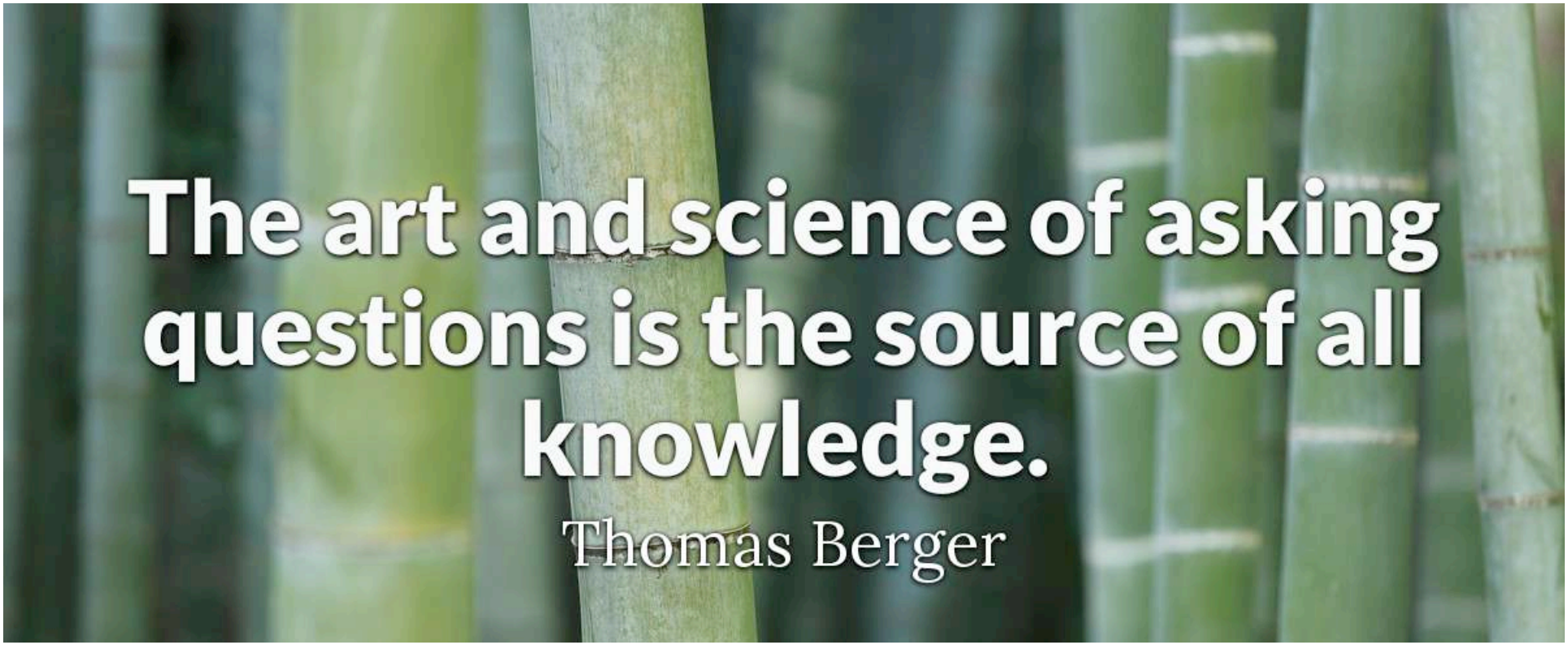

The art and science of asking questions is the source of all knowledge.
Thomas Berger

CASE STUDIES

Regenerative medicine

Perdita irreversibile di tessuti e cellule

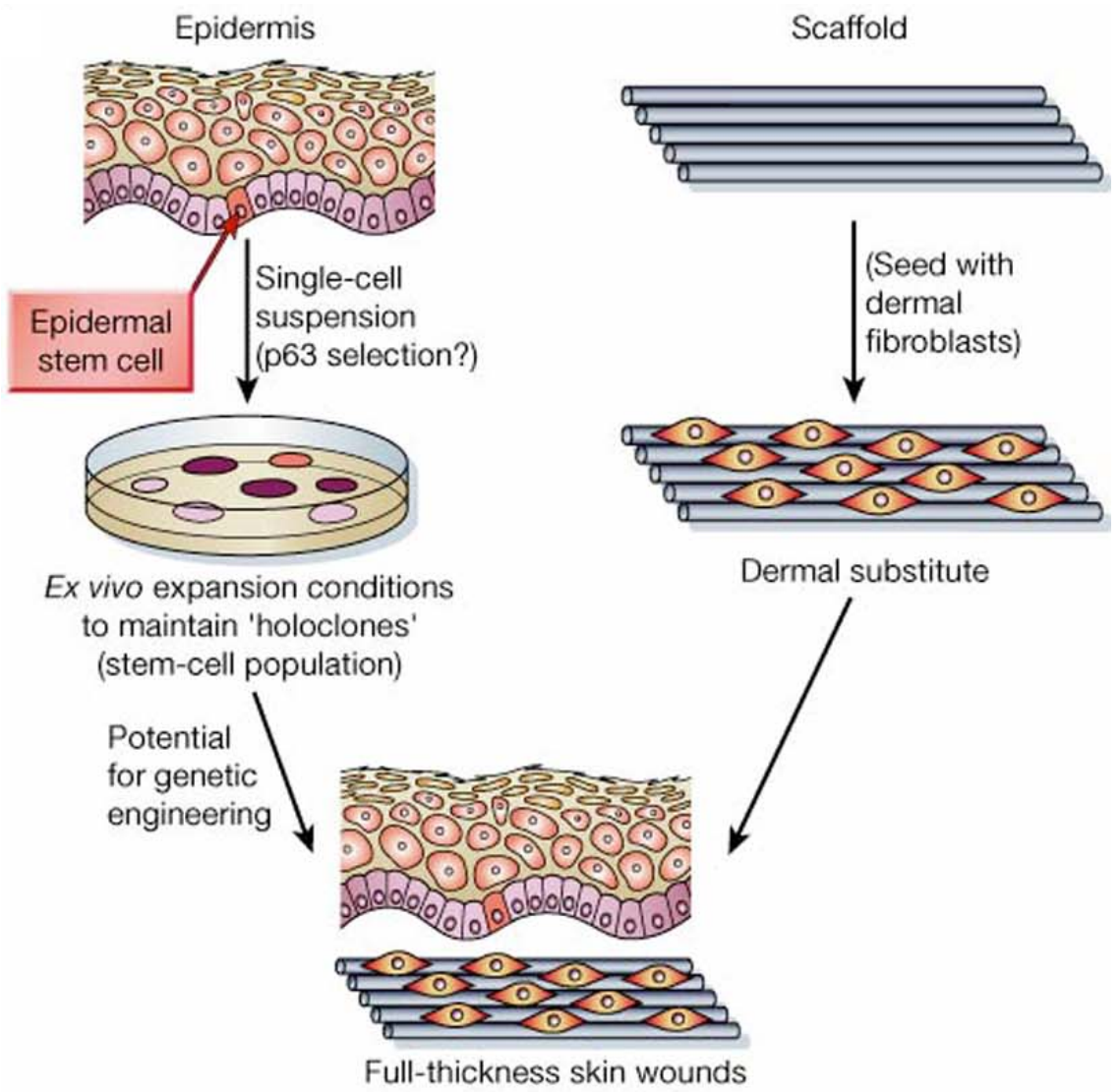
Infarto del miocardio
Ictus cerebrale
Diabete
m. Alzheimer

Anomalia irreversibile di tessuti e cellule

Malattie genetiche

Regenerative medicine

1. *Ingegneria dei tessuti*
2. *Terapia cellulare*
3. *Terapia genica*



Bianco & Robey, 2001

Cell therapy of alpha-sarcoglycan null dystrophic mice through intra-arterial delivery of mesoangioblasts.

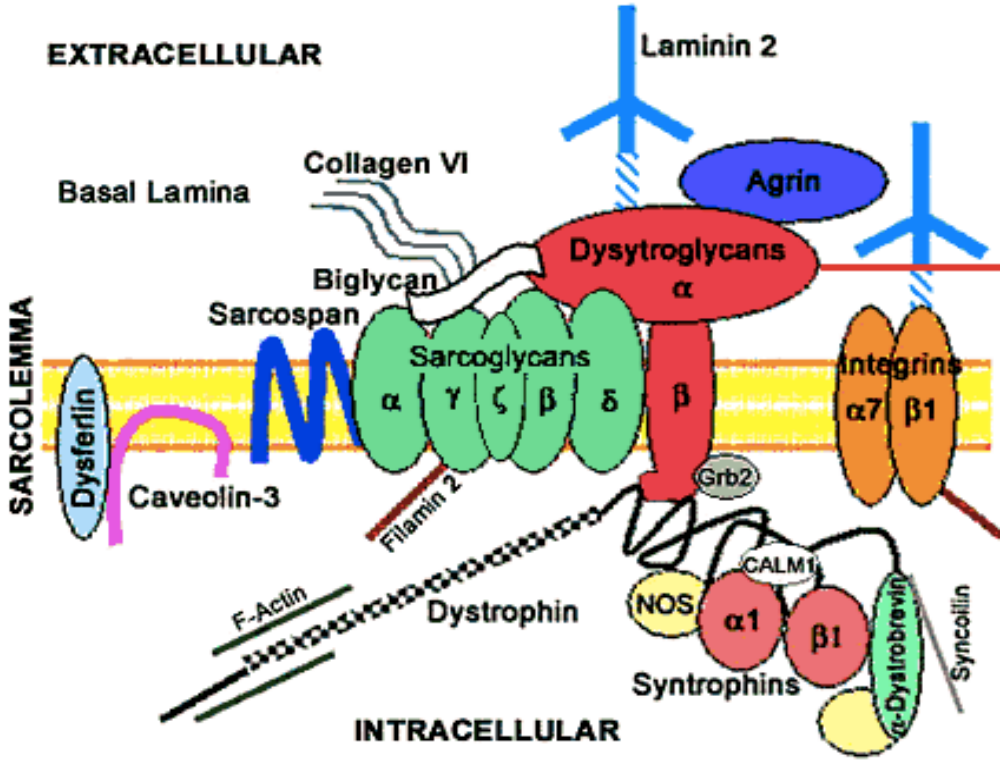
- knock out mice
- Cloned gene
- Genetically modified foetal cells

Science 2003 Jul 25

Muscular dystrophies

- Genetic disease
- Multiple genes involved; most common involving the dystrophin glyocprotein complex (DGC)
- typical trait is fiber necrosis

Dystrophin-glycoprotein complex



defective

Conventional therapy

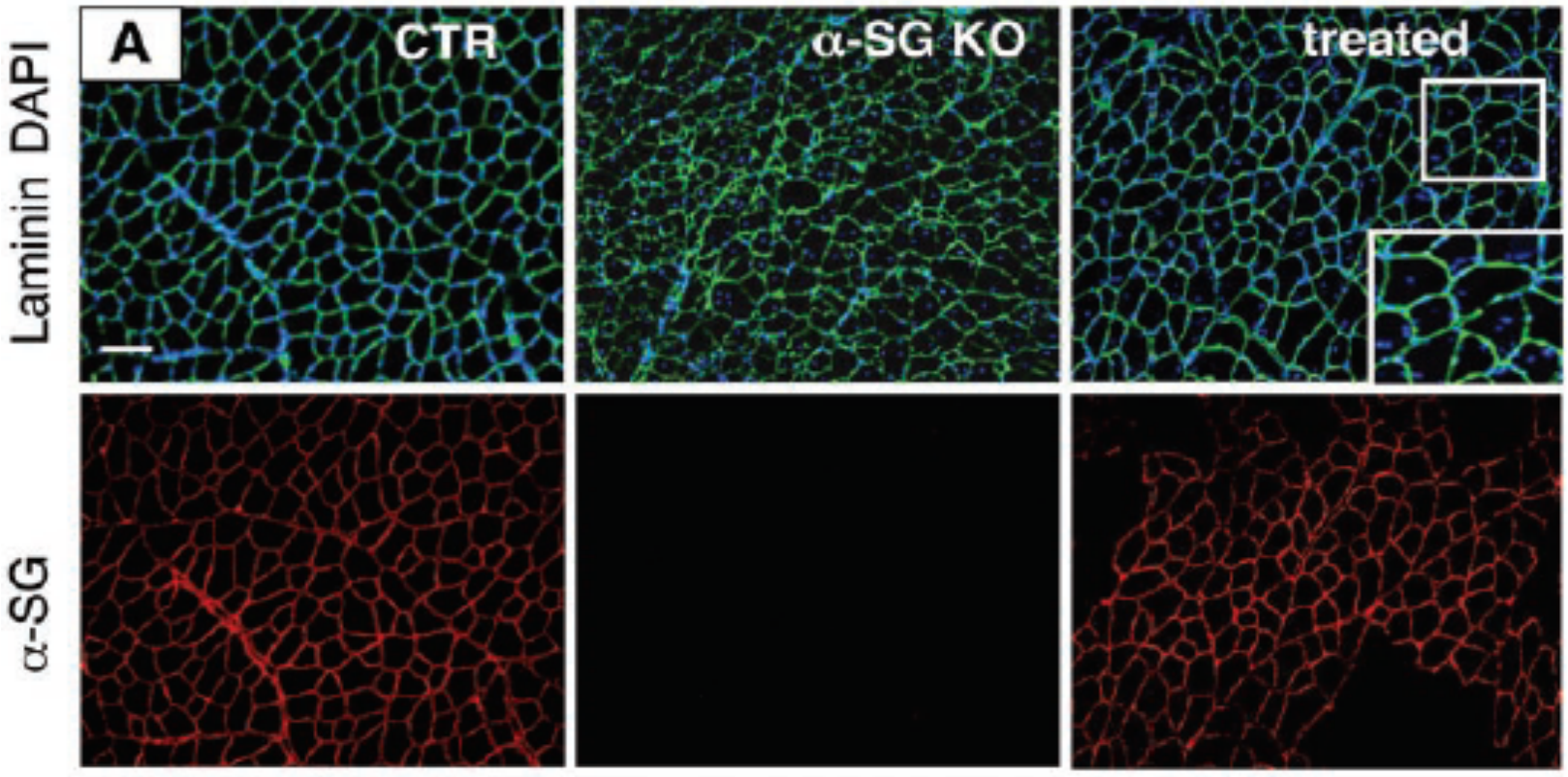
- Stretching of muscles ⇨ Does not cure
- Corticosteroid treatment ⇨ Side effectcs

- Drugs to induce protein symthesis similar to the absent (utrophin) ⇨ Mechanism validation to be assessed

Mesoangioblasts

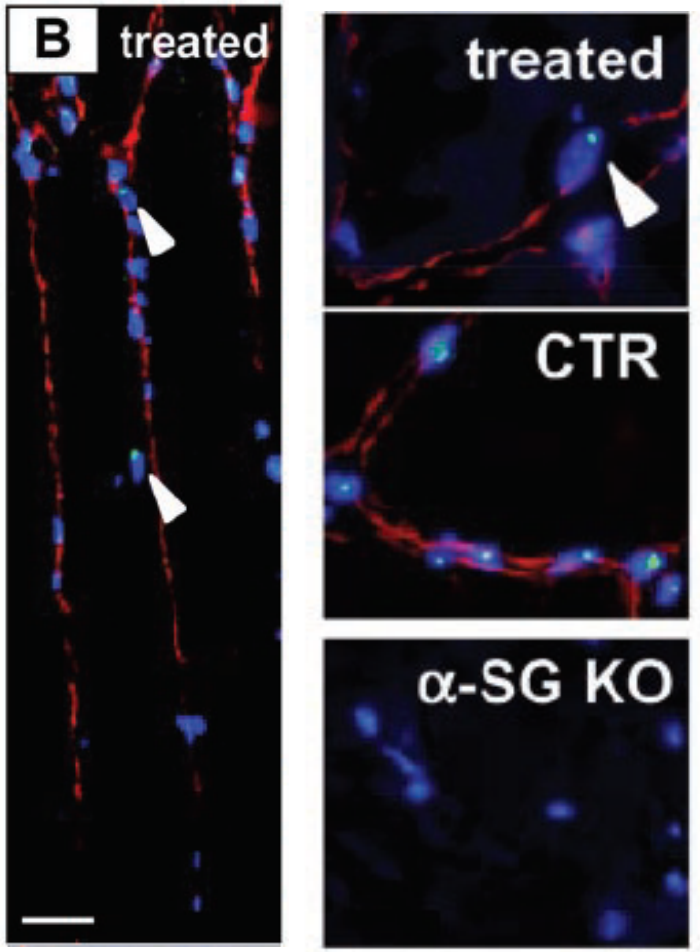
- Foetal stem cells associated with vascular system
- Highly proliferative
- Can move out of the vasculature in presence of inflammation
- Respond to necrotic cytokines

α-sarcoglican expression after mesoangioblasts (10e5) **wt,** heterologous in female -/- mice. Analysis at 2 months.



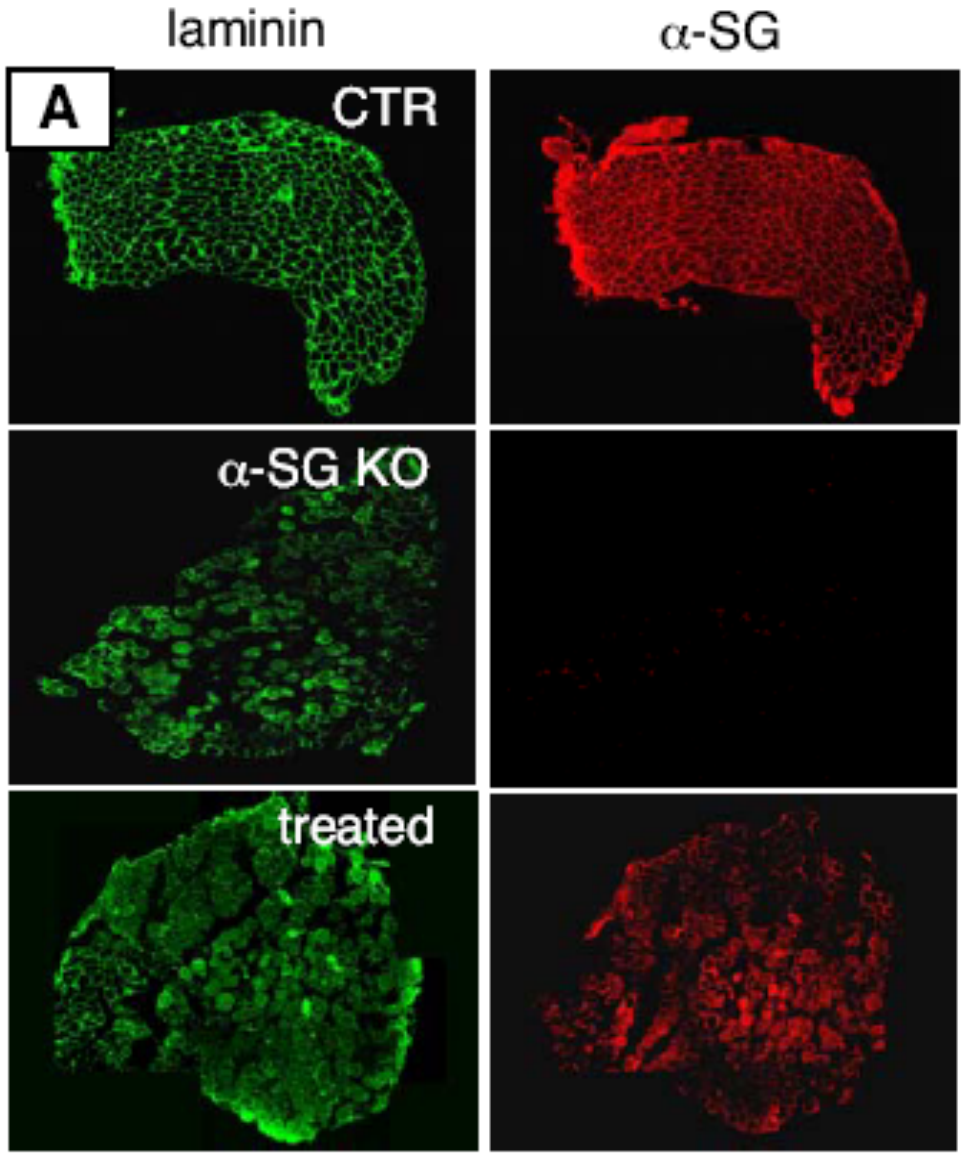
α-SG ab and tissue quality

αlpha-SG in mesoangioblasts



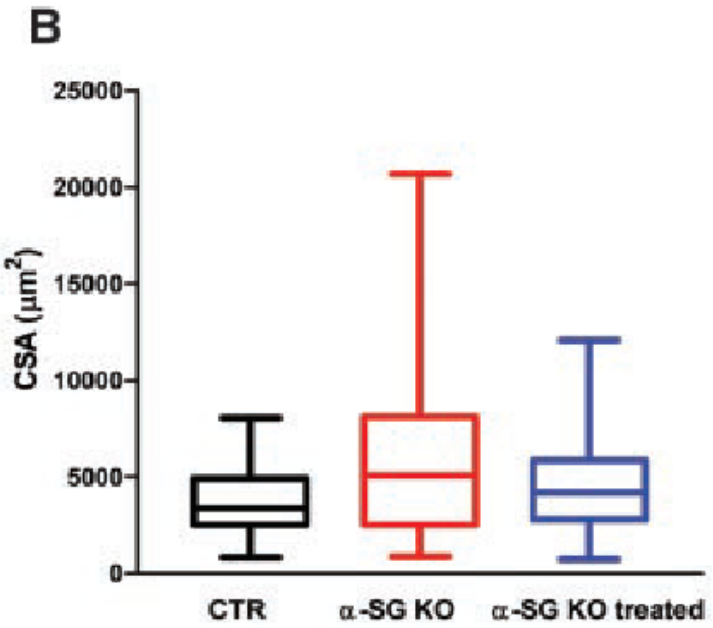
Fish (in blue) shows Y (arrow head), and α-SG positive (red)

3 injections at 40 days intervals; 5 x 10^5 mesoangioblasts male wt in female -/-. Assay 4 months after 1st injection



α-SG (in red), absent in diseases animals, is visible in treated mice

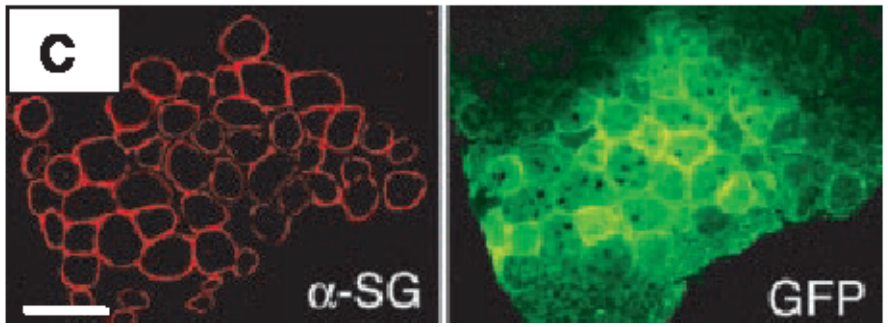
Triple injection. Muscle functionality evaluated ex vivo

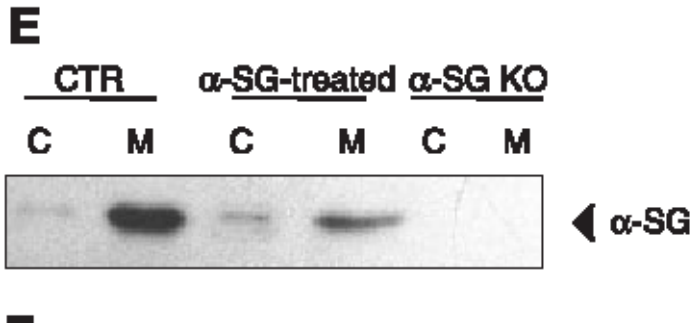


- Fibre section area

3 injections at 40 days intervals 5 x 10^5 autologous **mesoangioblasts**

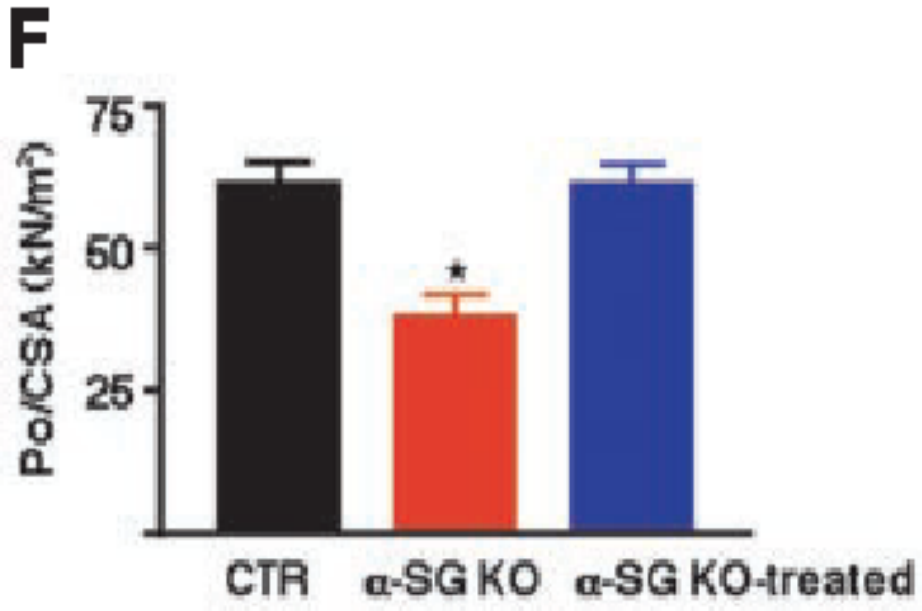
(from -/- mice aged **15d**) treated with lenti-PGK-SG-IRES-GFP





IF and WB show GFP and α-SG

Assay of muscular force in treated mice

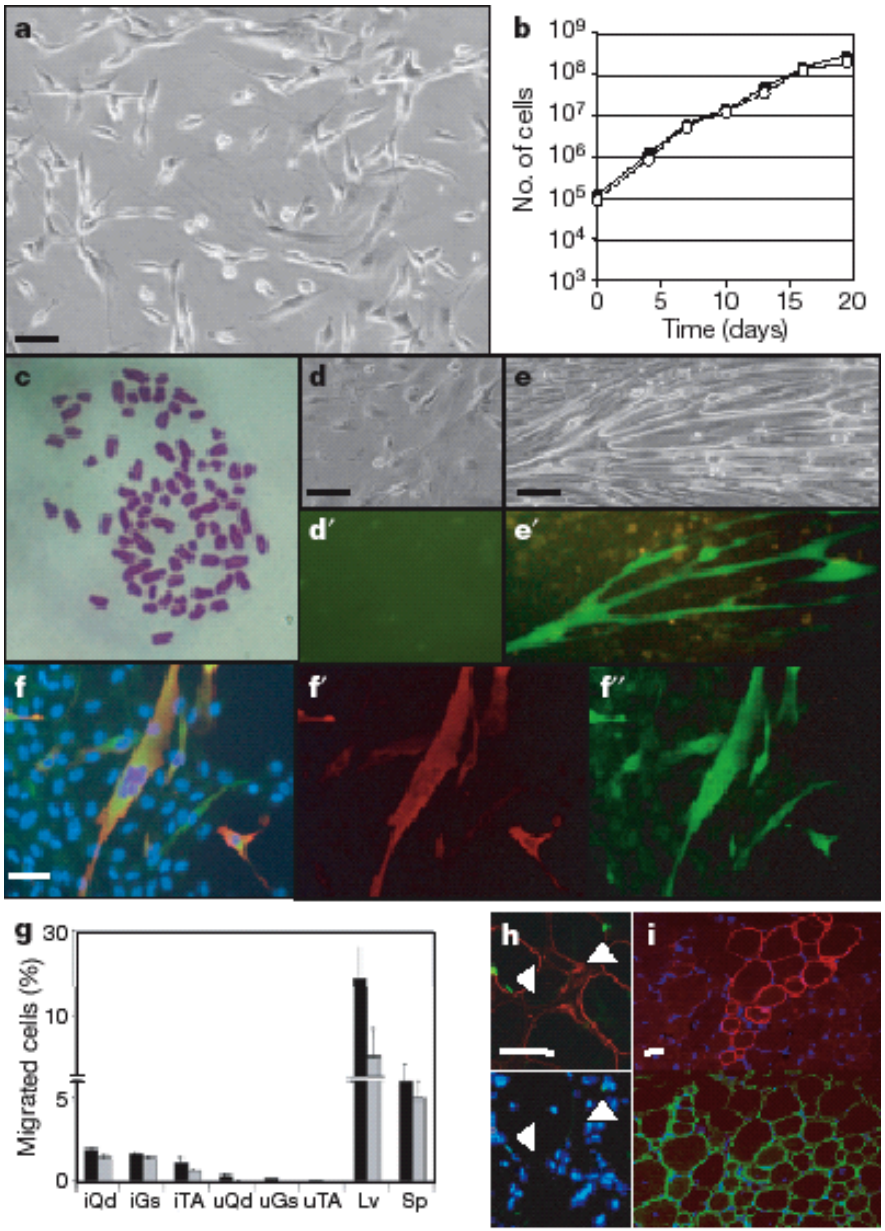


Mesoangioblast stem cells ameliorate muscle function in dystrophic dogs

Maurilio Sampaolesi[1,2]*, Stephane Blot[3]*, Giuseppe D'Antona[2], Nicolas Granger[3], Rossana Tonlorenzi[1], Anna Innocenzi[1], Paolo Mognol[4], Jean-Laurent Thibaud[3], Beatriz G. Galvez[1], Ines Barthélémy[3], Laura Perani[1], Sara Mantero[4], Maria Guttinger[5], Orietta Pansarasa[2], Chiara Rinaldi[2], M. Gabriella Cusella De Angelis[2], Yvan Torrente[6], Claudio Bordignon[1], Roberto Bottinelli[2] & Giulio Cossu[1,5,7]

Sanpaolesi Nature 2006

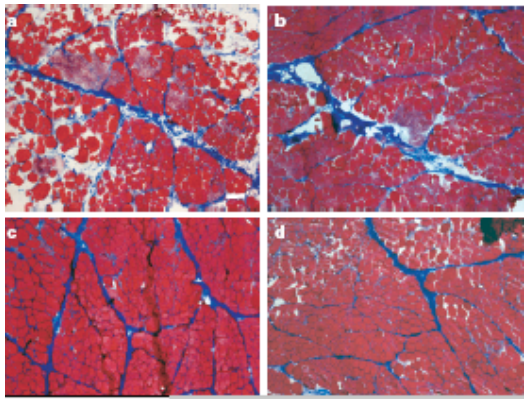
Characterization of dog mesoangioblasts in vitro and in mice



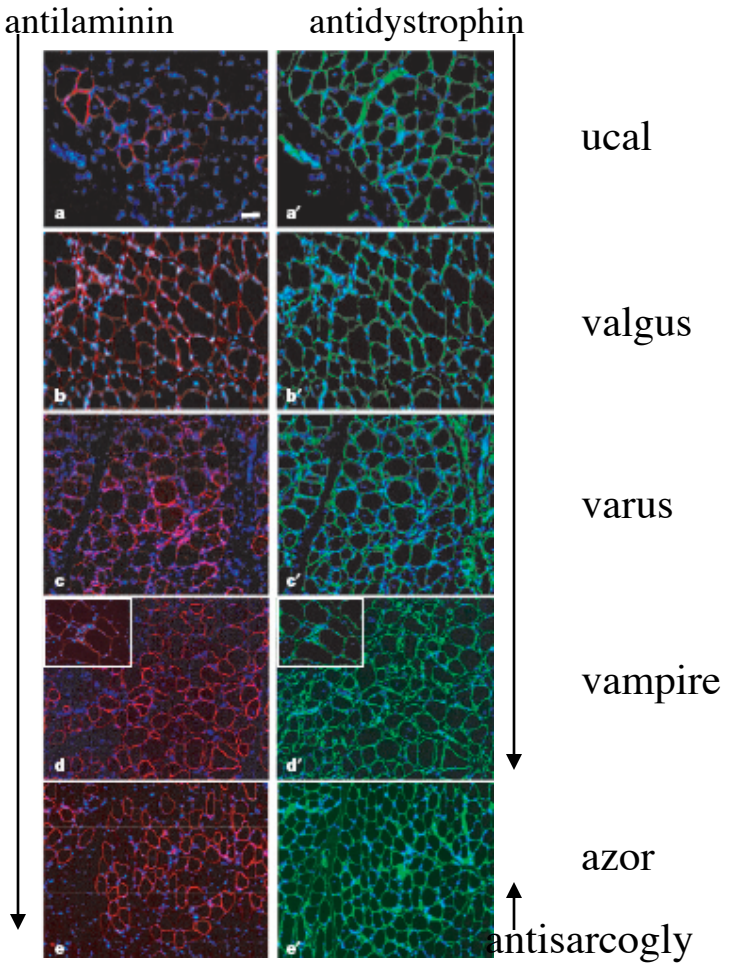
Dog mesangio
A-morphology
B-proliferation
C-karyotype
D-F transduction microdystro an GFP lenti
G-migration into skeletal muscle
H-histology in scid-mdx mice (laminin, dystro)

Sanpaolesi Nature 2006

Dogs (duchenne model) after intraartherial delivery of heterologous wt mesangioblasts

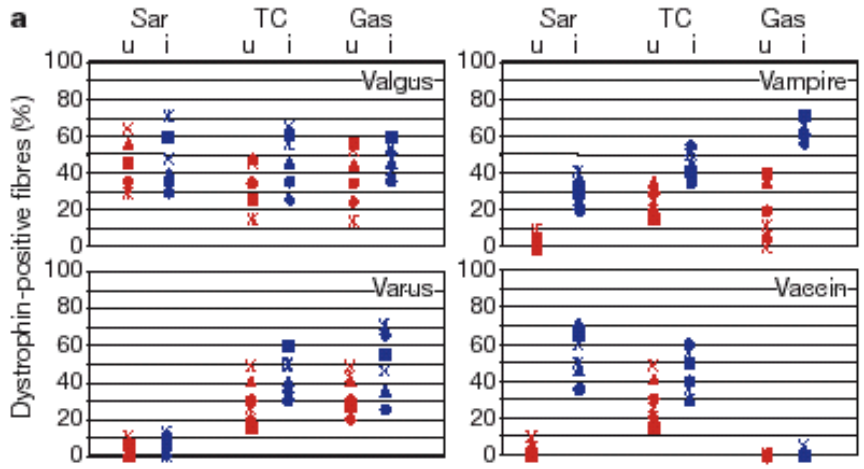


Histo (d-cured; a-c variable ill phehotype)



Immune histo on muscle

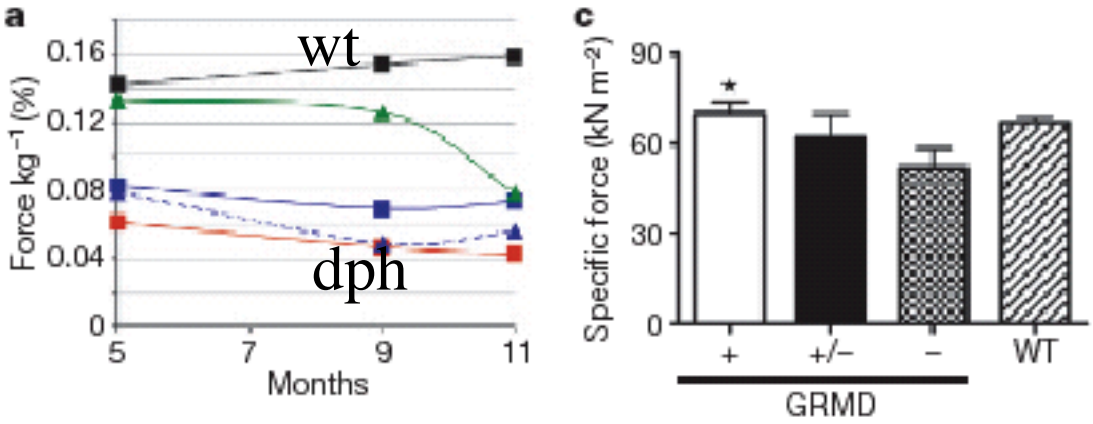
Quantitative analysis of dystrophin content in tissue from treated dogs



Physiology of treated dogs

Tetanic force

Fiber counting



http://www.telethon.it/comunicazione/cossu/Cossu.MP3

Test

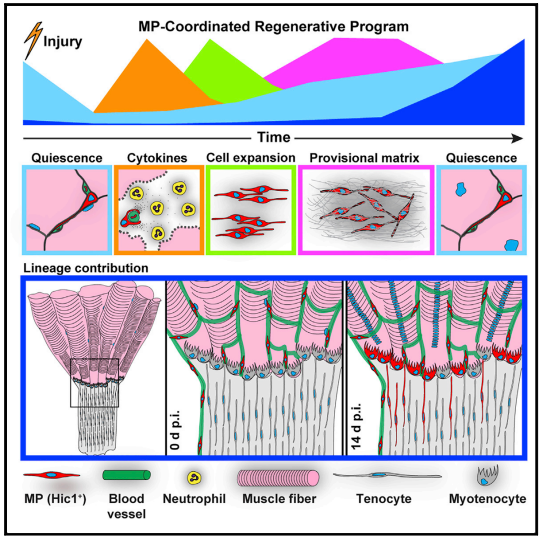
What would you do next

Article

Cell Stem Cell

Hic1 Defines Quiescent Mesenchymal Progenitor Subpopulations with Distinct Functions and Fates in Skeletal Muscle Regeneration

Graphical Abstract



Highlights

- *Hic1* marks multiple quiescent mesenchymal progenitor (MP) subsets within skeletal muscle
- Conditional deletion of *Hic1* leads to MP hyperplasia and an activated MP phenotype
- Hic1$^+$ MPs generate transit-amplifying progeny post-injury that support regeneration
- Following injury, select Hic1$^+$ progeny persist and regenerate the myotendinous junction

Authors

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In Brief

Multiple stem/progenitor populations, including stromal mesenchymal progenitors (MPs), participate in skeletal muscle regeneration. Scott and colleagues found that *Hic1* is a functional marker for MP quiescence, and Hic1$^+$ MPs coordinate multiple facets of the muscle regeneration program and contribute to several mesenchymal lineages, including "myotenocytes."

Scott et al., 2019, Cell Stem Cell *25*, 797–813
December 5, 2019
https://doi.org/10.1016/j.stem.2019.11.004

CellPress