STEM CELLS IN SPACE

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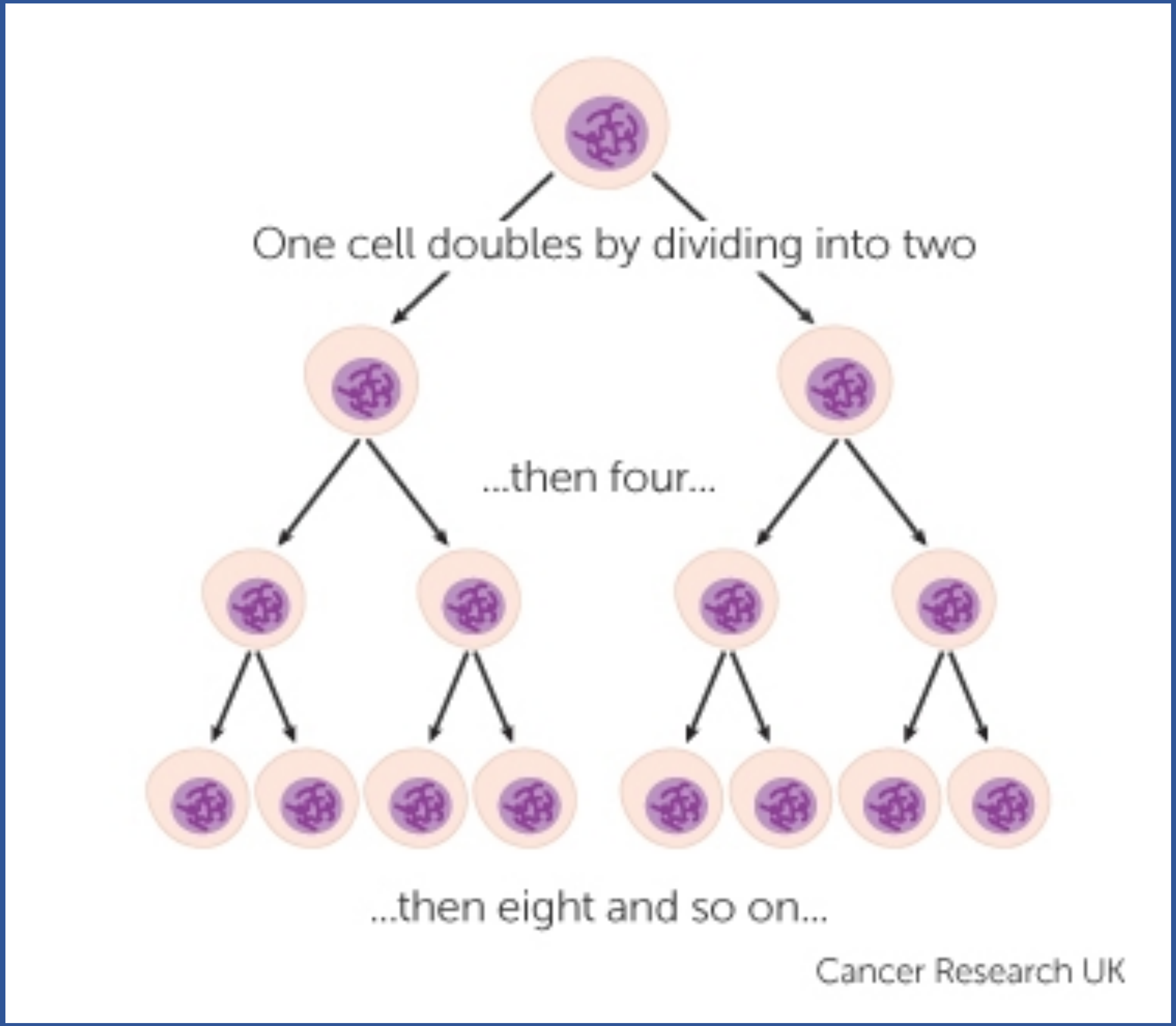
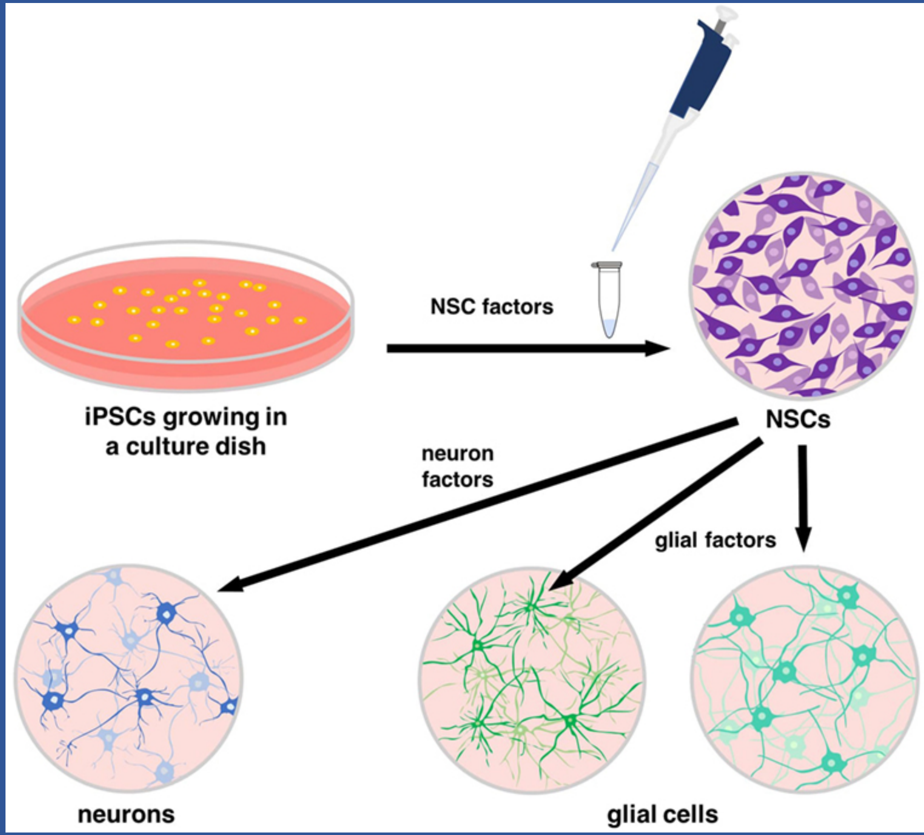
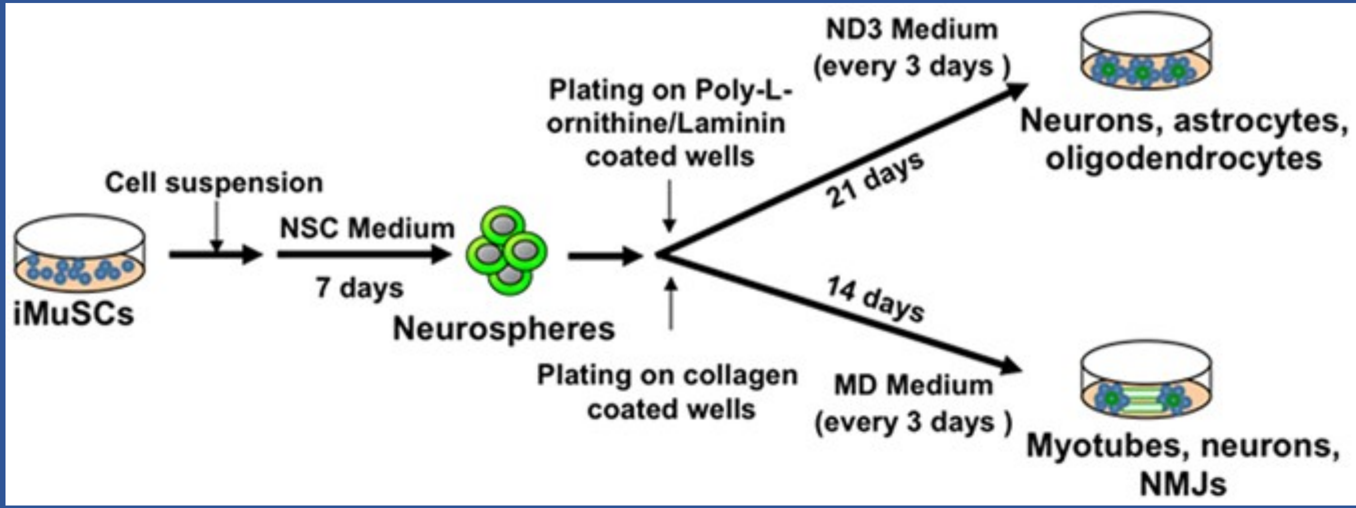
Stem cells


One cell doubles by dividing into two
...then four...
...then eight and so on...
Cancer Research UK

Chemical factors guide stem cell differentiation in vitro





https://www.nature.com/articles/s41598-017-01311-4

Making Neurons from Human Stem Cells · Frontiers for Young Minds (frontiersin.org)

Why is this important?

(i) the astronauts have stem cells in the body and in the brain and we need to understand how these cells are affected by space conditions and if they are able to maintain their property in space to replace damaged or dead cells;

(ii) since stem cells not only can produce new cells, but also can support other cells types, we want to know if space conditions will change the supportive capacity of stem cells;

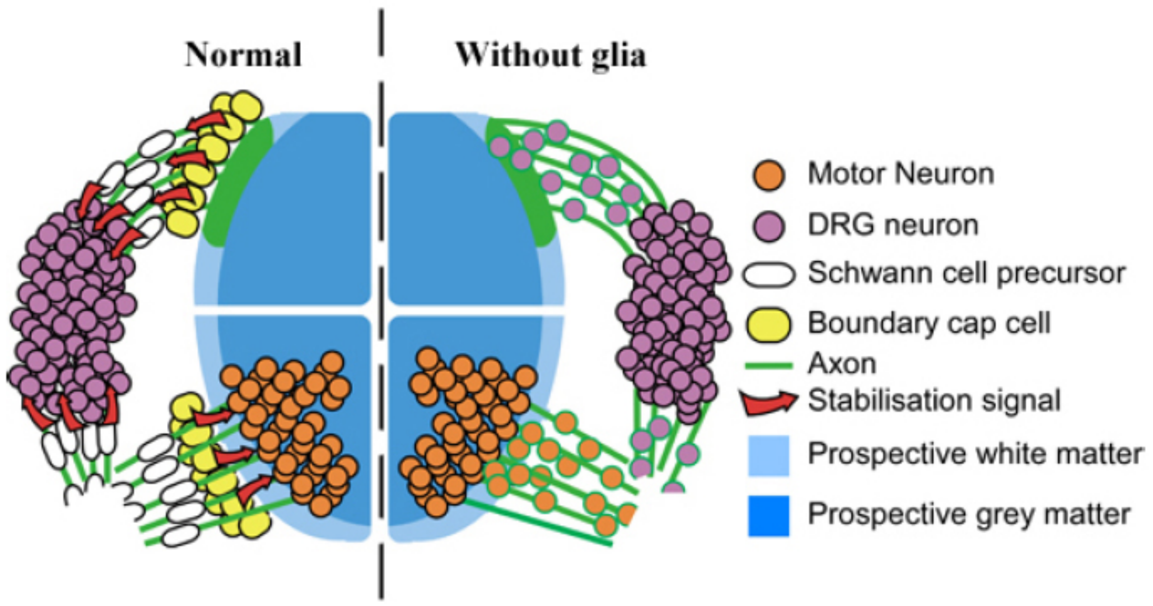
(iii) if we look to the future, we might speculate that instead of moving a lot of people to extraterrestrial settlements, it would be an option to produce new individuals from stem cells, which can be transported in large amounts to other planets;

(iv) it is also possible that stem cells, which have been in space may acquire novel features, which will be beneficial for medical purposes on earth;

(v) and finally, from stem cells we can generate new organs and tissues using 3D printing technology, which has a great potential for exploitation in long-lasting extraterrestrial voyages.

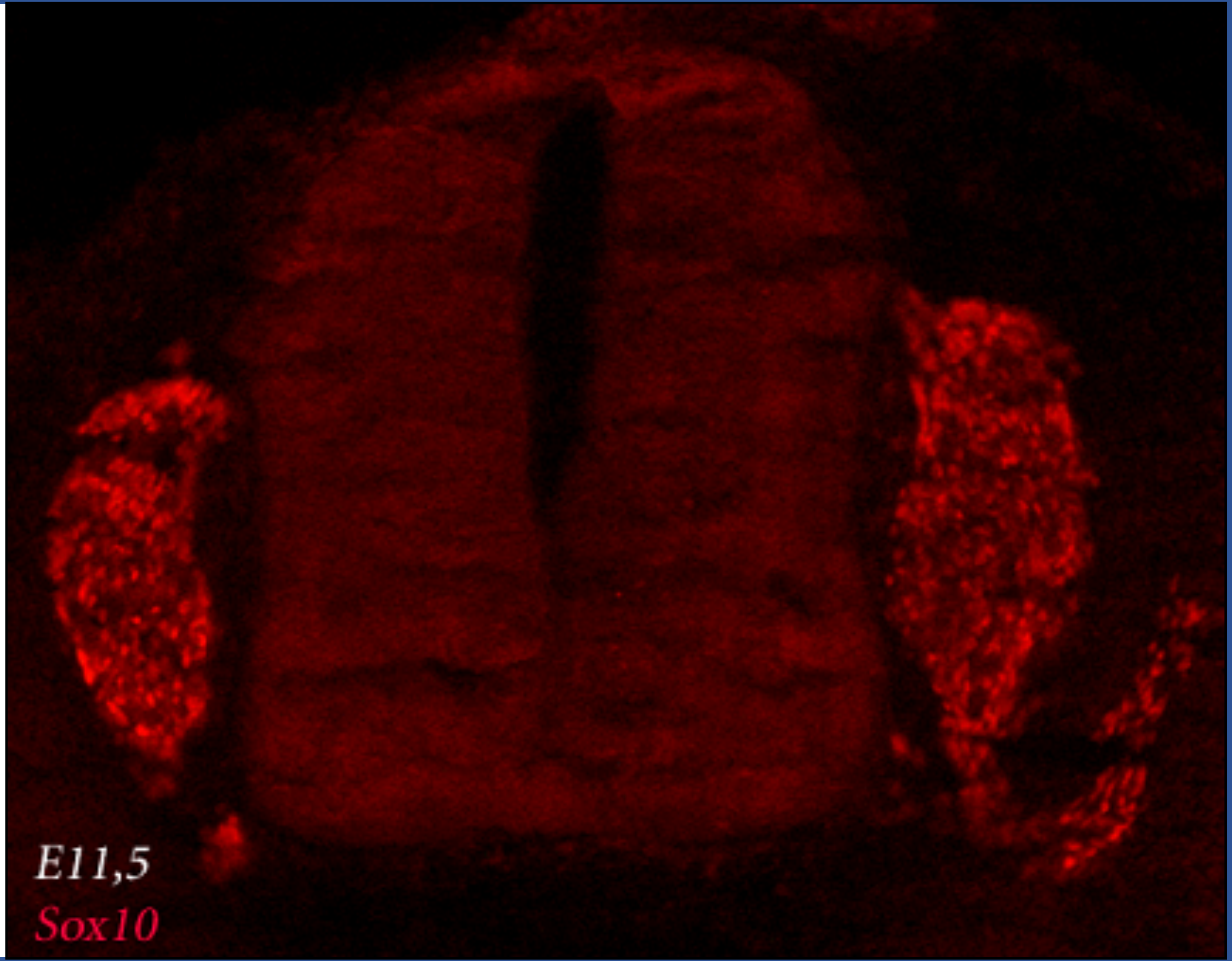
BC cell in mice

Model of neuron stabilisation.



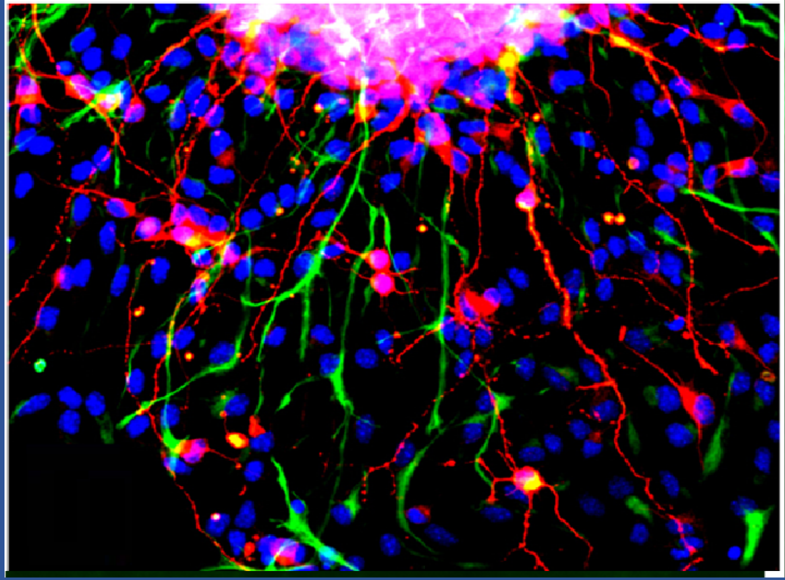
Left: during normal development, DRG neurons (purple) and motor neurons (orange) send axons (green) in and out of the spinal cord (blue). Motor neuron cell bodies are stabilised within the ventral spinal cord by a signal coming from the boundary cap cells (yellow) while DRG neurons are confined to their ganglia by peripheral glia (white)

Right: in the absence of boundary cap cells and peripheral glia, motor and DRG neurons are not stabilised and migrate off their normal position, by following their axons.

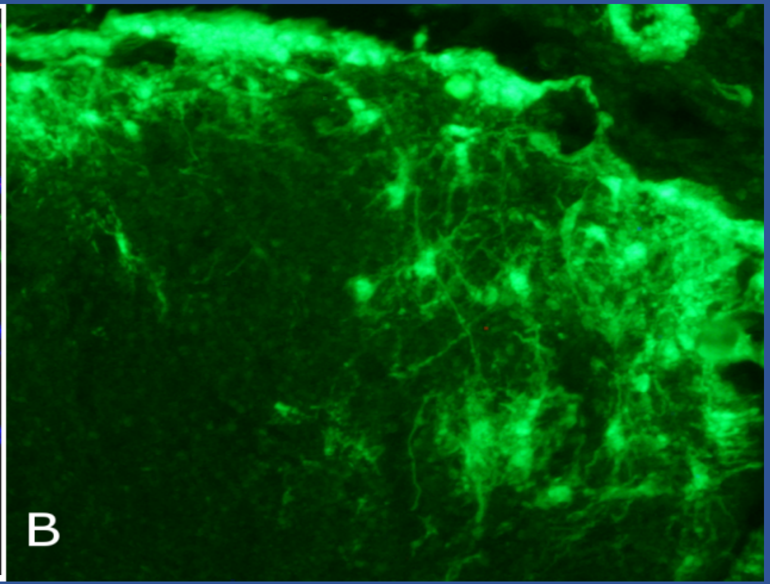


BC in avulsion model actively migrate and display advanced differentiation in CNS

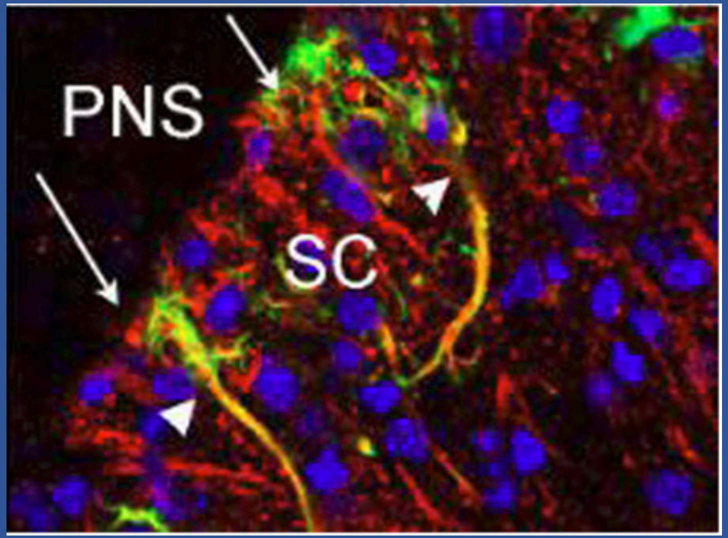
In vitro



In vivo after transplantation

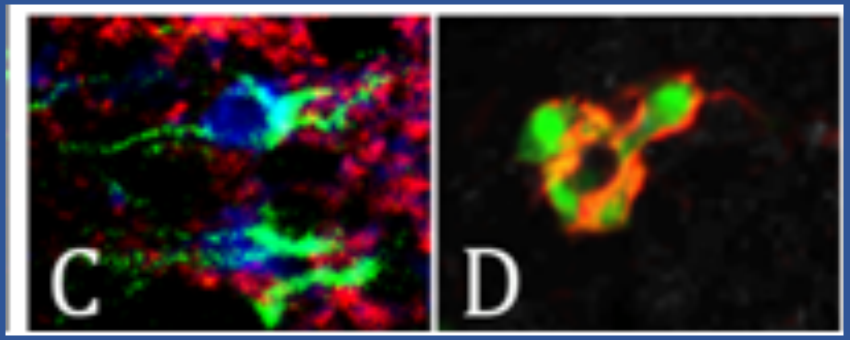


ChAT

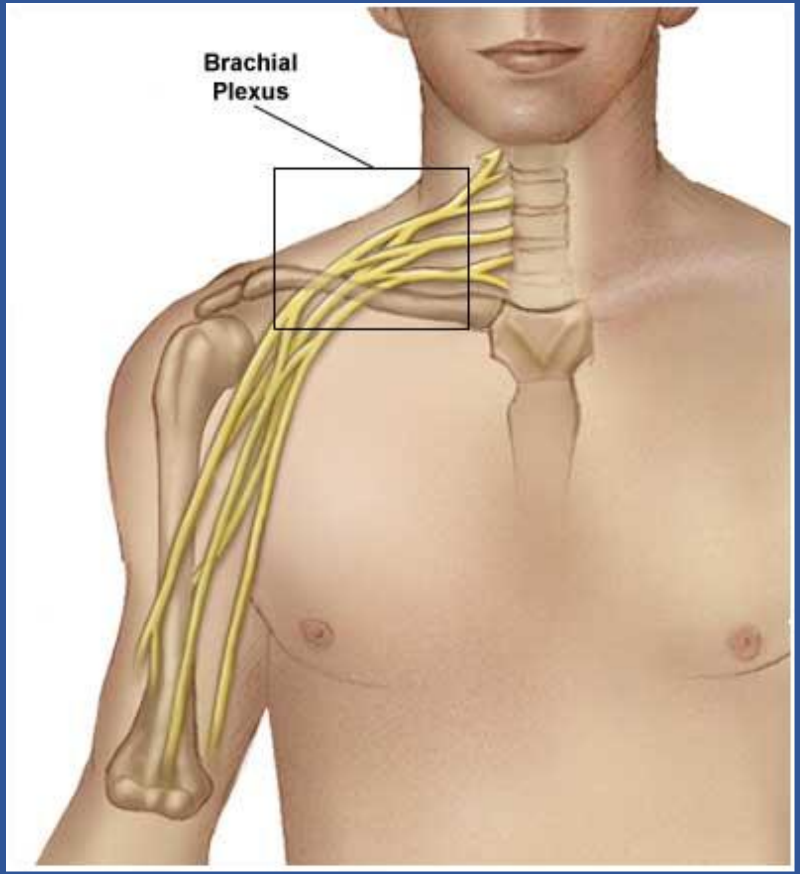


Calbindin
GFAP

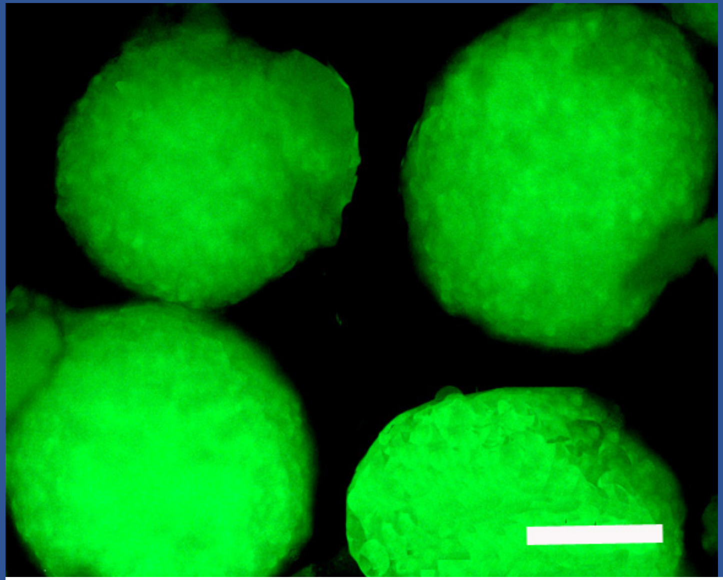
TrkB

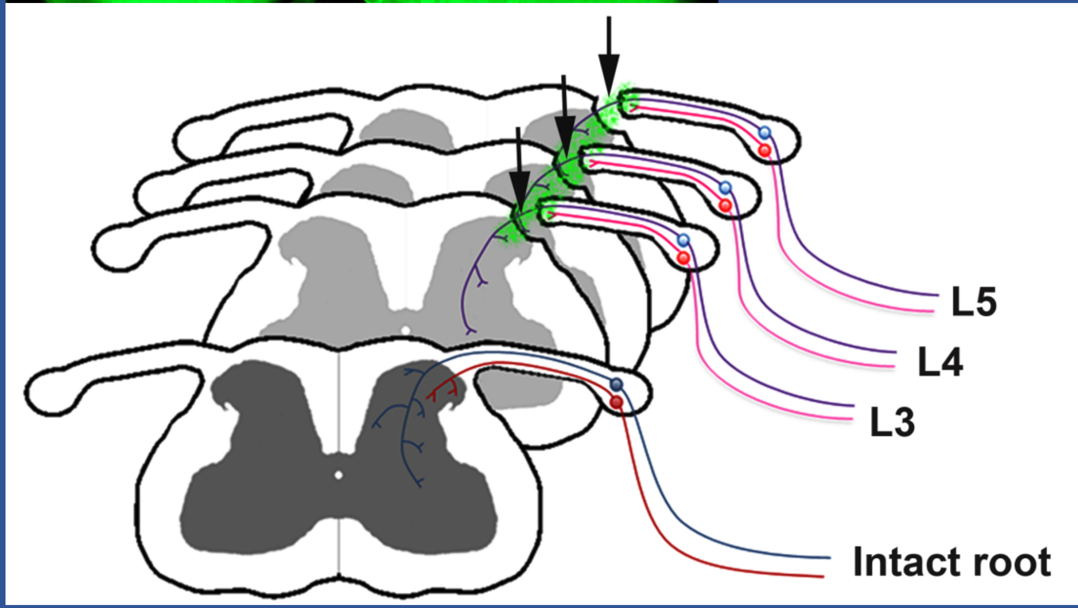


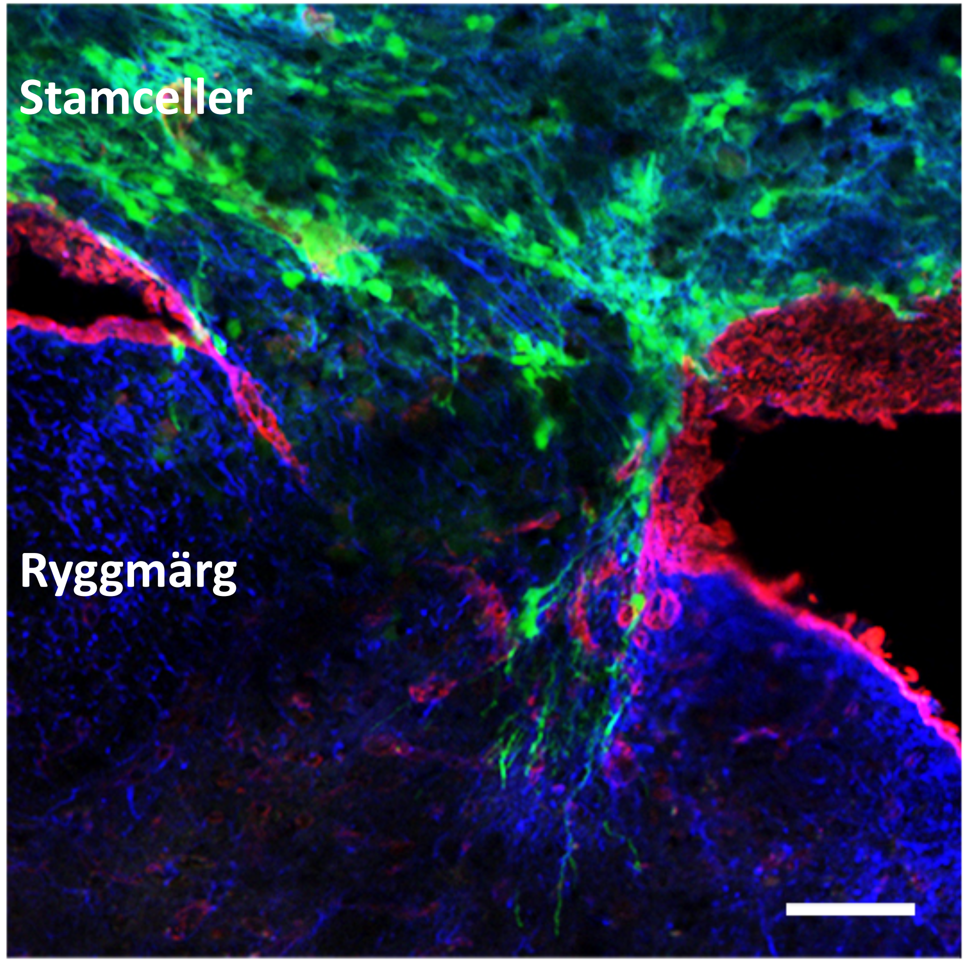
Avulsion injury



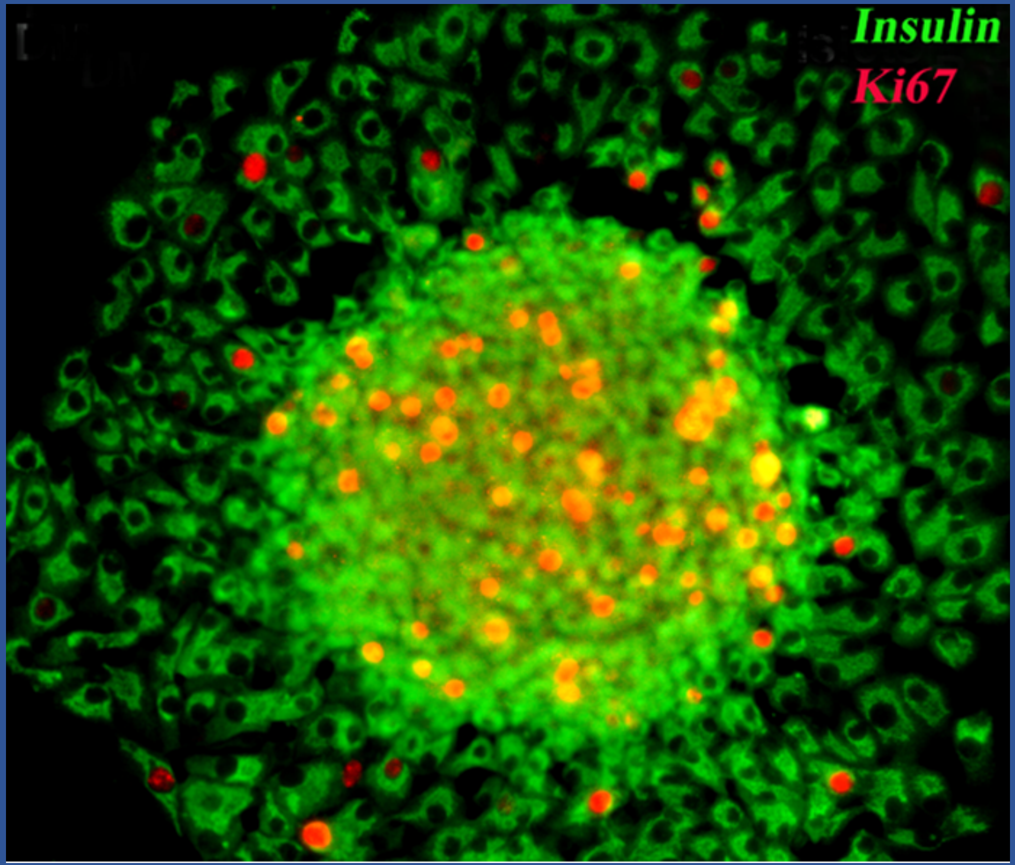
Implantation of Stem Cells in avulsed spinal cord results in sensory recovery







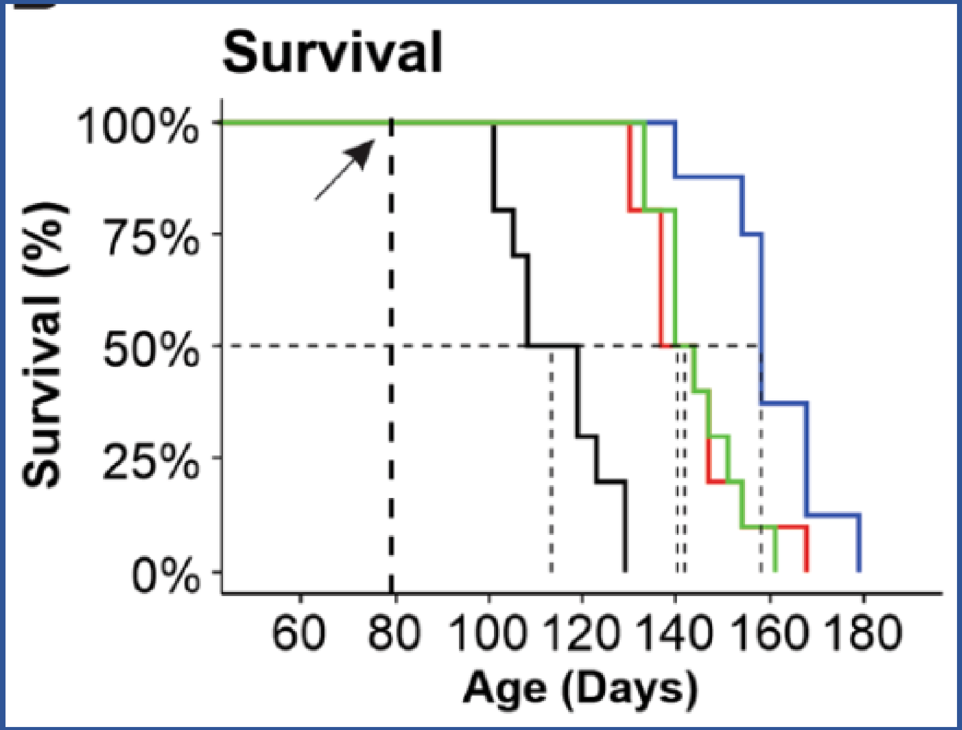
BC assist proliferation of insulin-producing beta cells

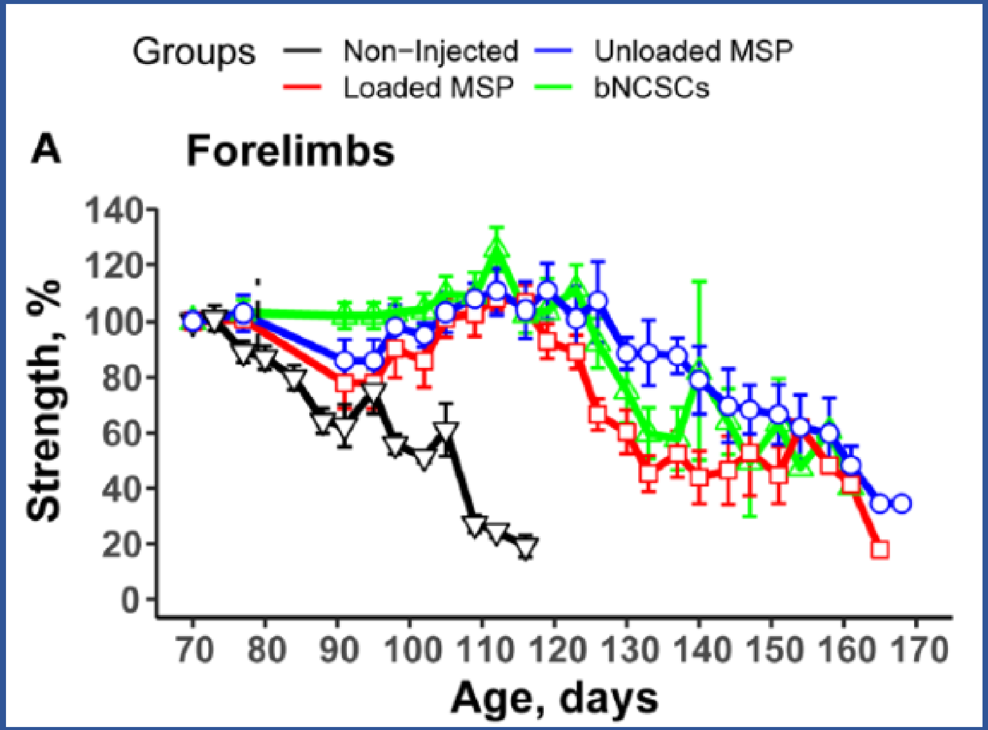


Collaboration with Ola Carlsson, UU MCB and
Harry Heimberg, Diabetes Research Center, Vrije Universiteit Brussel

bNCSCs delayed dissase progression and increased survival

in mouse ALS model

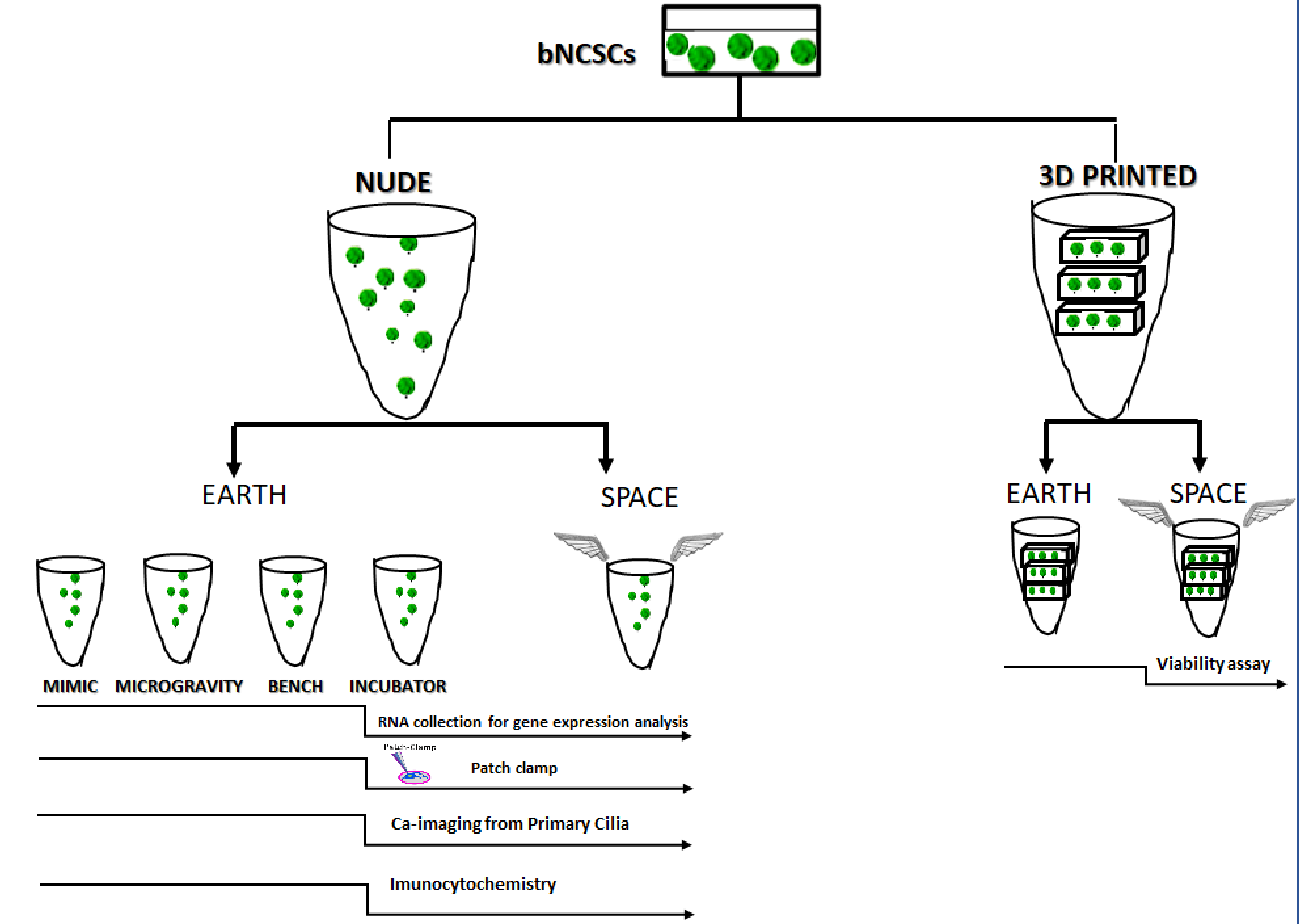


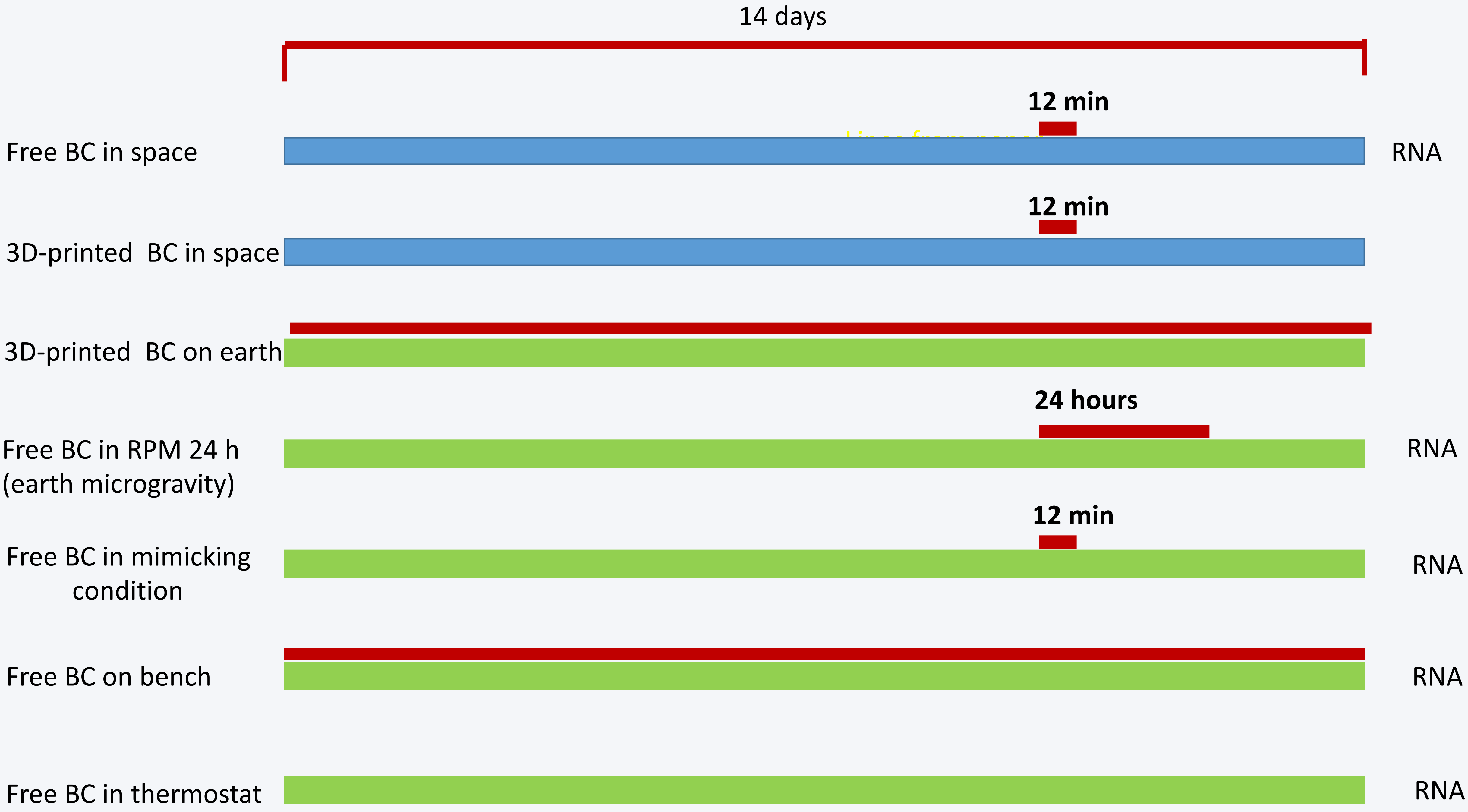


Leyton et al, SciRep, 2021

26 June 2019 Uppsala University in collaboration with Goteborg company CELLINK, AB and Swedish Space Corporation have sent bNCSCs with MASER 14 to SPACE.

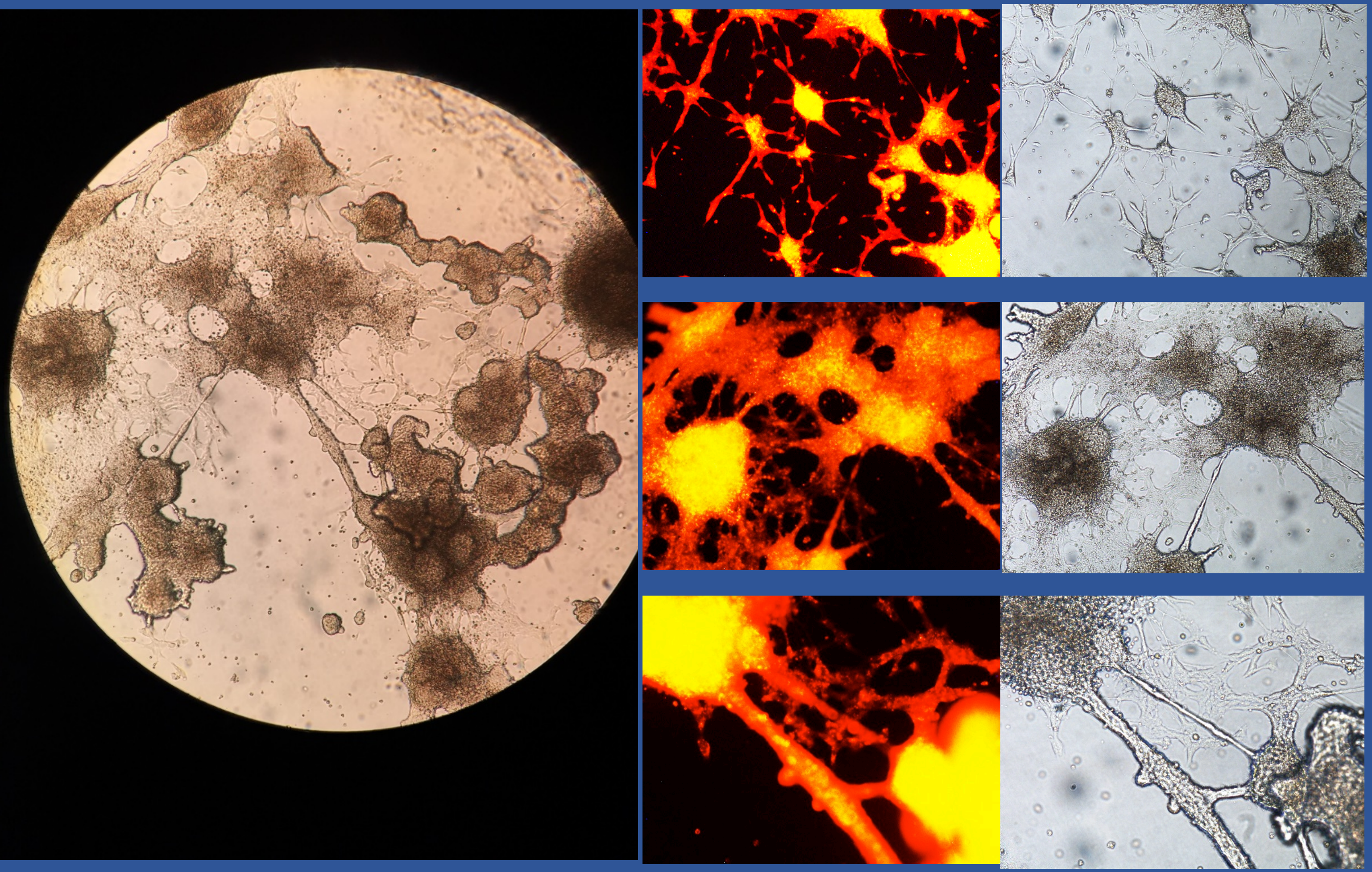
AIMs:
i) to determine the effect of hyper- and microgravity on stem cell ability to survive, differentiate and maintain previously documented characteristics
ii) to explore the possibility to protect neural stem cell viability under space flight with 3D printed scaffold
iii) to investigate if stem cells develop new useful properties from space joney
iv) to detect if “space” memory maintains after space voyage


bNCSCs
NUDE
3D PRINTED
EARTH
SPACE
EARTH
SPACE
MIMIC
MICROGRAVITY
BENCH
INCUBATOR
Viability assay
RNA collection for gene expression analysis
Patch clamp
Ca-imaging from Primary Cilia
Imunocytochemistry

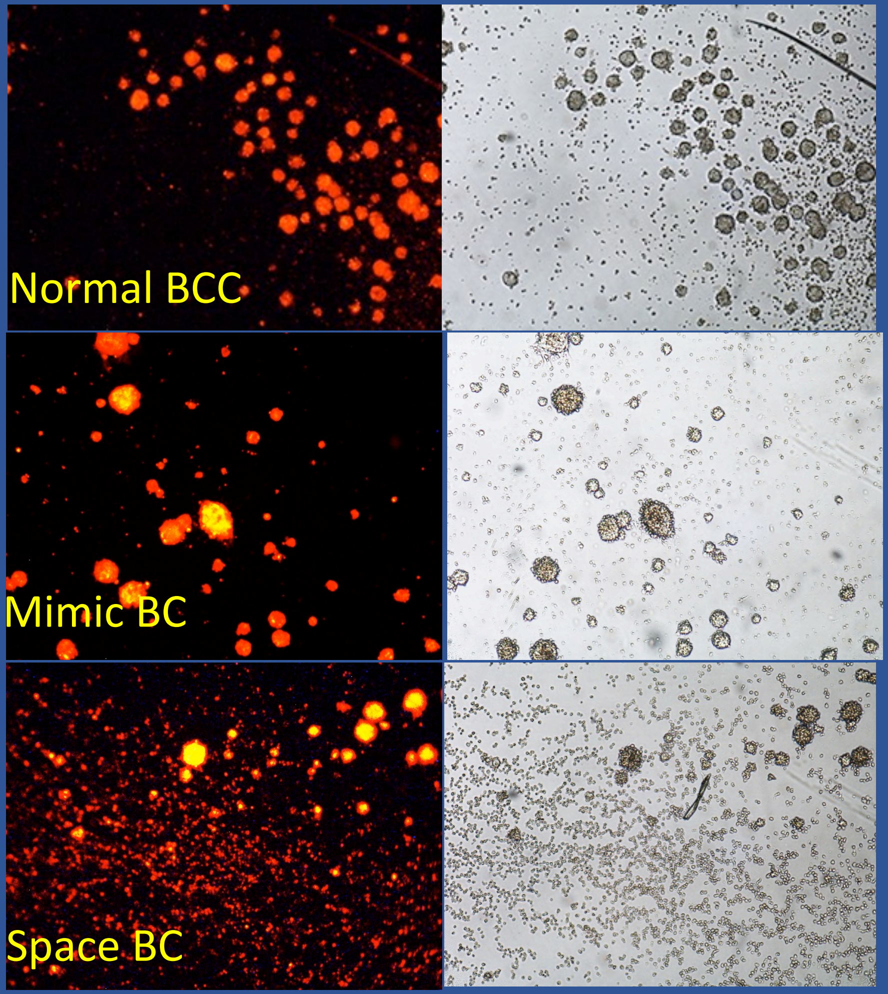

14 days
12 min
Free BC in space
RNA
12 min
3D-printed BC in space
3D-printed BC on earth
24 hours
Free BC in RPM 24 h (earth microgravity)
RNA
12 min
Free BC in mimicking condition
RNA
Free BC on bench
RNA
Free BC in thermostat
RNA

After Space Voyage

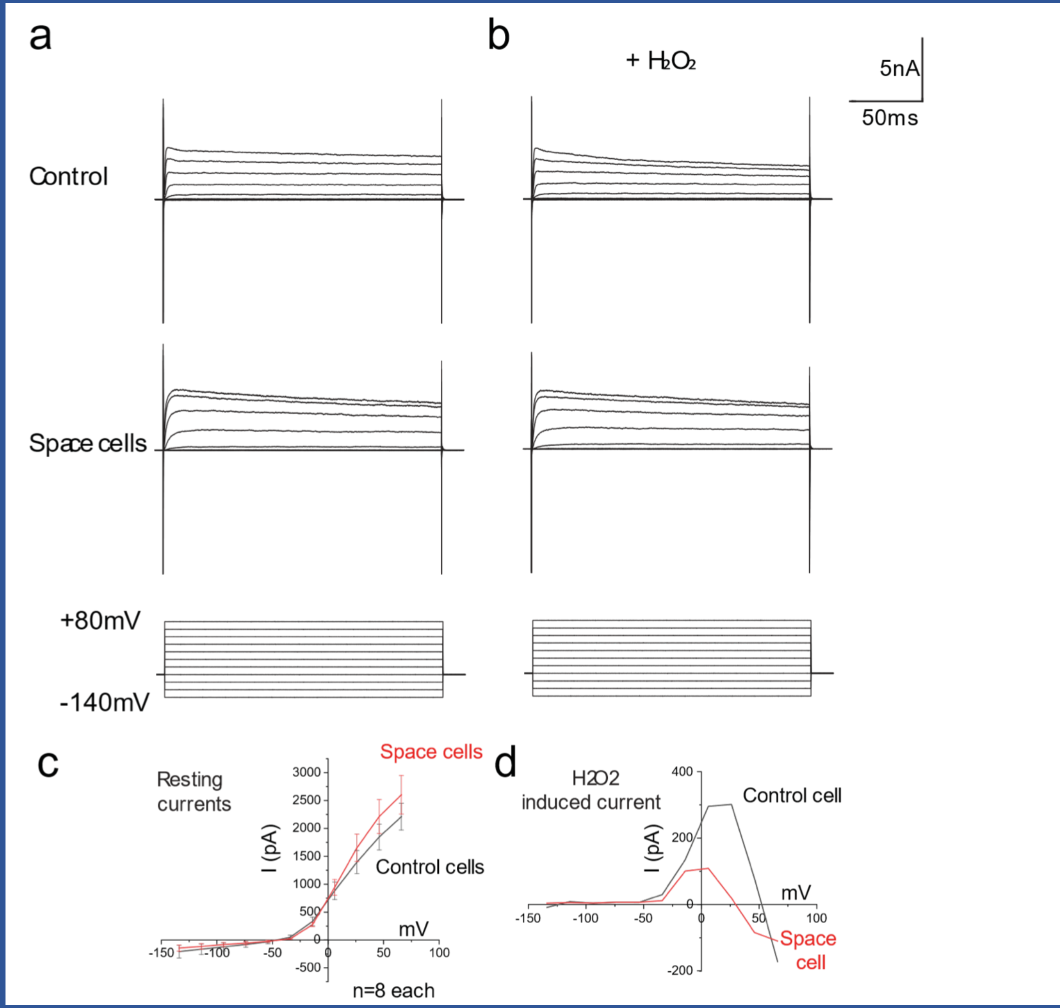
1st images



5 days in culture



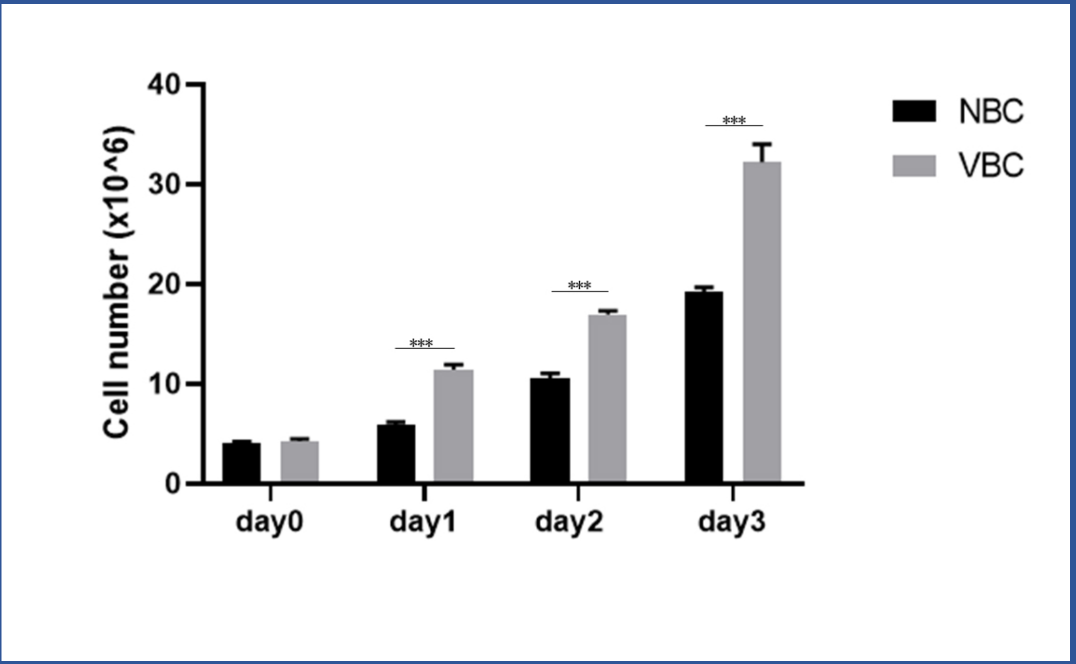
Patch clamp analysis 5 months after Space voyage have showed resistance of SPACE BC to oxidative stress compare to EARTH BC



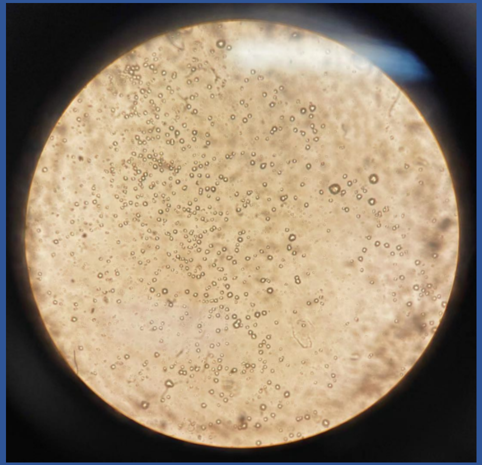
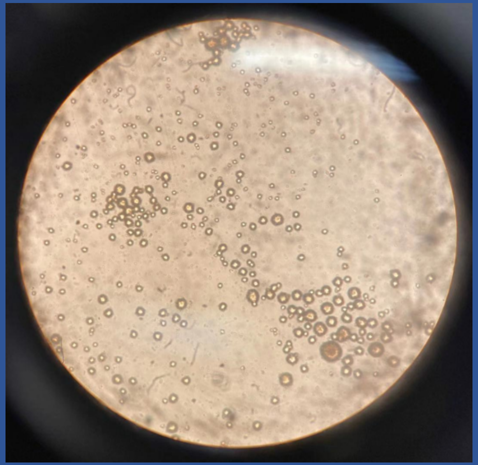
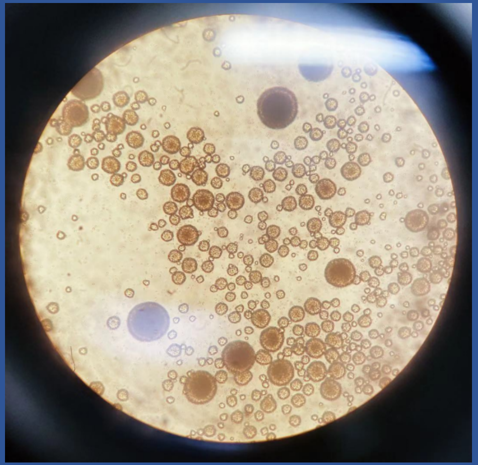
a, Representative I/V curves from patched control and space cells. b, Representative I/V curve after H2O2 application in both control and space cells. Steps of voltage from a holding potential of -60 mV to step potentials of 20 mV between -140 and 80 mV used. c, I-V curves of control (black) and space cells (red) summarized no changes in resting membrane currents and H2O2 induced current. d, I-V relationships obtained by the subtraction before and after H2O2.

Collaboration with N Hamilton-Whitaker, King's College, London

Space BC 5 months after Space voyage

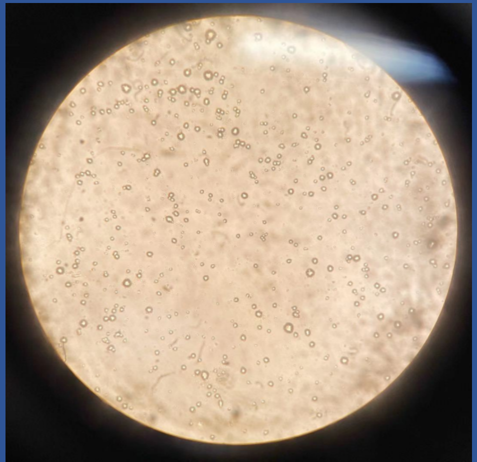
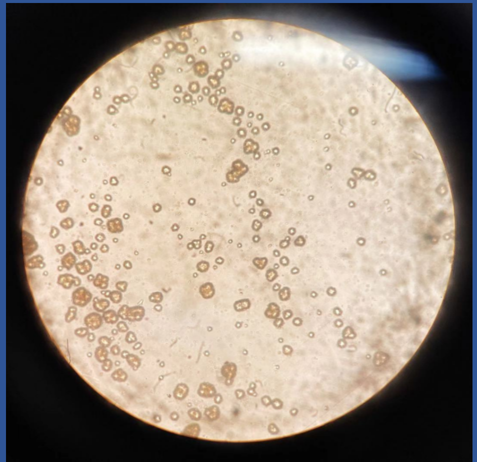
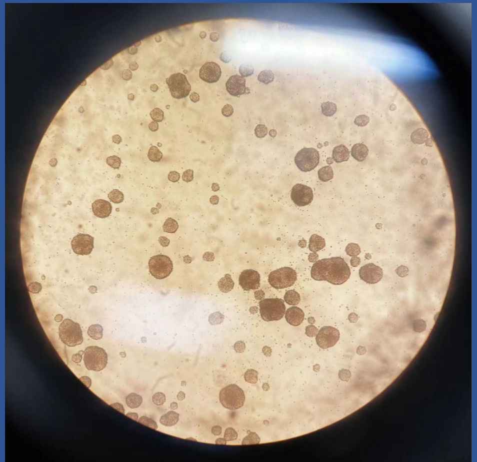


Space BC (V)

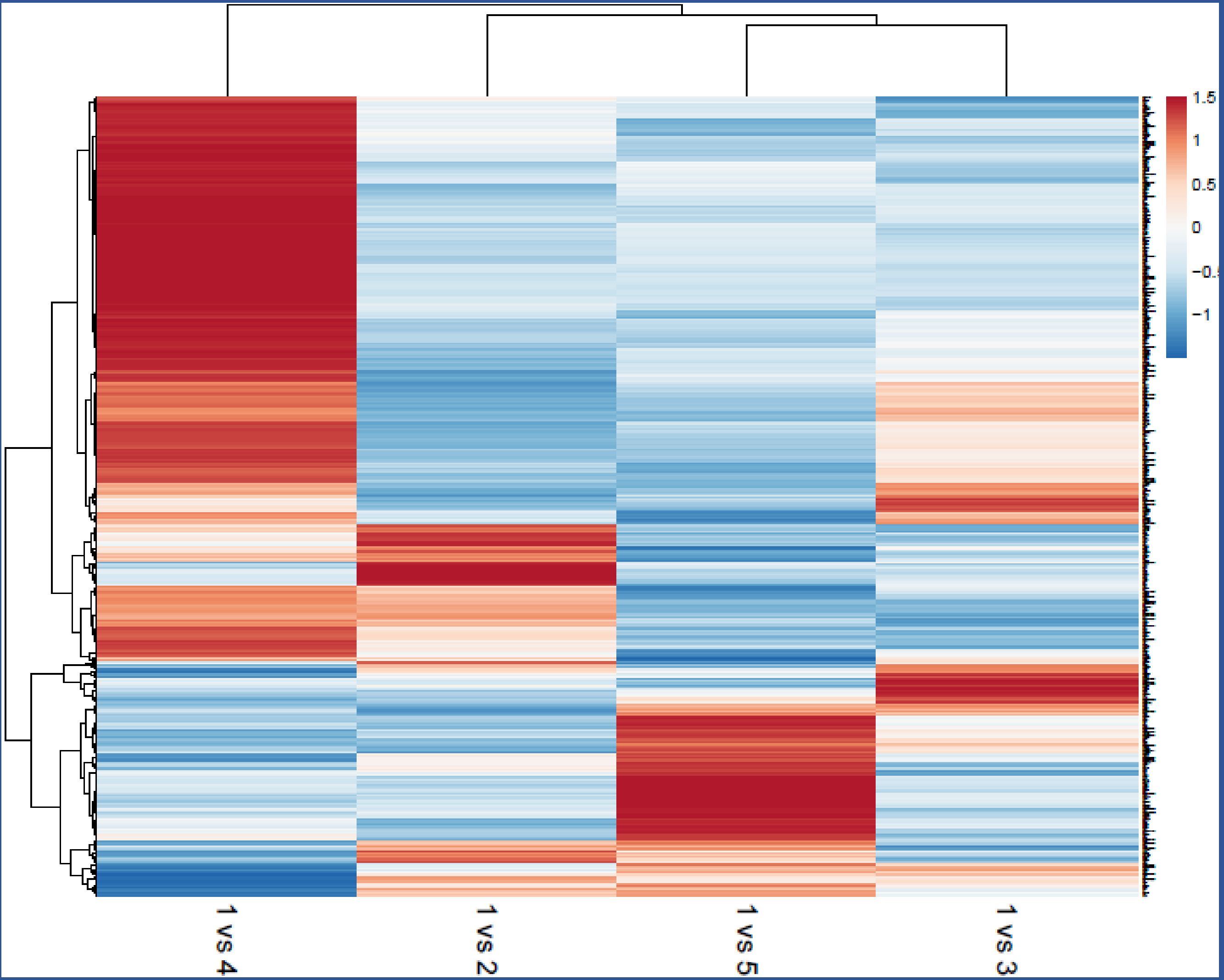




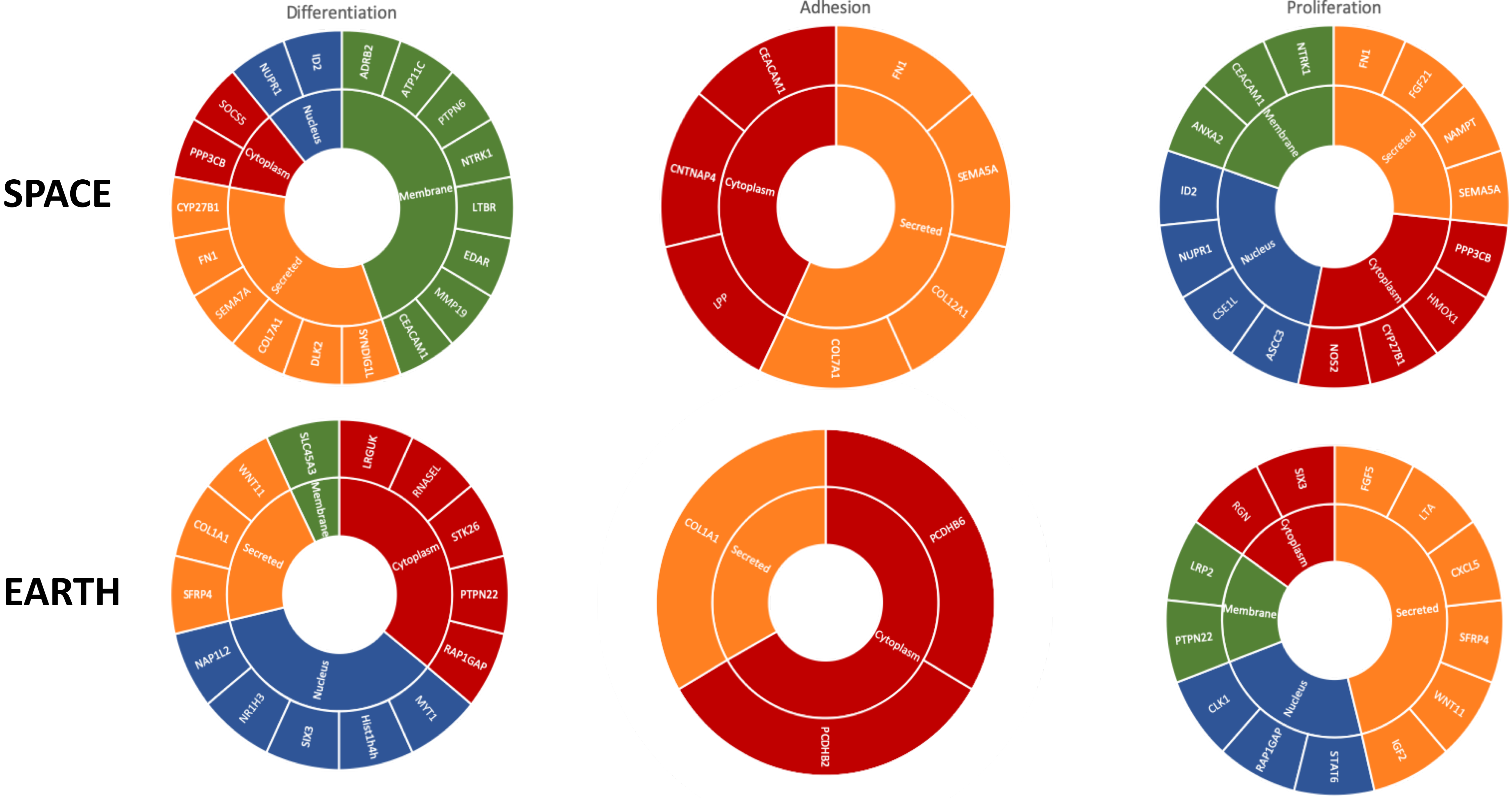
Day 1 Day 2 Day3

Earth BC (N)

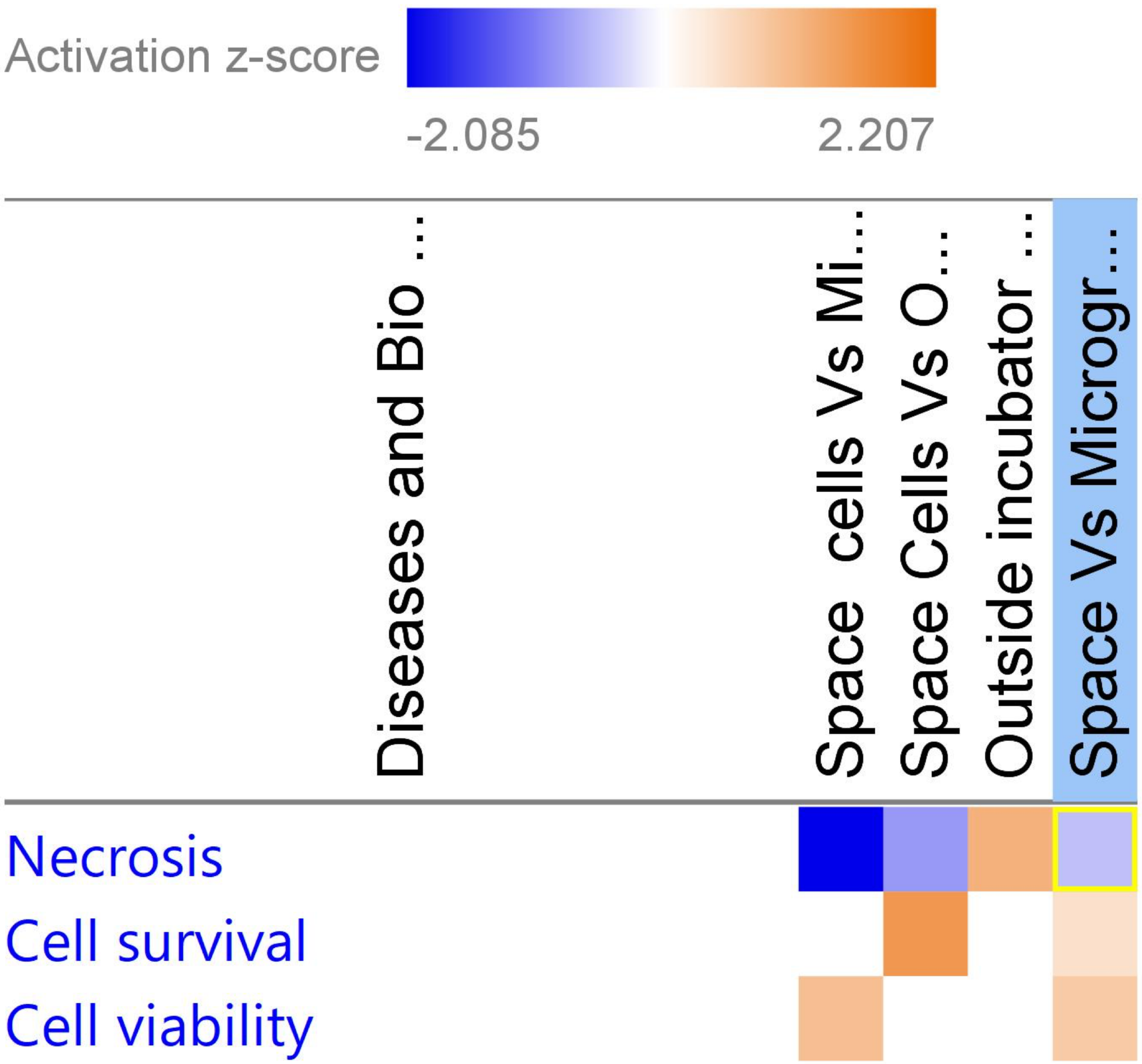
Cluster Heatmap: Space samples compare to Mimicing, Microgravity , Bench and Incubator control expresiments





Differentiation
Adhesion
Proliferation
SPACE
EARTH
Membrane
Secreted
Cytoplasm
Nucleus
ID2
NUPR1
SOCS5
PPP3CB
CYP27B1
FN1
SEMA7A
COL7A1
DLK2
SYNDIG1L
CEACAM1
MMP19
EDAR
LTBR
NTRK1
PTPN6
ATP11C
ADRB2
SEMA5A
COL12A1
LPP
CNTNAP4
FGF21
NAMPT
HMOX1
NOS2
ASCC3
CSE1L
ANXA2
SLC45A3
LRGUK
RNASEL
STK26
PTPN22
RAP1GAP
MYT1
Hist1h4h
SIX3
NR1H3
NAP1L2
SFRP4
COL1A1
WNT11
PCDHB6
PCDHB2
FGF5
LTA
CXCL5
IGF2
STAT6
CLK1
LRP2
RGN

Comparision 2021



Conclusions from 1st Space experiment

- Space conditions improved proliferation capacity of bNCSC
- This proliferation capacity is inherited by stem cell progenies and maintains for several months
- After space conditions bNCSCs become more resistant to oxidative stress
- They increase expression of genes responsible for cell survival
- They increase capacity to support other cells

We now have received support from ESA to test if space cells can induce proliferation of insulin producing beta cells in space, and if beta cells themselves can be induced to proliferate under space conditions.

This experiment is now in preparation for next MASER trip scheduled for 2022.

UU

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Swedish National Space Agency

Kristine Dannenberg

Swedish Space Corporation

Christian Lockowandt and Gunnar Florin

CellINK

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ESA

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