Sustained Intermittent Hypoxaemia as a component of COPD pathophysiology: which effect on skeletal muscle?

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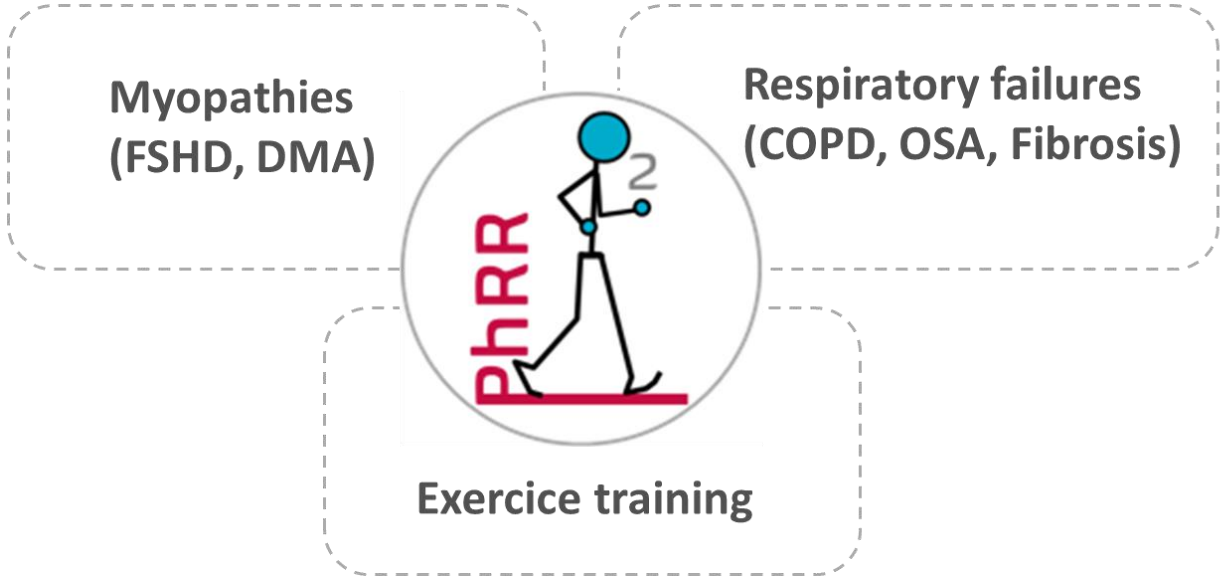

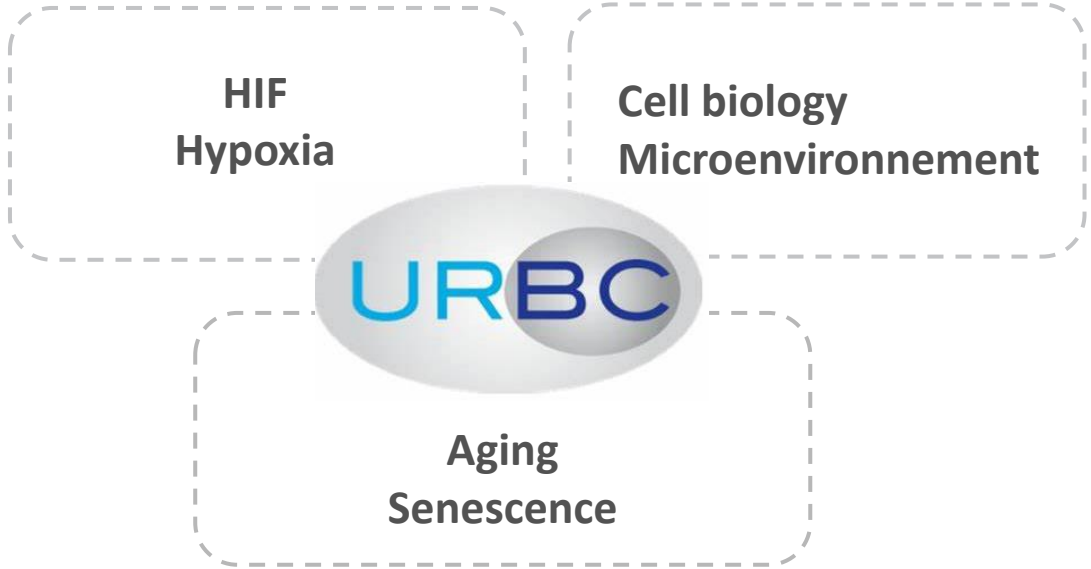

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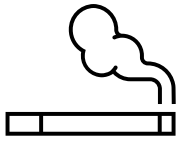
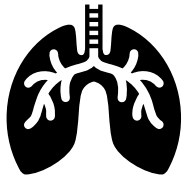
Chronic **O**bstructive **P**ulmonary **D**isease



COPD

Inflammation

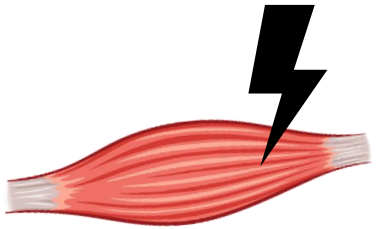
Medication



Malnutrition

Deconditioning

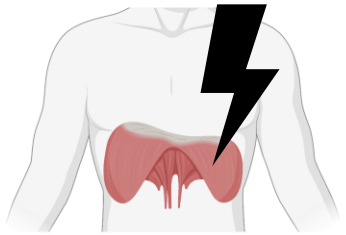
Hypoxaemia



Locomotor muscles

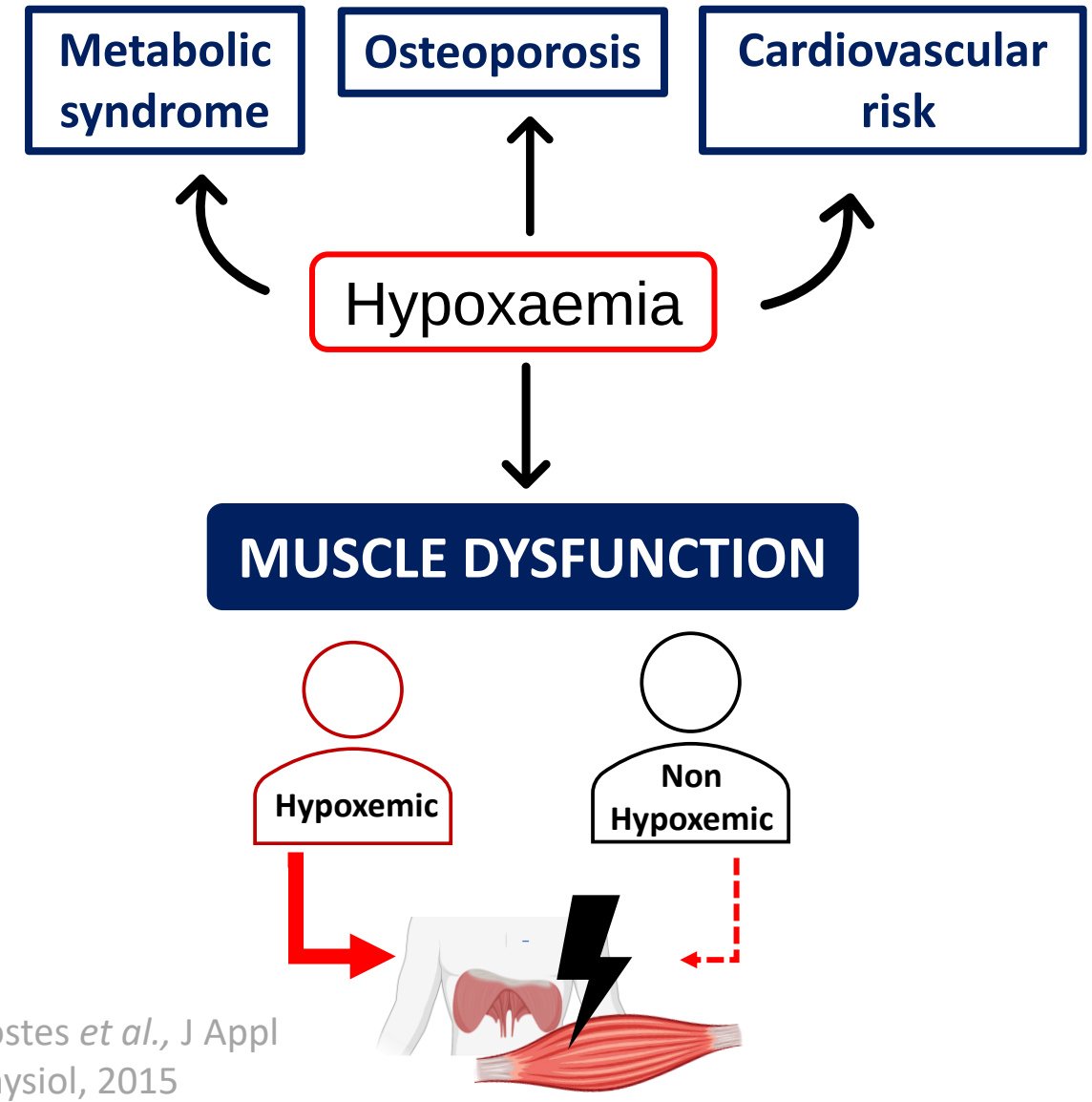
MUSCLE DYSFUNCTION

Atrophy | **Regeneration defect** | **Senescence**



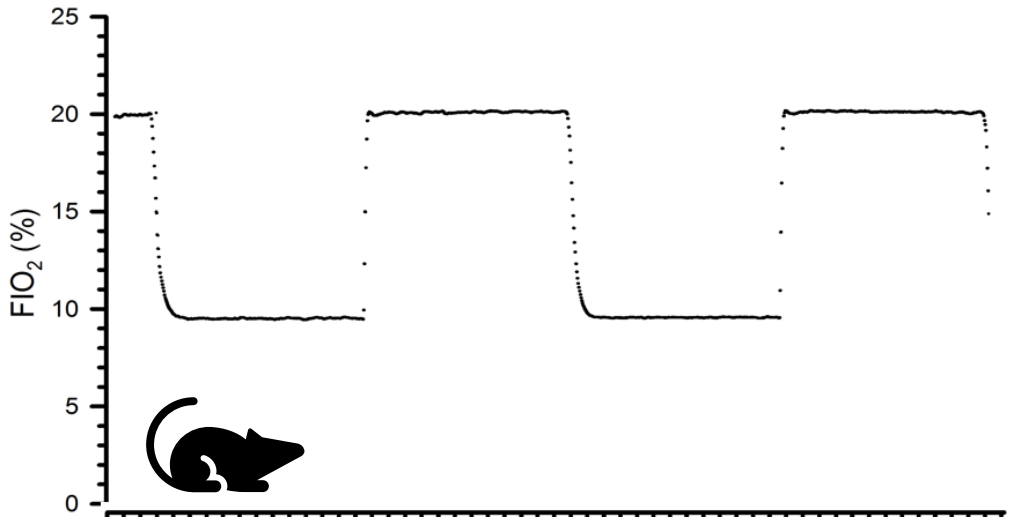
Respiratory muscles

Hypoxaemia in **COPD**



Episodic desaturations

Sleep Exercise training

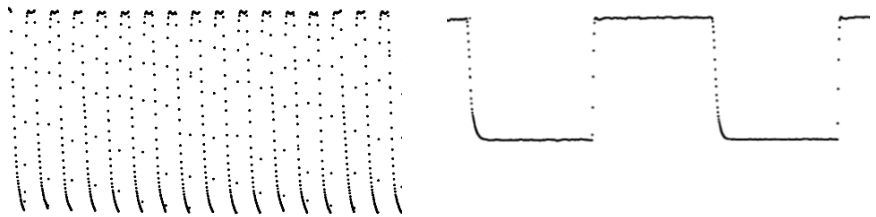


Costes *et al.*, J Appl Physiol, 2015

Hypoxaemia & muscle dysfunction

Pattern of exposure

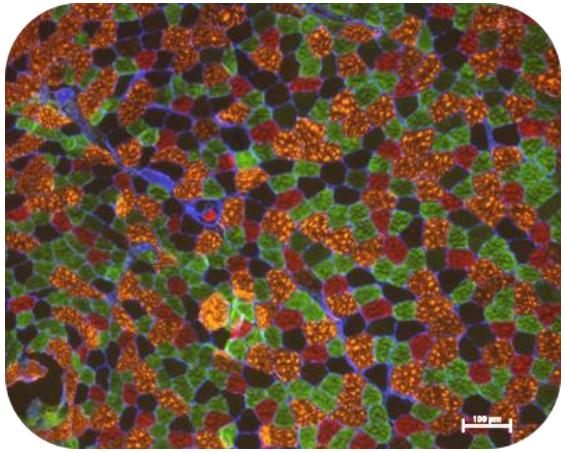
- depth
- duration



Hypoxaemia

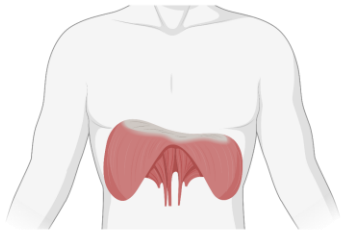
↑↓ ?

Locomotor muscles



Slow fiber type → Fast fiber type

Respiratory muscles



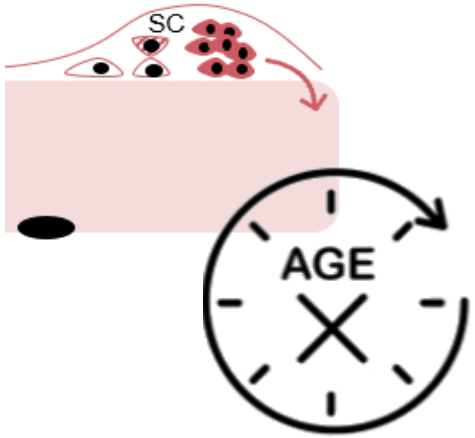
↗ strength, fatigue resistance

MUSCLE DYSFUNCTION

+

Altered muscle **regeneration**

Muscle cell **Senescence**



Itoh *et al*, 1990 ; Cao 2022

Murine model of SIH

PLoS One. 2013;8(4):e59973. doi: 10.1371/journal.pone.0059973. Epub 2013 Apr 2.

A new device to mimic intermittent hypoxia in mice

Kamil J Chodzyński [1], Stephanie Conotte, Luc Vanhamme, Pierre Van Antwerpen, Myriam Kerkhofs, J L Legros, Michel Vanhaeverbeek, Alain Van Meerhaeghe, Gregory Coussement, Karim Zouaoui Boudjeltia, Alexandre Legrand

Affiliations + expand

PMID: 23565179 PMCID: PMC3615002 DOI: 10.1371/journal.pone.0059973

Free PMC article

frontiers in Physiology

Sustained Intermittent Hypoxemia Induces Adiponectin Oligomers Redistribution and a Tissue-Specific Modulation of Adiponectin Receptor in Mice

Mélany Pierard[1], Alexandra Tassin[1†], Stéphanie Conotte[1†], Karim Zouaoui Boudjeltia[2] and Alexandre Legrand[1]*

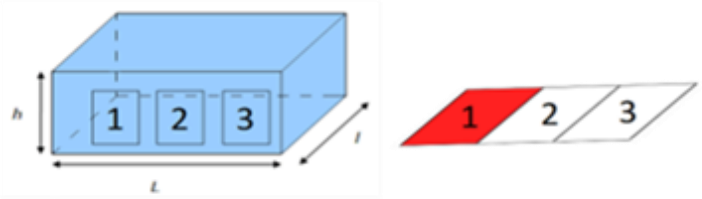
Respir Physiol Neurobiol. 2018 Oct;256:157-173. doi: 10.1016/j.resp.2018.02.015. Epub 2018 Mar 6.

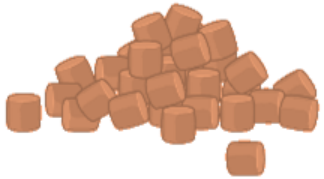
Metabonomic profiling of chronic intermittent hypoxia in a mouse model

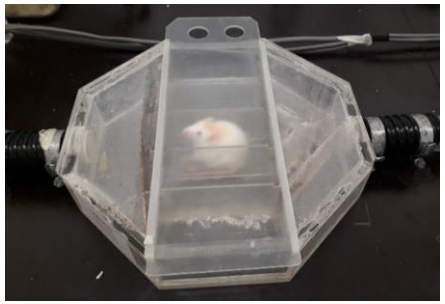
Stéphanie Conotte [1], Alexandra Tassin [1], Raphaël Conotte [2], Jean-Marie Colet [2], Karim Zouaoui Boudjeltia [3], Alexandre Legrand [4]

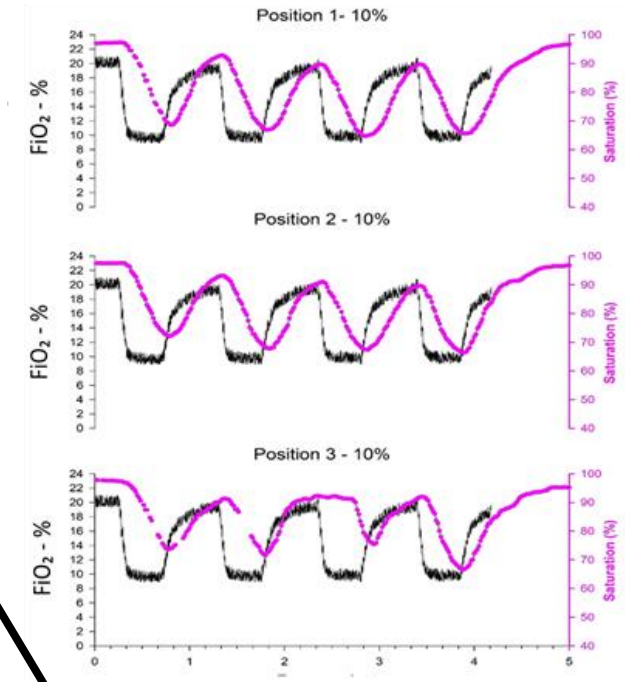
Affiliations + expand

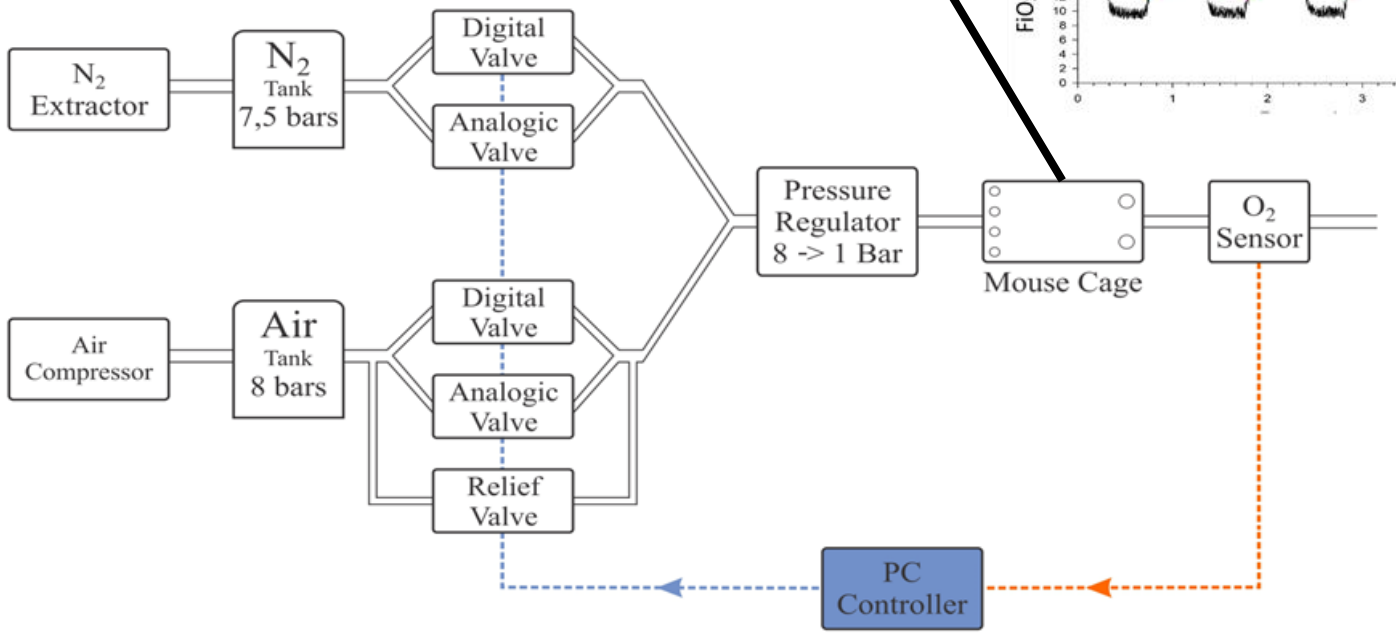
PMID: 29522877 DOI: 10.1016/j.resp.2018.02.015







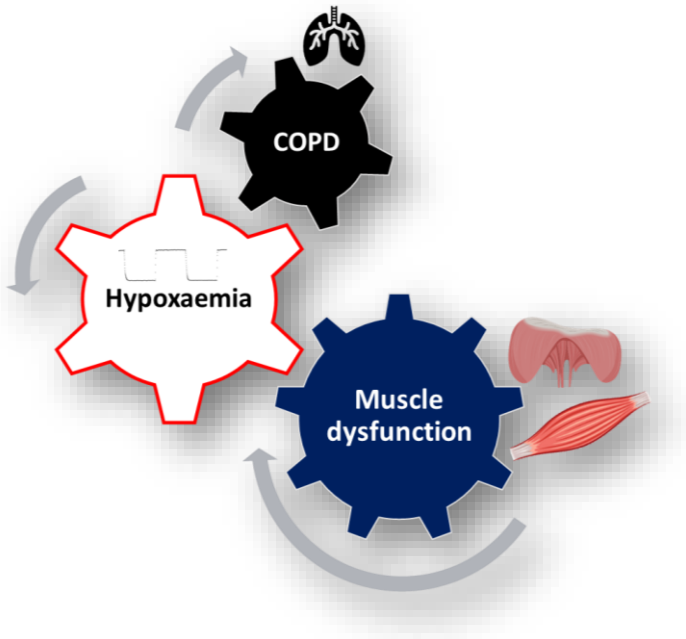


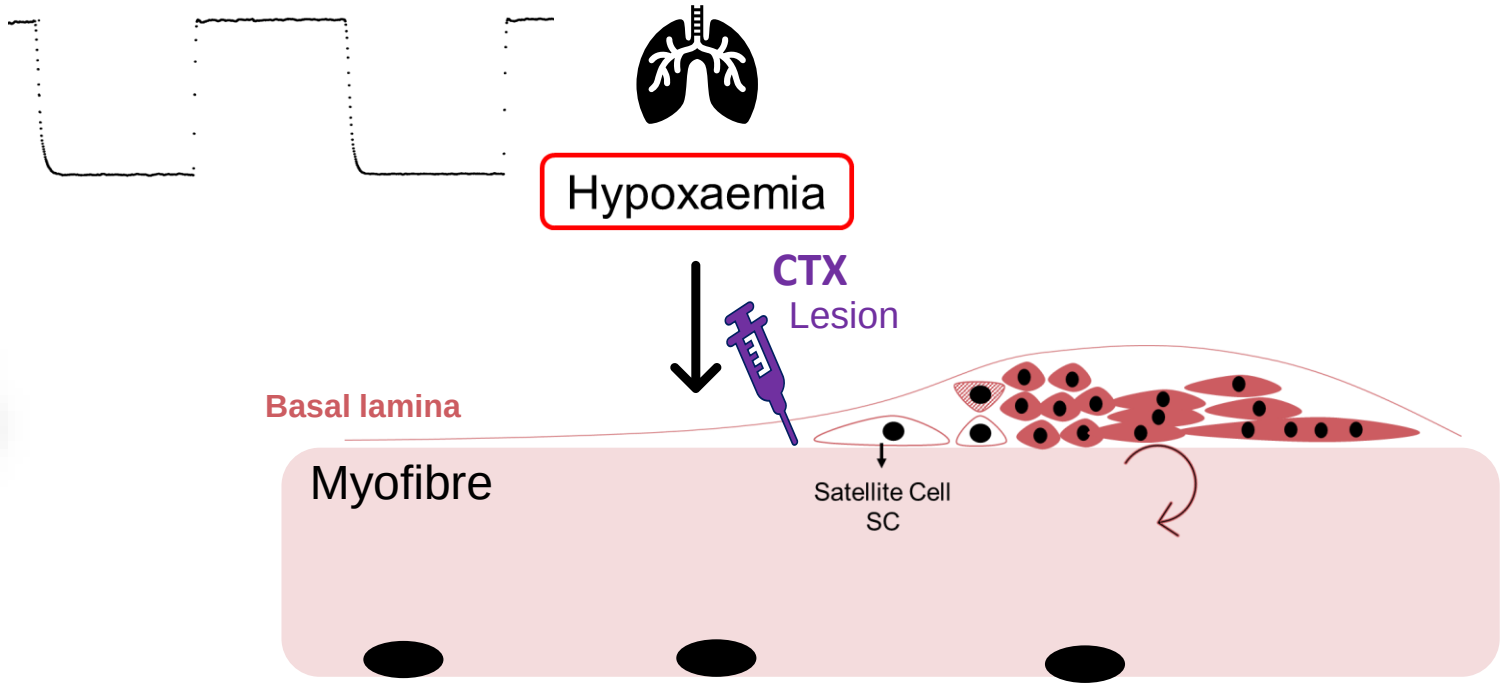


AIM #1. To determine specific effects of the **hypoxemic component** of COPD on **muscle structure, mass, functions, senescence and regeneration.**

#1.1. To characterize **muscle alterations** caused by **Sustained Intermittent Hypoxia (SIH)** *in vivo*.

#1.2. To study SIH effects on skeletal muscle **regeneration.**





Muscle alterations: **Atrophy** | **Muscle dysfunction** | **Senescence** | **Regeneration defect**

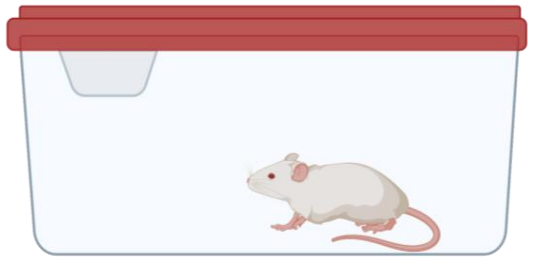
Material and methods

CTL

SIH

D0 D7 D14 D21 D28 D35

FiO_2 10%
8h/day
7d/week



FiO_2

21%

10%

8h

Myogenic factor expression

RTqPCR

Morphometry

CSA
Myofiber size distribution
Fibre type

Material and methods

CTL

SIH

D0 **D7** D14 D21 D28 **D35**

FiO_2 10%
8h/day
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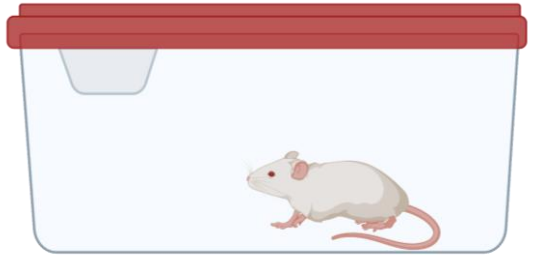


FiO_2

21%

10%

8h

Myogenic factor expression

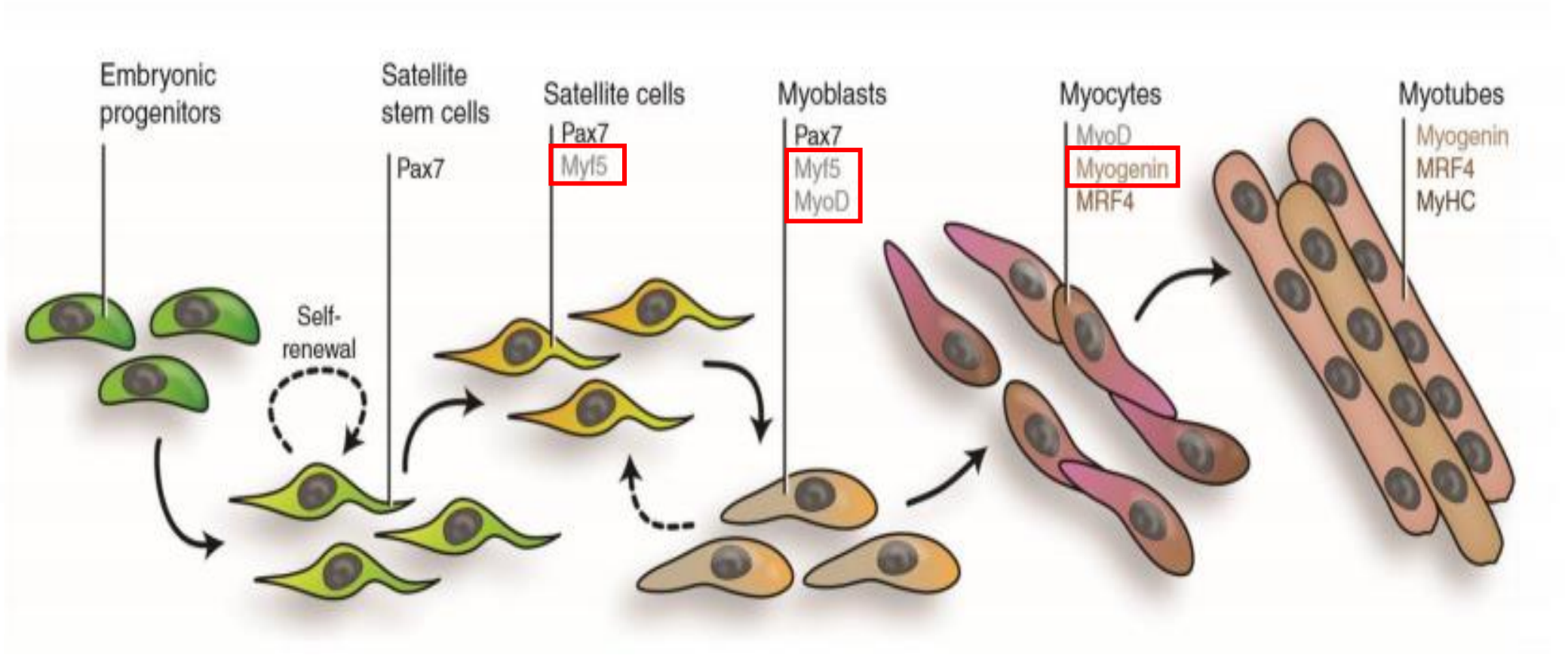
RTqPCR

Morphometry

CSA
Myofiber size distribution
Fibre type

AIM #1.1..

Myogenesis



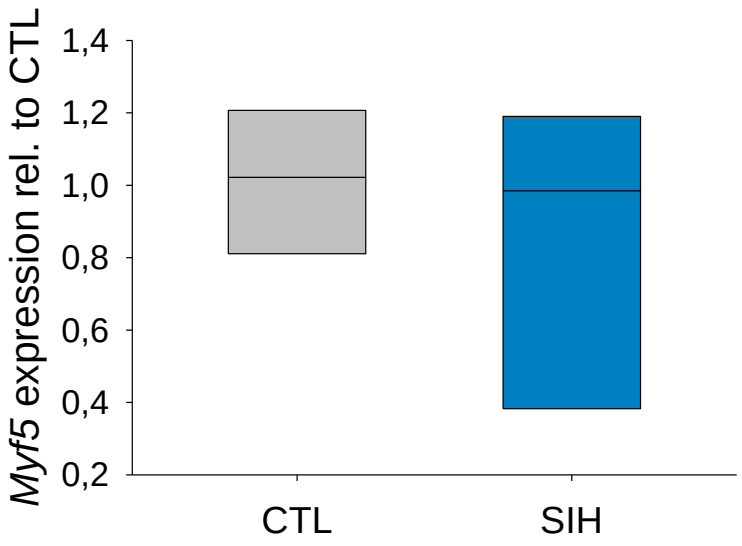
Preliminary data

AIM #1.1..

Gastrocnemius

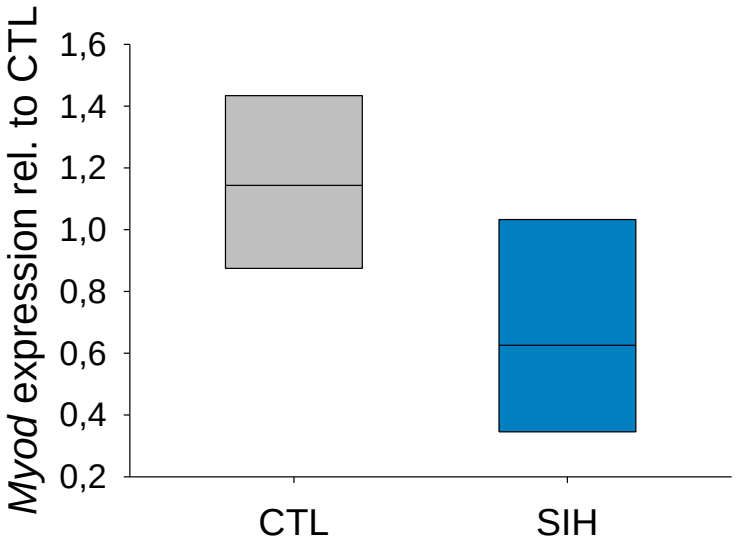
7 days of SIH

Myf5



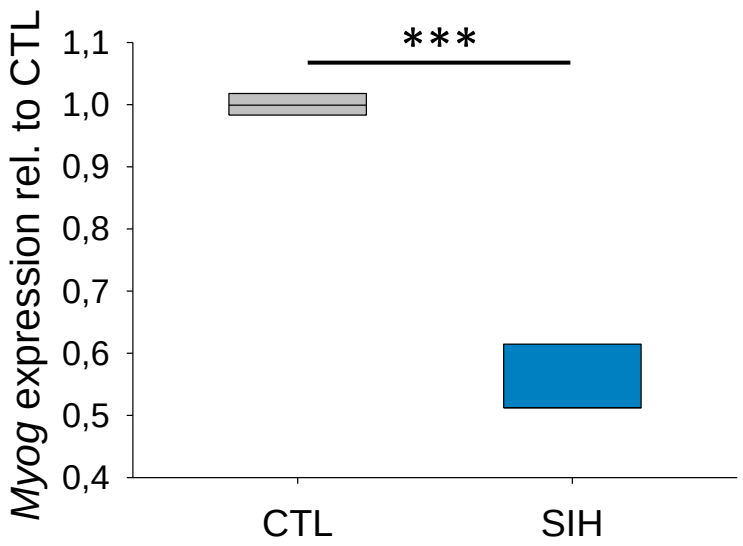
t-test, NS (p = 0,581)

Myod



t-test, NS (p = 0,133)

Myog



t-test, ***p < 0,001

n = 3

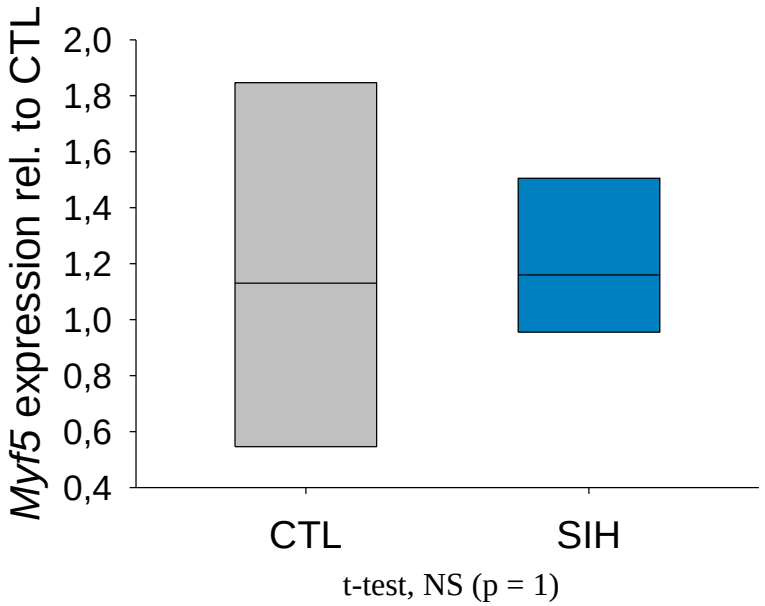
Preliminary data

AIM #1.1..

Gastrocnemius

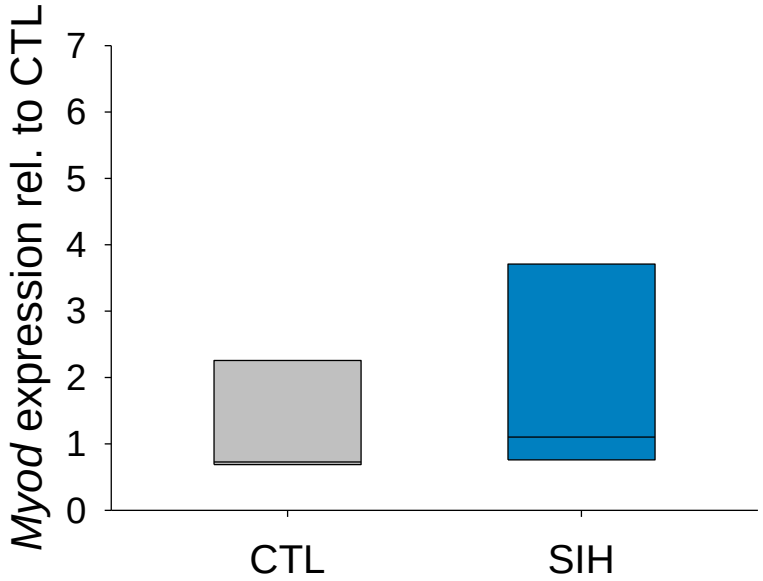
35 days of SIH

Myf5



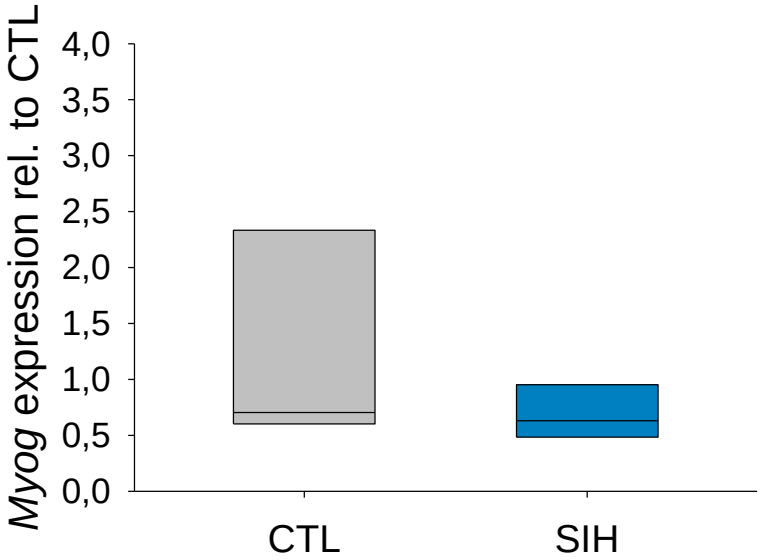
t-test, NS (p = 1)

Myod



t-test, NS (p = 0,286)

Myog



t-test, NS (p = 0,421)

n = 5

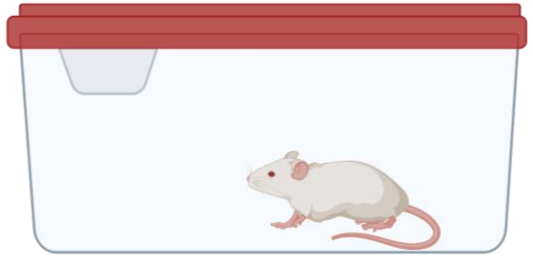
Material and methods

CTL

SIH

D0 **D7** D14 D21 D28 **D35**

FiO_2 10%
8h/day
7d/week



FiO_2

21%

10%

8h

Myogenic factor expression

RTqPCR

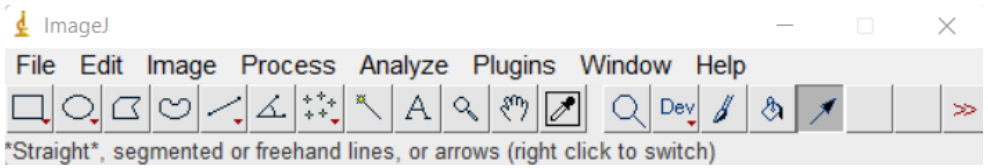
Morphometry

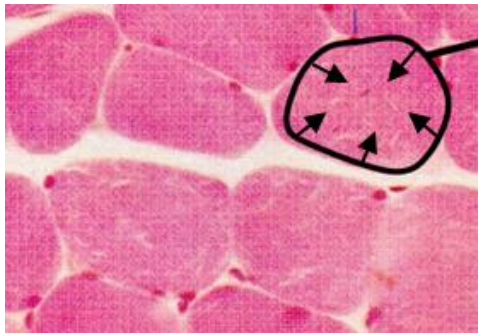
CSA
Myofiber size distribution
Fibre type

Preliminary data

AIM #1.1..

Cross-Sectional Area (CSA)





Myofibre area

Mean CSA

Fast MyHC, counter-staining

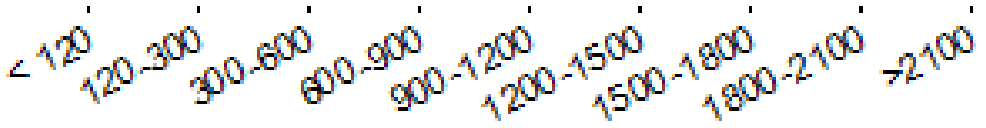
Results

	Area	Mean	Min	Max
1	2585	58.745	23	116
2	1749	74.799	39	158
3	1385	58.471	27	152
4	1633	73.735	39	130
5	1869	67.530	31	130
6	2292	66.480	39	122
7	2217	60.444	23	118
8	1464	60.797	27	122
9	2433	64.250	23	112
10	1521	64.517	39	142
11	1978	64.315	23	115
12	1214	65.626	31	103
13	1291	63.391	35	122
14	1668	61.976	27	118
15	1745	75.694	39	140
16	1870	74.904	39	152

→ Area

Clustering

Fibre size distribution



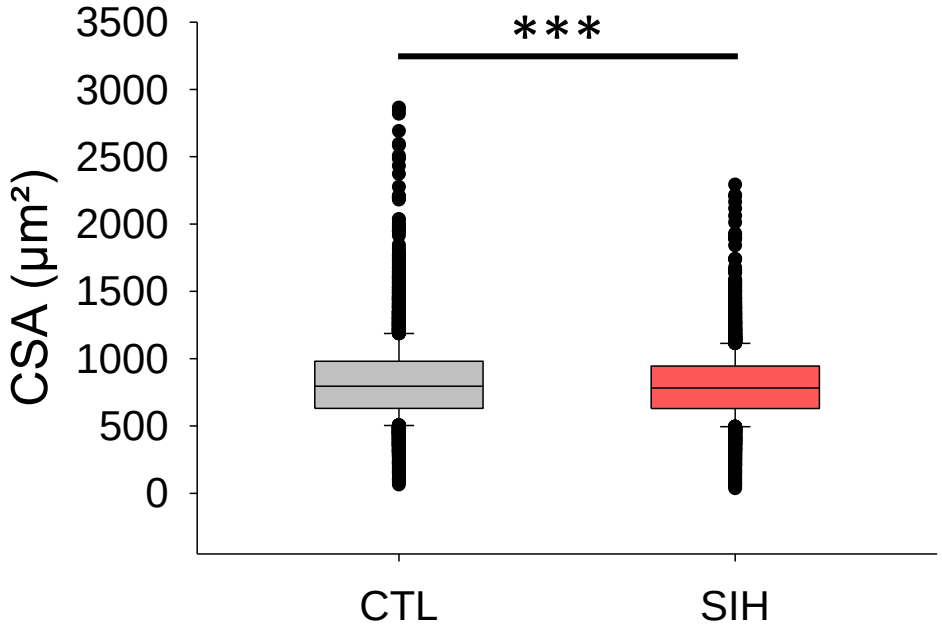
Soleus

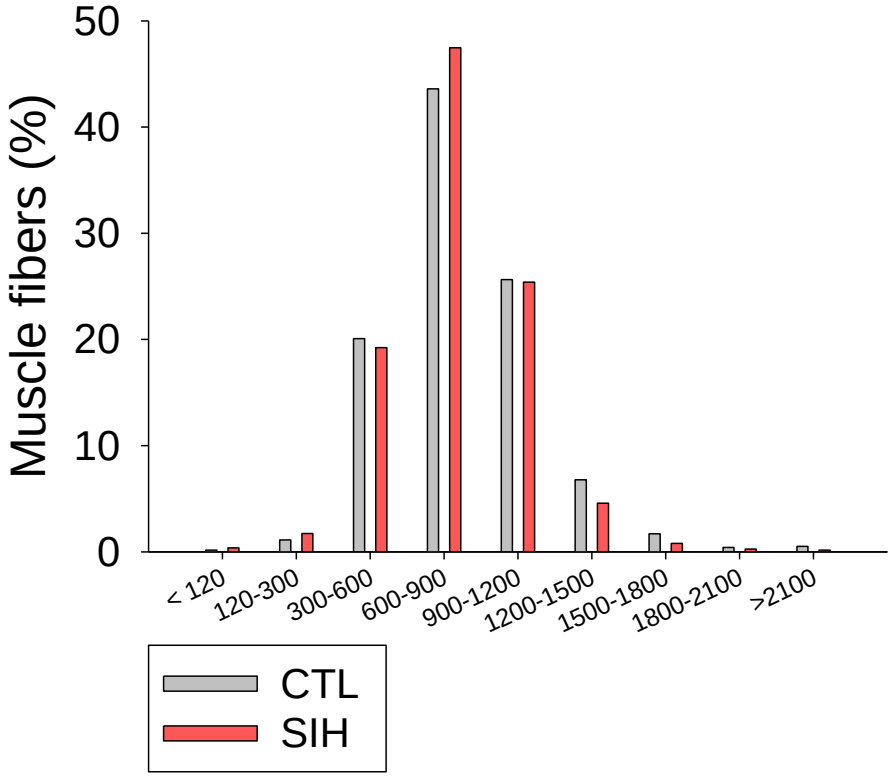
35 days of SIH

Preliminary data

AIM #1.1..

Global fibers





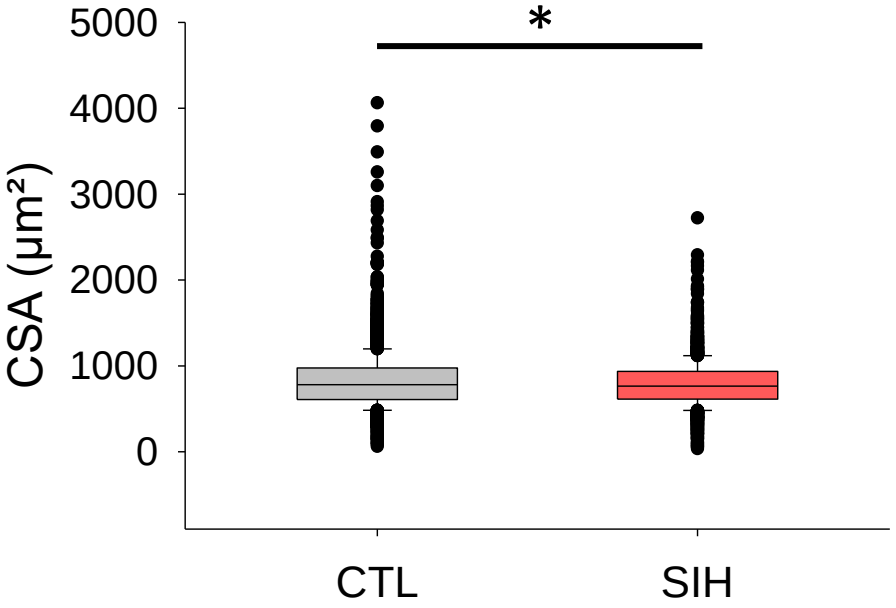
t-test, ***p = 0,001

Preliminary data

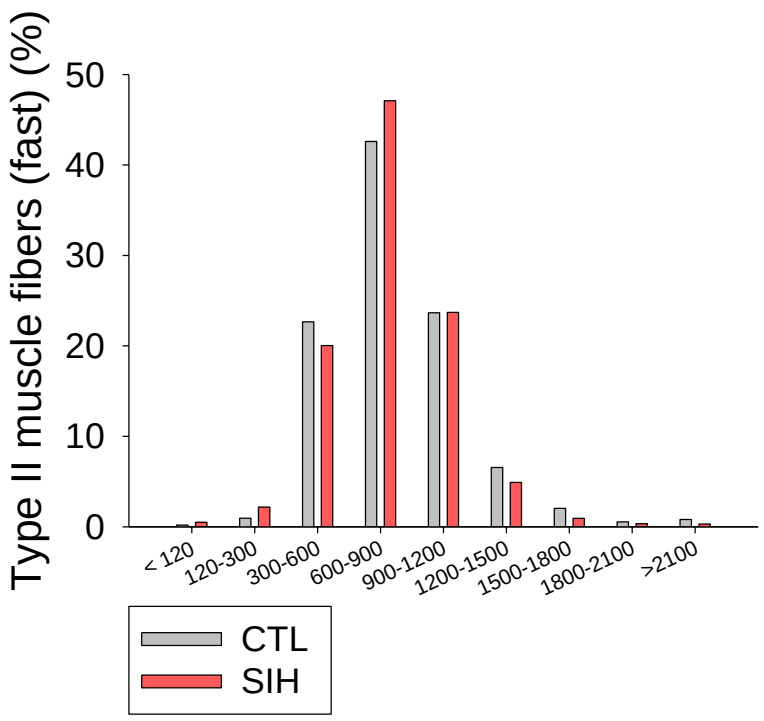
AIM #1.1..

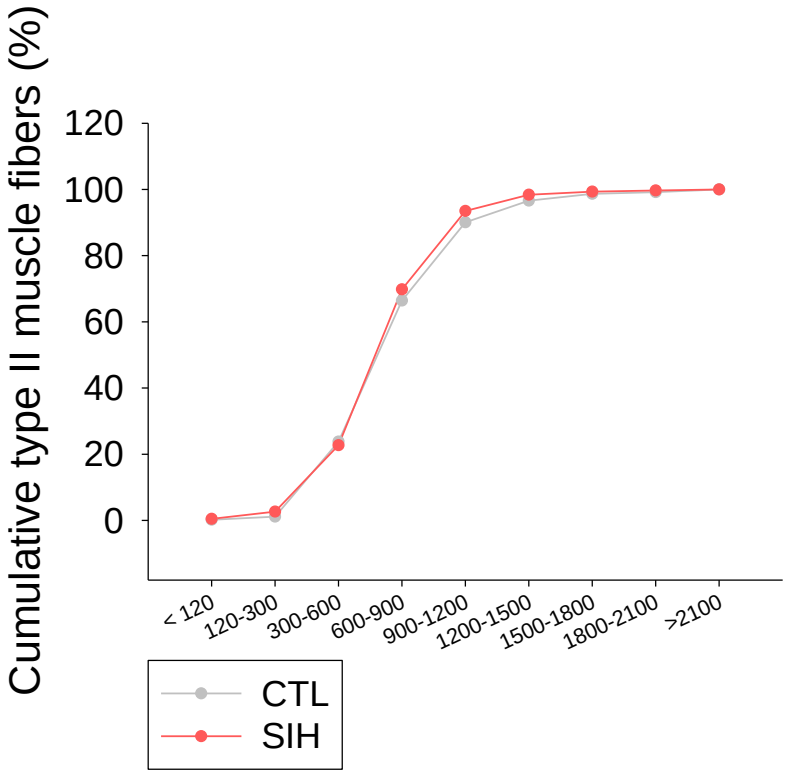
Soleus

35 days of SIH

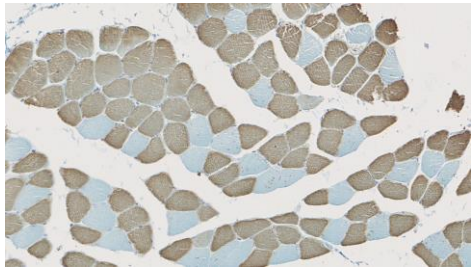


Fast fibers

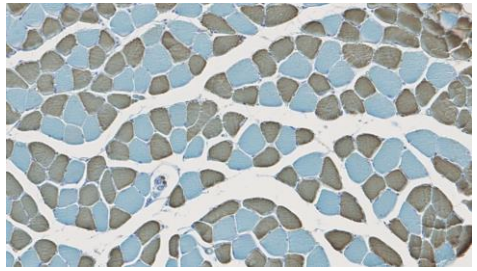




CTL



SIH



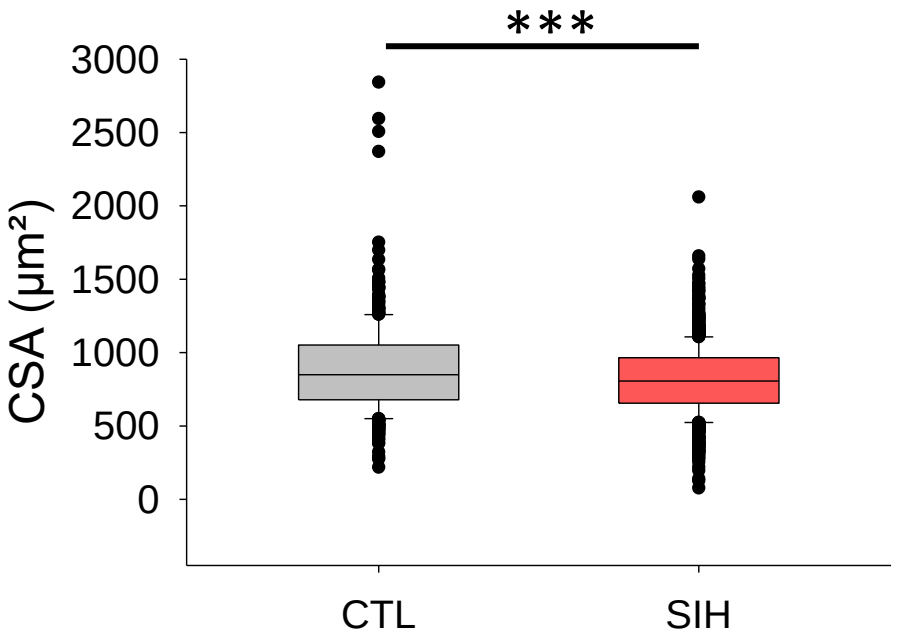
t-test, *p = 0,019

Preliminary data

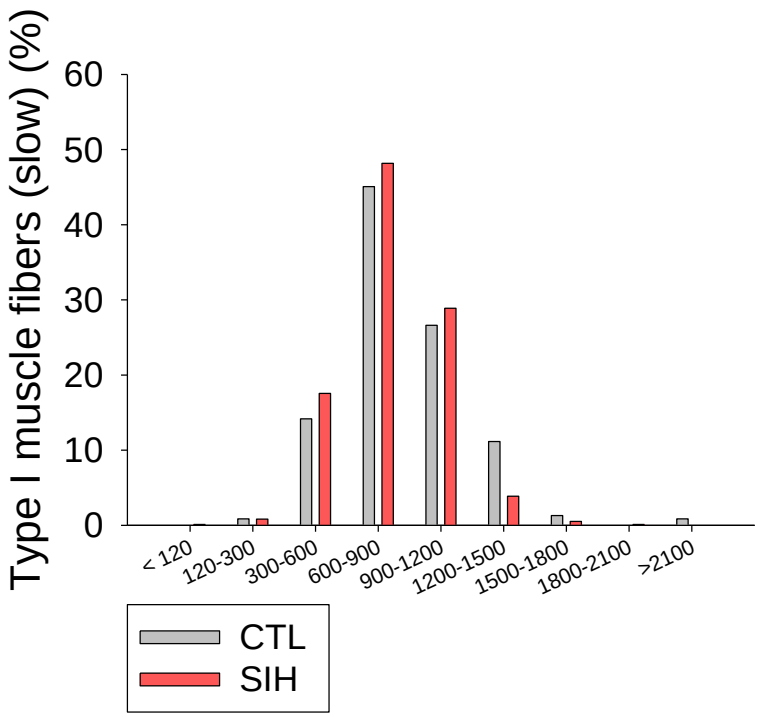
AIM #1.1..

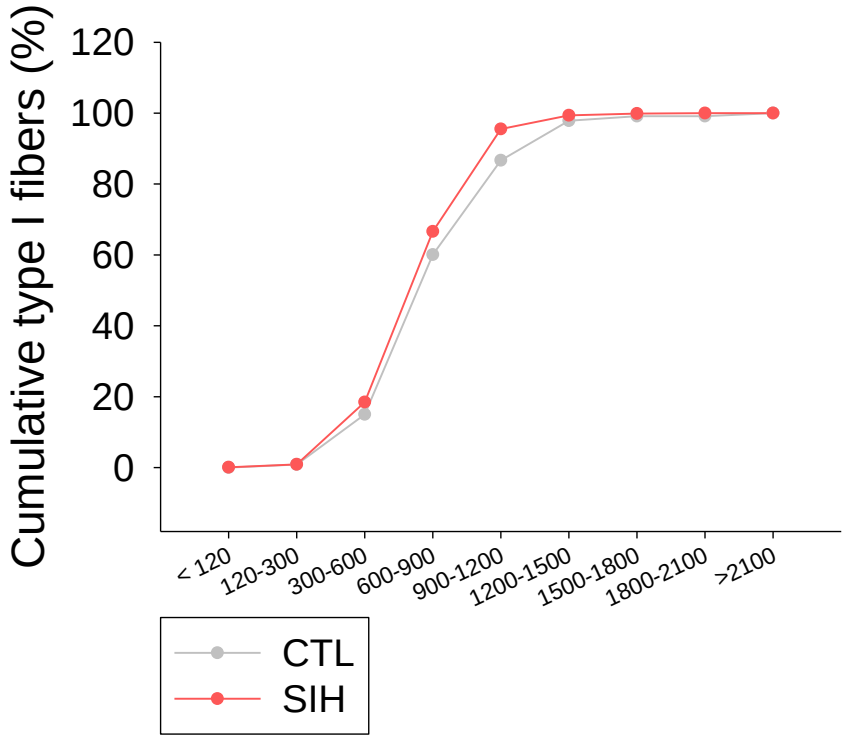
Soleus

35 days of SIH



Slow fibers





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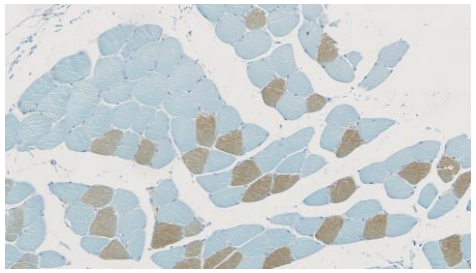

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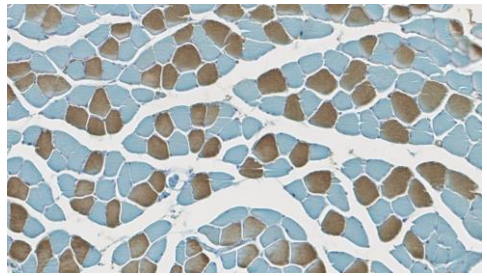
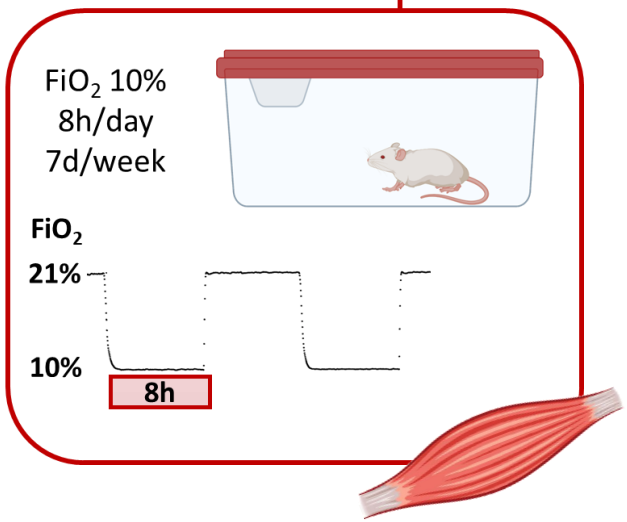


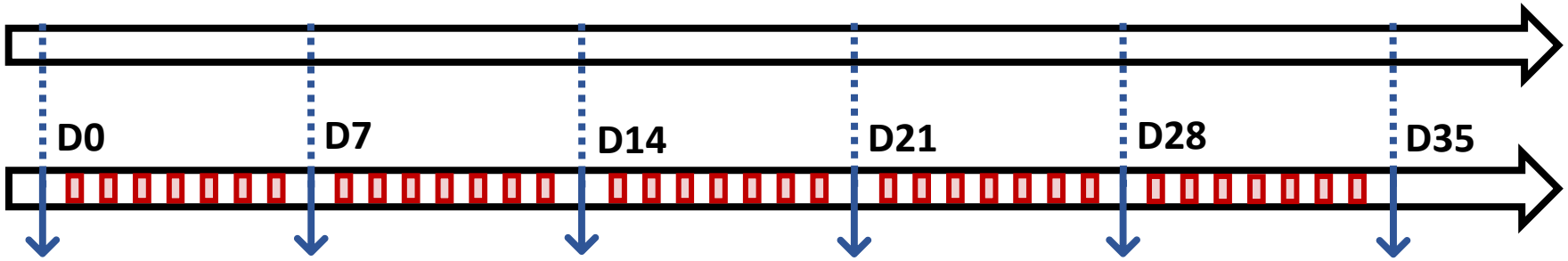
t-test, ***p = 0,001

Conclusion

CTL

SIH





Myogenic factor expression

Myog

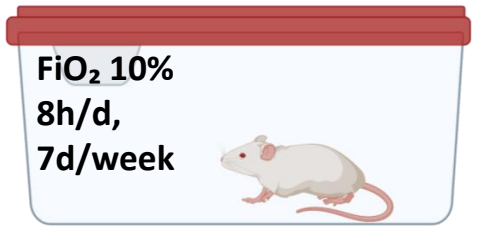
Morphometry

CSA

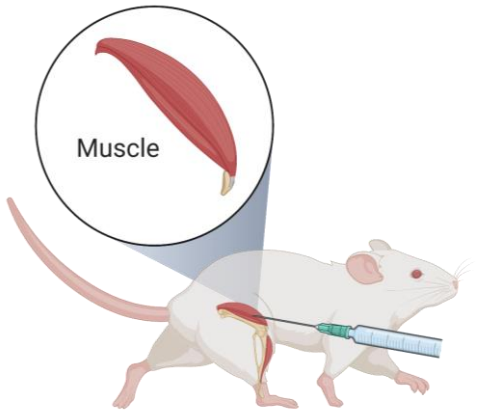
Prospects

AIM #1.2..

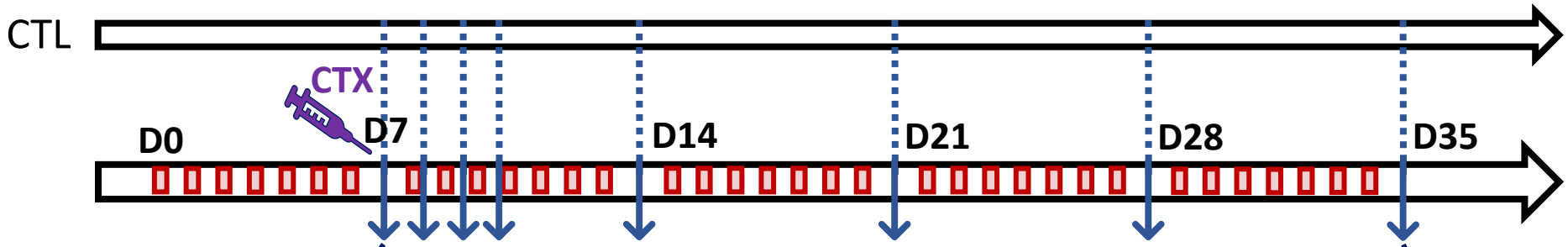
In vivo



SIH

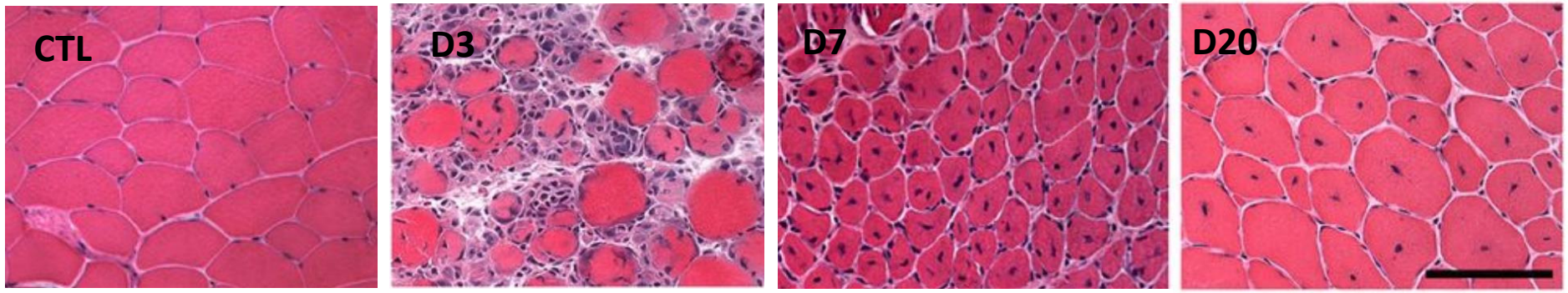


CTX-induced lesion



Lesion evolution & regeneration process

-Necrotic areas
-Number of inflammatory macrophages
-Regenerating myofibres and myofibre CSA distribution
-Myogenic markers

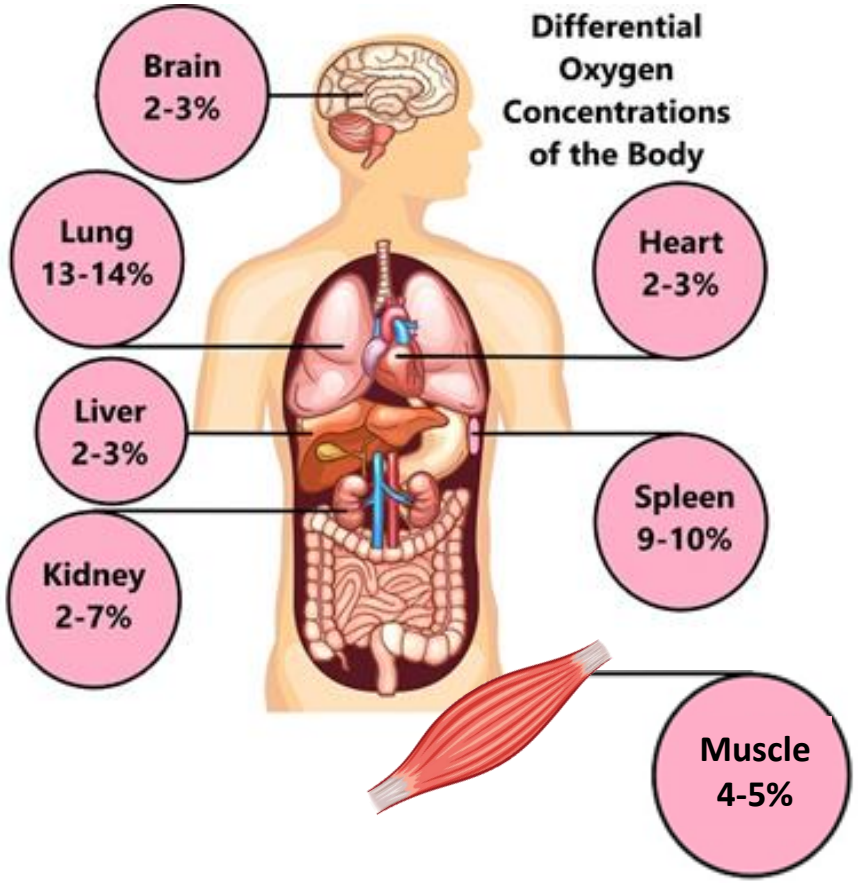


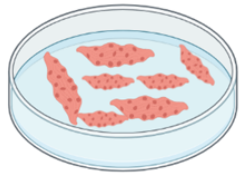
Dalle *et al.*, J Muscle Res Cell Motil, 2020

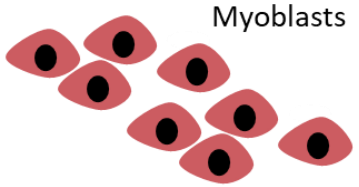
Liu et al., PNAS, 2014

Prospects

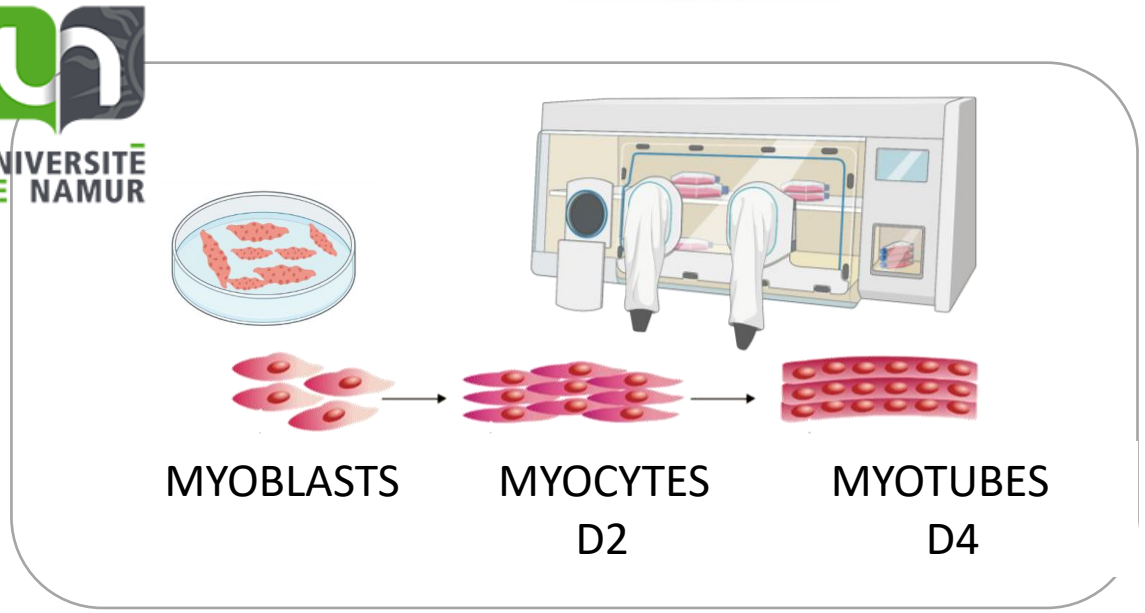
AIM #1.2..

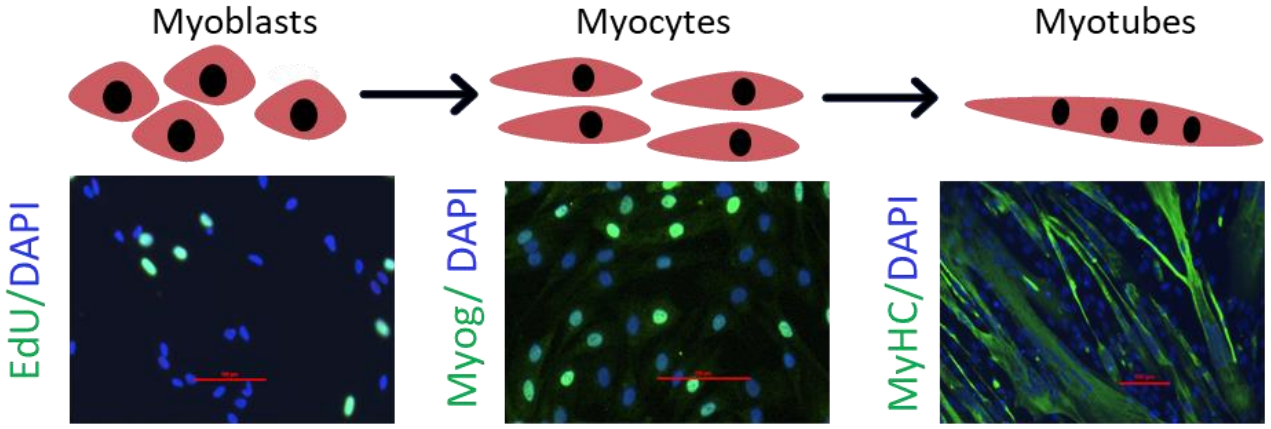






Acclimatation to **physioxia**





Proliferation and differentiation under **hypoxia**

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