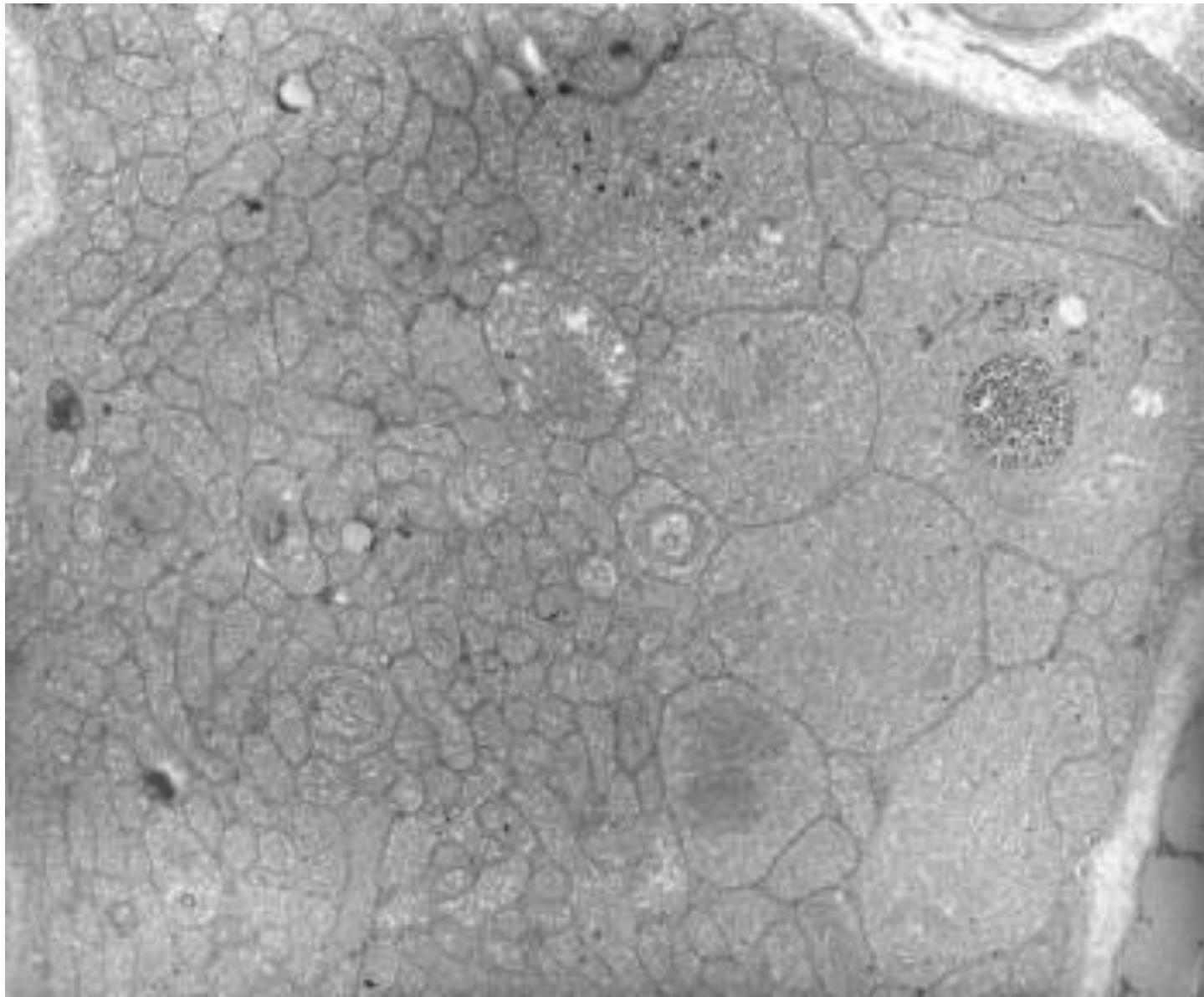
Mitochondrial myopathies



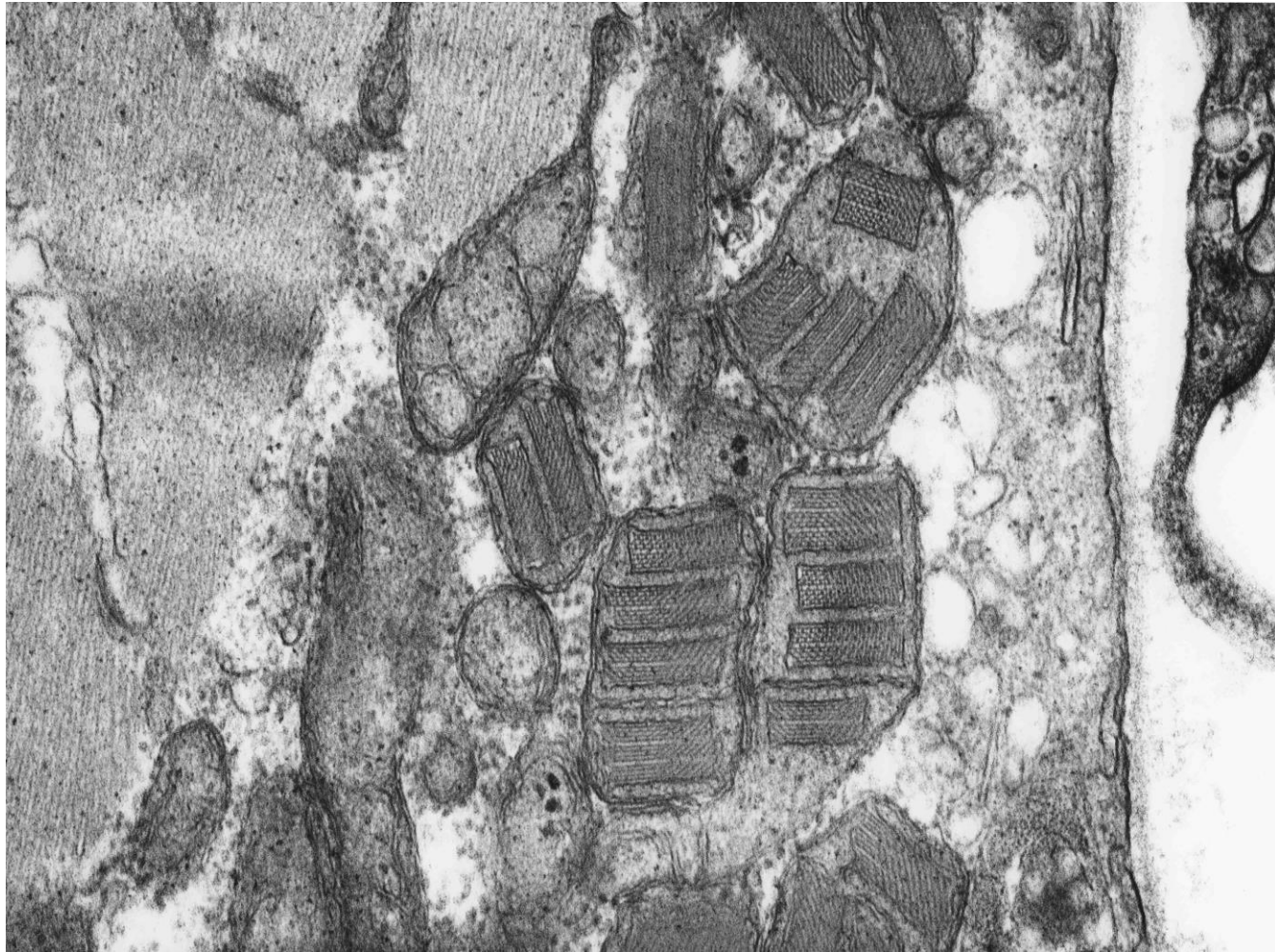
Mitochondrial Cytopathy (Myopathy)



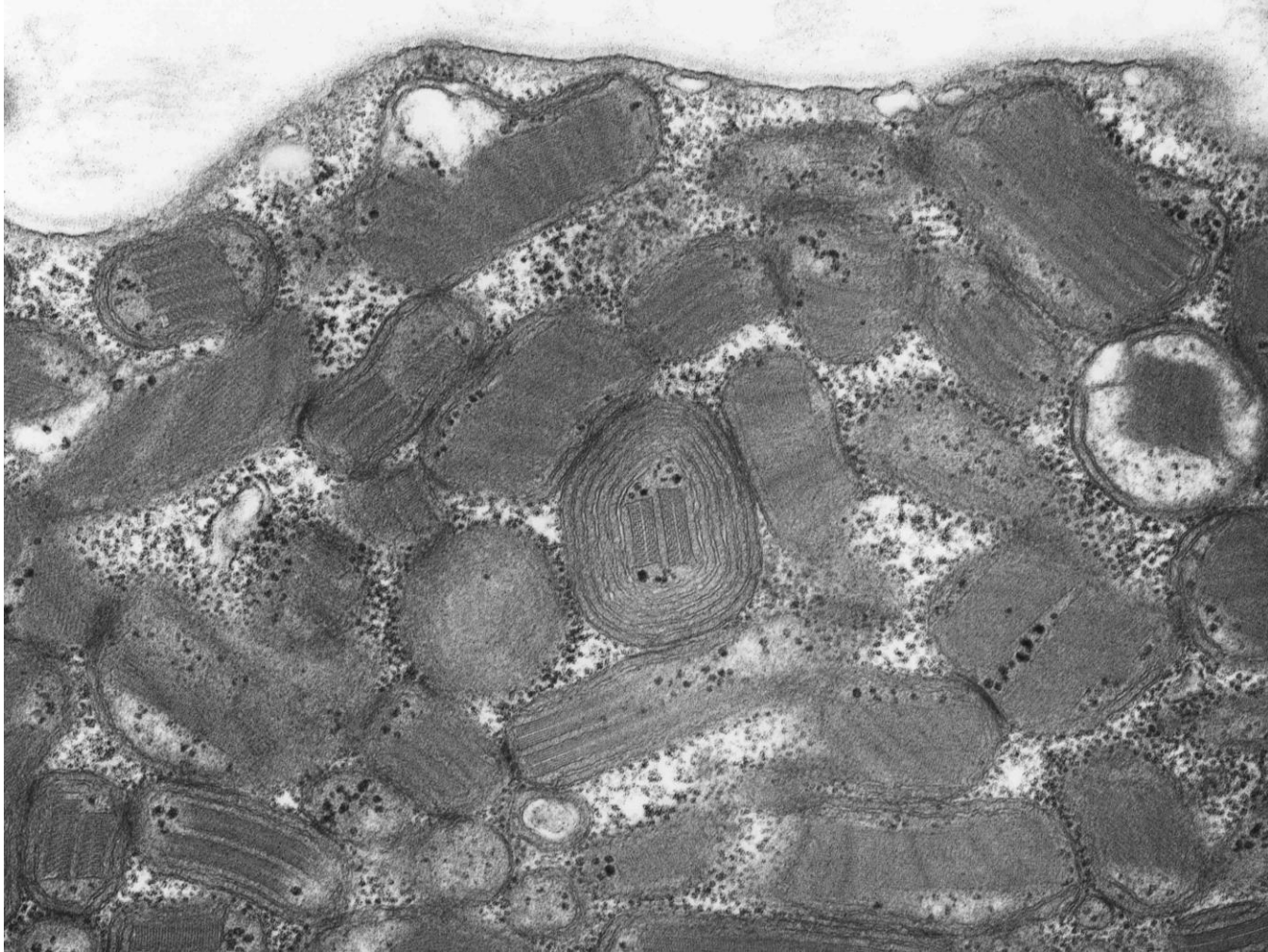
Mitochondrial myopathy – 1 μ m resin section



Mitochondrial Cytopathy (Myopathy) – (megaconial)

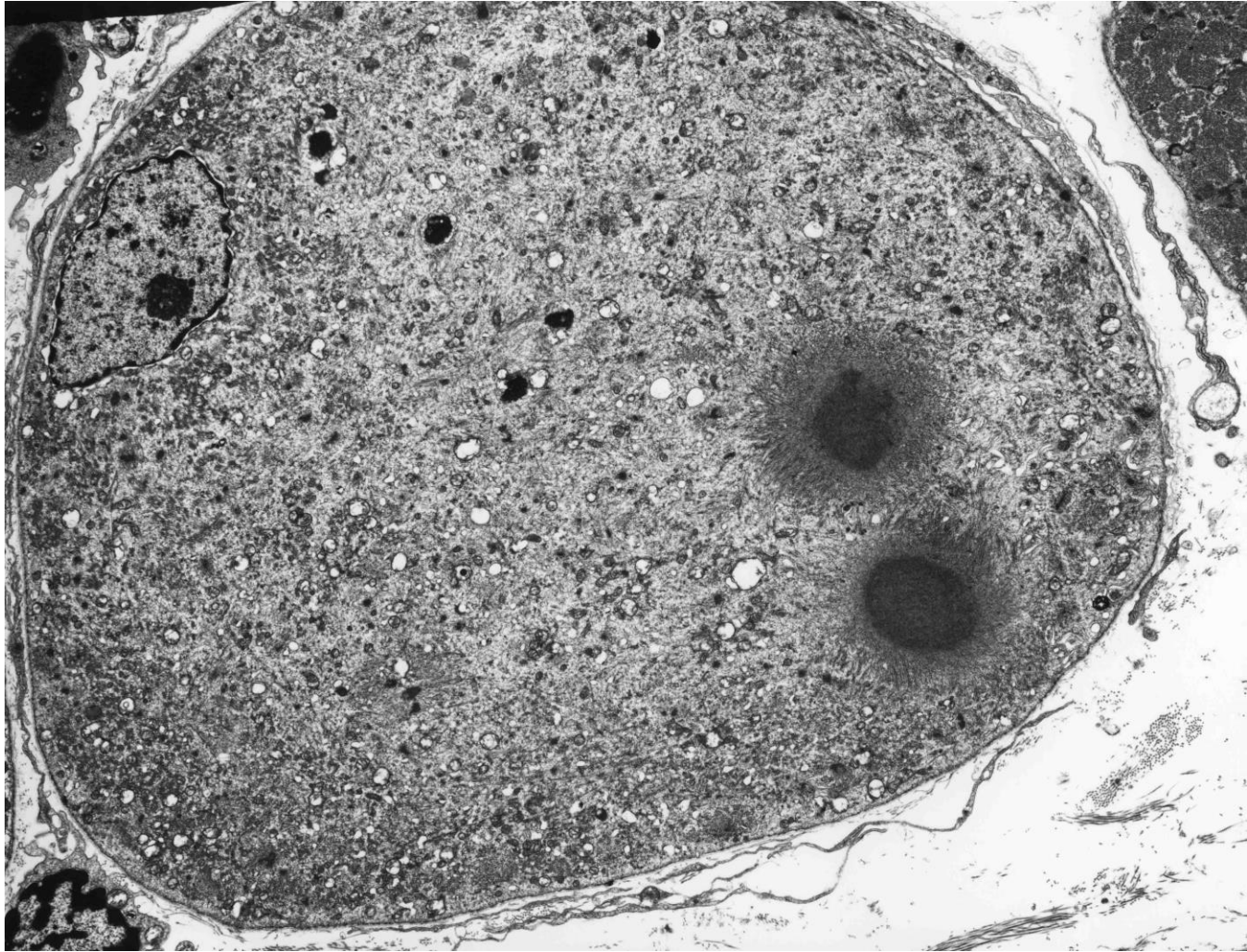


Inclusions in Mitochondrial Cytopathy (Myopathy)

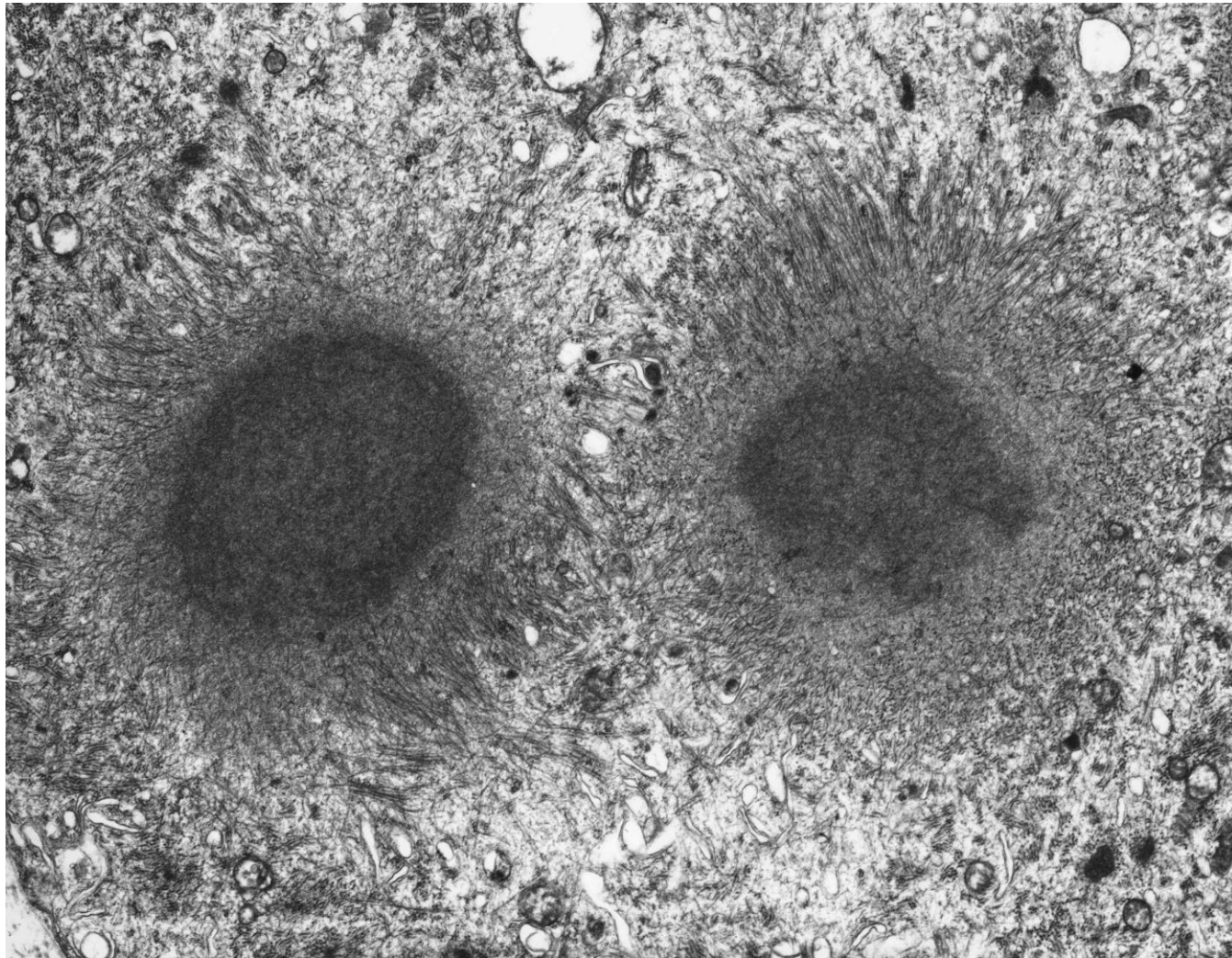


Inclusions in Mitochondrial Cytopathy (Myopathy)

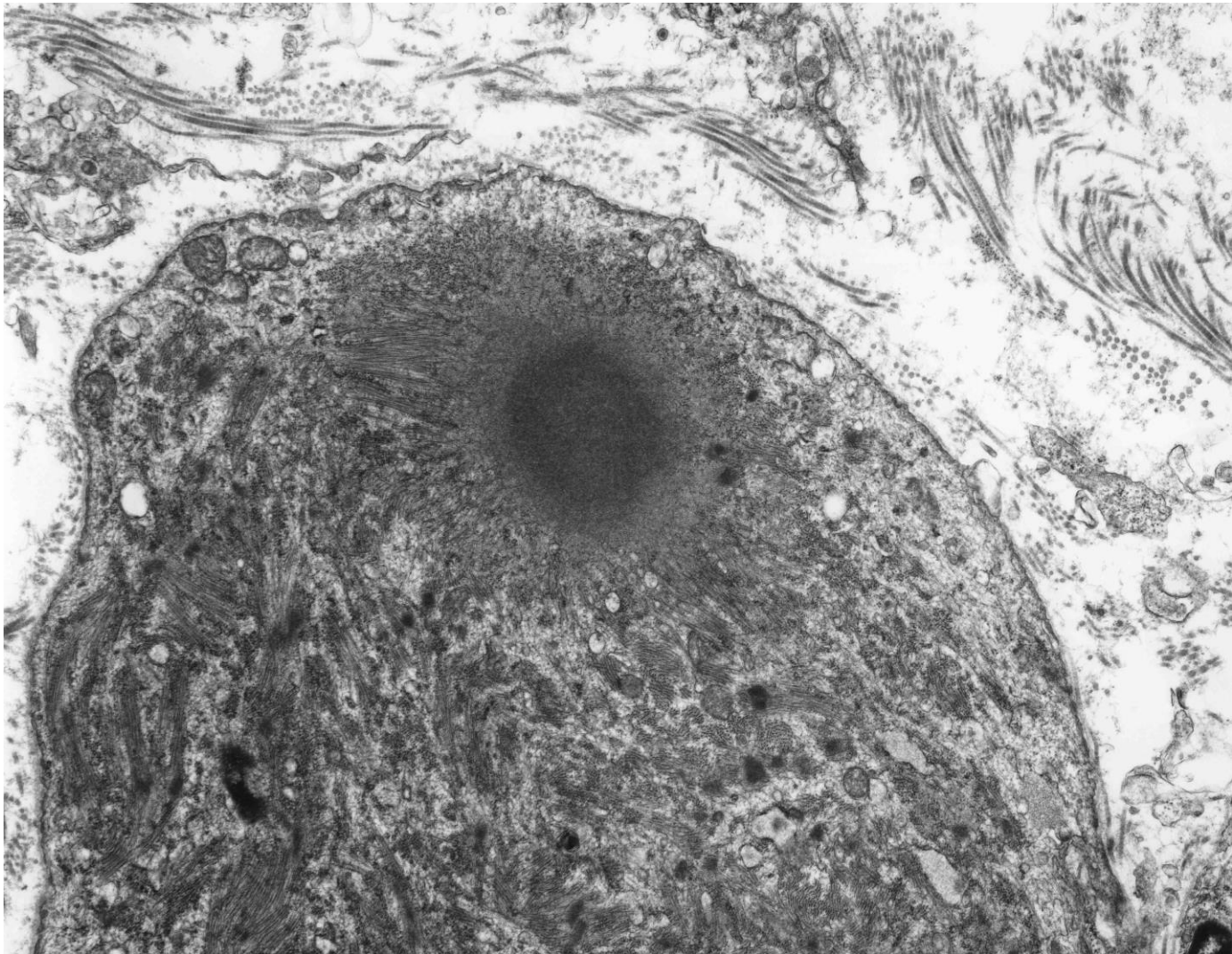
Cytoplasmic Inclusions



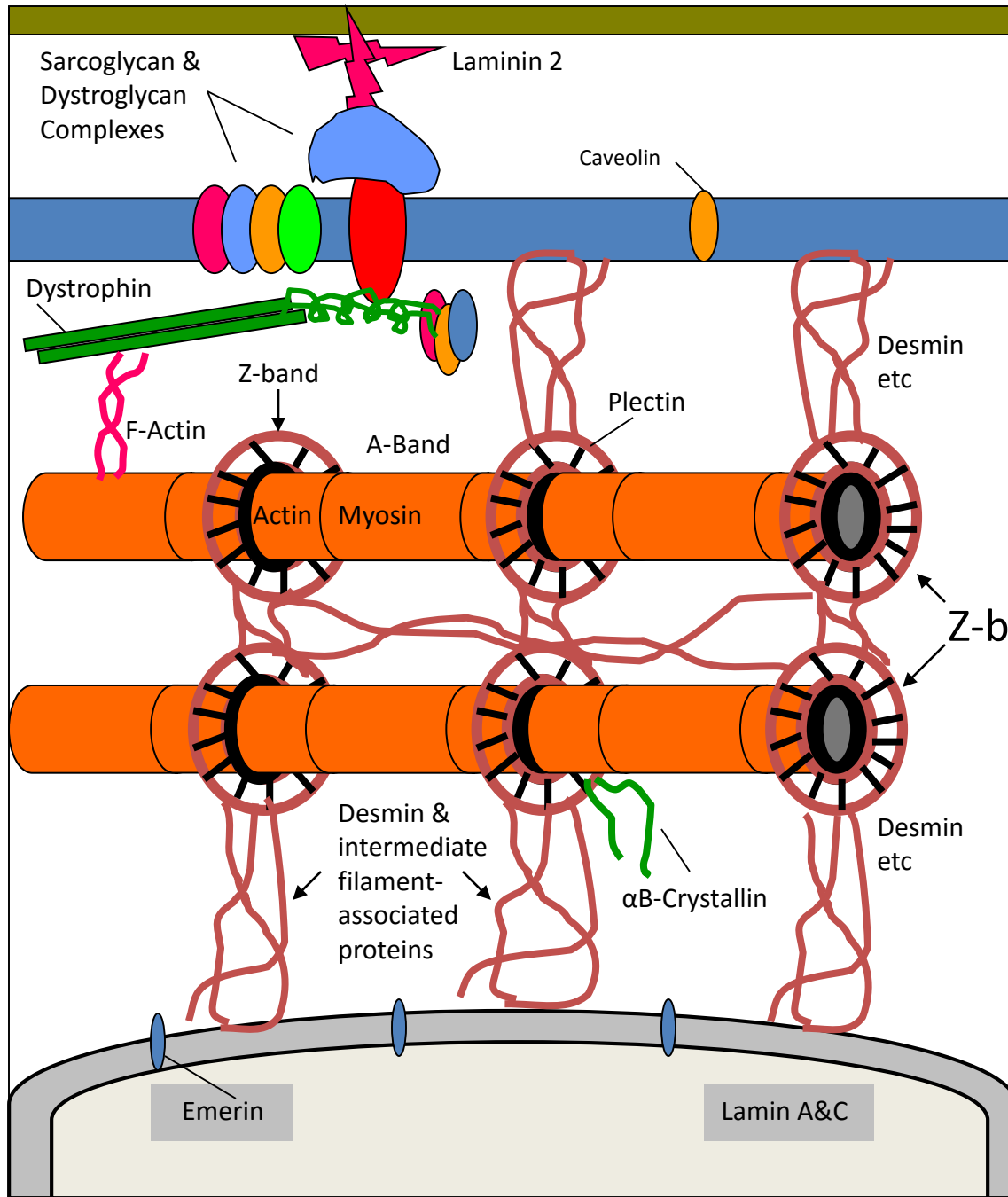
Cytoplasmic Inclusions



Cytoplasmic Inclusions – some myofibrillar myopathies



Cytoplasmic Inclusion



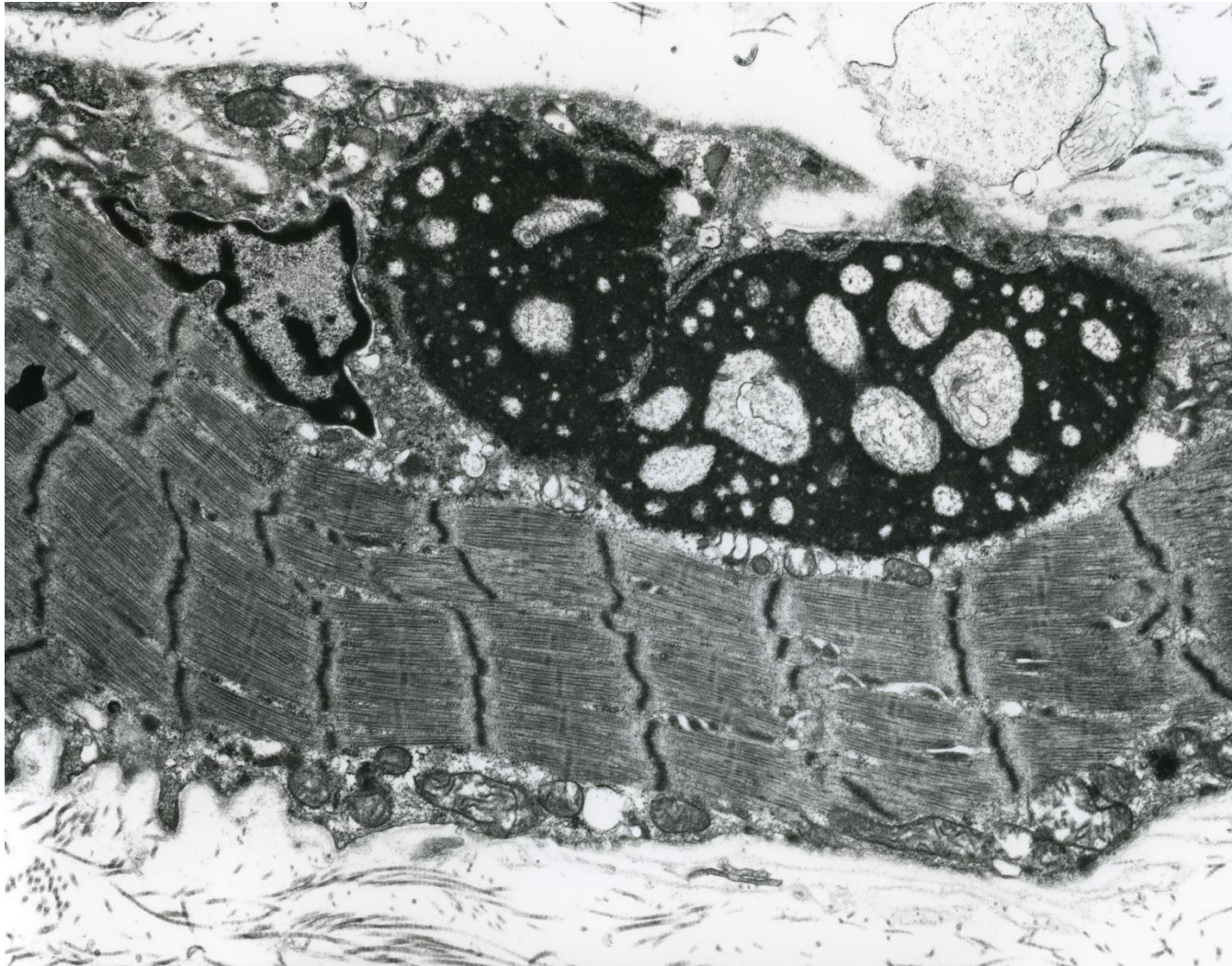
Basement Membrane

Sarcolemma

Z-bands

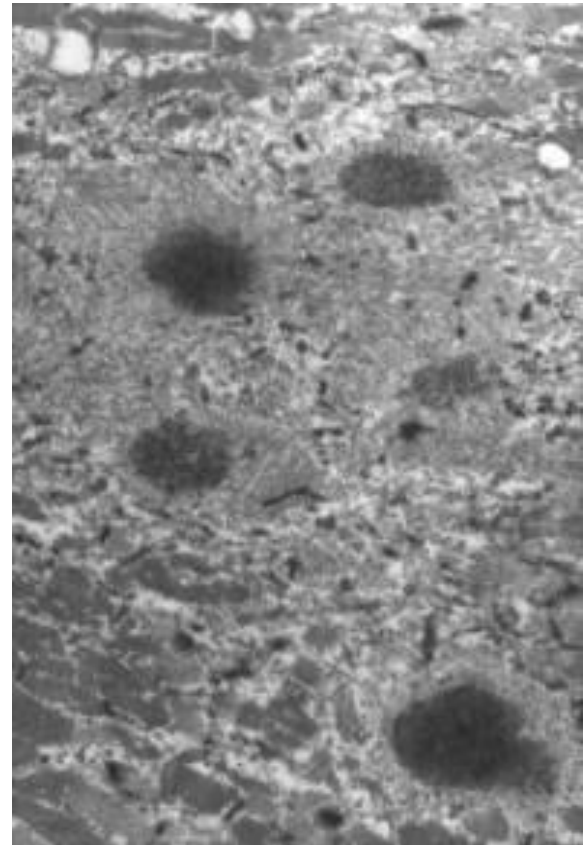
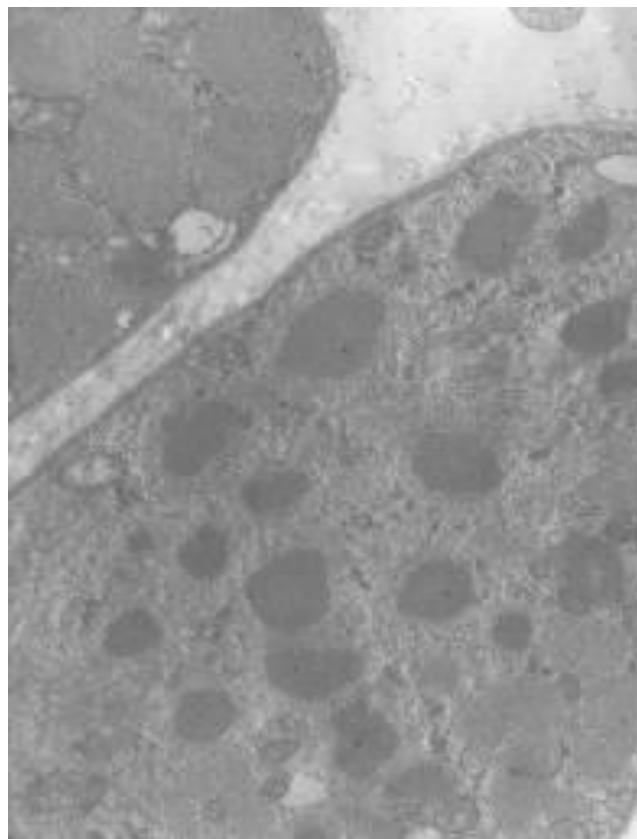
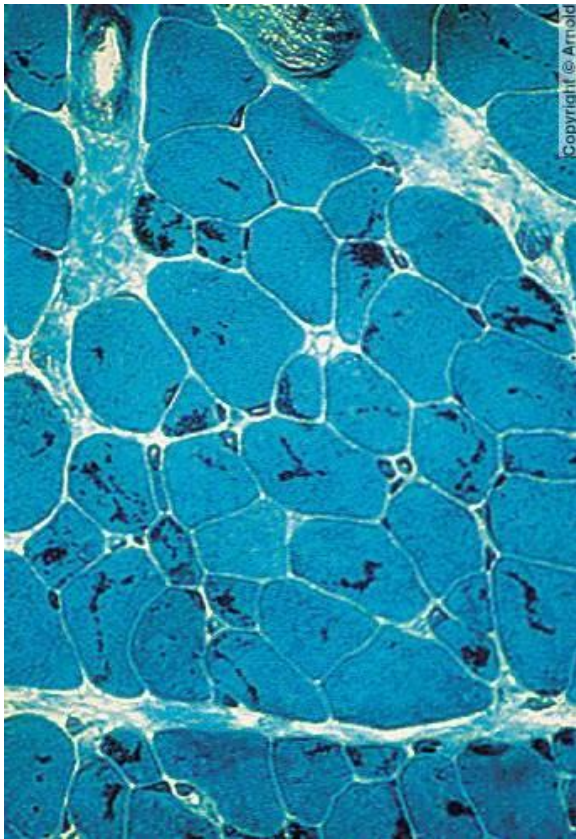
**Myofibrillar
myopathies**

Nucleus

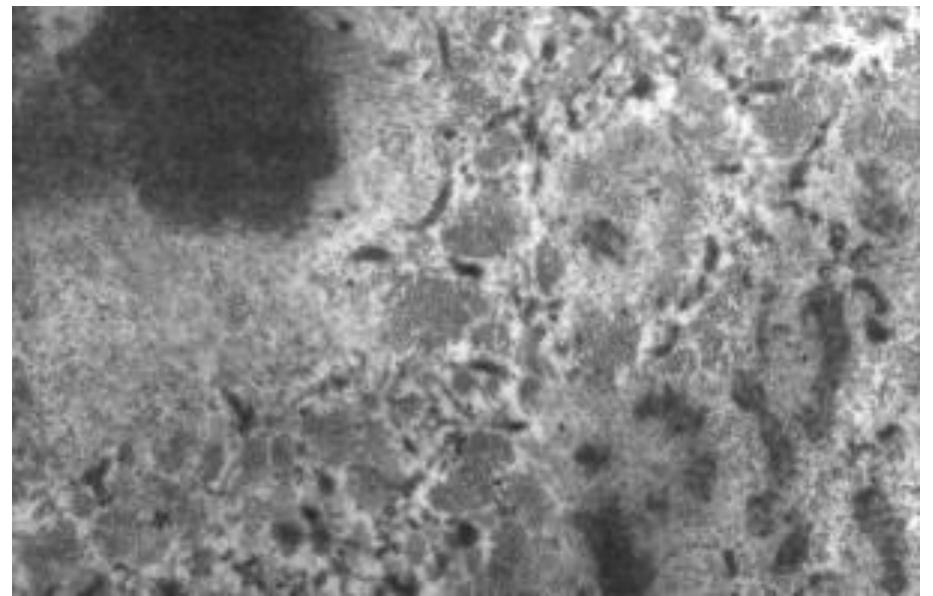
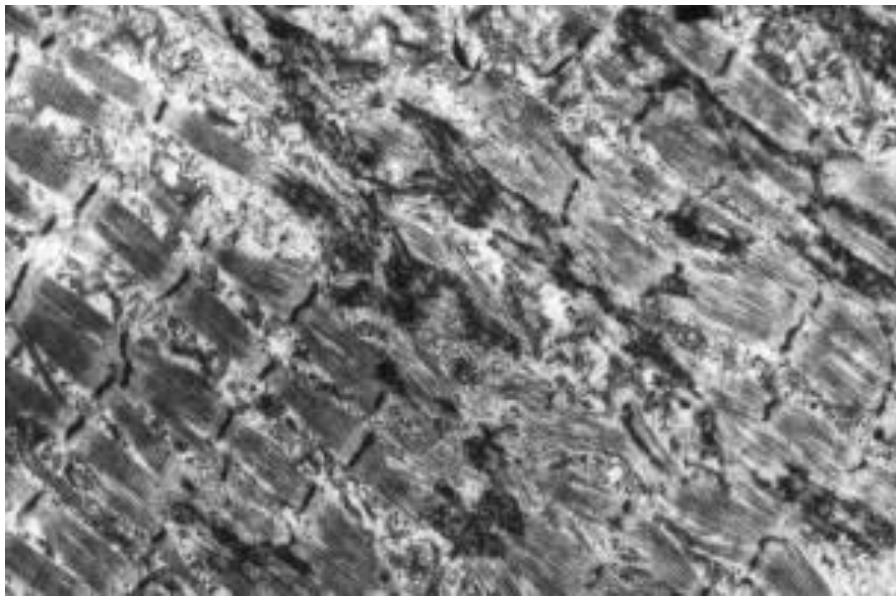
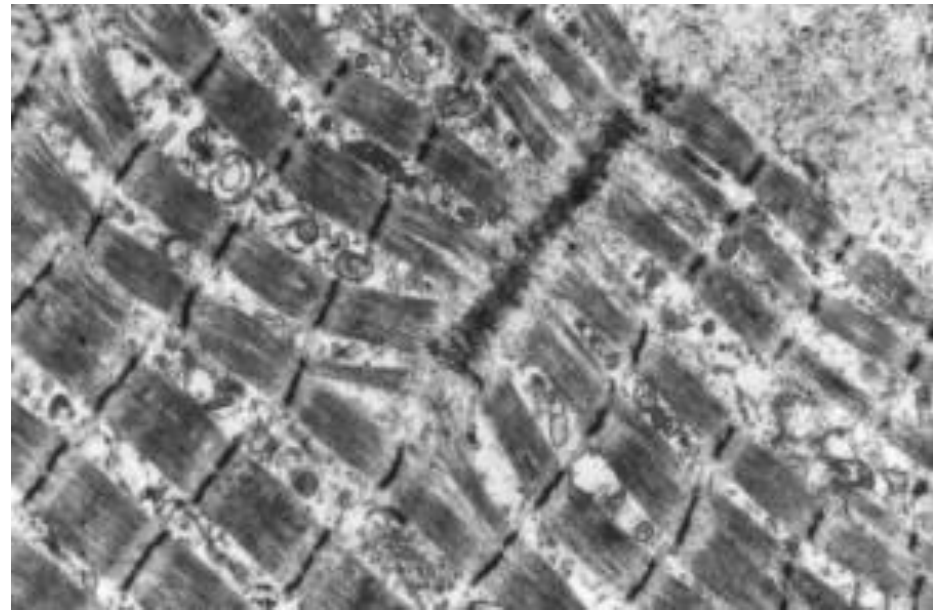
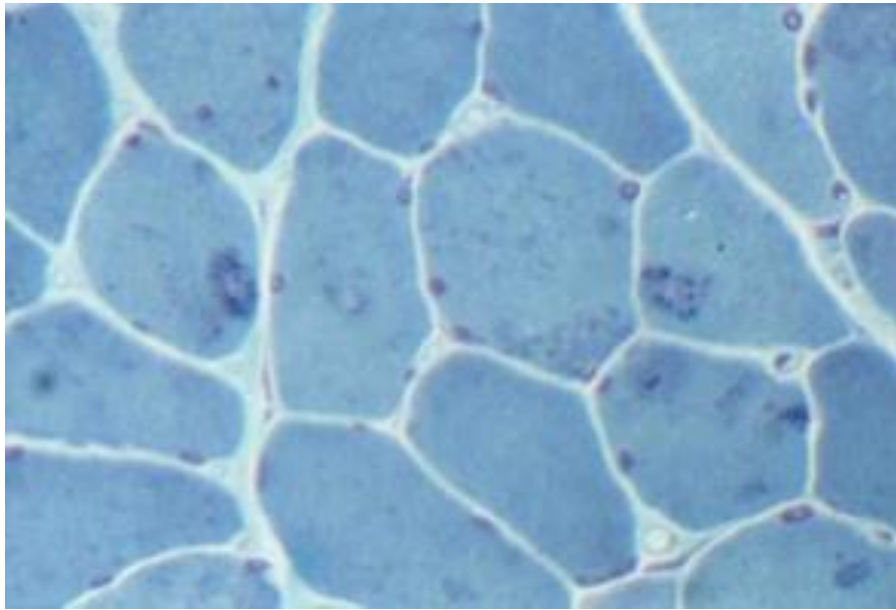


Reducing body – reduces menadione nitro-blue-tetrazolium (NBT) – mutation in the *FHL1* gene and other disorders

Z-band disorders – rod bodies



Nemaline myopathy – defects in thin filament proteins eg actin



Toxic myopathy due to Senna

Muscle fibre destruction and regeneration

For example “inflammatory myopathies”

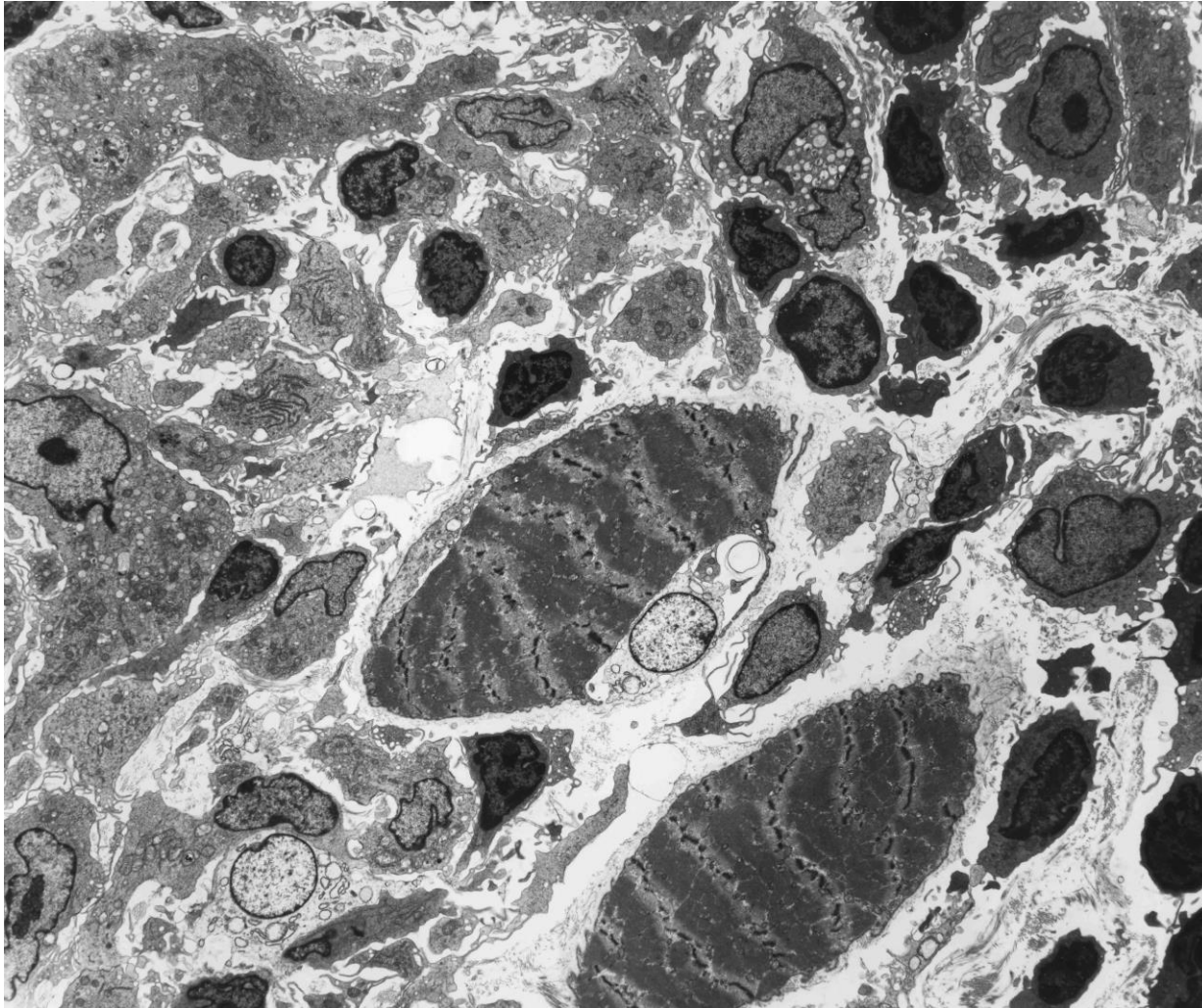
Polymyositis,

dermatomyositis,

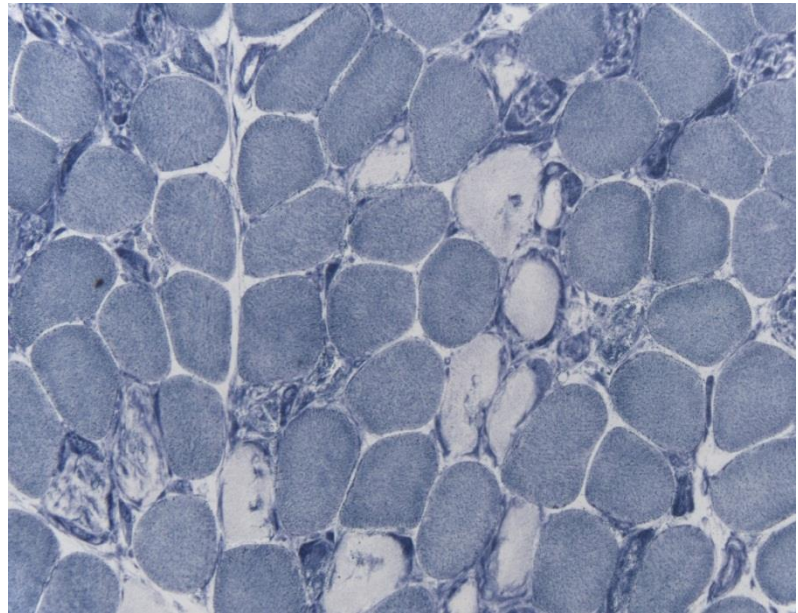
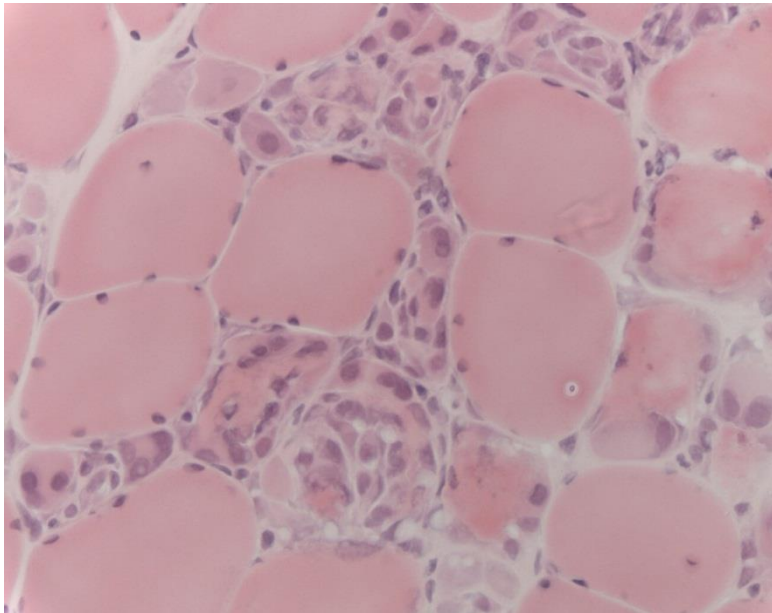
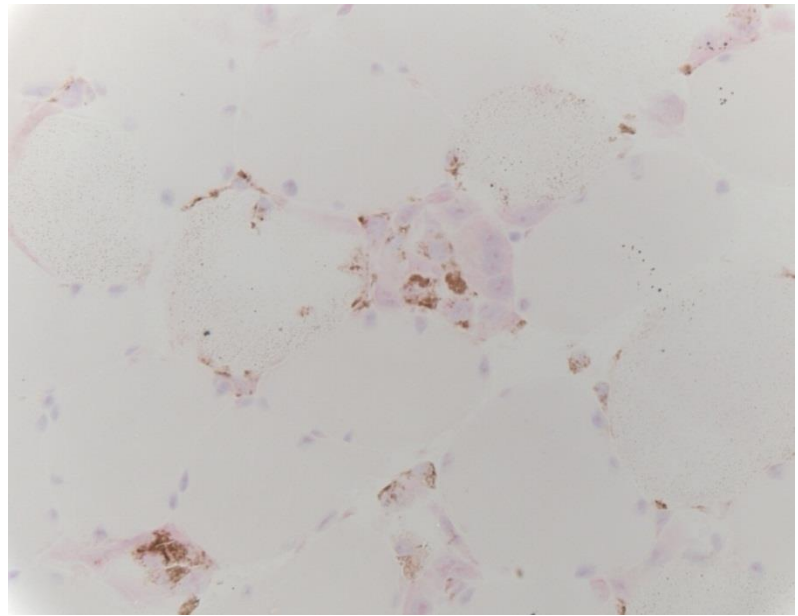
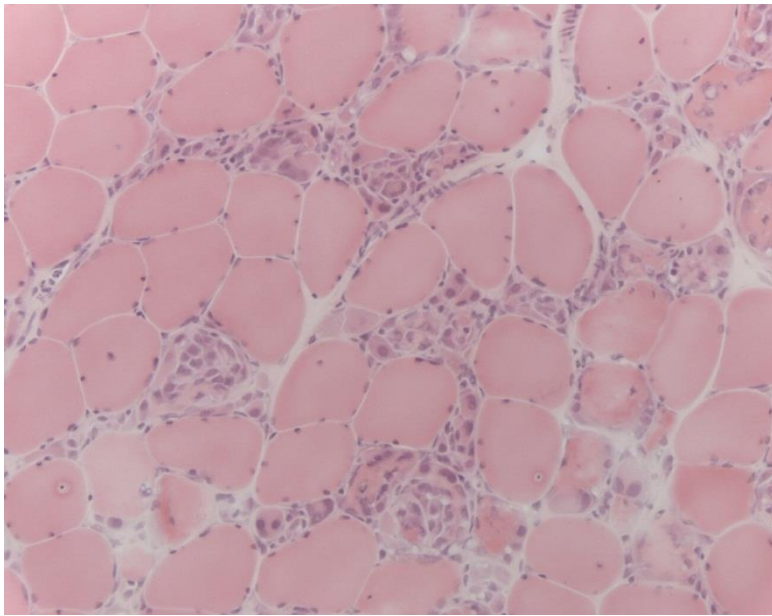
Inclusion Body Myositis,

parasitic infections

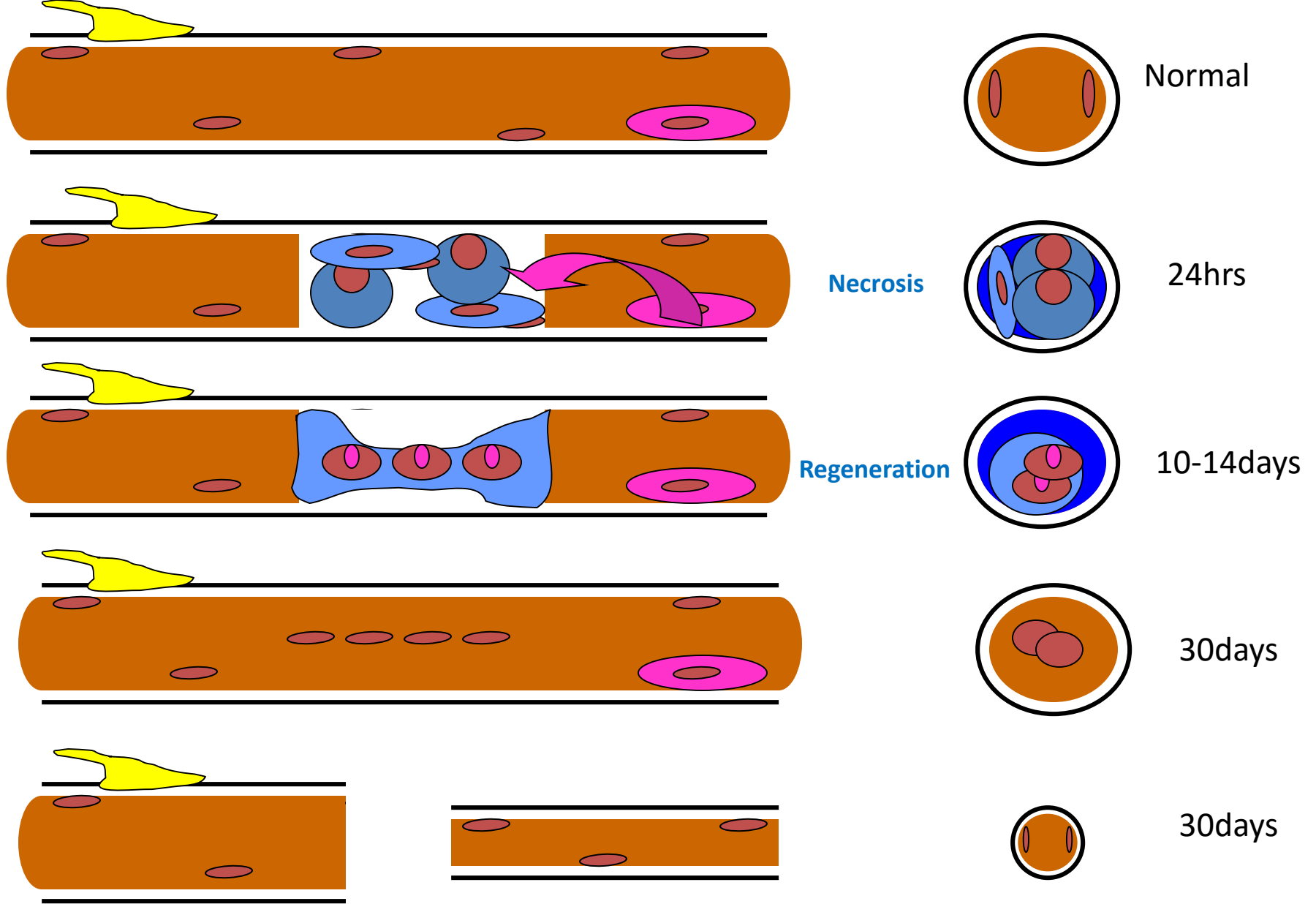
But also Dystrophies



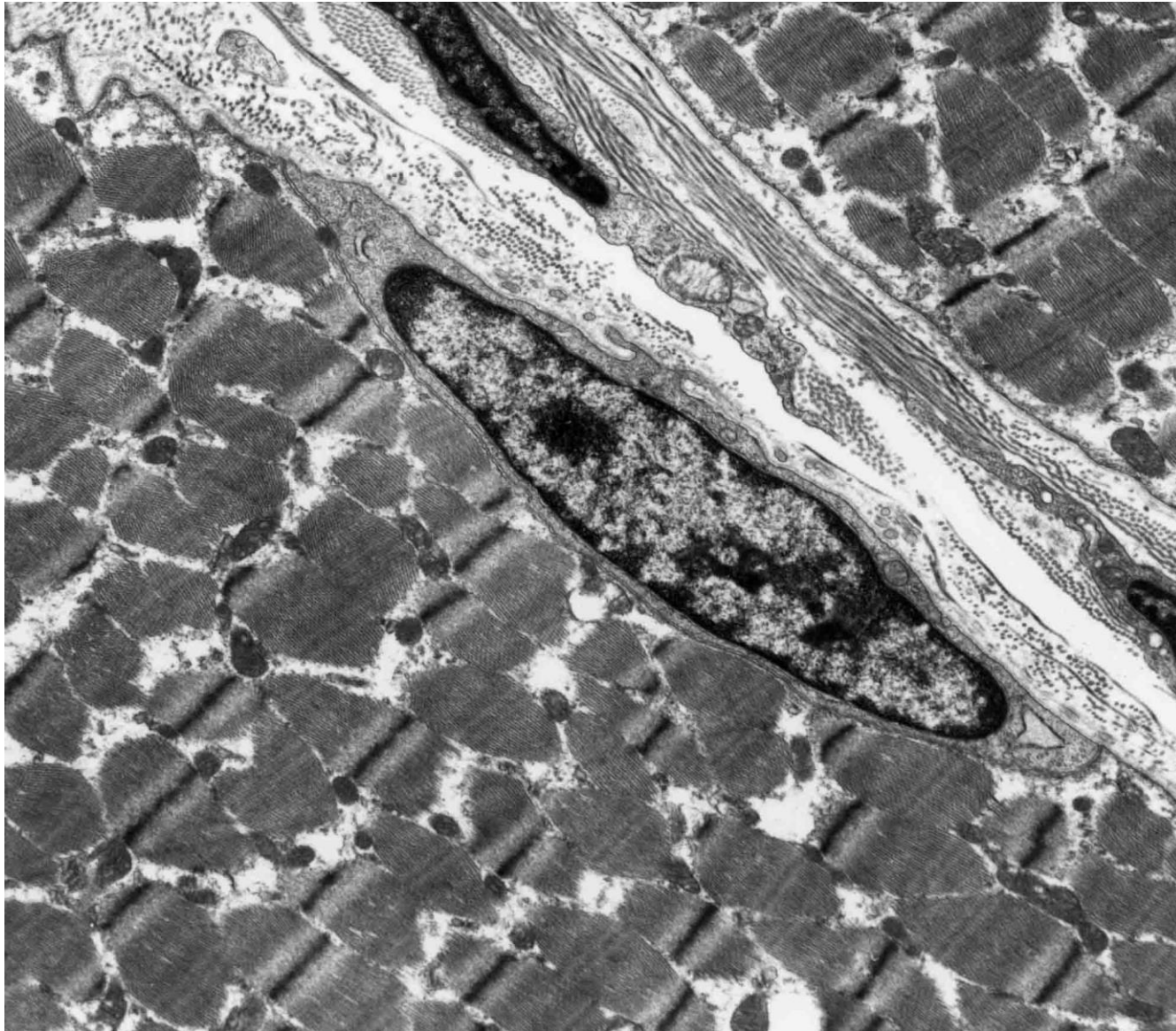
**Inflammatory cells in the endomysium
surrounding atrophic muscle fibres**



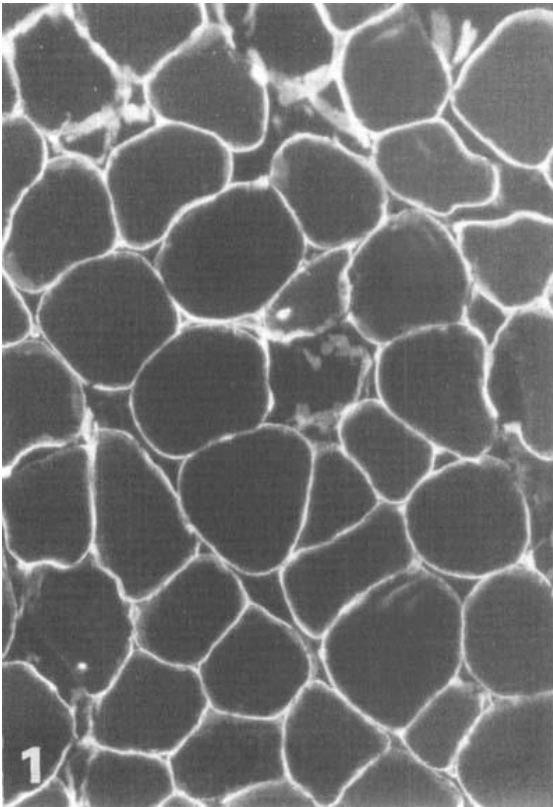
Muscle fibre destruction – influenza-A myopathy – macrophages and regenerating myoblasts



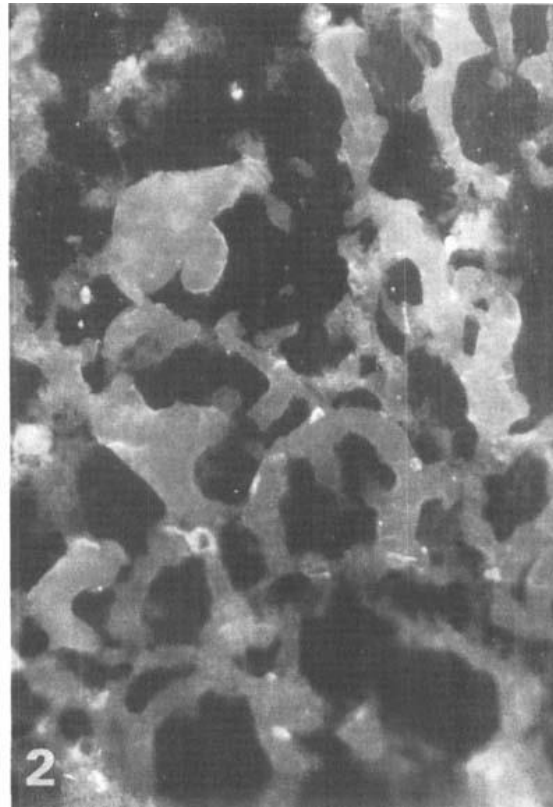
Focal necrosis and regeneration of skeletal muscle



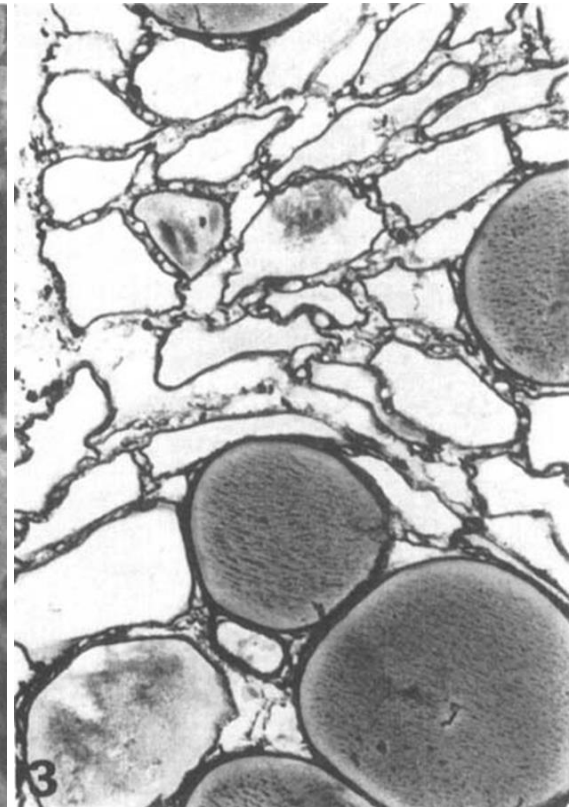
Satellite Cell – source of regenerating myoblasts



**Normal basement membrane
(Laminin)**



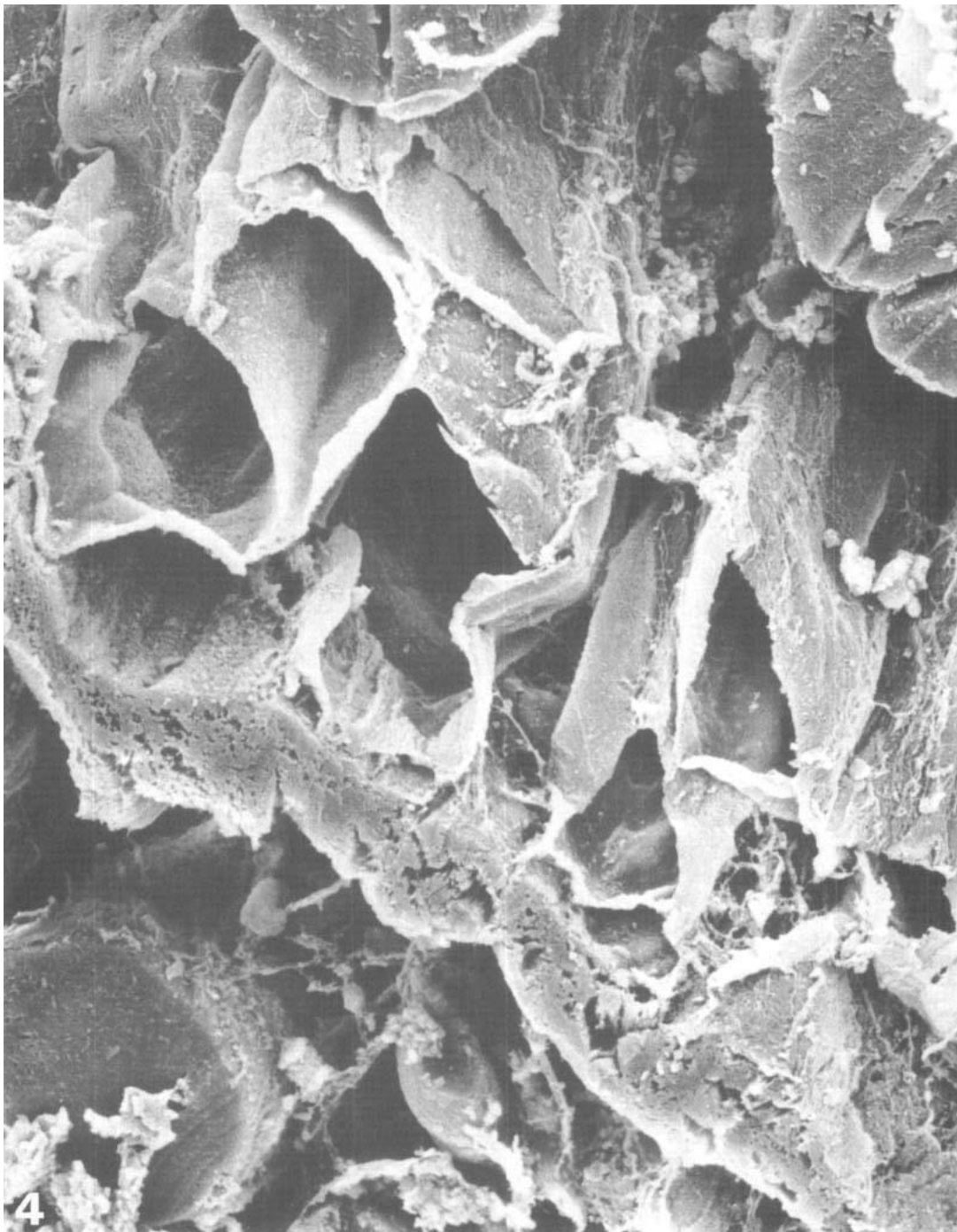
**Trypsin destroys the
basement membrane**



**Barium chloride destroys
only the muscle fibres**

Is an intact basement membrane tube essential for successful muscle fibre regeneration?

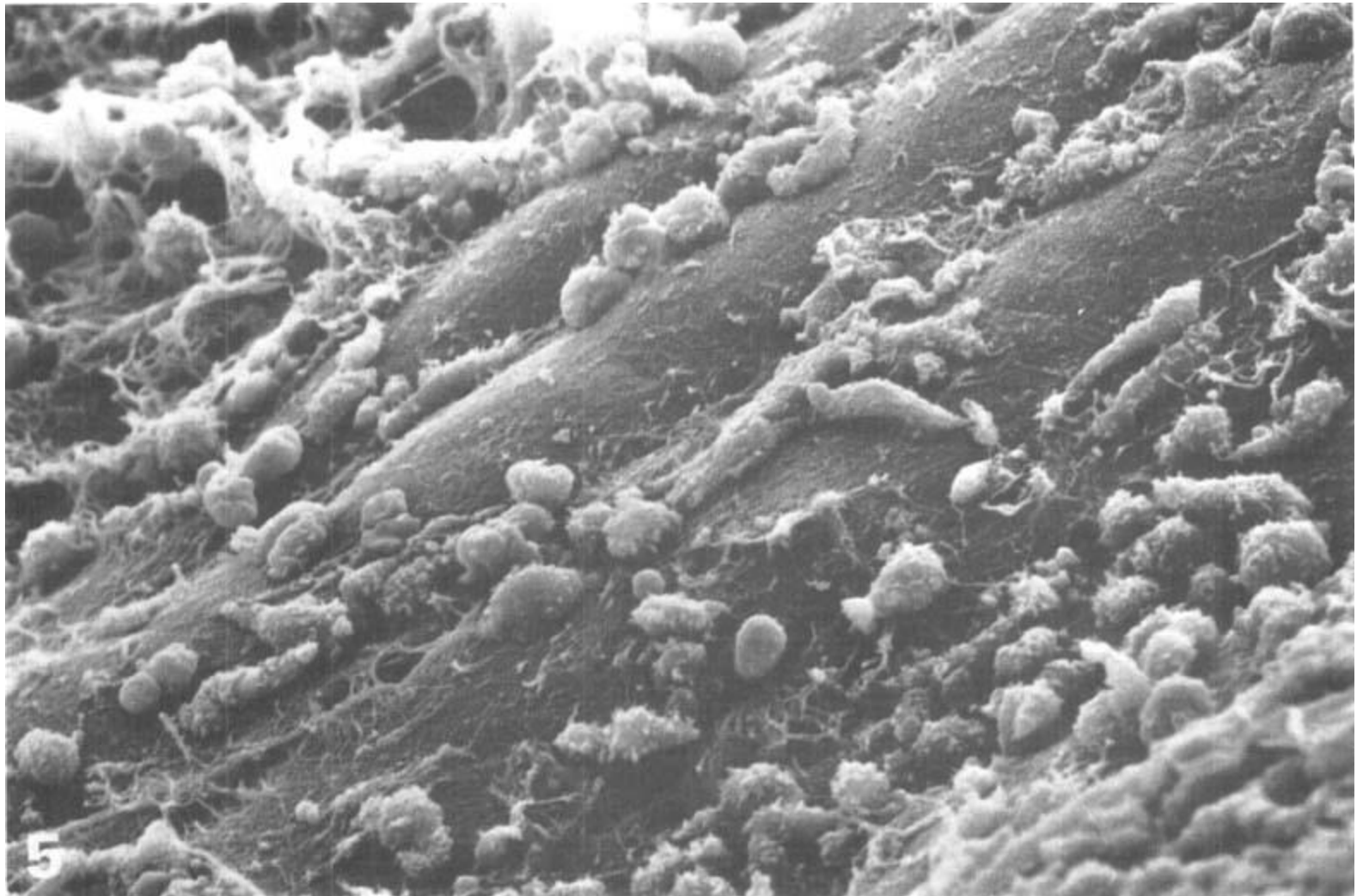
Role of the basement membrane in the regeneration of skeletal muscle. [Caldwell CJ, Matthey DL, Weller RO](#)
Neuropathol Appl Neurobiol. 1990 Jun;16:225-38.



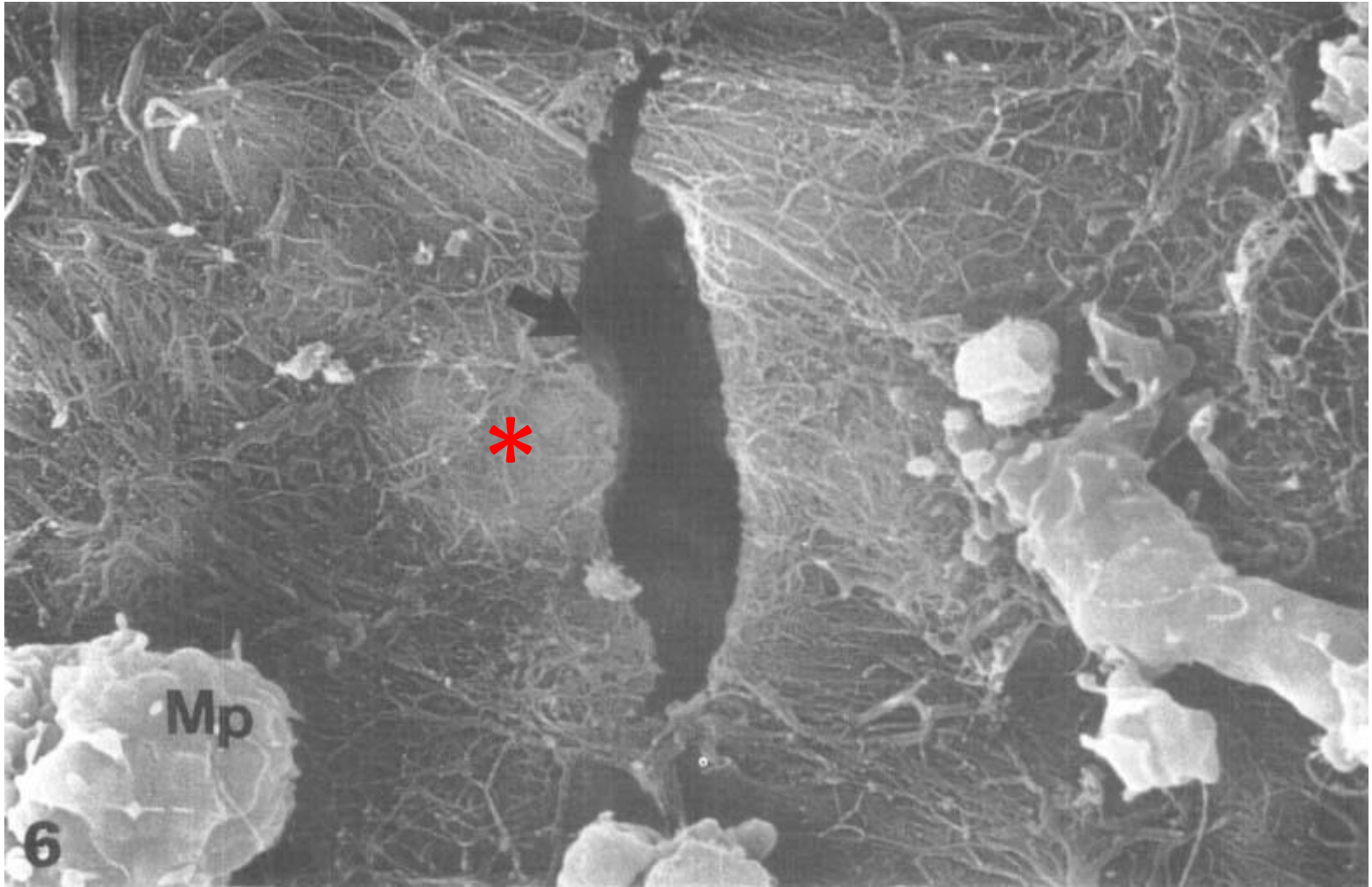
Scanning Electron microscopy

**Barium chloride destroys
only the muscle fibres**

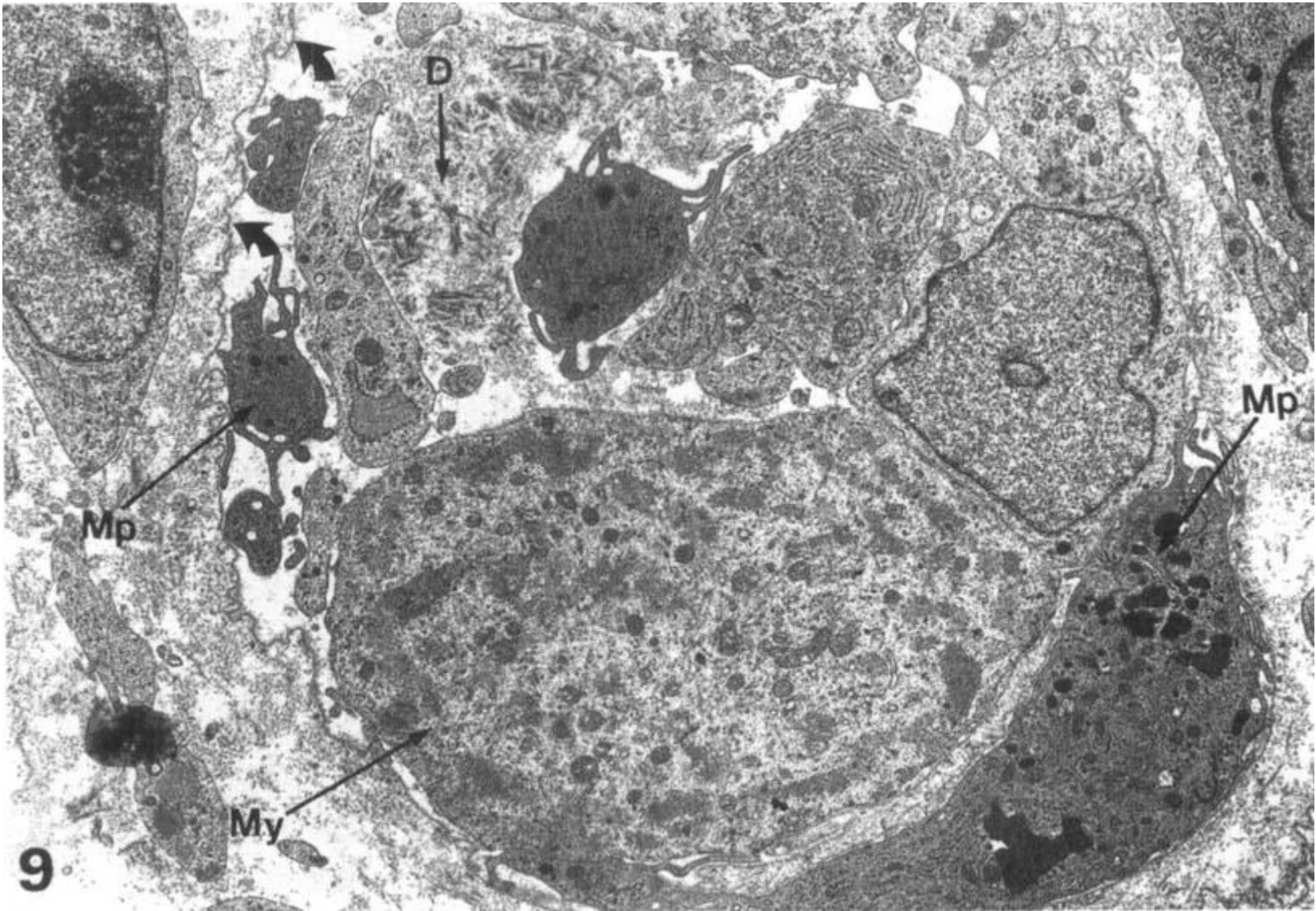
**Basement membrane
tubes are preserved**



**Scanning Electron microscopy: Macrophages on basement membrane tubes:
-- Barium chloride treated muscle**



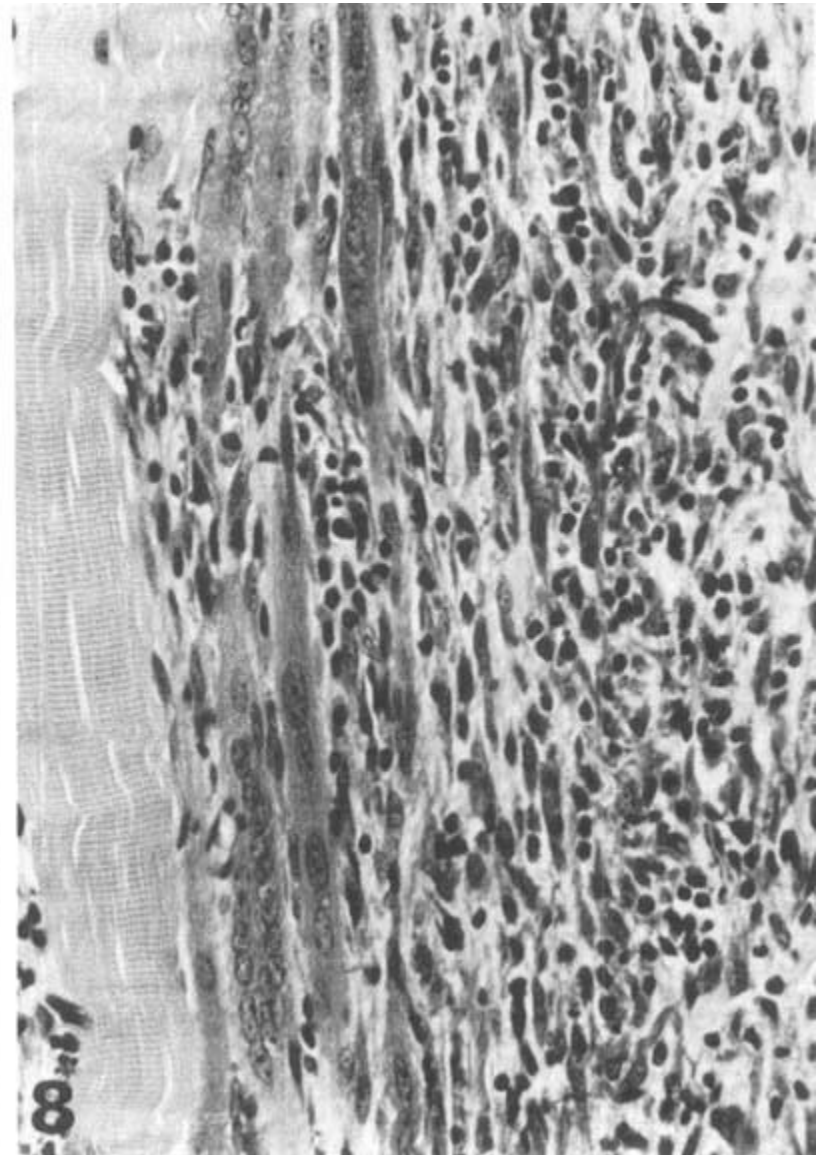
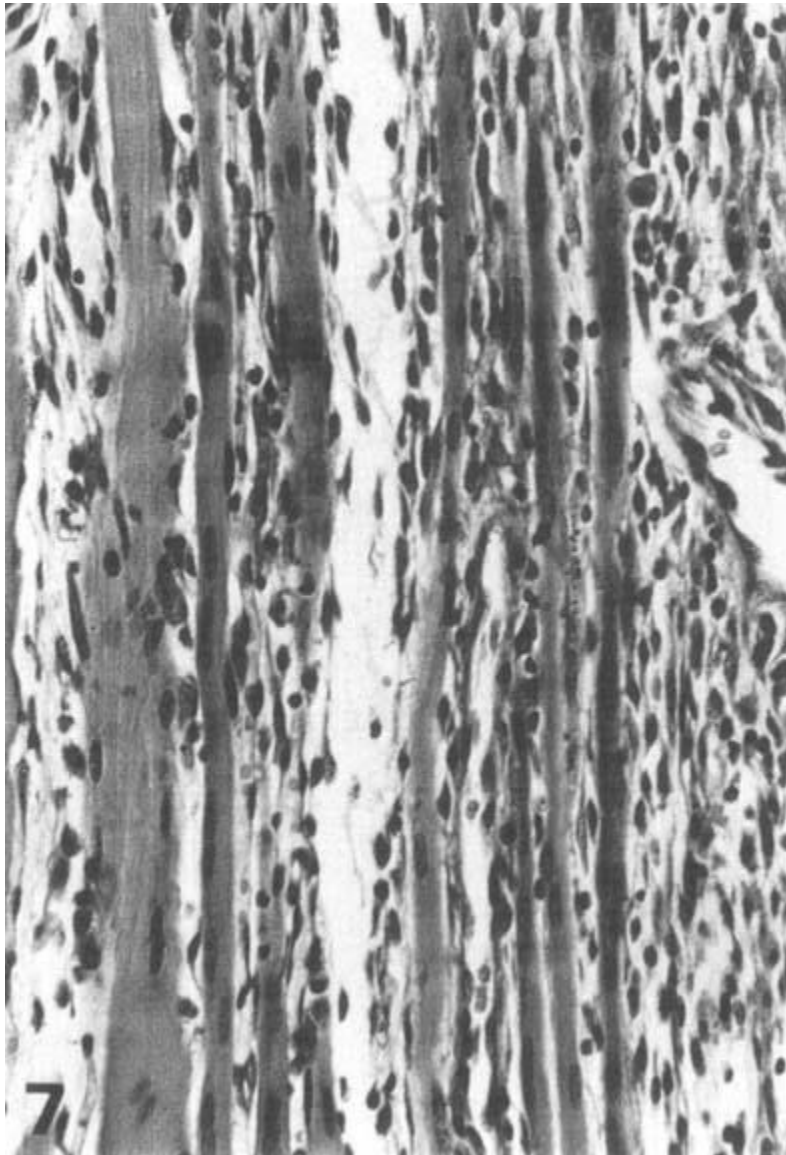
**Scanning Electron microscopy: Macrophages within basement membrane tube: -
- Barium chloride treated muscle**



**Macrophages and regenerating myoblast within basement membrane tube: --
Barium chloride treated muscle**

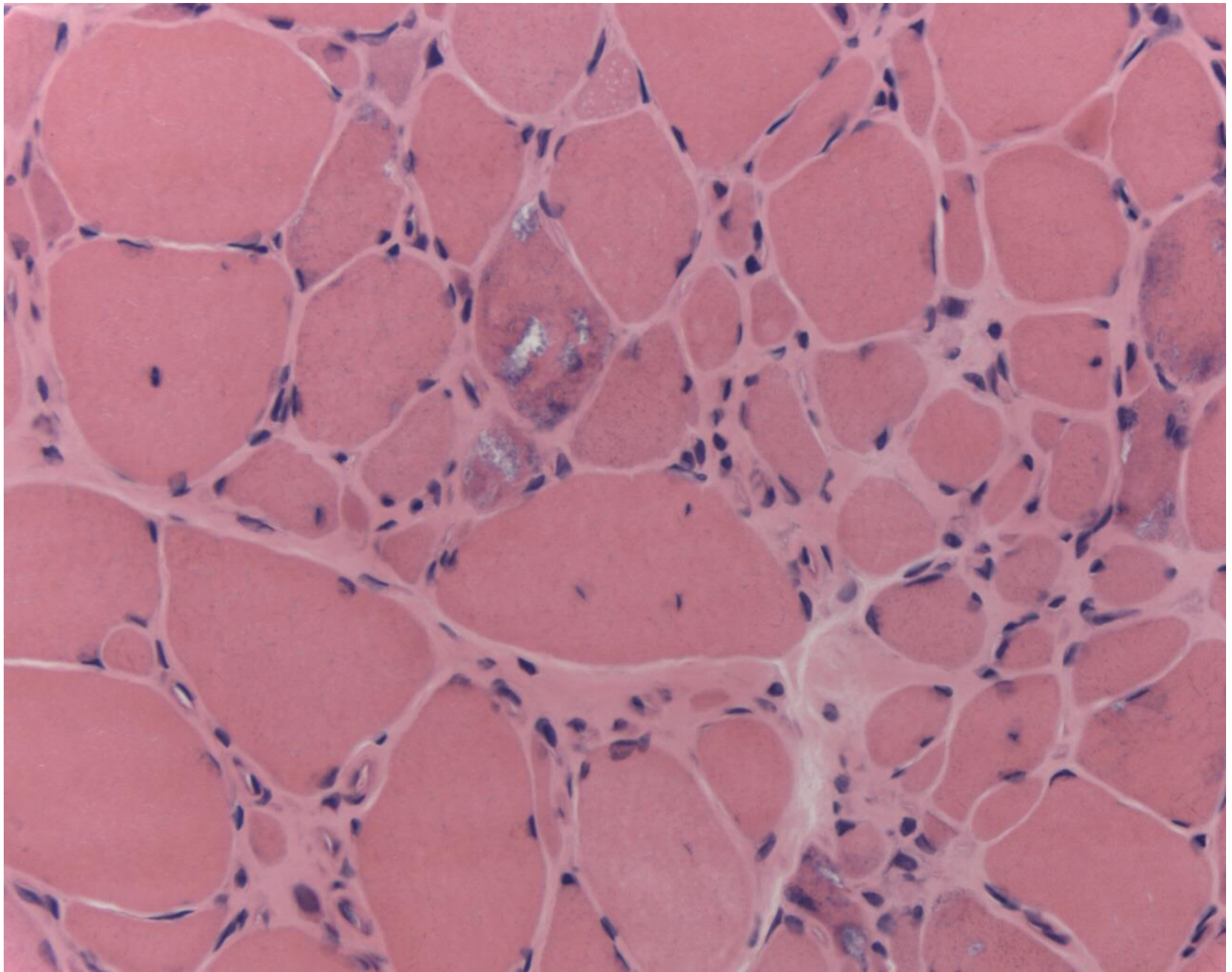


Basement membrane closely invests a regenerating myoblast in Trypsin treated muscle in which the muscle fibre and the basement membrane were destroyed

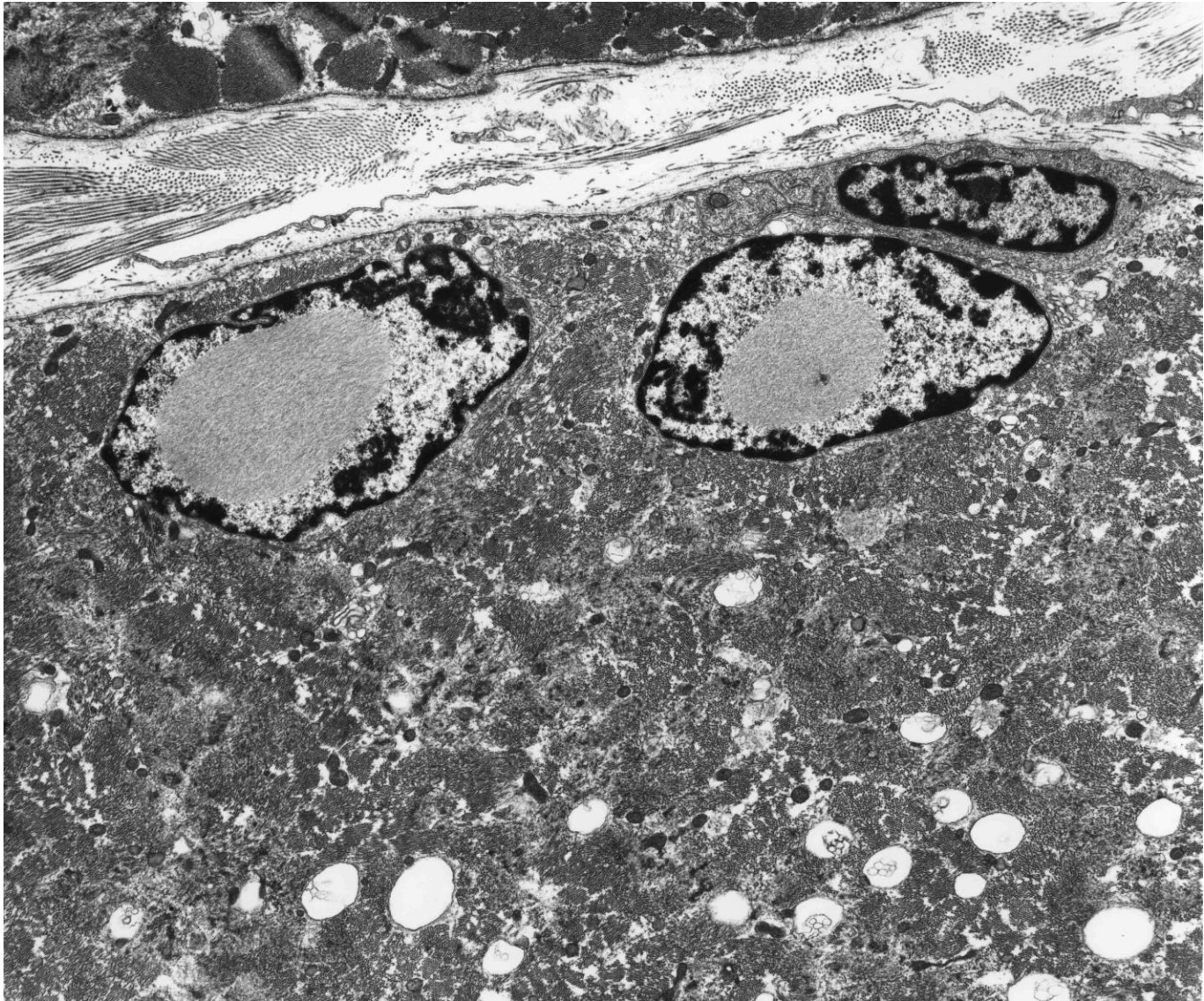


5 days recovery: which is the Trypsin-treated muscle?

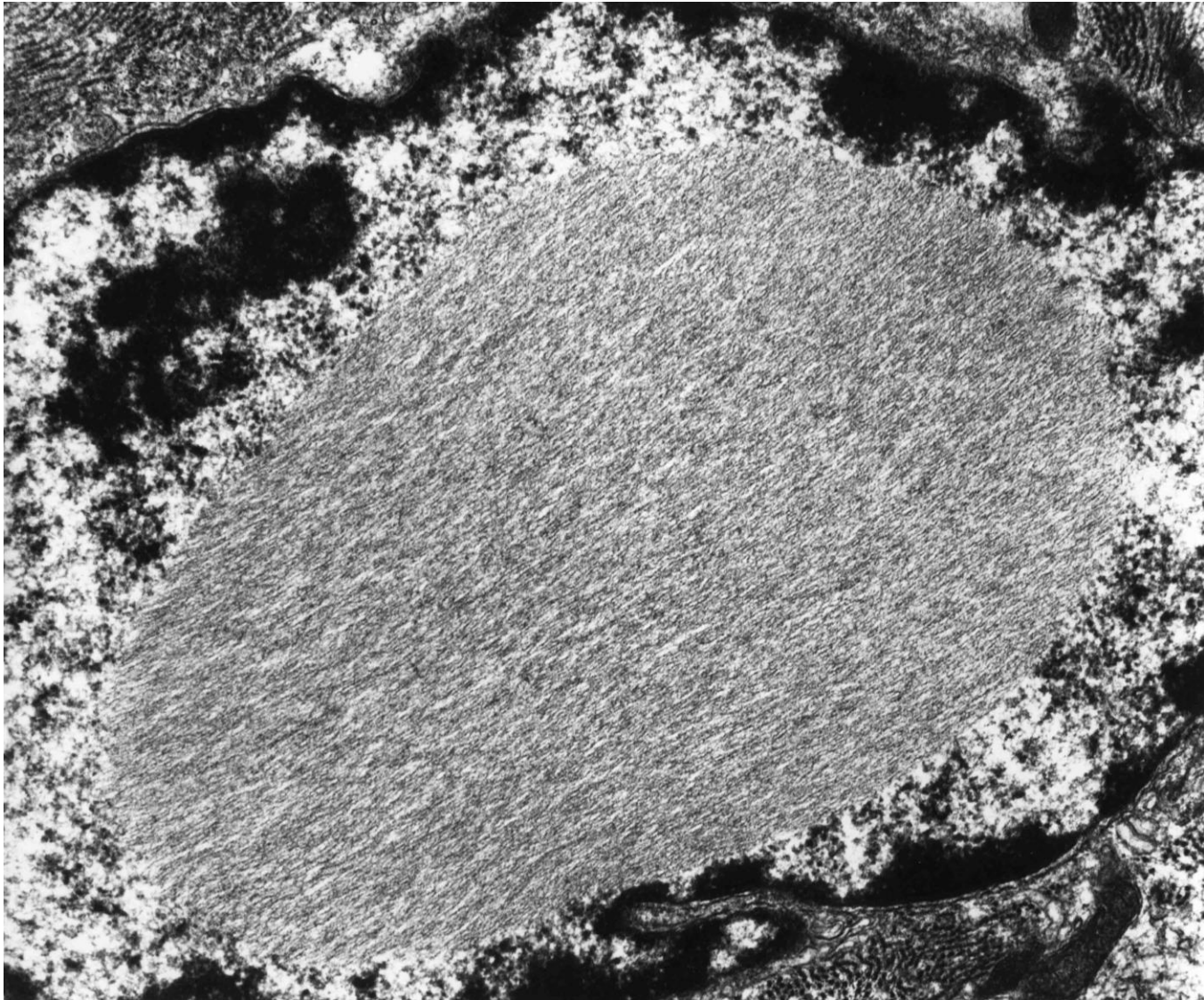
Inclusion Body Myositis



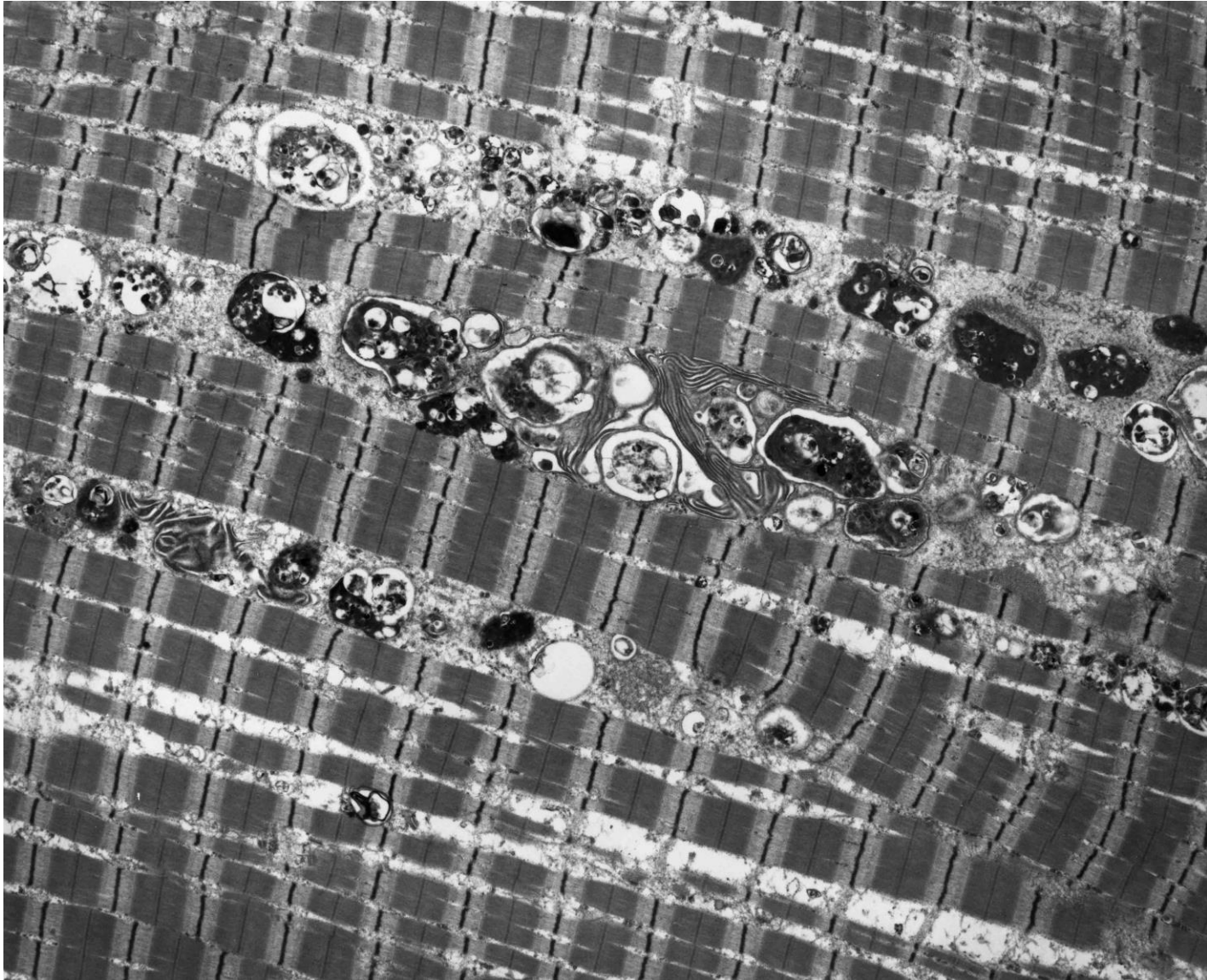
Inclusion Body Myositis



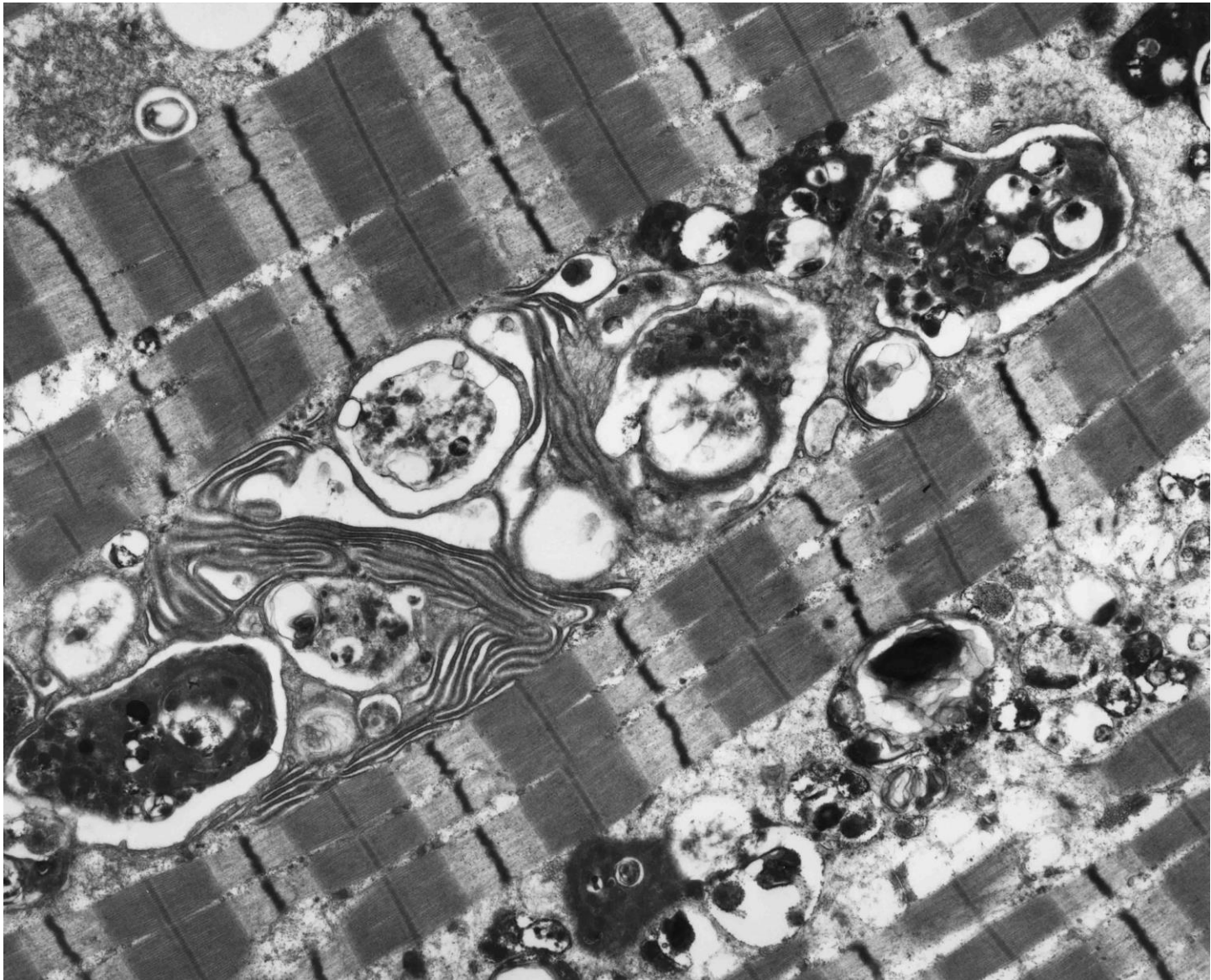
Inclusion Body Myositis



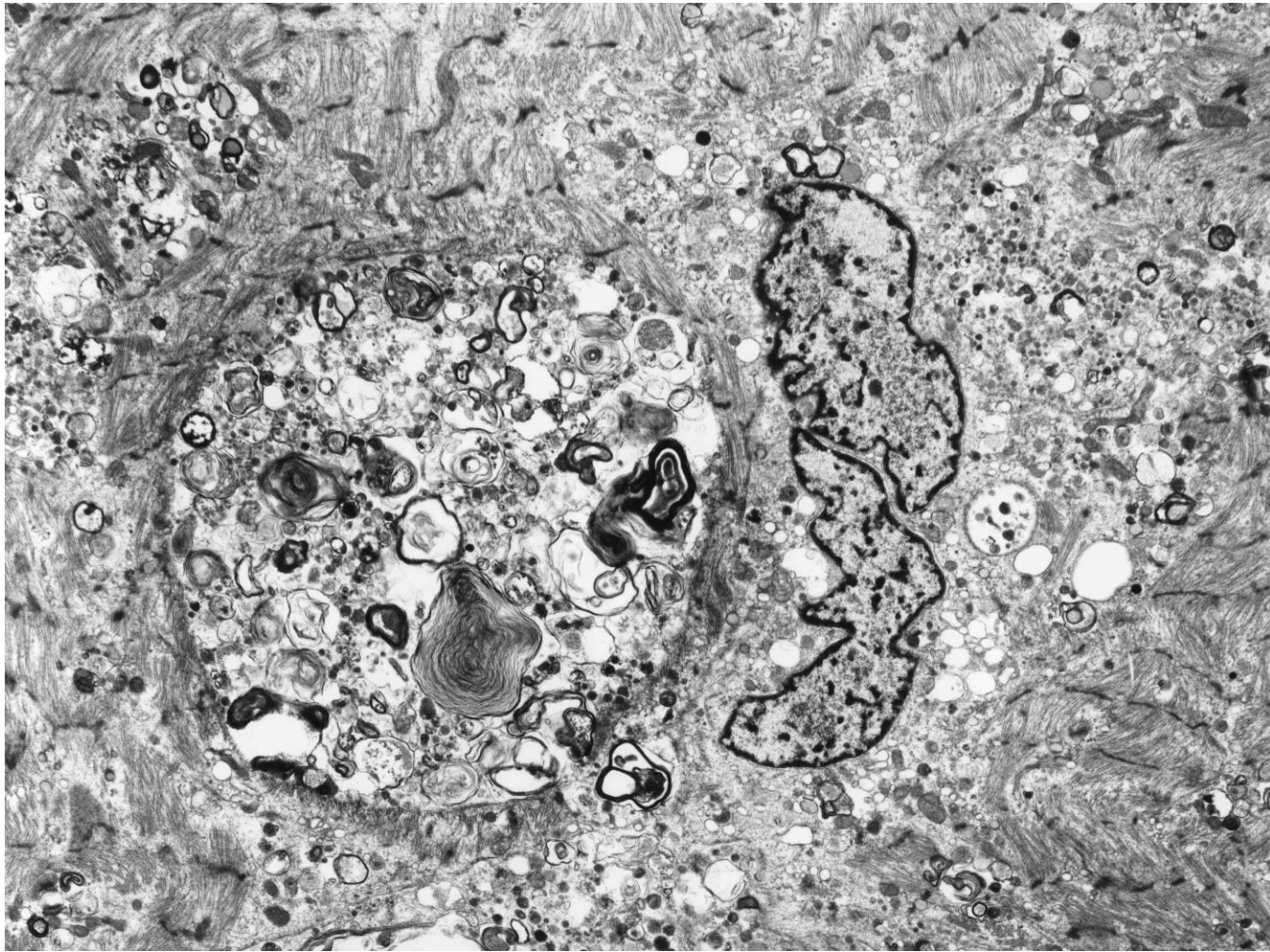
Inclusion Body Myositis



Inclusion Body Myositis



Inclusion Body Myositis



Inclusion Body Myositis

Electron microscopy in the evaluation of individual cases

Dr Ingrid Mazanti

Dr Mark Walker

