Neuromuscular Plasticity

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The **PIEZO family**

The existence of a “piezo-electric substance” capable **of converting mechanical force into membrane depolarization** date back to 1950 (Sir B. Katz). This substance received a name in 2010, and the Nobel Prize in 2021:

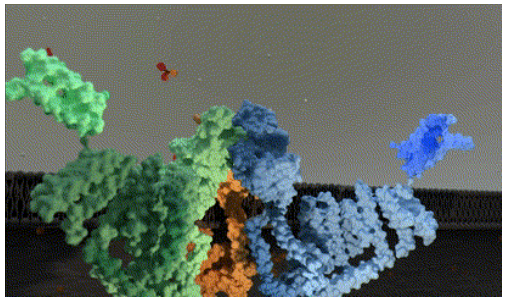
Piezo1 and Piezo2 Are Essential Components of Distinct Mechanically Activated Cation Channels

Bertrand Coste,[1] Jayanti Mathur,[2] Manuela Schmidt,[1] Taryn J. Earley,[1] Sanjeev Ranade,[1] Matt J. Petrus,[2] Adrienne E. Dubin,[1] Ardem Patapoutian[1,2]*

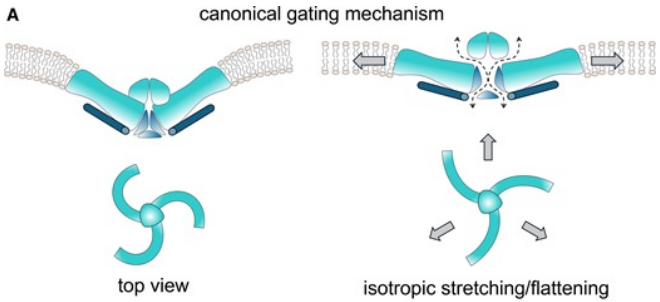
Mechanical stimuli drive many physiological processes, including touch and pain sensation, hearing, and blood pressure regulation. Mechanically activated (MA) cation channel activities have been recorded in many cells, but the responsible molecules have not been identified. We characterized a rapidly adapting MA current in a mouse neuroblastoma cell line. Expression profiling and RNA interference knockdown of candidate genes identified *Piezo1* (*Fam38A*) to be required for MA currents in these cells. Piezo1 and related Piezo2 (Fam38B) are vertebrate multipass transmembrane proteins with homologs in invertebrates, plants, and protozoa. Overexpression of mouse Piezo1 or Piezo2 induced two kinetically distinct MA currents. Piezos are expressed in several tissues, and knockdown of Piezo2 in dorsal root ganglia neurons specifically reduced rapidly adapting MA currents. We propose that Piezos are components of MA cation channels.

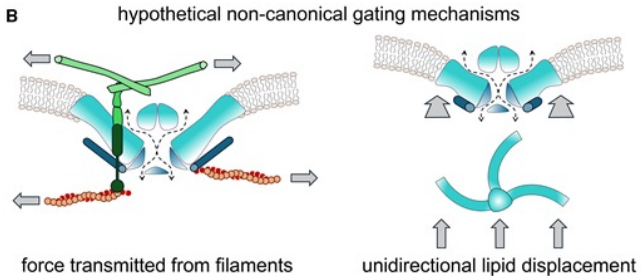
Figure 2. With Bertrand Coste and his electrophysiology rig where PIEZO was identified (La Jolla, CA, 2010).

PIEZO1 open channel mechanism

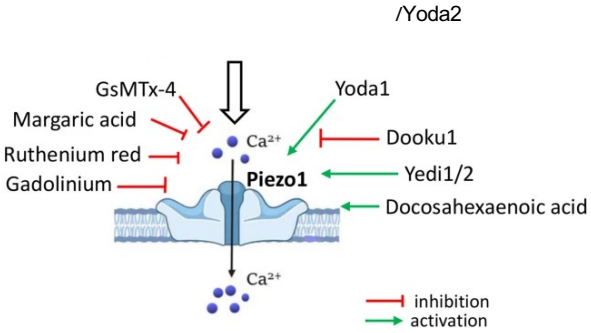


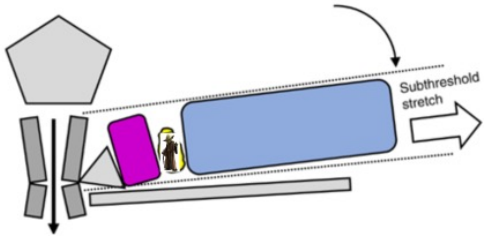
Mechanical signals





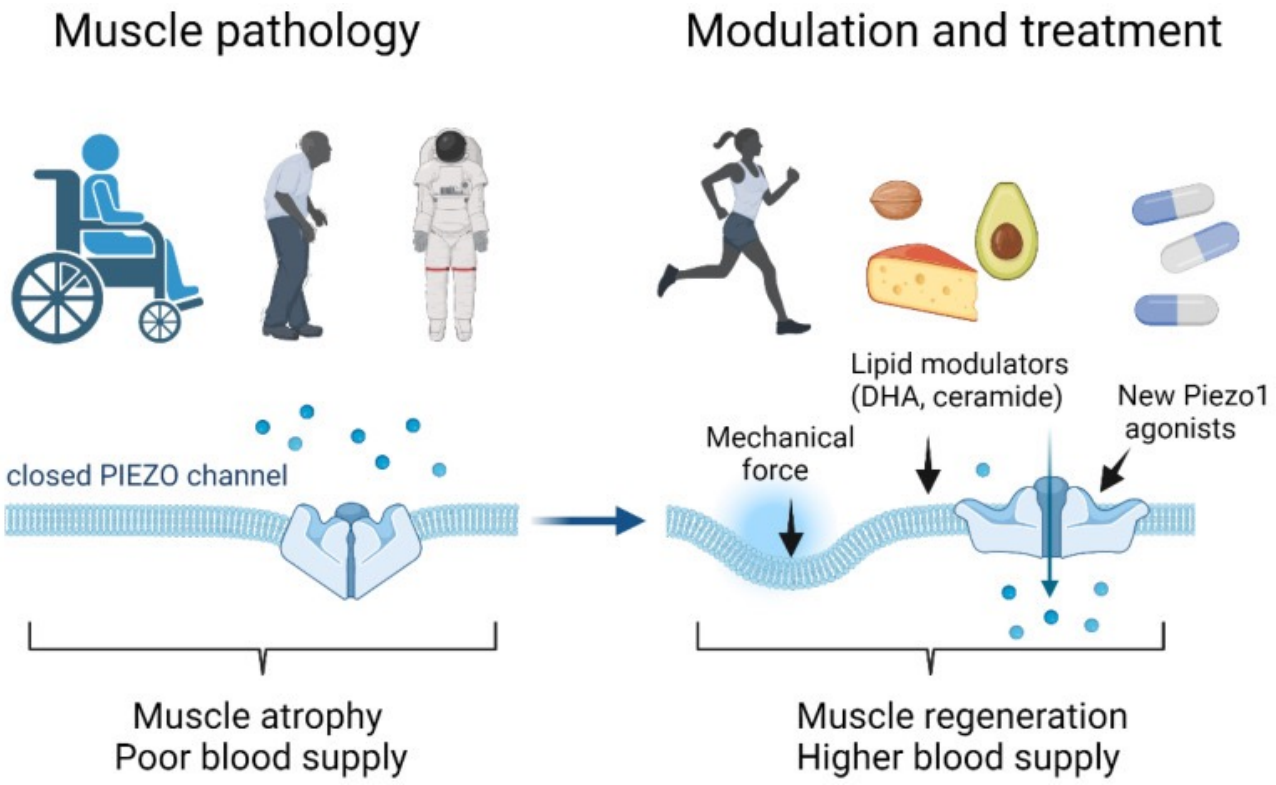
Chemical (exogenous) signals





Aim:

Role of PIEZO1 channels in skeletal muscle physiology and pathology

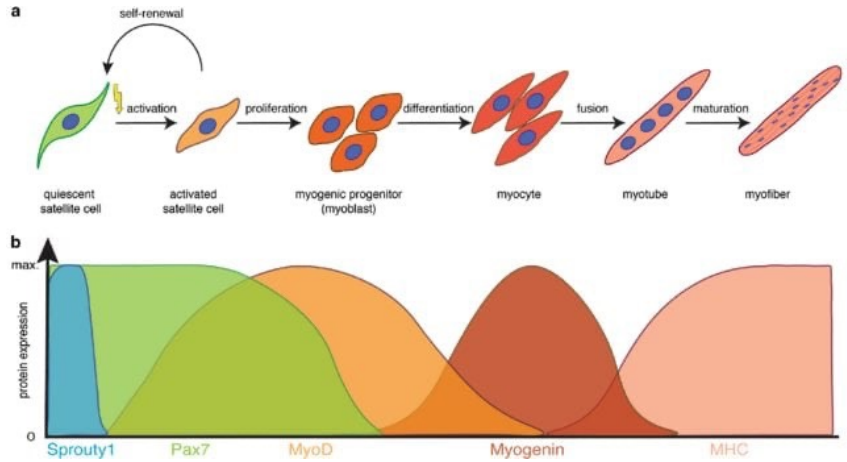


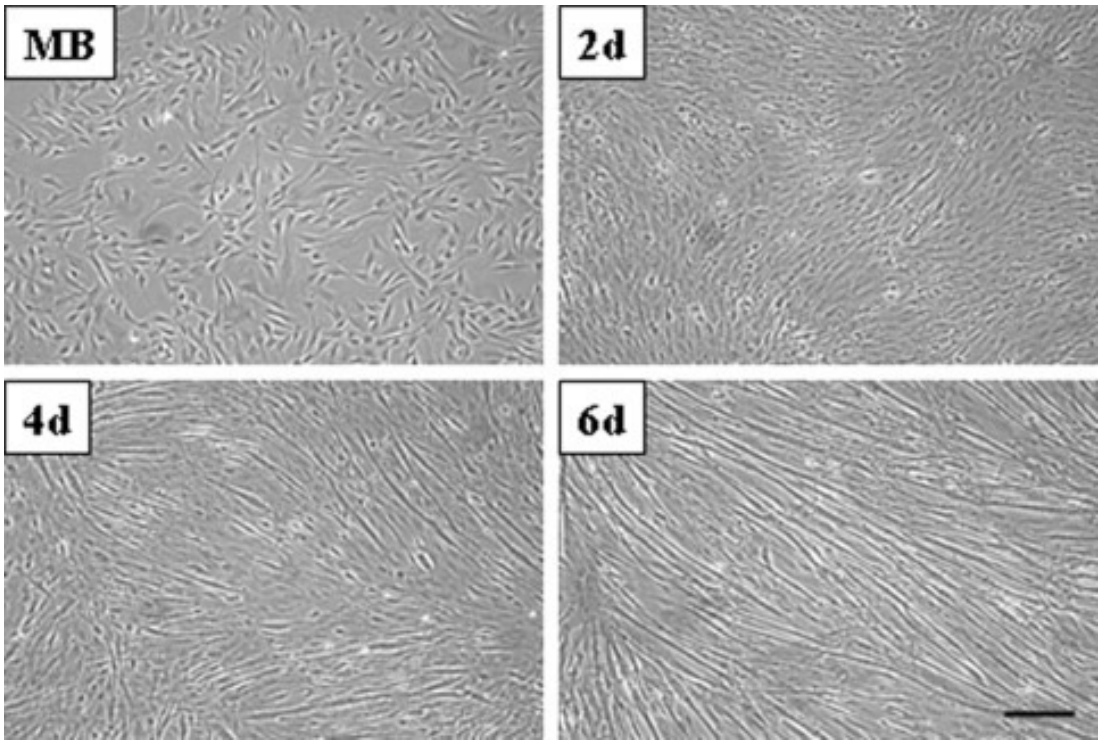
1. Effect of Piezo1 on myogenesis (impact on muscle regeneration)

Cell model:

myogenic precursor cells

to mimic *in vitro* myogenesis (C2C12)





2. Effect of Piezo1 on adult muscle

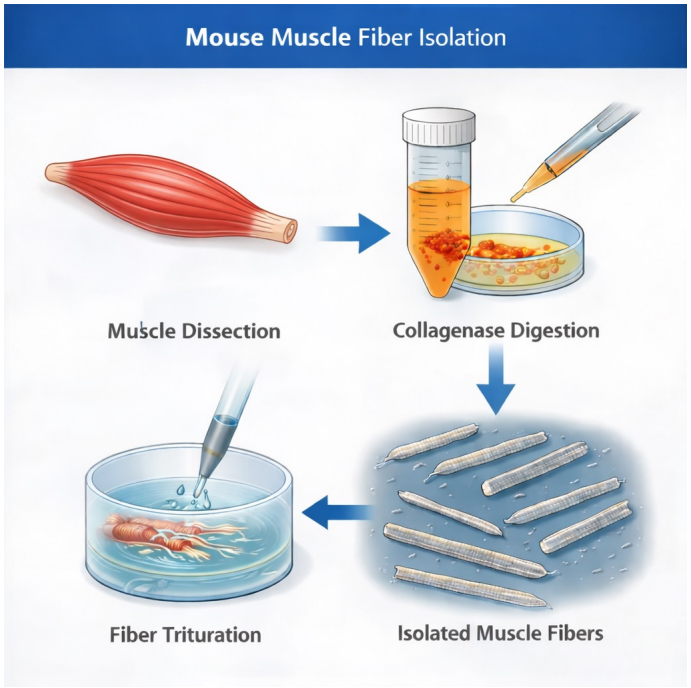
Cell model:

Adult muscle fiber

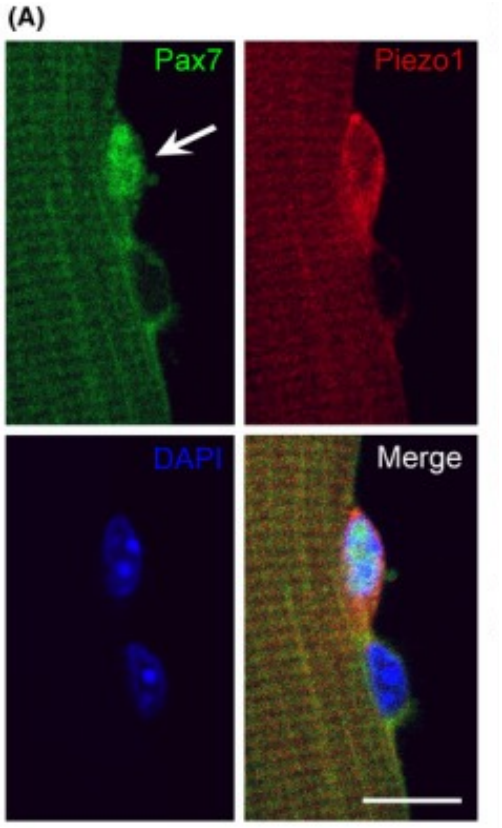
(e.g. *FDB*)

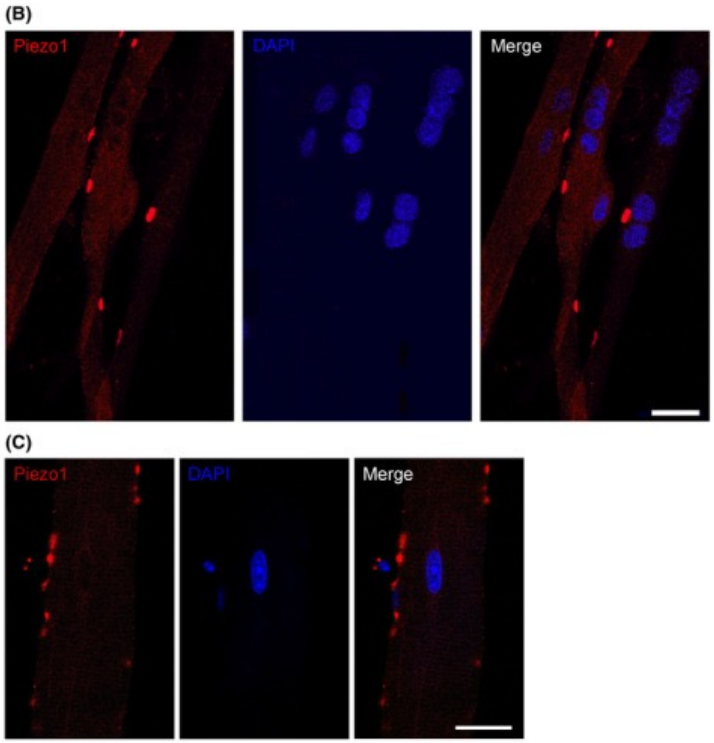
Muscle tissue

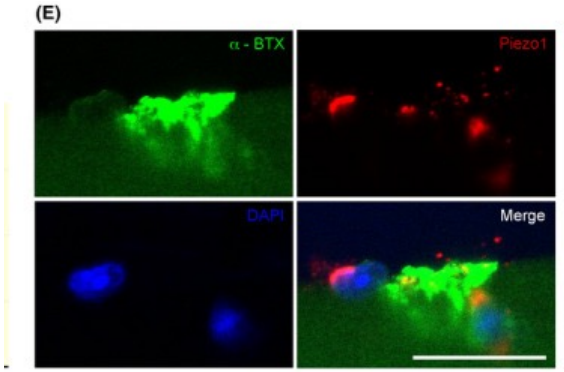
(e.g. mouse/rat/human)

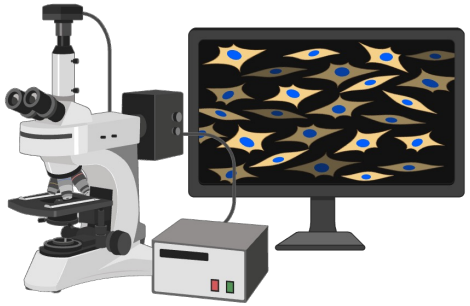


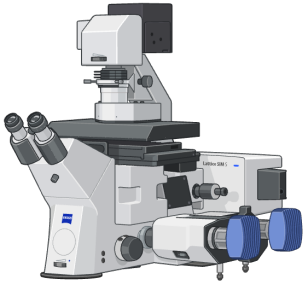
Methods:

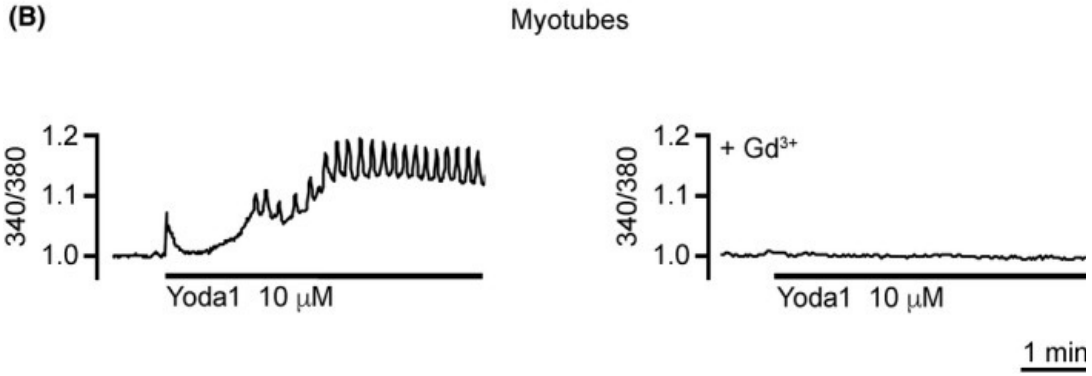

(A)
Pax7
Piezo1
DAPI
Merge

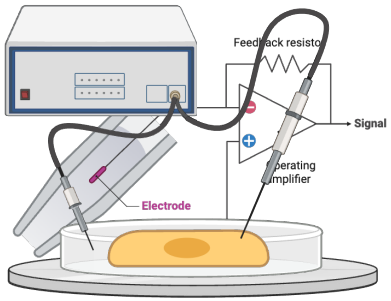

(B)
Piezo1
DAPI
Merge
(C)
Piezo1
DAPI
Merge

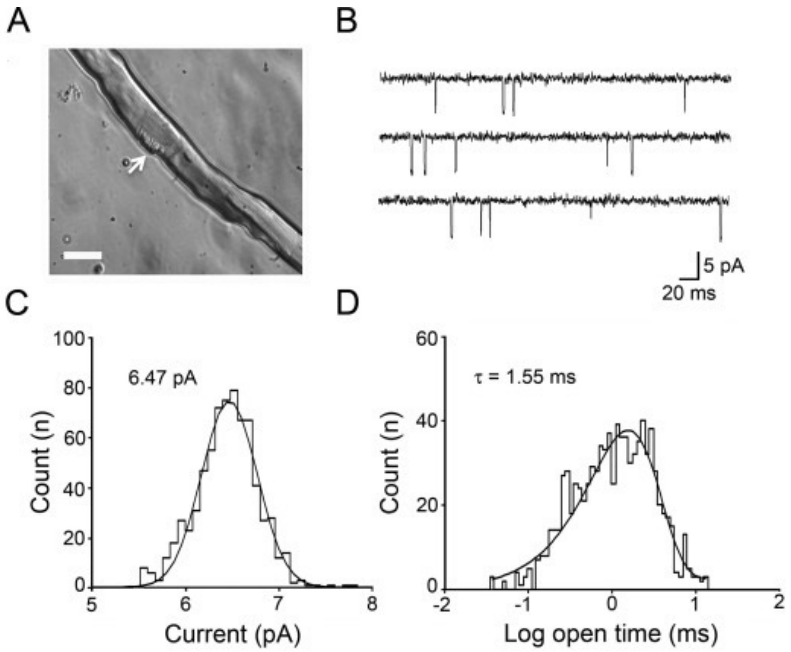

(E)
α - BTX
Piezo1
DAPI
Merge

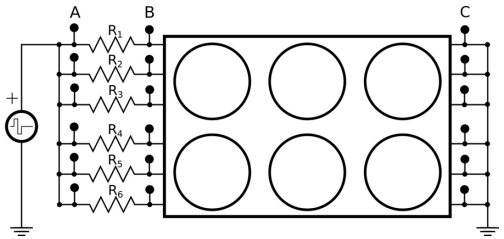


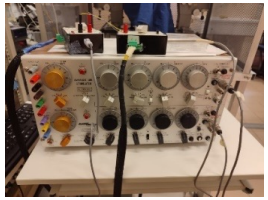


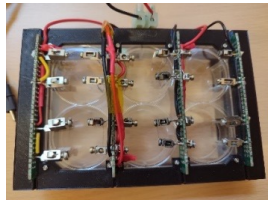

(B)
Myotubes
340/380
1.2
1.1
1.0
Yoda1 10 μM
+ Gd3+
1 min


Feedback resisto
Signal
Electrode

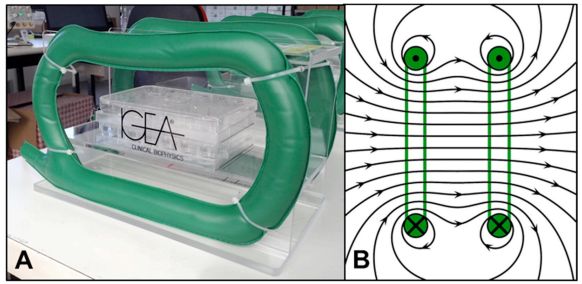

A
B
5 pA
20 ms
C
D
6.47 pA
τ = 1.55 ms
Count (n)
Current (pA)
Log open time (ms)



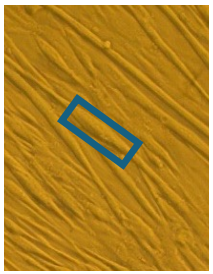


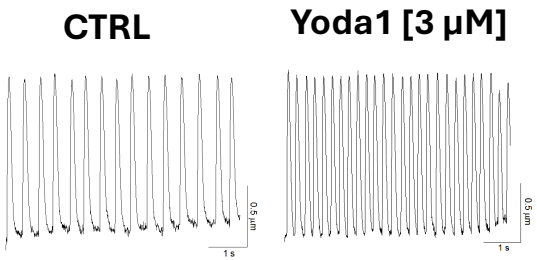


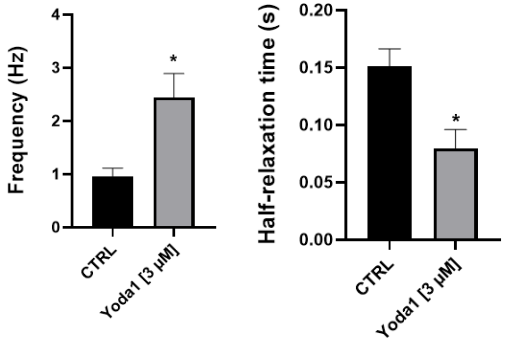
Electrical pulse stimulation currents. The electric current acts more superficially on the musculature, causing a submaximal muscle contraction.

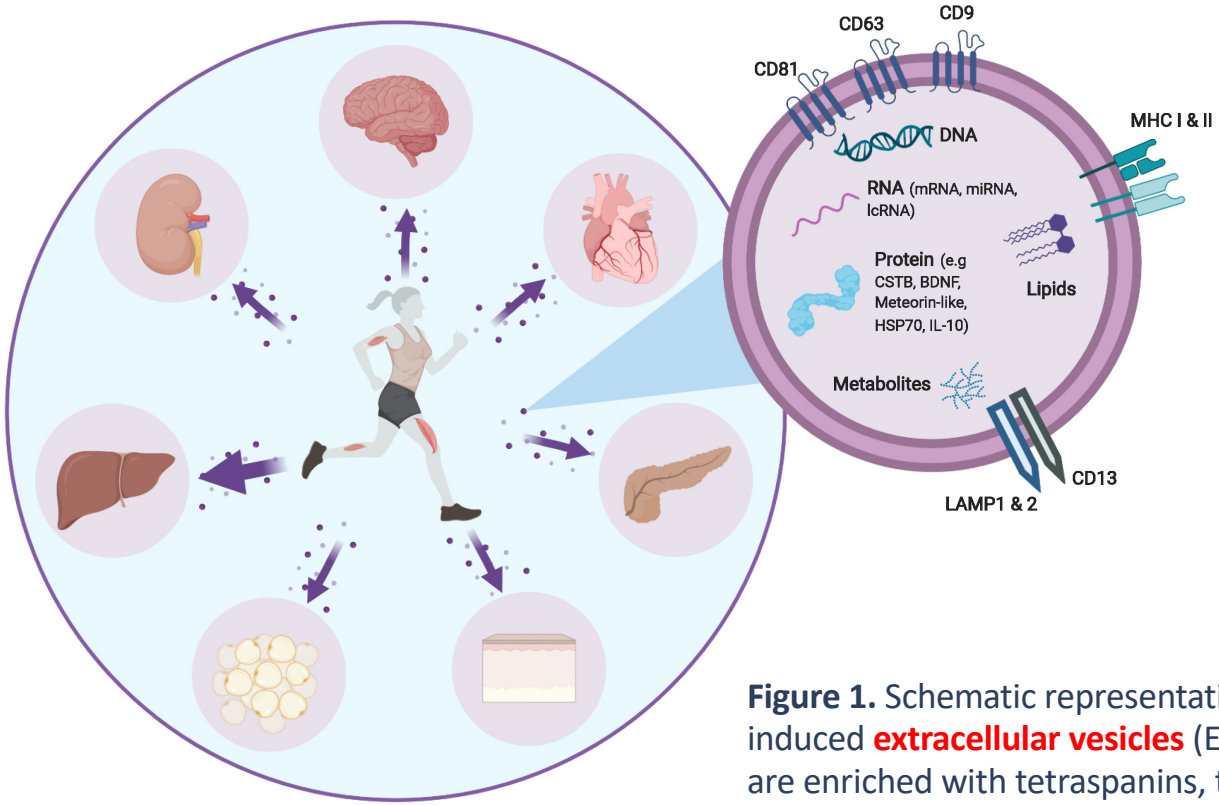


Pulsed electromagnetic field potentially evolves the whole muscle, it promotes maximal muscle contraction without the need for contact. The risk of infection is reduced. It is cheap, very simple to use, painless, non-invasive, no side effects.



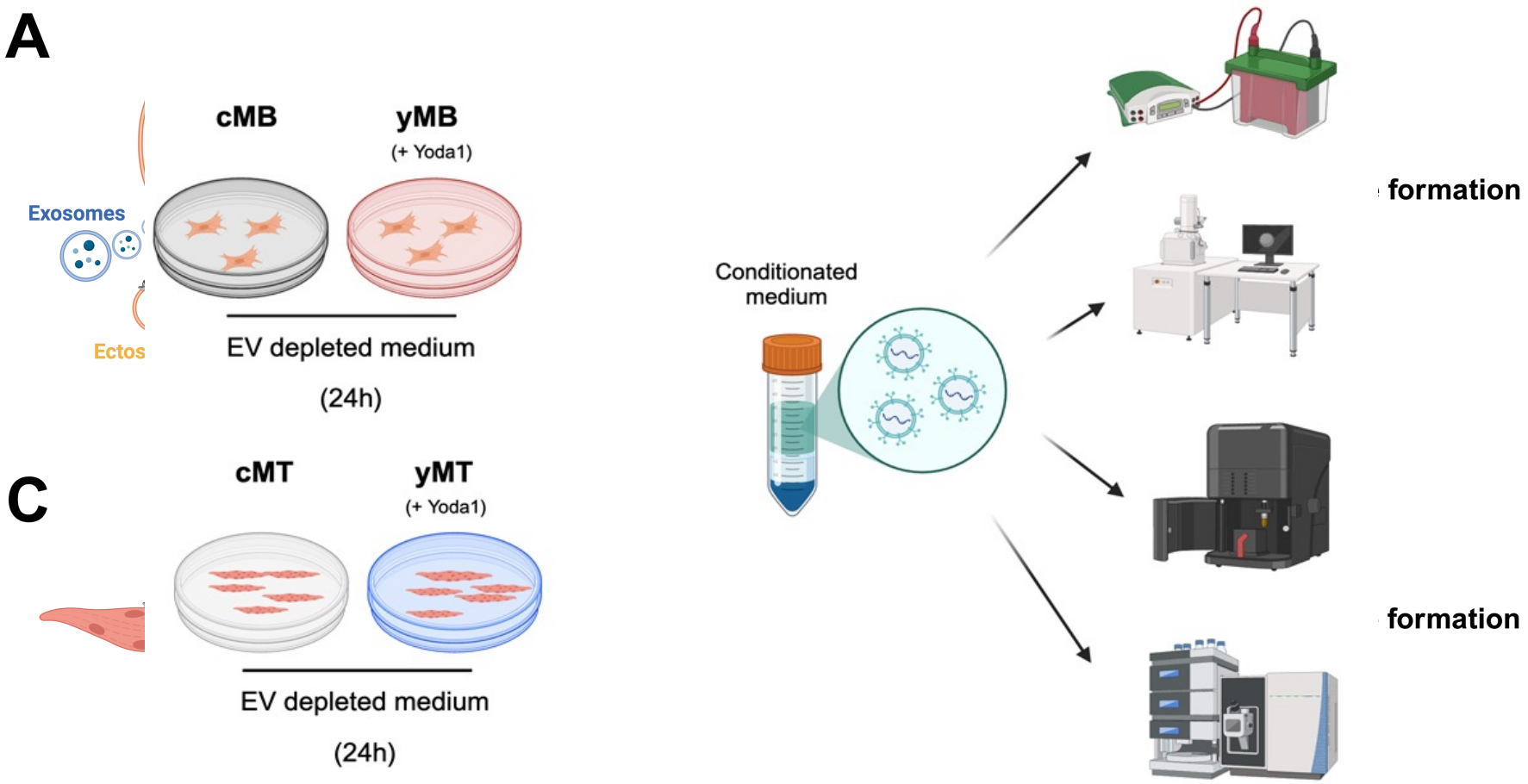






Y, Liu B, Gong W, Wu W, Peng R, Wang C, Shen T, **itive dysfunction in Alzheimer's disease mice via nce by microglia**. Nat Aging. 2026 Mar;6(3):579-58.

Figure 1. Schematic representation of inter-organ cross-talk mediated via exercise-induced **extracellular vesicles** (EVs) released from contracting skeletal muscle. EVs are enriched with tetraspanins, transmembrane proteins involved in transport and fusion, and contain bioactive cargo, including proteins (examples of protein cargo which might play a role in neurodegenerative diseases), DNA, RNA (mRNA, miRNA, lncRNA), lipids and metabolites.


A
cMB
yMB
(+ Yoda1)
Exosomes
Ectos
EV depleted medium
(24h)
C
cMT
yMT
(+ Yoda1)
EV depleted medium
(24h)
Conditionated medium
formation
formation

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