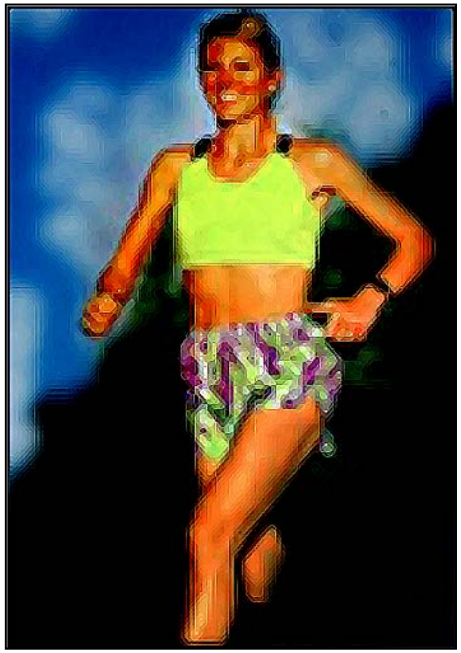
STARS

Mini-Symposium

Skeletal Muscle:
Development, Adaptation & Disease

"Gain Without Pain"

Rhonda Bassel-Duby, Ph.D.
Associate Professor of Molecular Biology



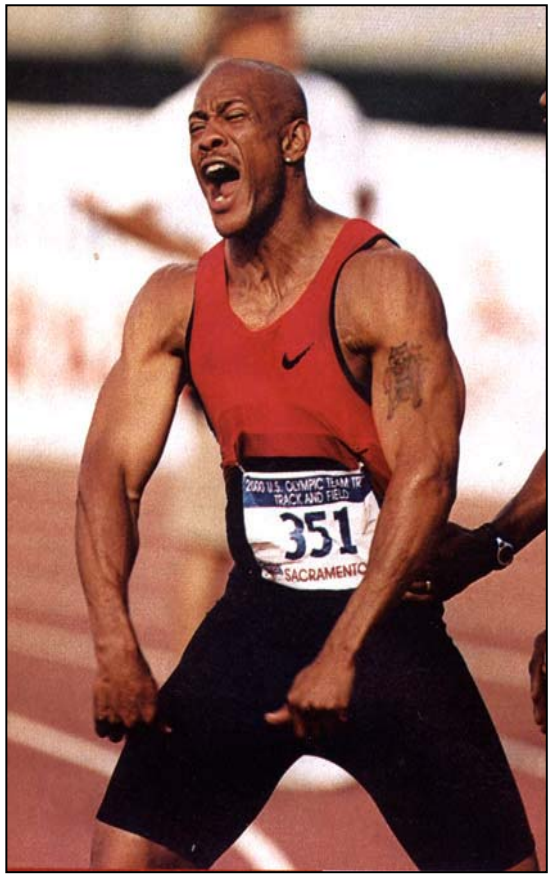
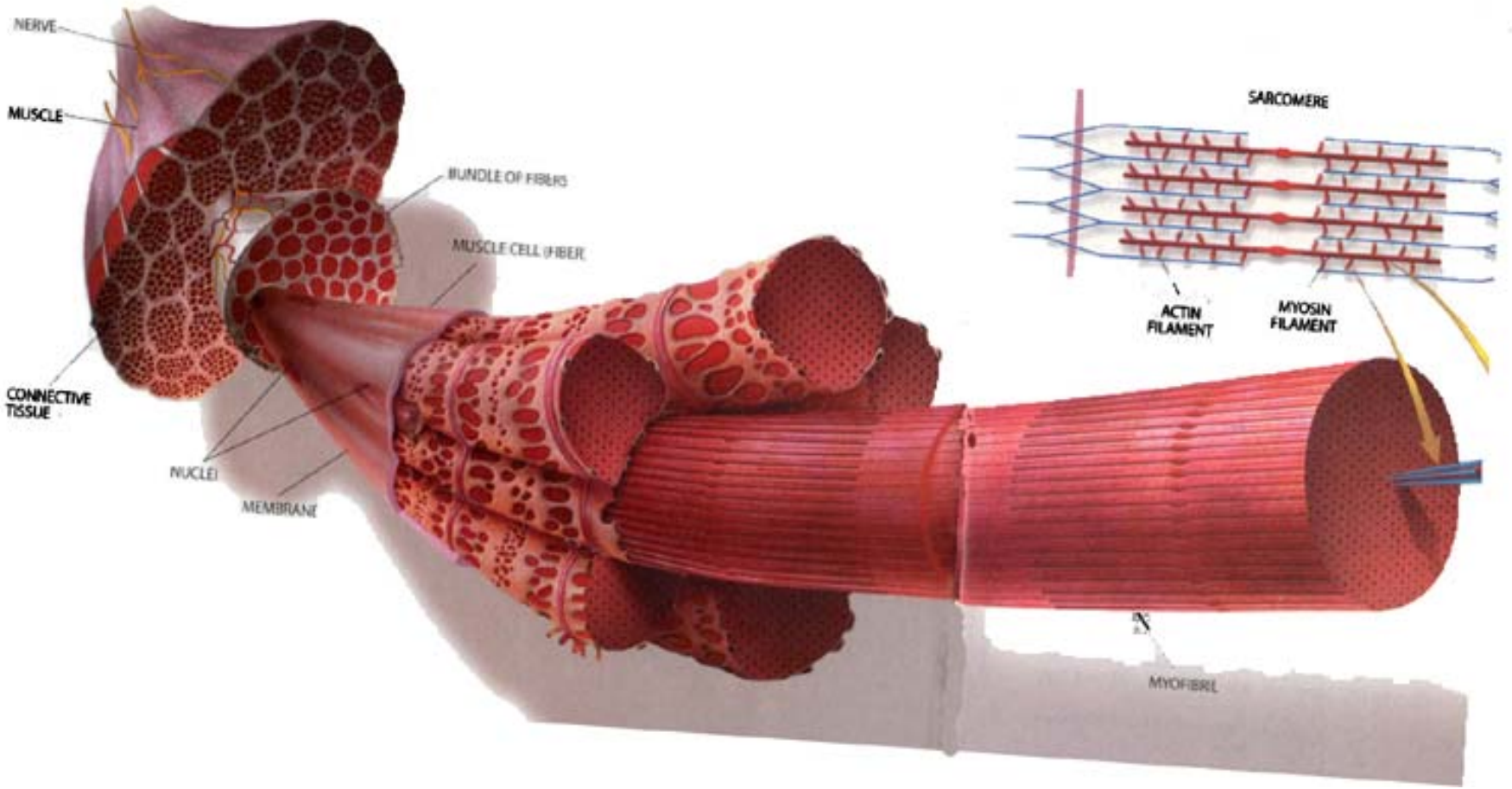
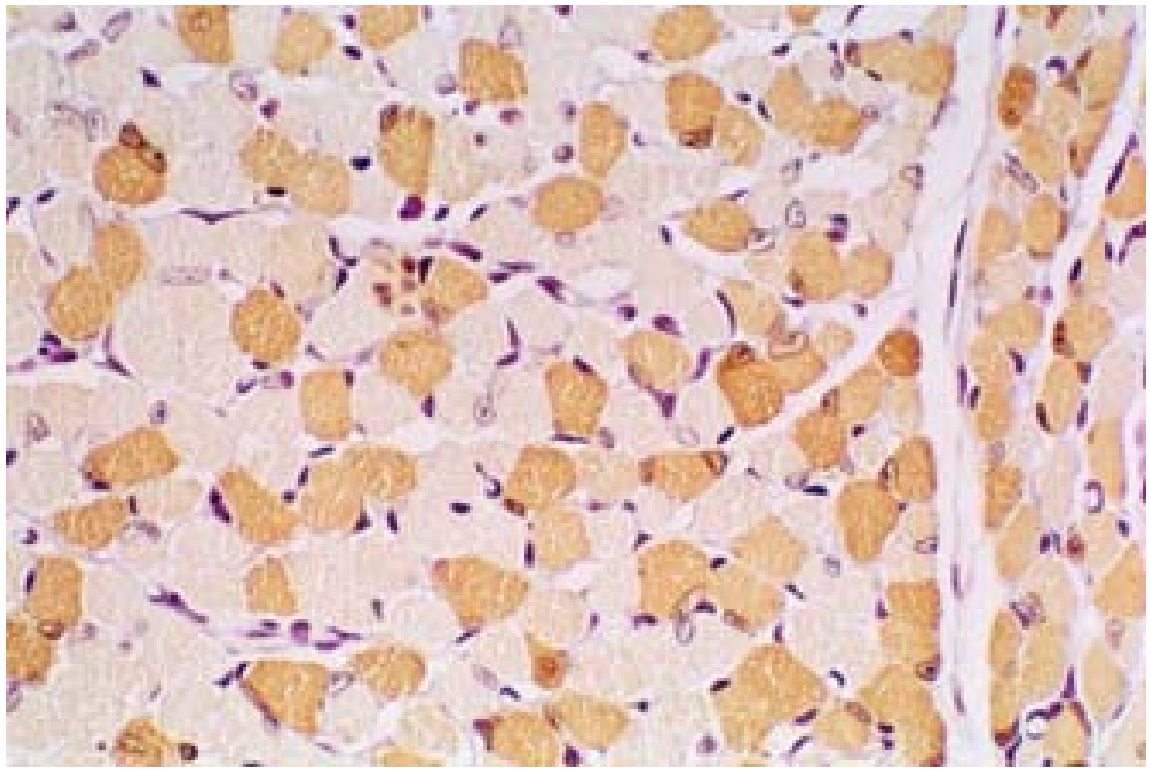

2000 U.S. OLYMPIC TEAM TRY
TRACK AND FIELD
351
SACRAMENTO

Diagram of Skeletal Muscle



Myoglobin Immunohistochemistry



Subtypes of Skeletal Myofibers

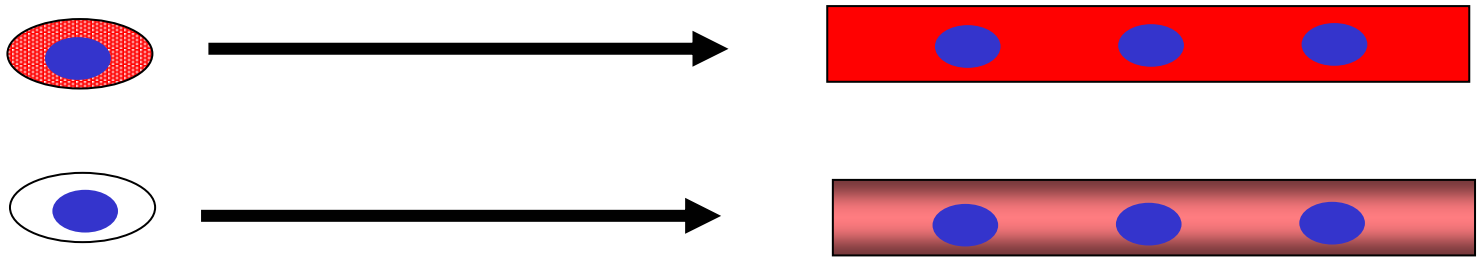
Type I (slow)	Type IIa	Type IIb (fast)
red, oxidative fatigue-resistant slow contraction insulin-sensitive		white, glycolytic fatigue rapidly rapid force development insulin-resistant

endurance training, nerve stimulation

inactivity, disease, hypogravity

Establishing Myofiber Specialization

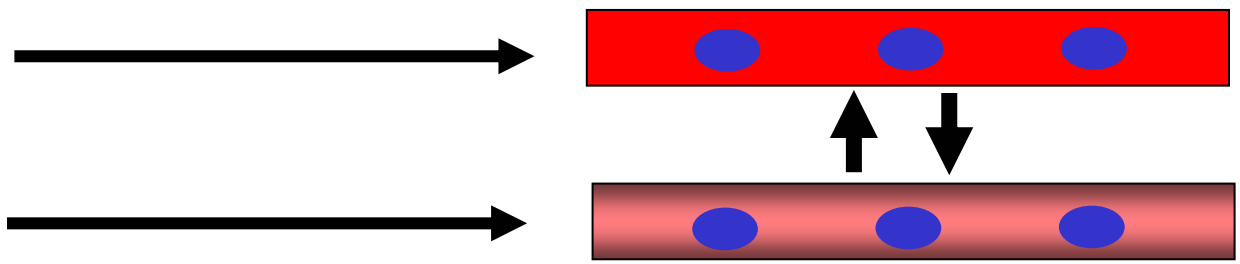
Preprogramming of myoblasts



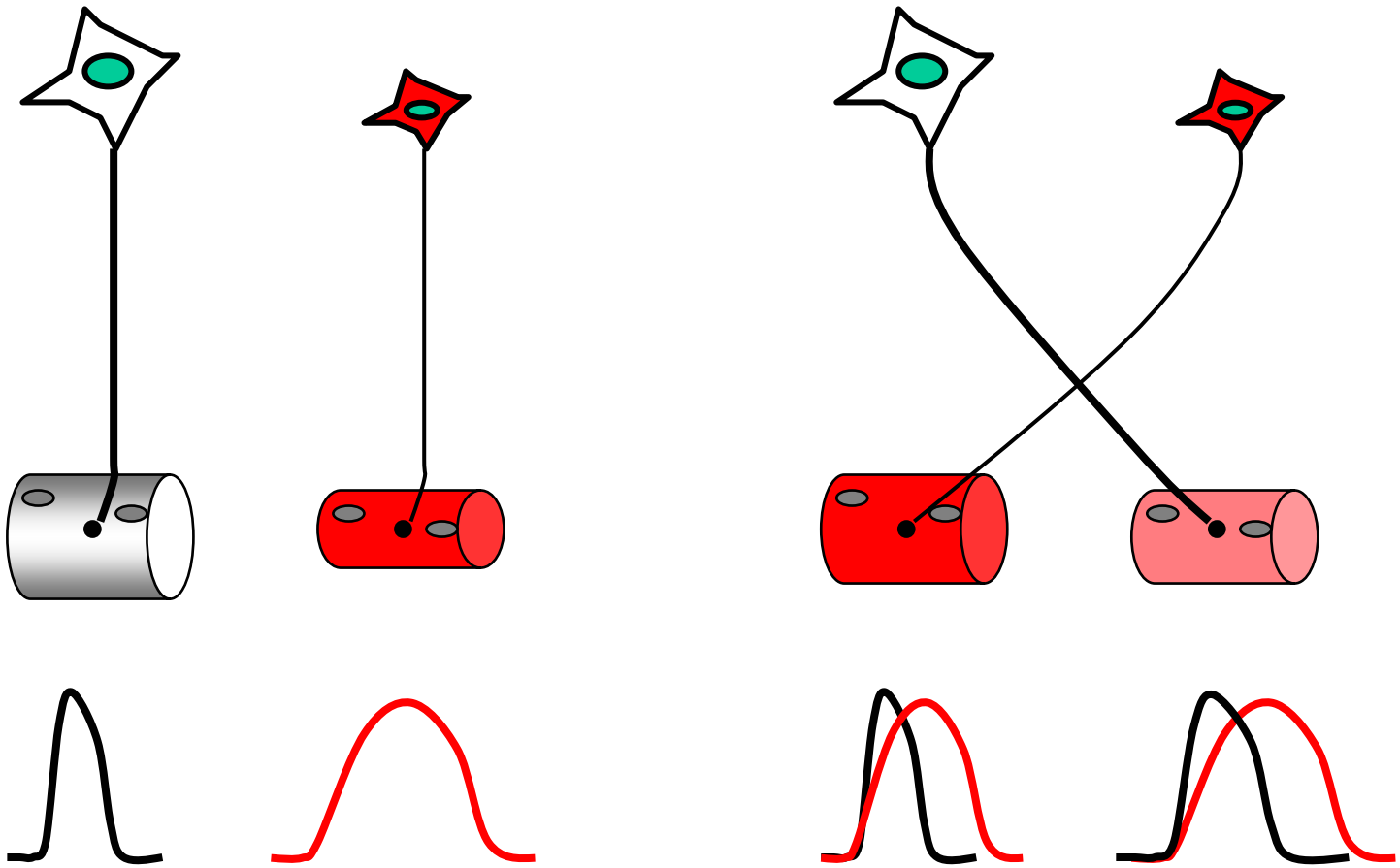
Pattern imposed by motor nerve

tonic

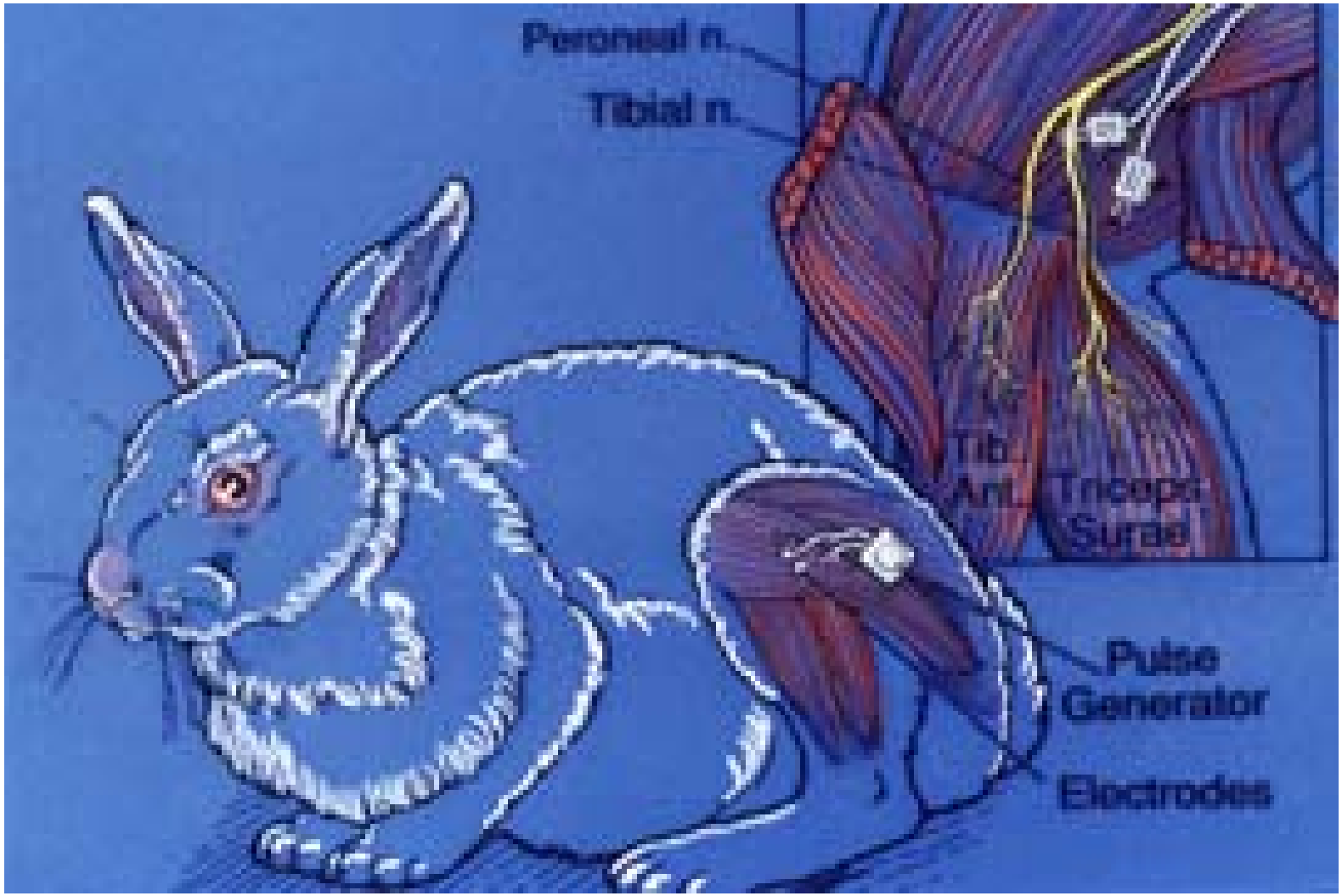
phasic



Cross-innervation Switches Fiber Types



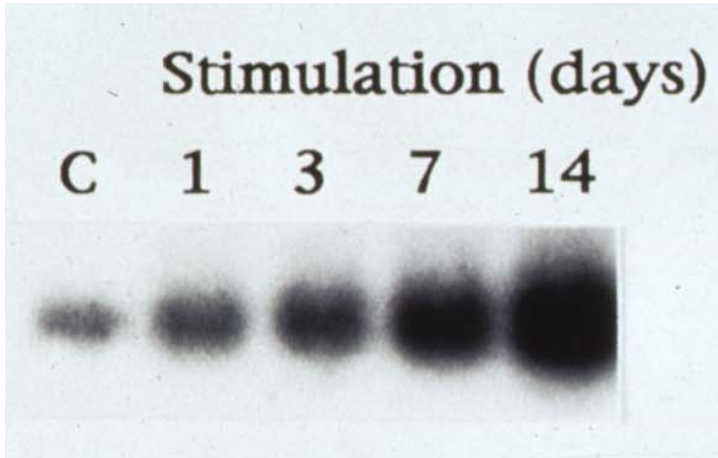
Electrical Stimulation Model



unstimulated stimulated

Molecular Marker of Muscle Plasticity

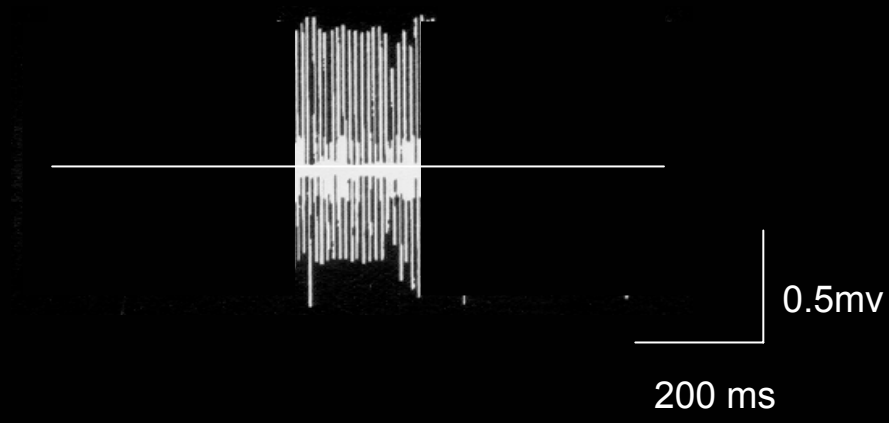
myoglobin

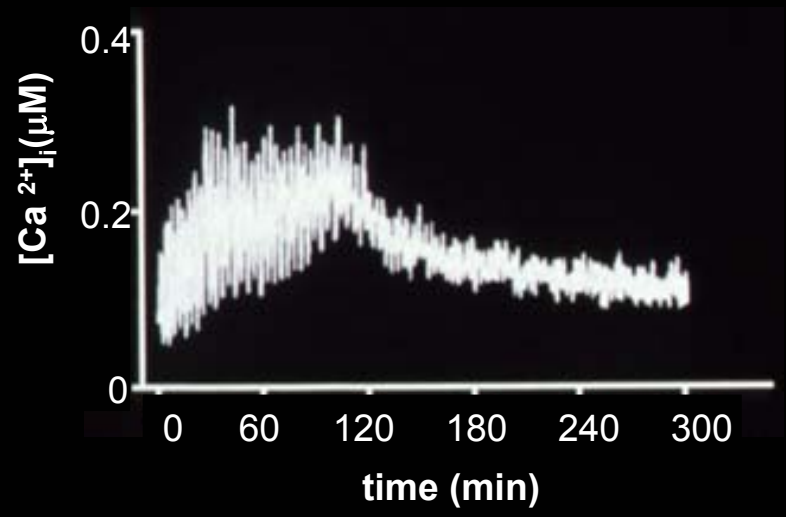


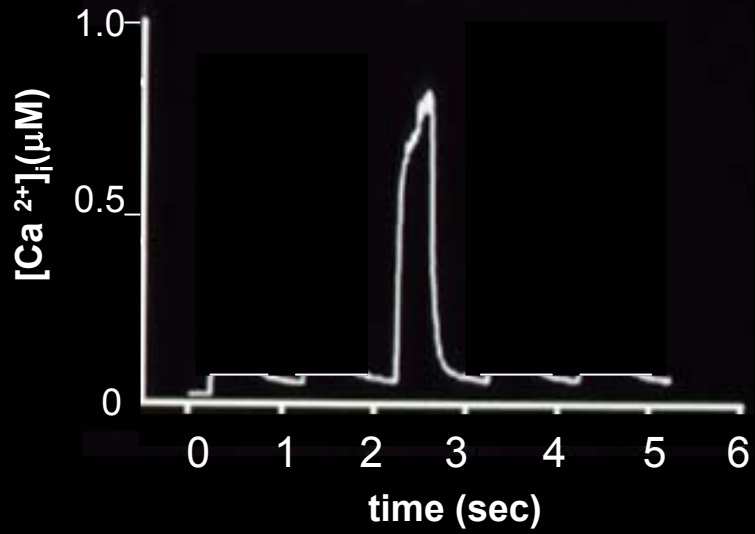
Electrical Signals Alter Intracellular Calcium

10 Hz continuous

100 Hz intermittent



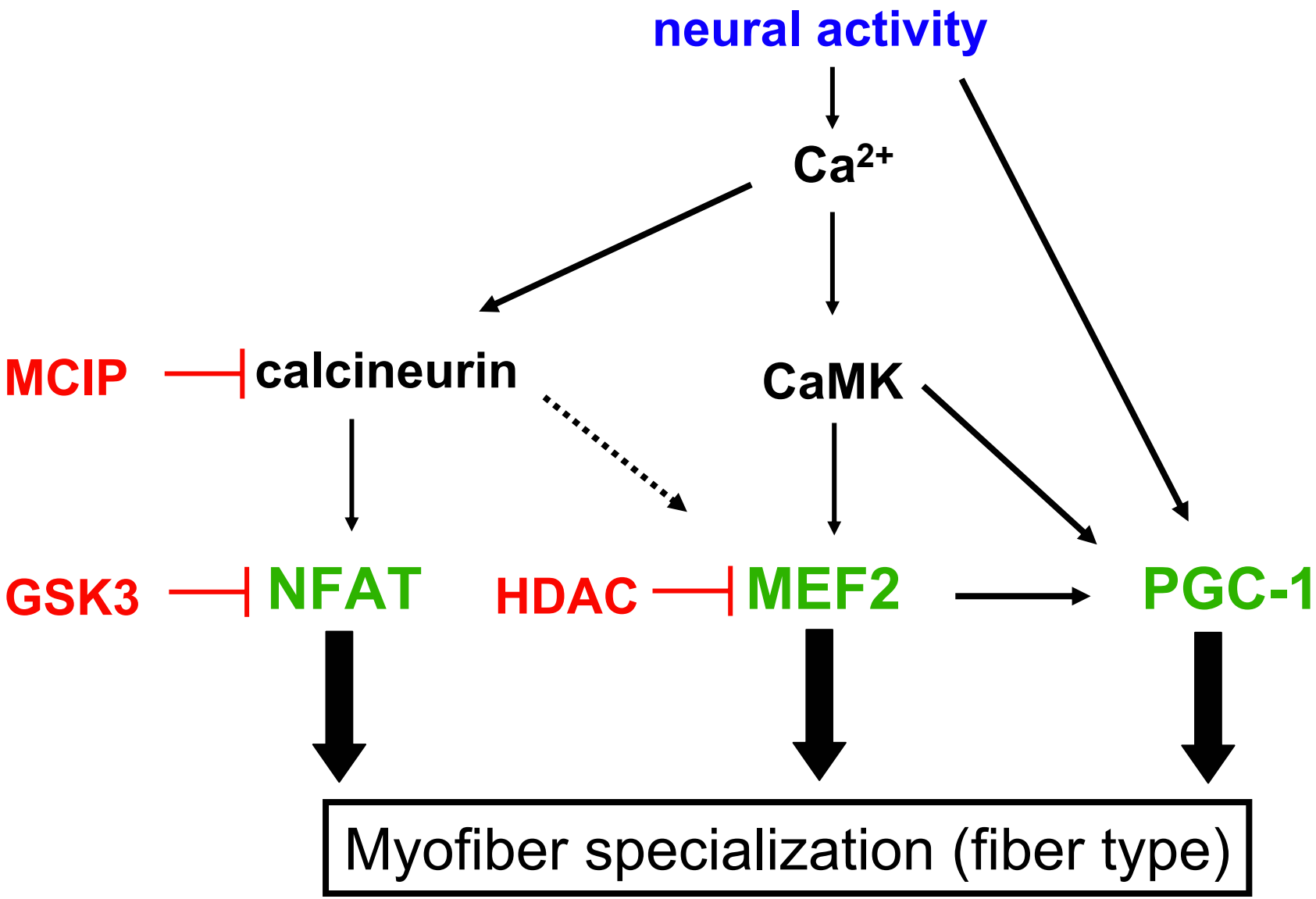




Type I fibers

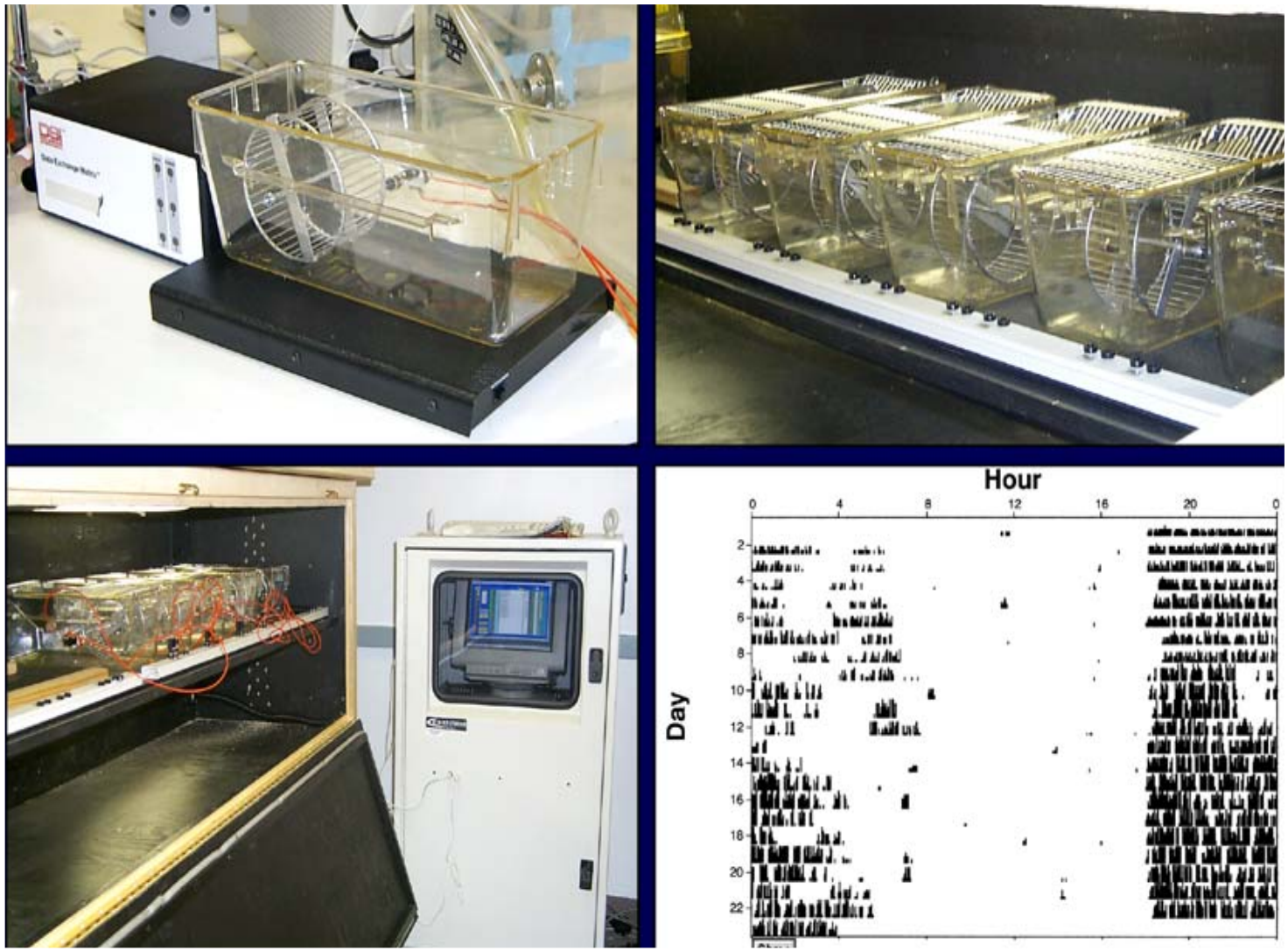
Type II fibers

Genetic Reprogramming of Skeletal Muscle

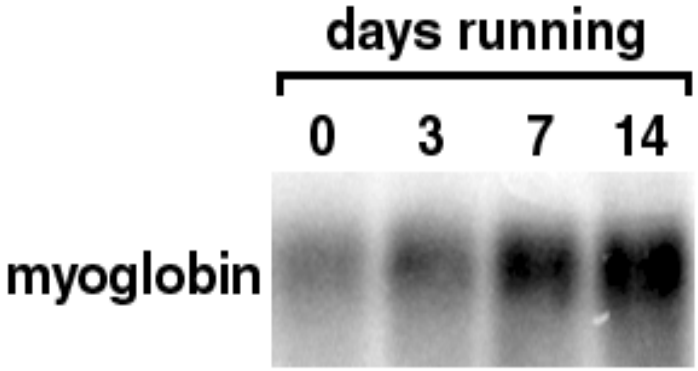


Genetic Manipulation of Signal Transduction Pathways in Muscle

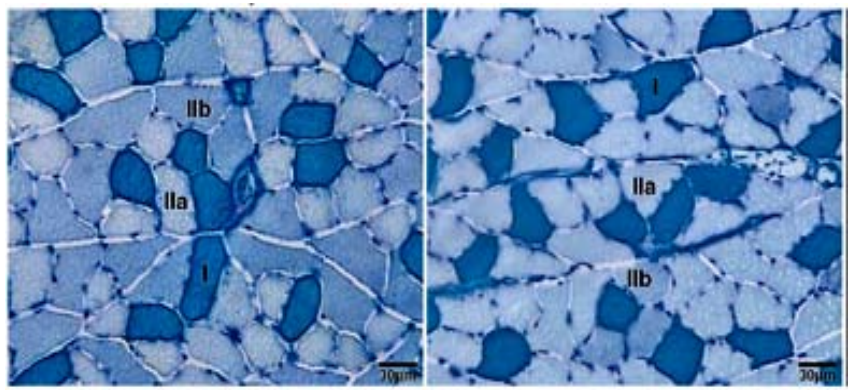
Voluntary Running Cages



Voluntary Wheel Running Enhances Muscle Oxidative Capacity

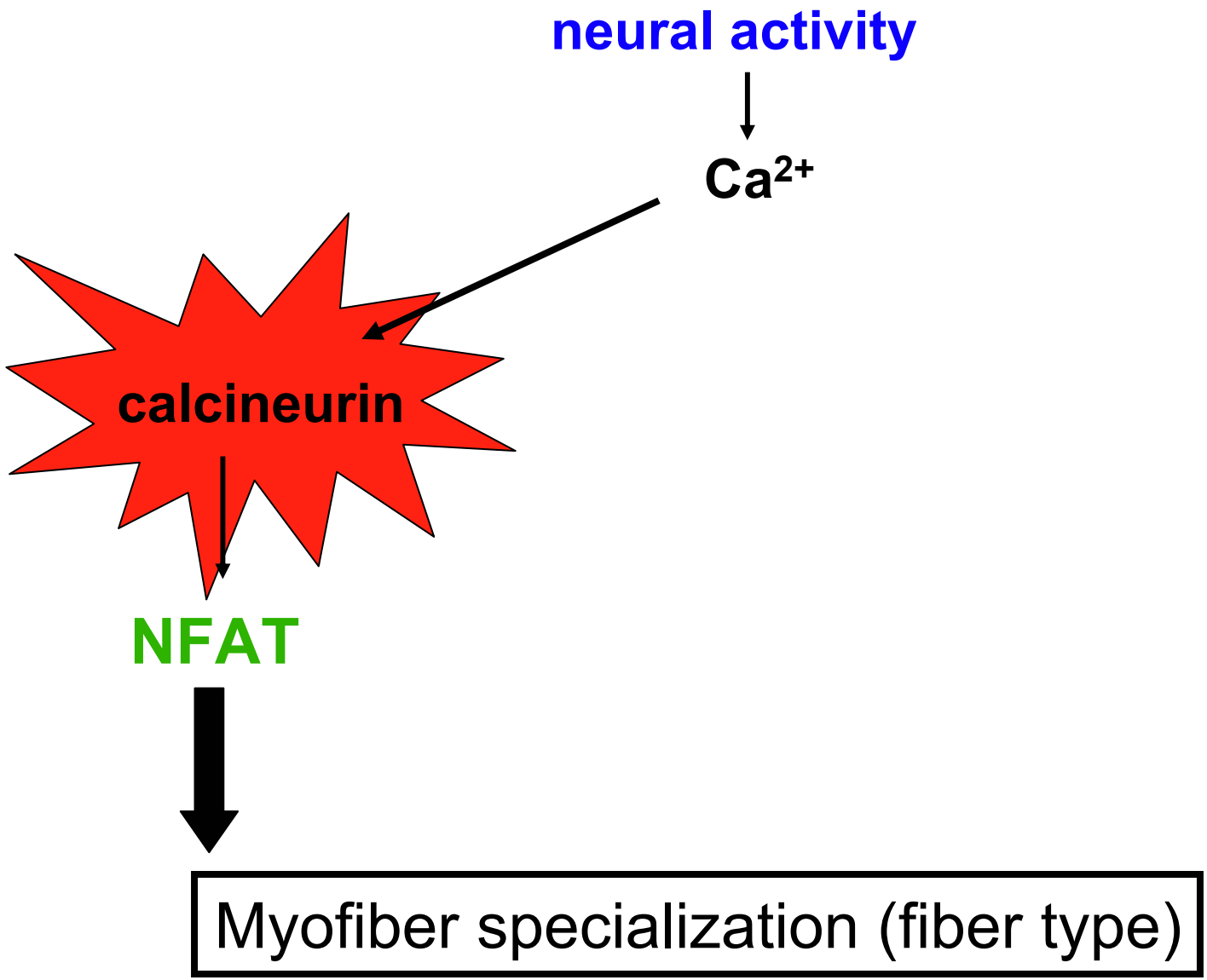


Sedentary 4 wk run



% fiber	Sedentary	Run
Type I	24.7+3.9	21.6+1.6
Type IIa	26.5+5.6	61.2+12.3
Type IIb	48.8+2.0	17.2+10.9

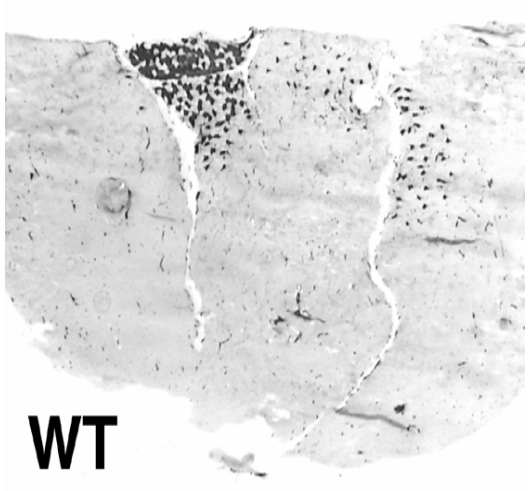
Genetic Reprogramming of Skeletal Muscle



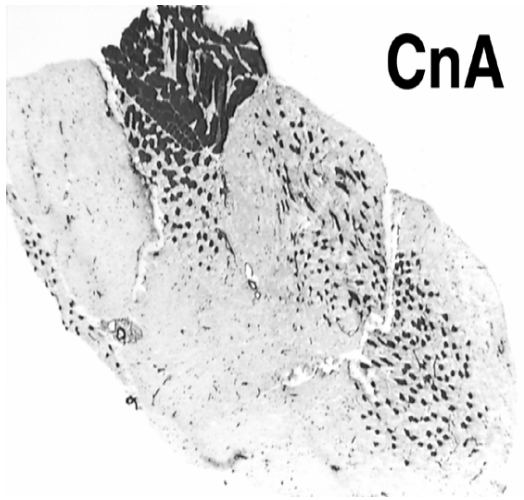
Genetic Manipulation of Signal Transduction Pathways in Muscle

Calcineurin Promotes Slow Fiber Transformation

Wild-type



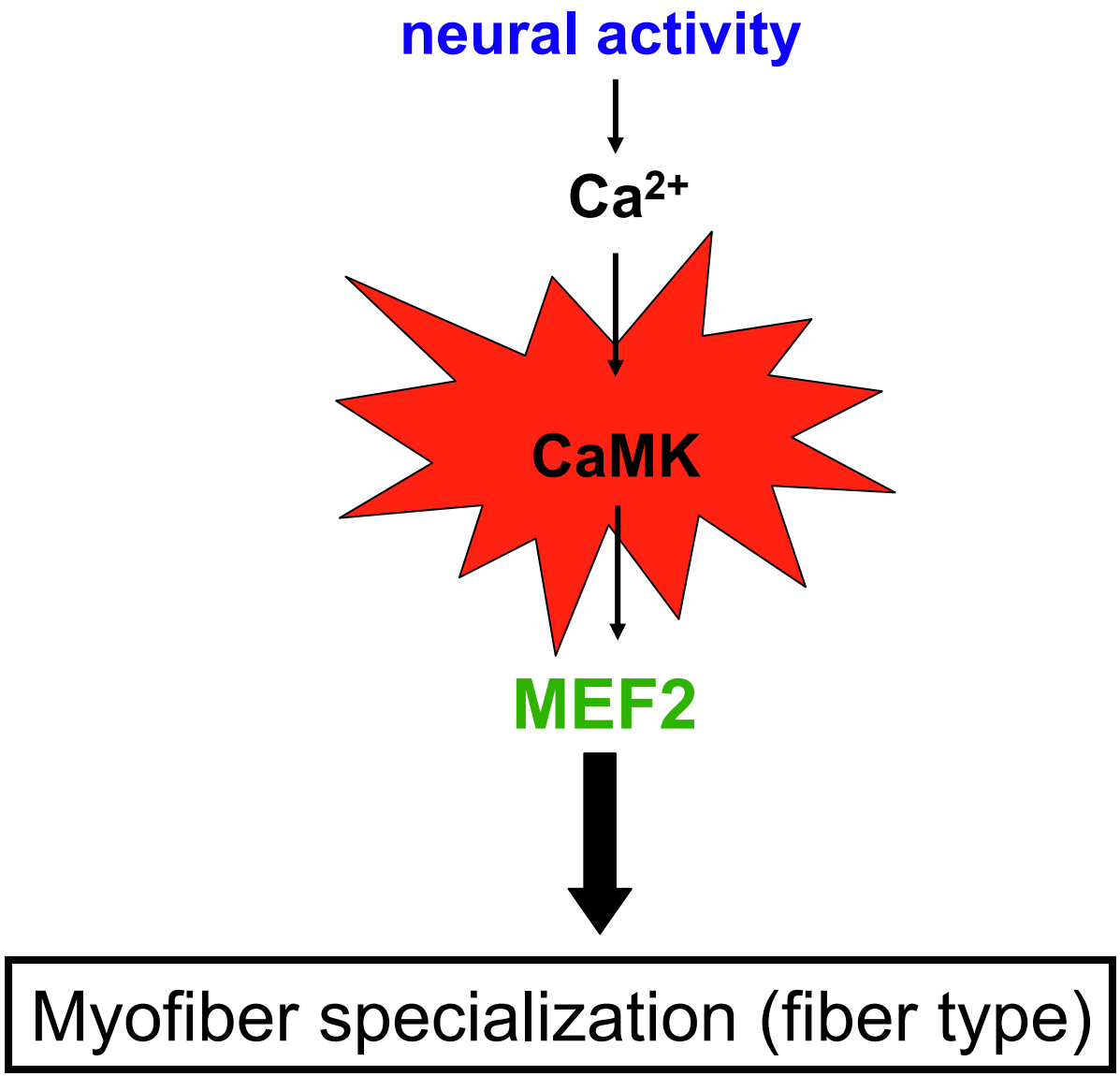
MCK-CnA*



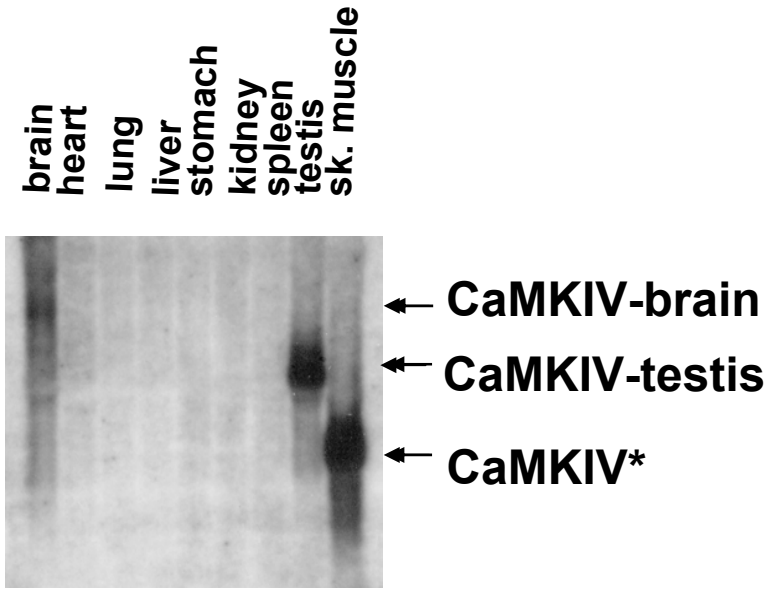
Slow myosin ATPase
(gastrocnemius)

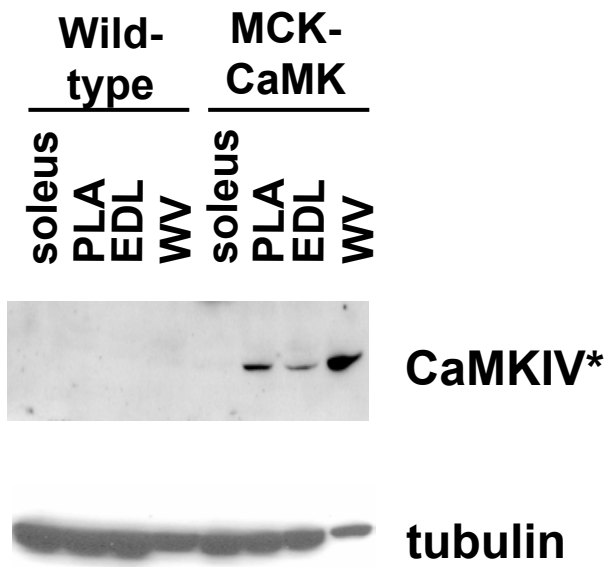
Naya *et al.* J Biol Chem, 1999.

Genetic Reprogramming of Skeletal Muscle



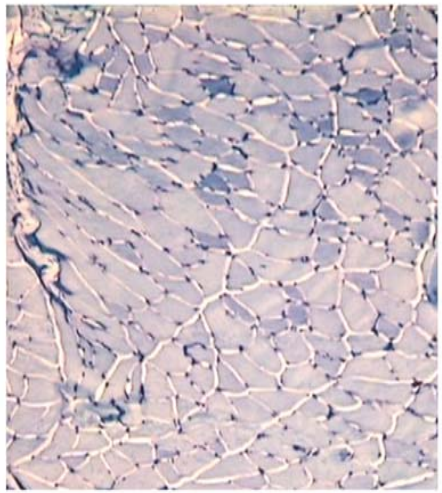
Expression of CaMKIV* in Skeletal Muscle



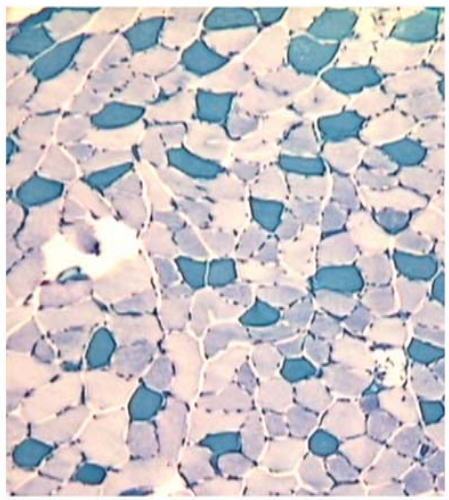


CaMK Promotes Slow Fibers Transformation

Wild-type

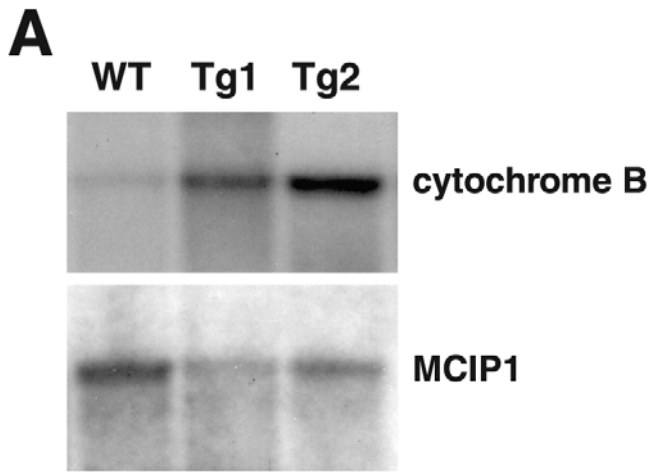


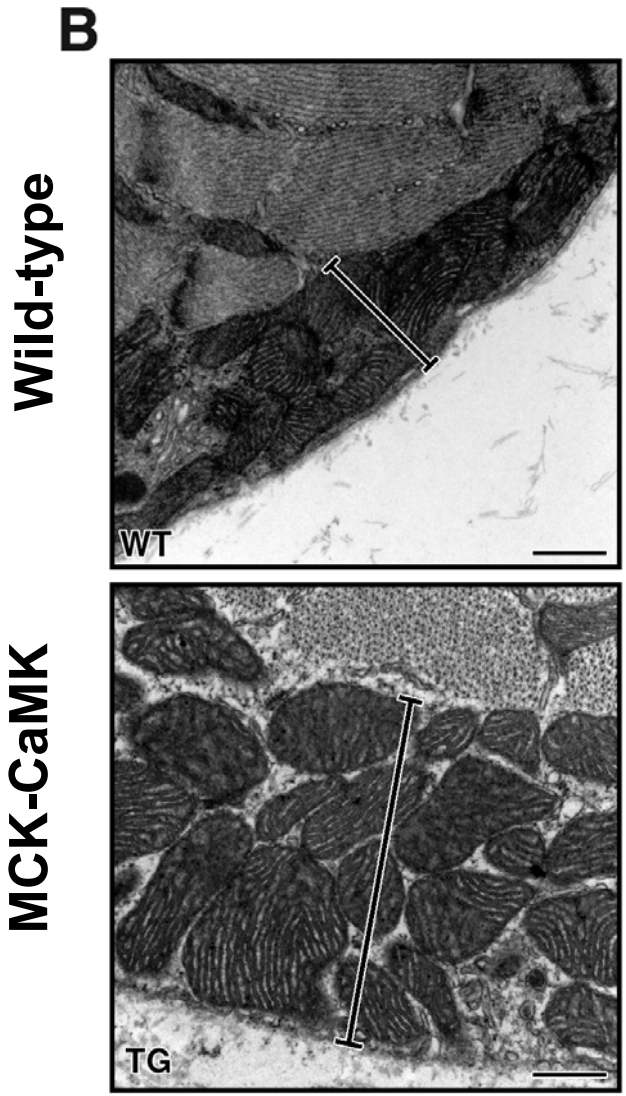
MCK-CaMK



Wu *et al.* Science, 2002.

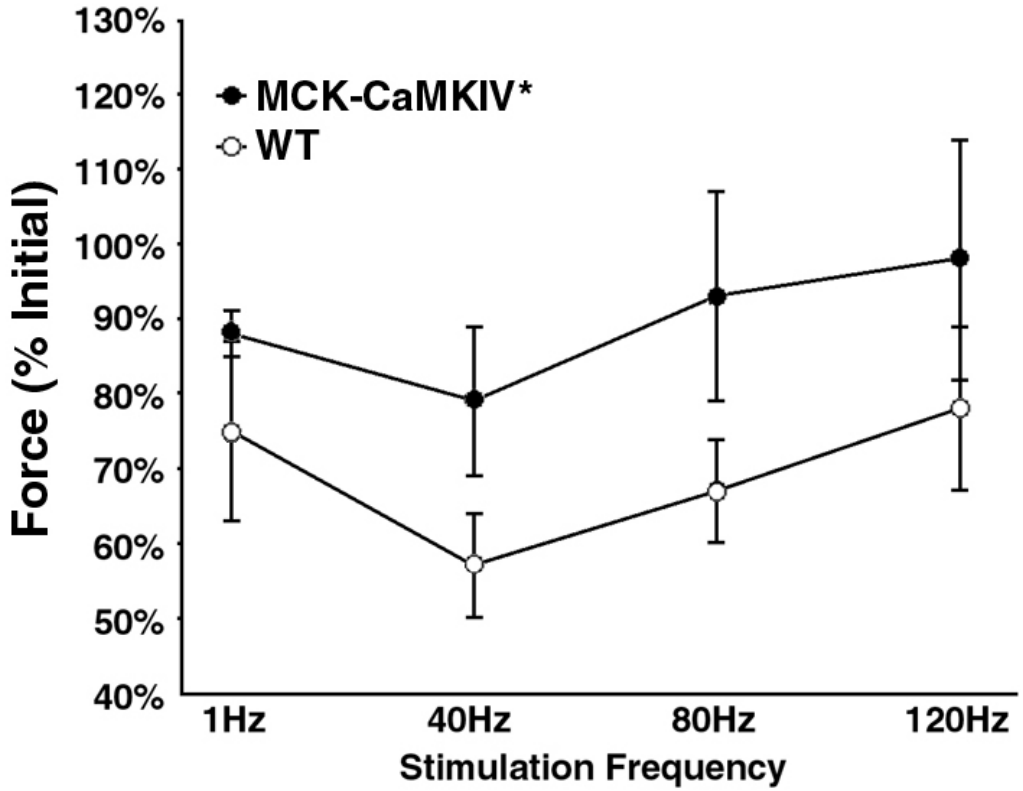
CaMK Stimulates Mitochondrial Biogenesis





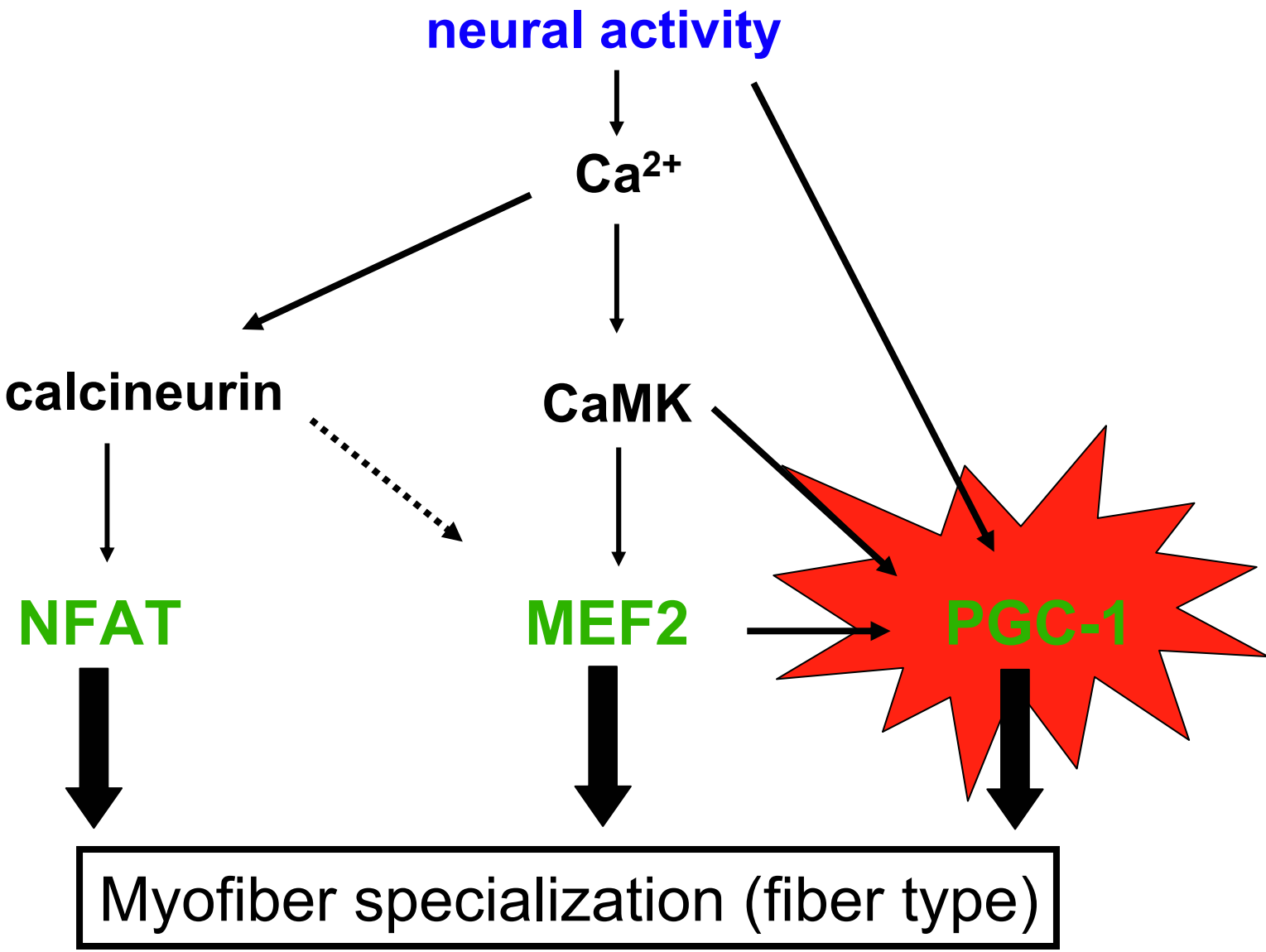
Wu *et al.* Science, 2002.

MCK-CaMK Muscle Shows Improved Function

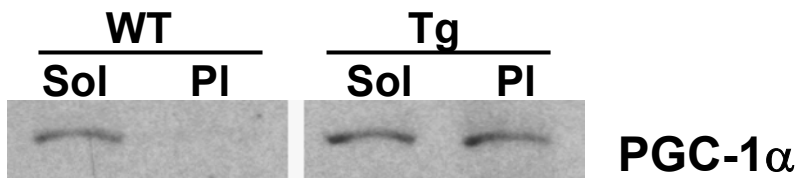


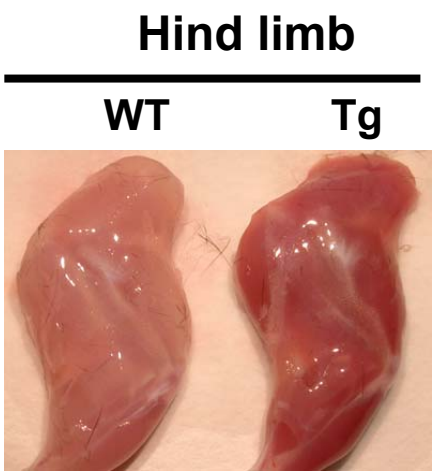
Wu *et al.* Science, 2002.

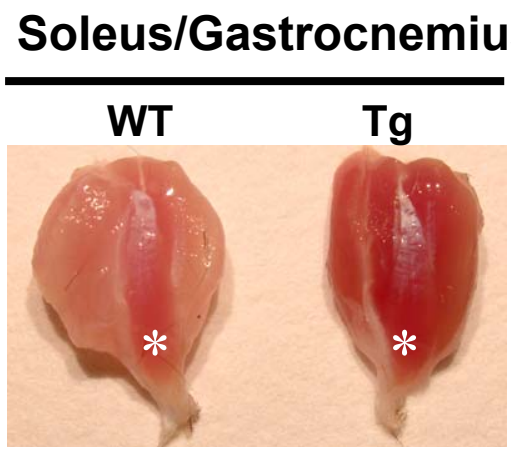
Genetic Reprogramming of Skeletal Muscle

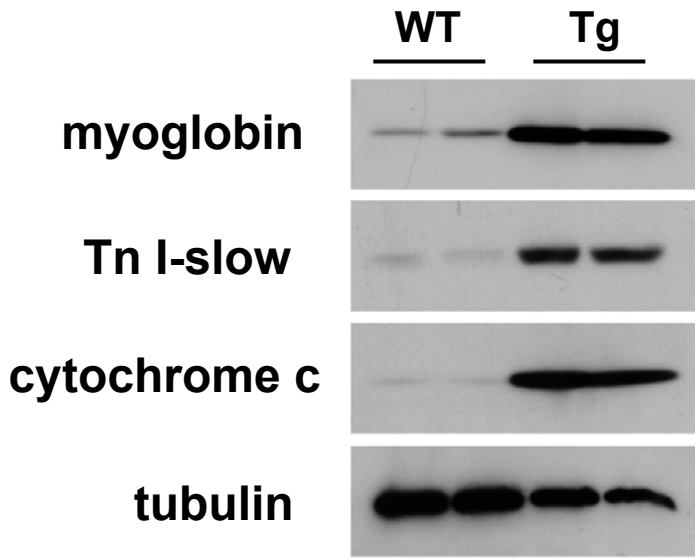


PGC-1α Promotes Slow Fiber Transformation



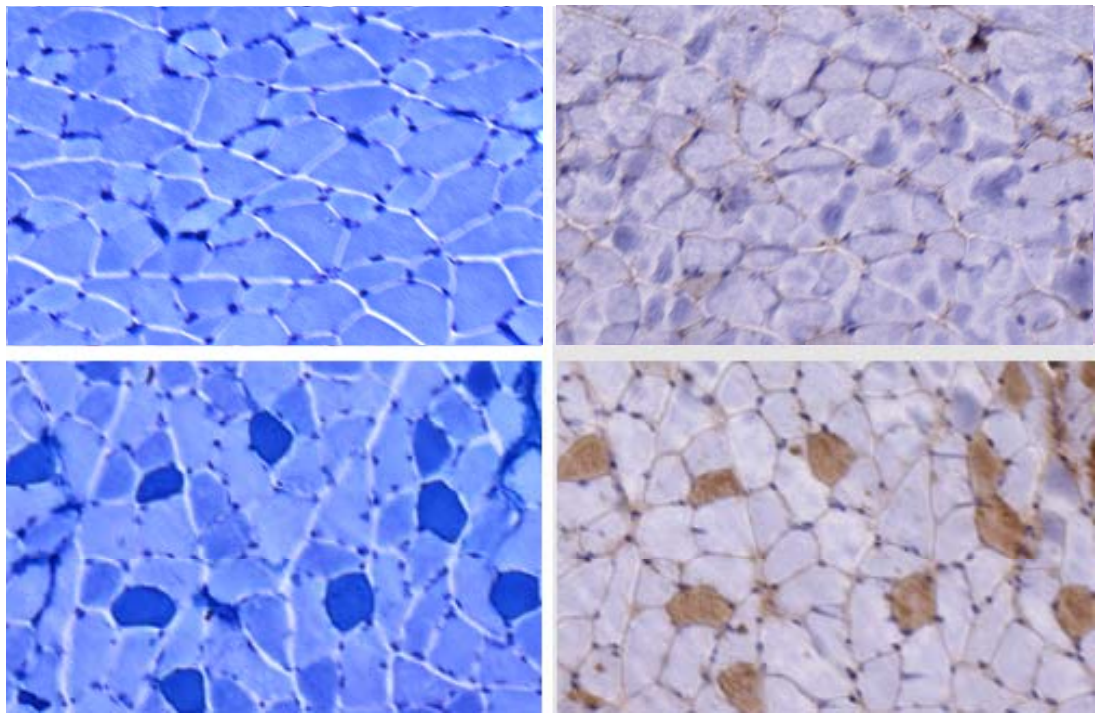




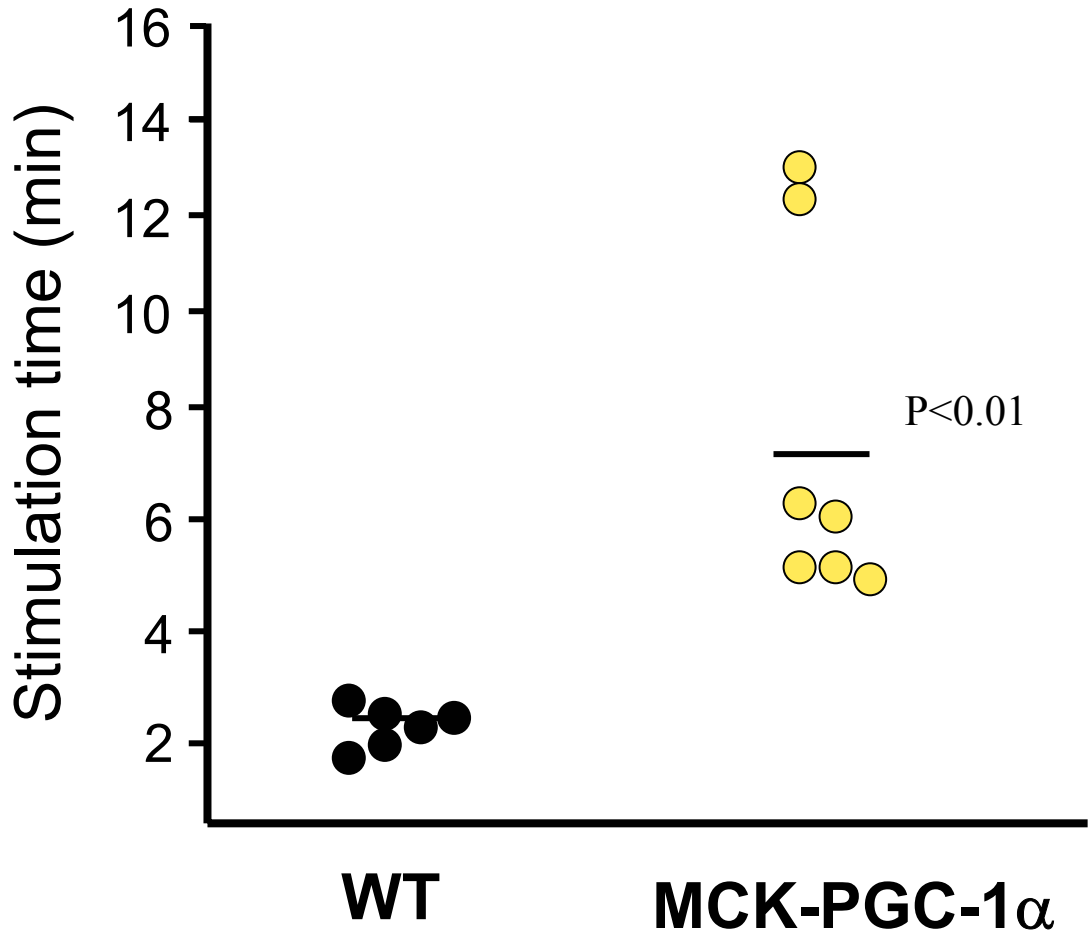


Lin *et al.* Nature, 2002.

PGC-1α Promotes Slow Fiber Transformation

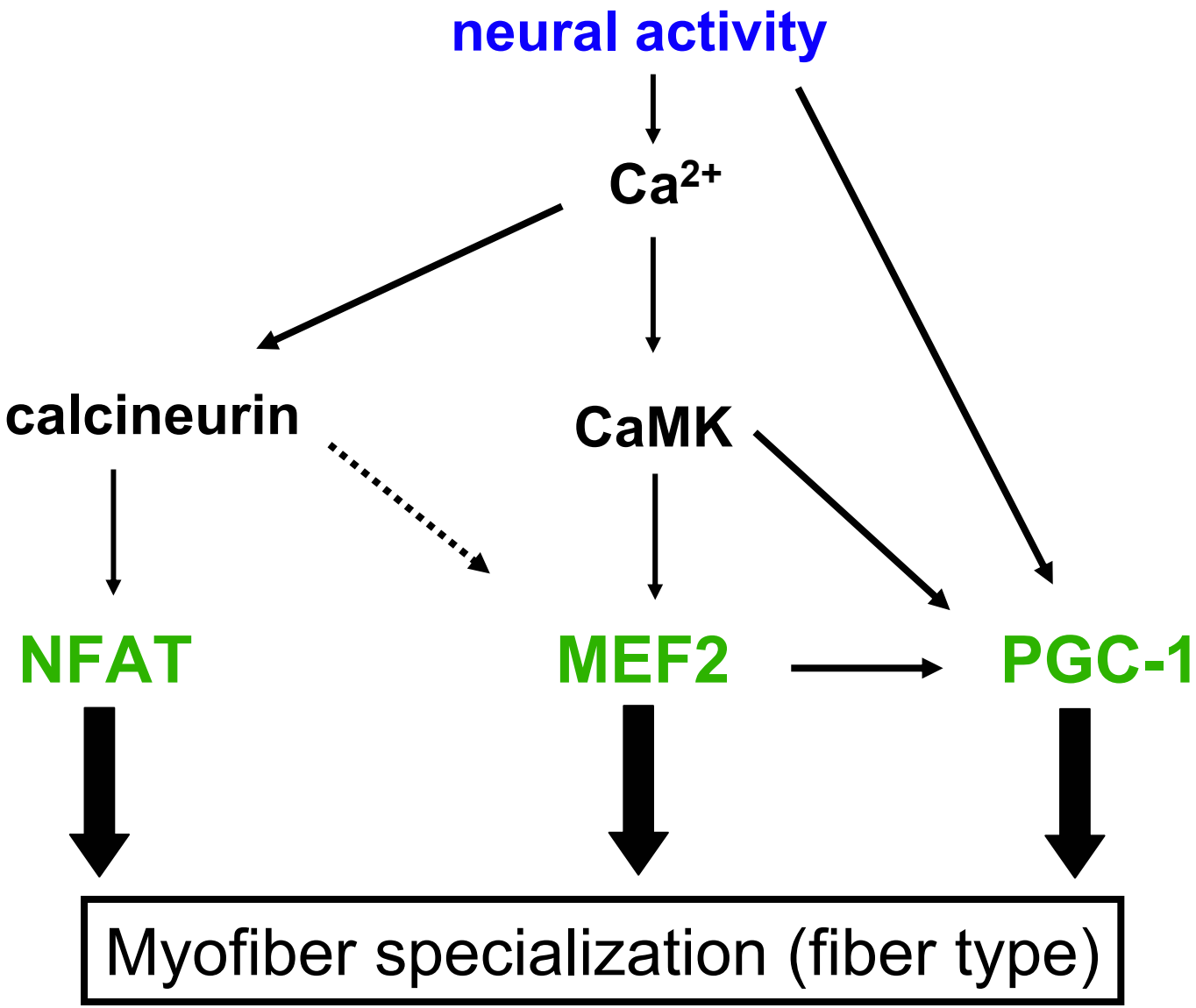


MCK-PGC-1 Muscle is More Resistant to Fatigue

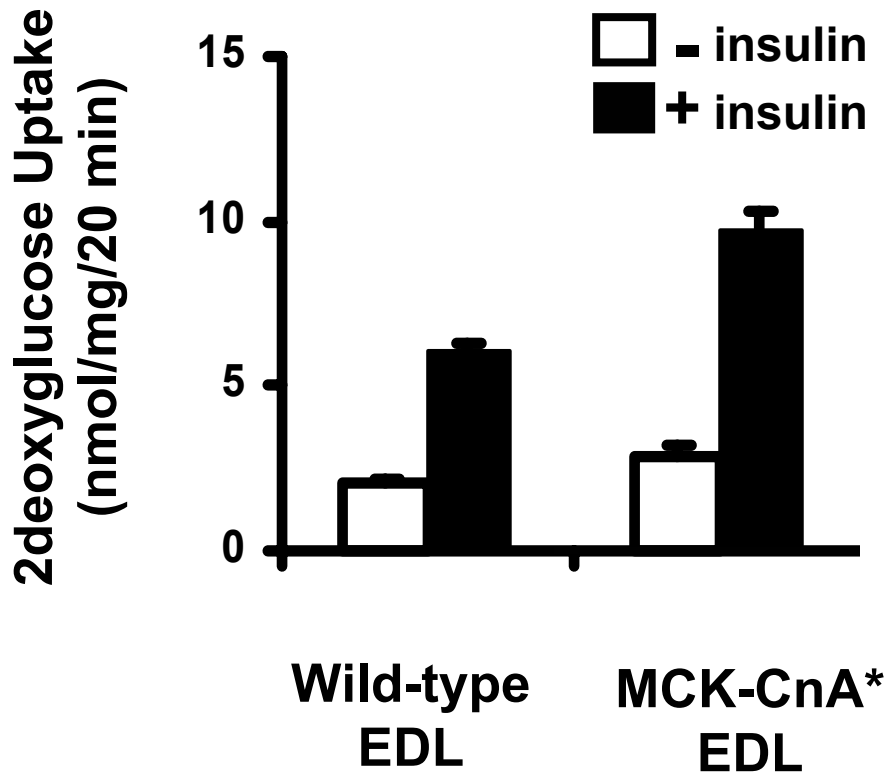


Lin *et al.* Nature, 2002.

Genetic Reprogramming of Skeletal Muscle

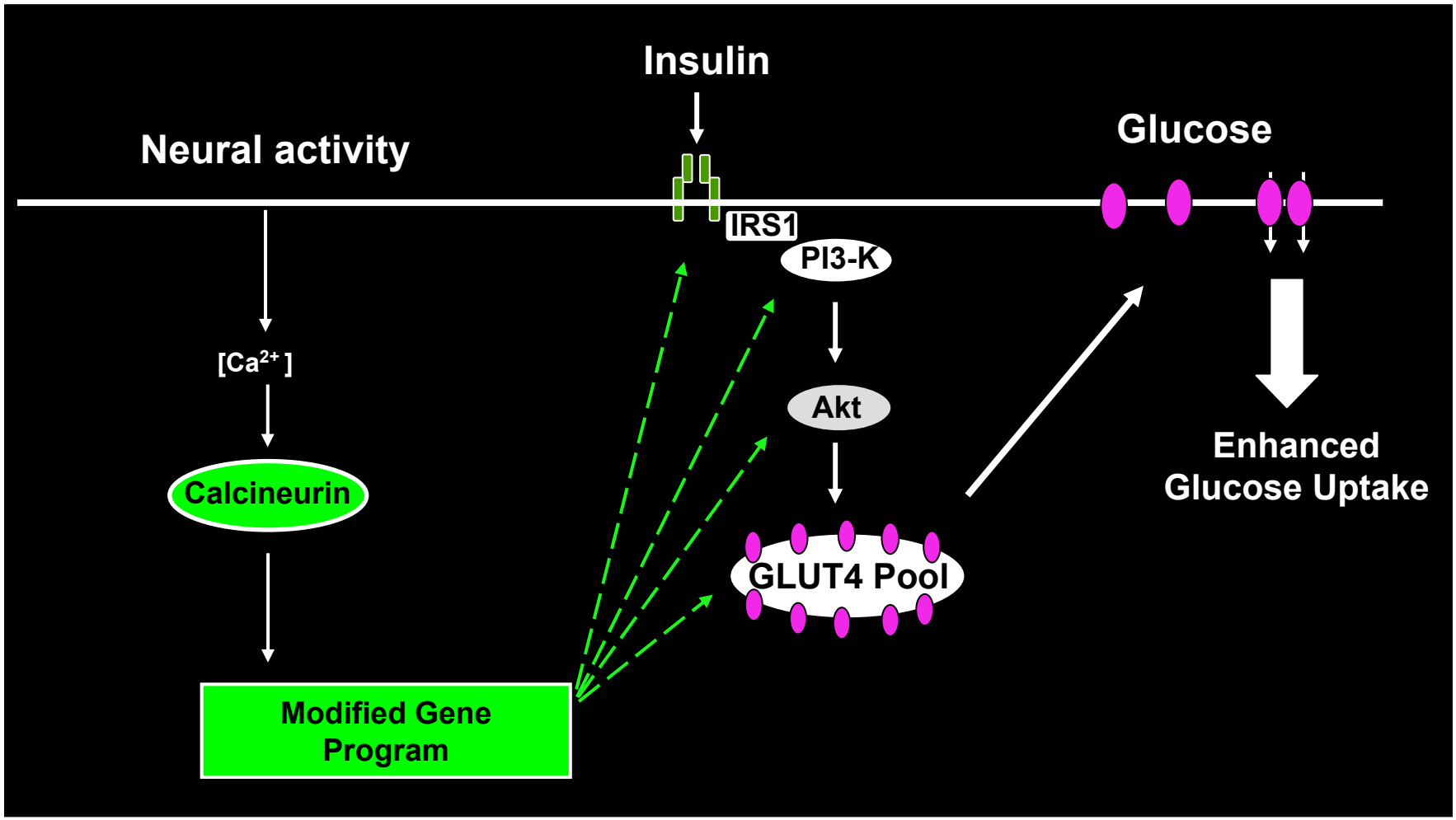


Calcineurin Enhances Insulin-Stimulated Glucose Transport in Muscle

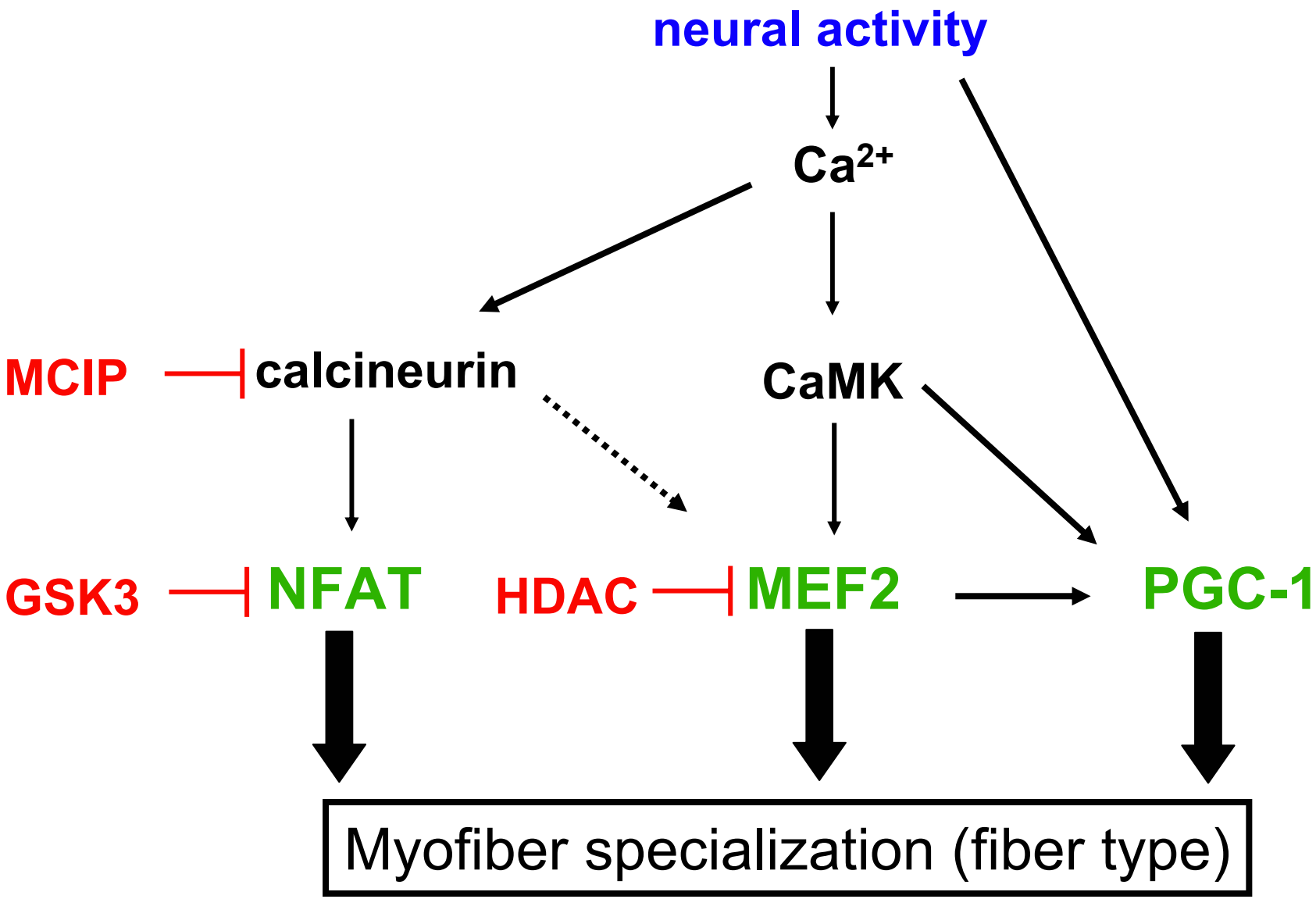


Ryder et al. JBC, 2003

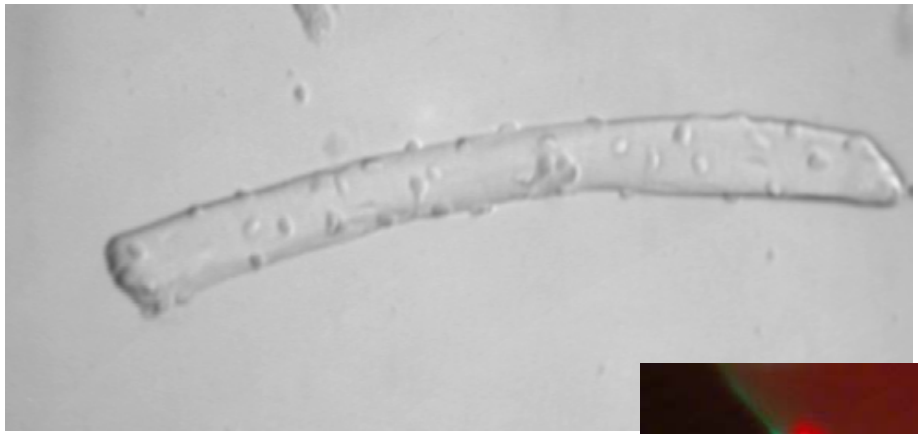
Calcineuirn Modulates Insulin-Stimulated Glucose Uptake in Muscle

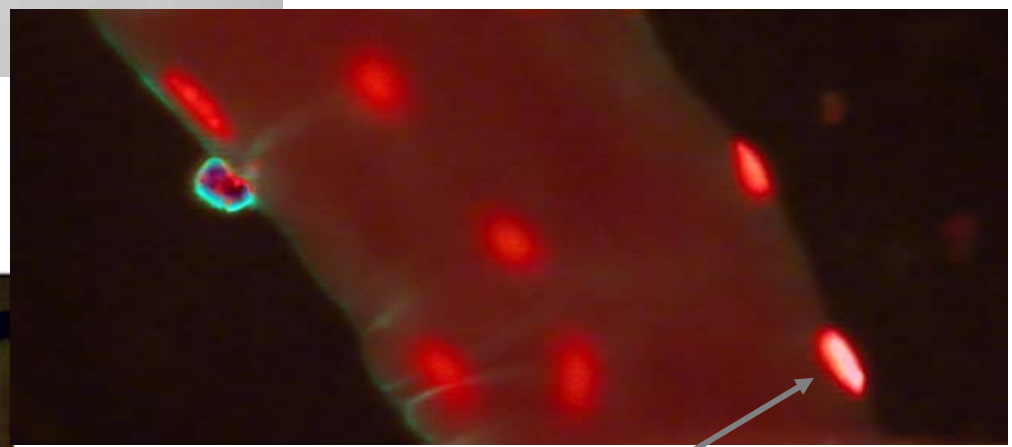


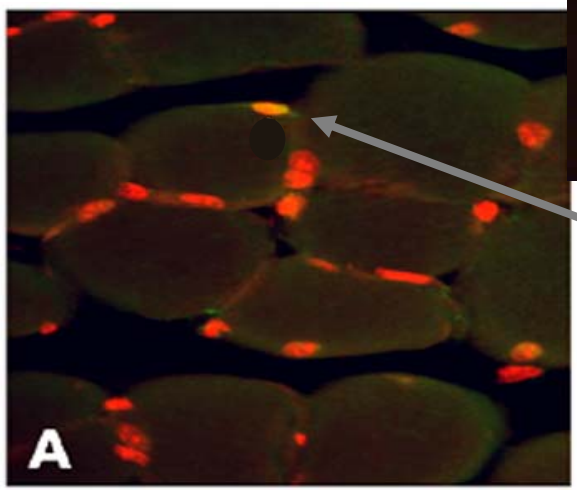
Genetic Reprogramming of Skeletal Muscle



Skeletal Muscle Regenerates

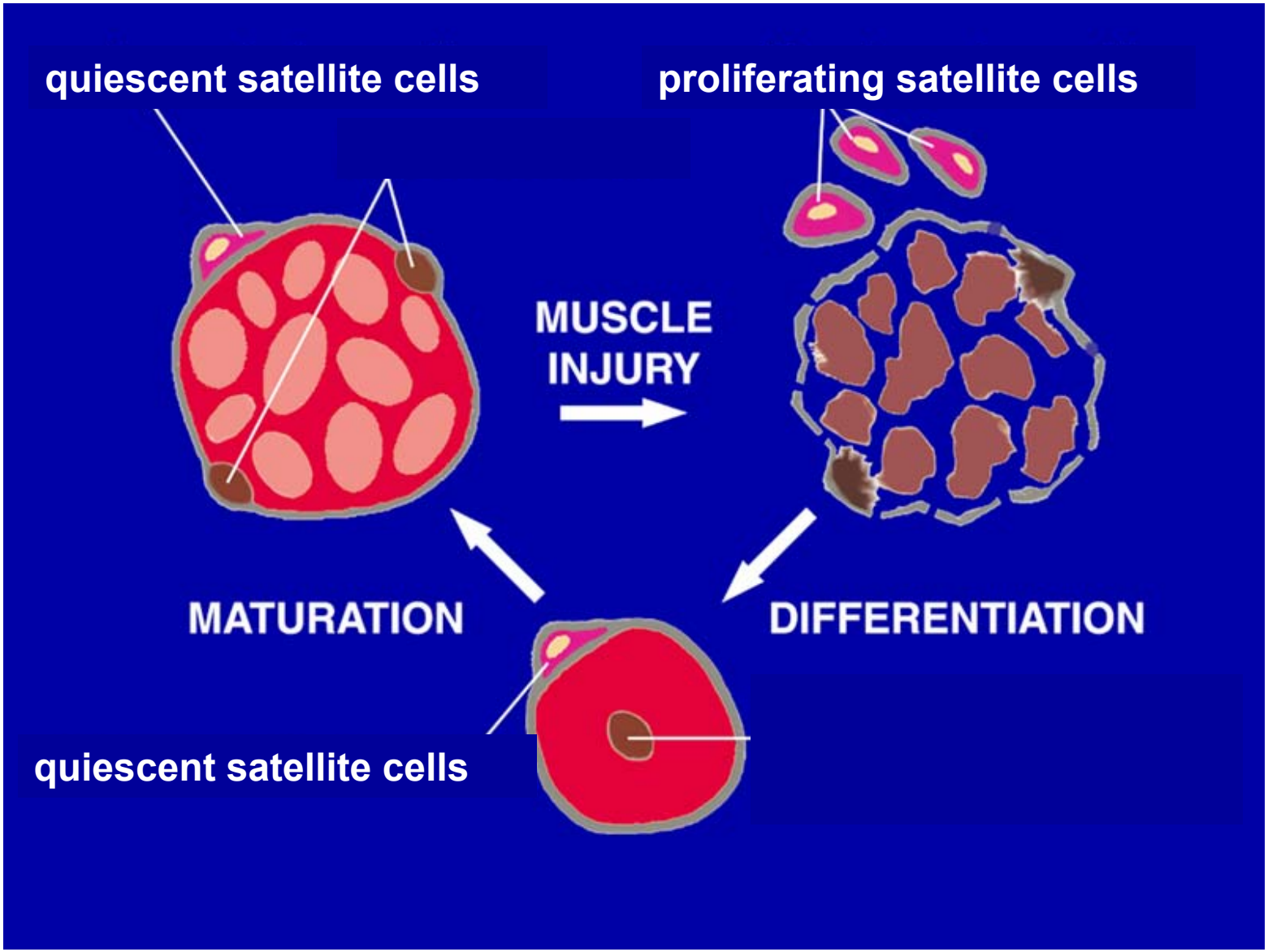




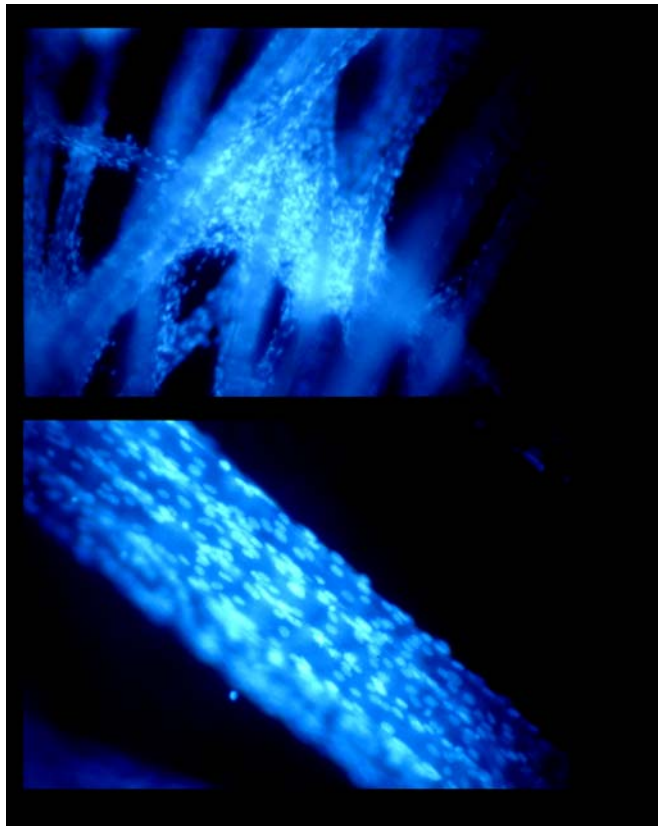


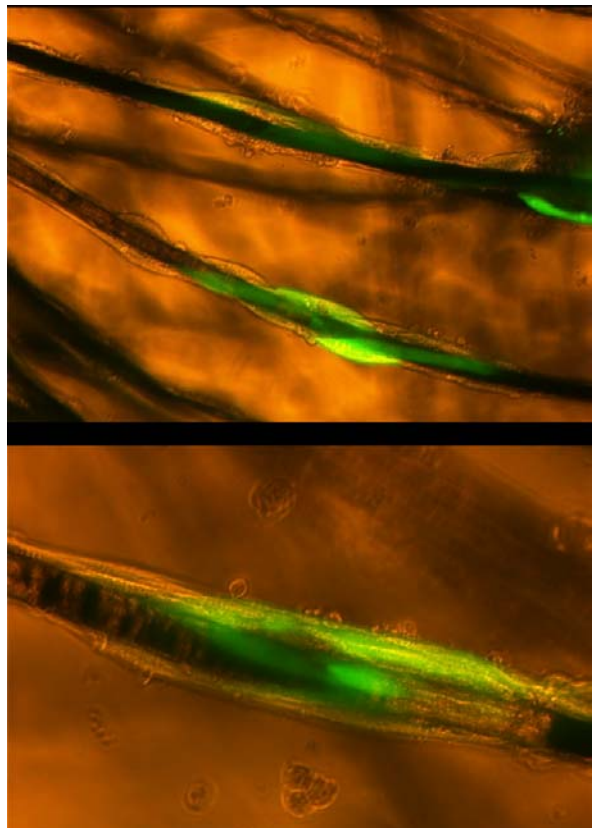
satellite cells

Muscle Regeneration



Growing Muscle on Synthetic Fibers





Acknowledgements

Hai Wu

Fritz Thurmond

Elizabeth Cronin

Darrell Neufer

Eva Chin

Frank Naya

Sandy Williams

Eric Olson

Daniel Garry

Joseph Garcia

Jim Stull

George Ordway

John Shelton

Jim Richardson

Harvard Medical School

Jiandie Lin

Bruce Spiegelman

Karolinska, Sweden

Jeffrey Ryder