Kan vi lage ALS i en petriskål?

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NORWEGIAN CENTER FOR STEM CELL RESEARCH

JA !

JA !

ved bruk av stamceller.

Dog med visse begrensninger…

Hvilken type stamceller?

Pluripotente – kan bli til en hvilken som helst av kroppens celletyper

Enten hentes fra veldig tidlige embryoer (embryonale stamceller = ES-celler)

Hvilken type stamceller?

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✔ Eller ***lages*** i laboratoriet (induserte pluripotente stamceller = **iPS-celler**)

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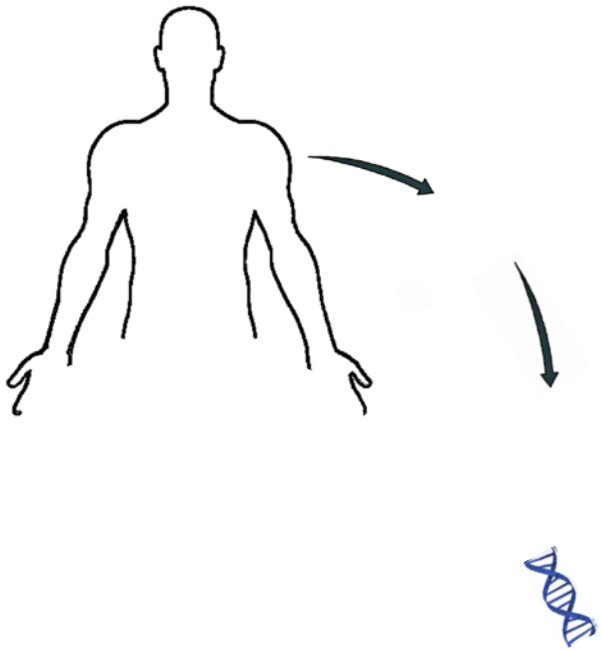
Norwegian Core Facility for Human Pluripotent Stem Cells

v/Nasjonalt senter for stamcelleforskning

NORWEGIAN CENTER FOR STEM CELL RESEARCH

Shinya Yamanaka John Gurdon

induserte pluripotente stamceller (iPS celler)



NORWEGIAN CENTER FOR STEM CELL RESEARCH

NORWEGIAN CENTER FOR STEM CELL RESEARCH

Currently organizing a Phase II Center

Focused on stem cell-based *in vitro* human disease models

The Neuron Factory

Standardized differentiation from iPS cells:

Neural progenitors
Various neuron types (including MNs)
Astrocytes

Norwegian Core Facility for Human Pluripotent Stem Cells

National Core Facility for human pluripotent stem cell production and characterization

The National Core Facility for Human Pluripotent Stem Cells provides researchers throughout Norway with established human ES and iPS cell lines and also the technical services and instruction required for the derivation of iPS cells and the characterization of ES and iPS cell-derived cells. Researchers can obtain ES and iPS cell-related services or make use of the facility to differentiate and characterize cells themselves. The National Core Facility has a staff of 3 highly trained cell culture technicians and a laboratory technician, and is supported by grants from the Norwegian Research Council (NFR) and the SouthEast Regional Health Authority (HSØ).

Only such facility in Norway
First of its kind in Scandinavia

Over 500 iPS cell lines made (140 donors)
25-30 new lines each year

iPS cell-related services offered

National Allogeneic iPS Cell Bank

Collaboration between Stem Cell Center, National Bone Marrow Donor Registry, Ex Vivo Lab, and Dept of Ophthalmology

Hva kan iPS-celler brukes til?

Forskning på sykdommer

Medikamenttesting/toksikologi

Behandling (erstatning av syke celler og organer)

Hva kan iPS-celler brukes til?

- ✔**Forskning** på sykdommer
- ✔**Medikamenttesting**/toksikologi
- Behandling (erstatning av syke celler og organer)

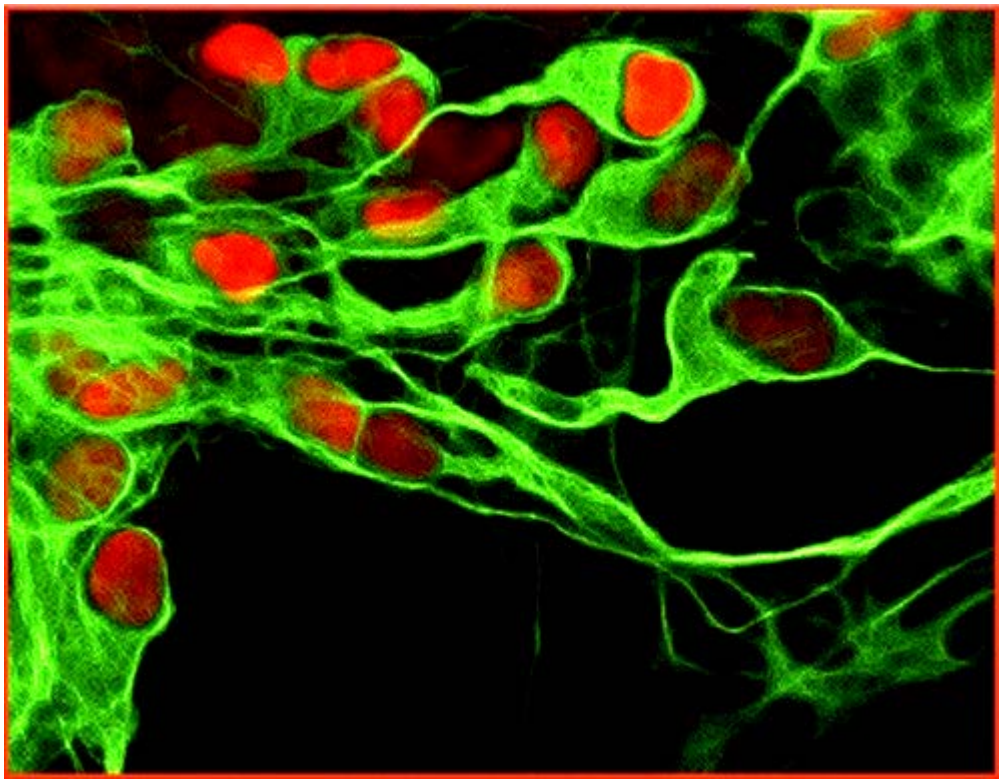
Science 29 August 2008:
Vol. 321. no. 5893, pp. 1218 – 1221
DOI: 10.1126/science.1158799

2008

REPORTS

Induced Pluripotent Stem Cells Generated from Patients with ALS Can Be Differentiated into Motor Neurons

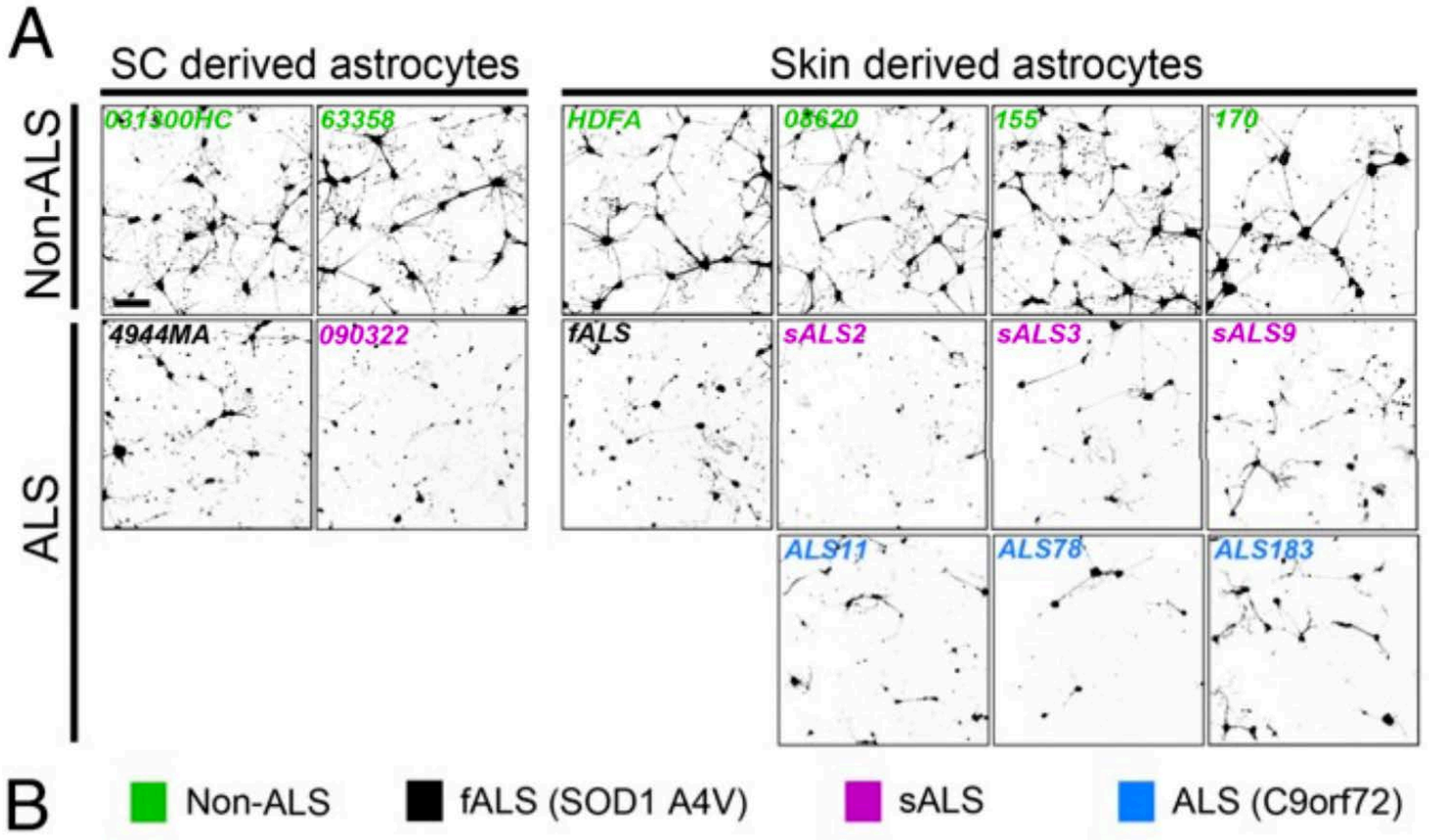
John T. Dimos,[1*] Kit T. Rodolfa,[1,2*] Kathy K. Niakan,[1] Laurin M. Weisenthal,[1] Hiroshi Mitsumoto,[3,4] Wendy Chung,[4,5] Gist F. Croft,[4,6] Genevieve Saphier,[1] Rudy Leibel,[5] Robin Goland,[7] Hynek Wichterle,[4,6] Christopher E. Henderson,[4,6] Kevin Eggan[1†]



2014

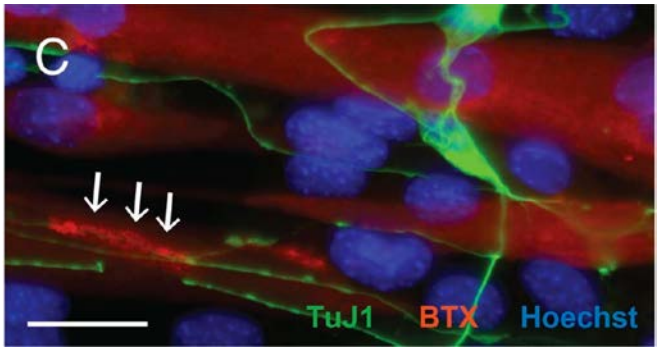
Direct conversion of patient fibroblasts demonstrates non-cell autonomous toxicity of astrocytes to motor neurons in familial and sporadic ALS

Kathrin Meyer[a], Laura Ferraiuolo[a], Carlos J. Miranda[a], Shibi Likhite[a,b], Sohyun McElroy[a], Samantha Renusch[c], Dara Ditsworth[d], Clotilde Lagier-Tourenne[d,e], Richard A. Smith[f], John Ravits[e], Arthur H. Burghes[g], Pamela J. Shaw[h], Don W. Cleveland[d,i], Stephen J. Kolb[g,j,k], and Brian K. Kaspar[a,b,c,1]



Mechanically patterned neuromuscular junctions-in-a-dish have improved functional maturation

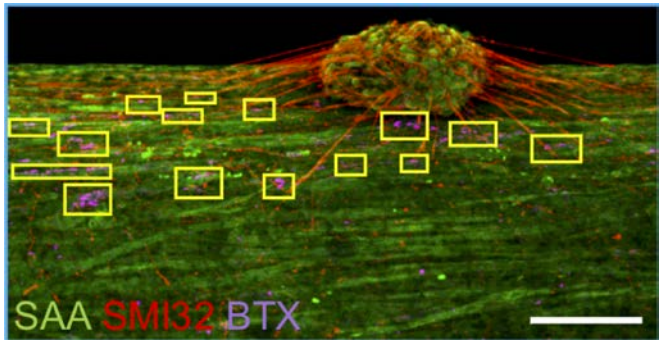
Cassandra L. Happe[a], Kevin P. Tenerelli[a], Anastasia K. Gromova[b], Frederic Kolb[a,†], and Adam J. Engler[a,b,c,*]
[a]Department of Bioengineering and [b]Biomedical Sciences Program, University of California, San Diego, La Jolla, CA 92093; [c]Sanford Consortium for Regenerative Medicine, La Jolla, CA 92037



2017

A 3D culture model of innervated human skeletal muscle enables studies of the adult neuromuscular junction

Mohsen Afshar Bakooshli[1,2], Ethan S Lippmann[3,4], Ben Mulcahy[5], Nisha Iyer[3,4], Christine T Nguyen[6], Kayee Tung[7], Bryan A Stewart[6,8], Hubrecht van den Dorpel[2,9], Tobias Fuehrmann[1,10], Molly Shoichet[1,2,10], Anne Bigot[11], Elena Pegoraro[12], Henry Ahn[7,13], Howard Ginsberg[2,7,13], Mei Zhen[5,14,15], Randolph Scott Ashton[3,4], Penney M Gilbert[1,2,6,16]*



2019

Mechanically patterned neuromuscular junctions-in-a-dish have improved functional maturation

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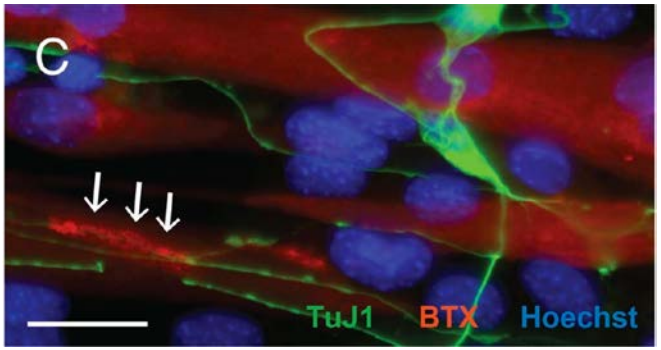

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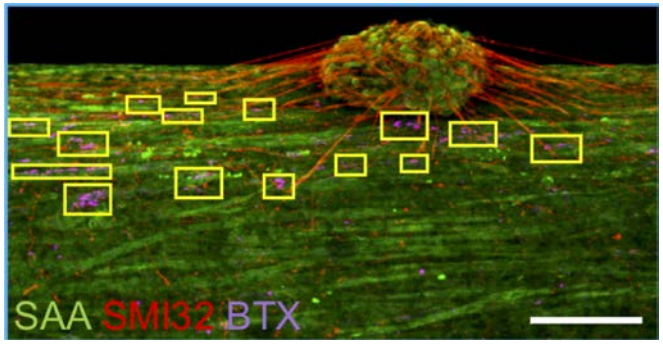


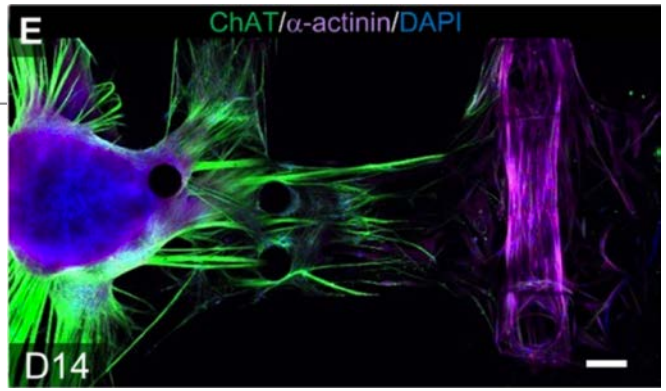
2019

SCIENCE ADVANCES | RESEARCH ARTICLE

HEALTH AND MEDICINE

Microphysiological 3D model of amyotrophic lateral sclerosis (ALS) from human iPS-derived muscle cells and optogenetic motor neurons

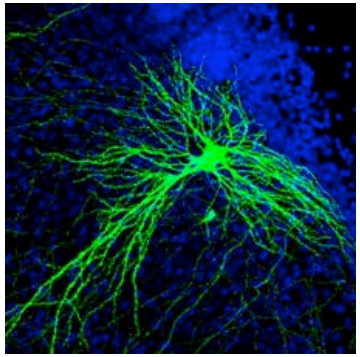
Tatsuya Osaki[1], Sebastien G. M. Uzel[1,2,3], Roger D. Kamm[1,4,5]*



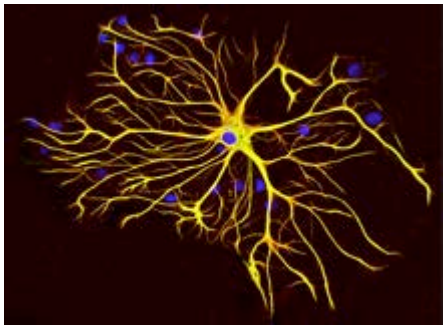
2018

4 hovedcelletyper i ALS:

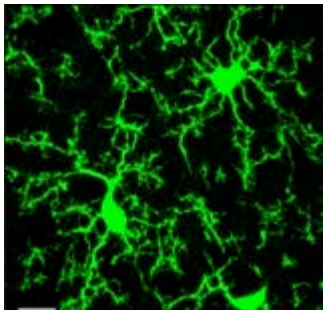
De motoriske nervecellene



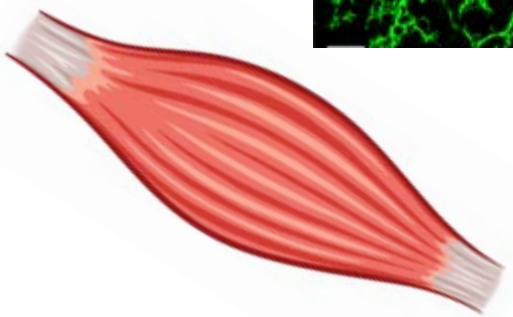
Astrocyttene (en type gliacelle)



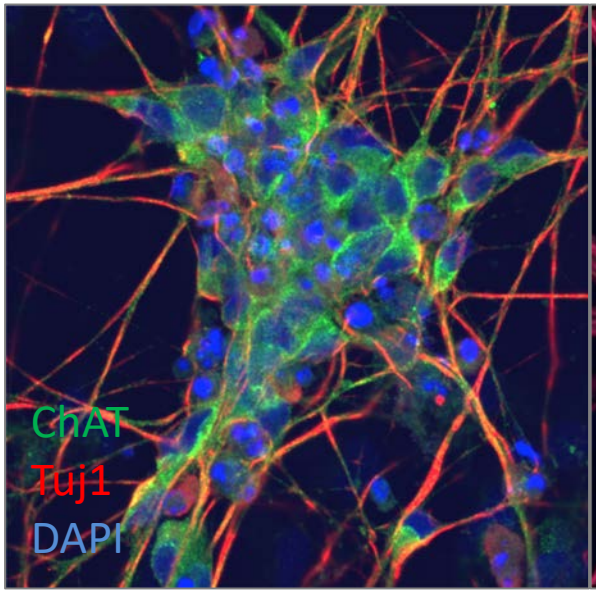
Mikroglia (en type gliacelle)

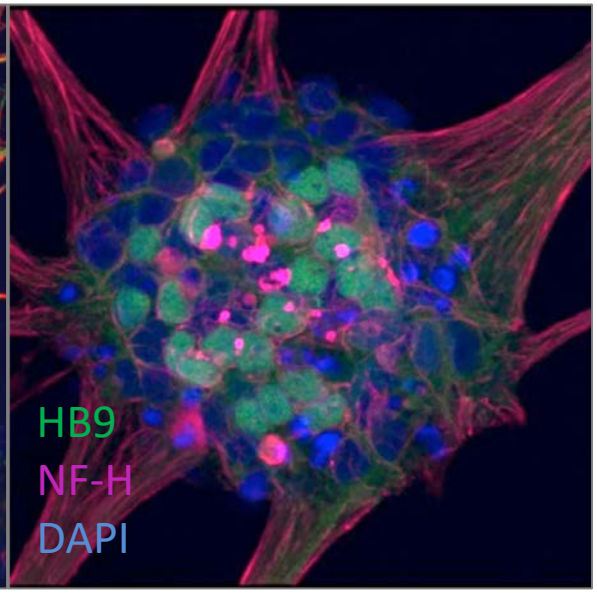


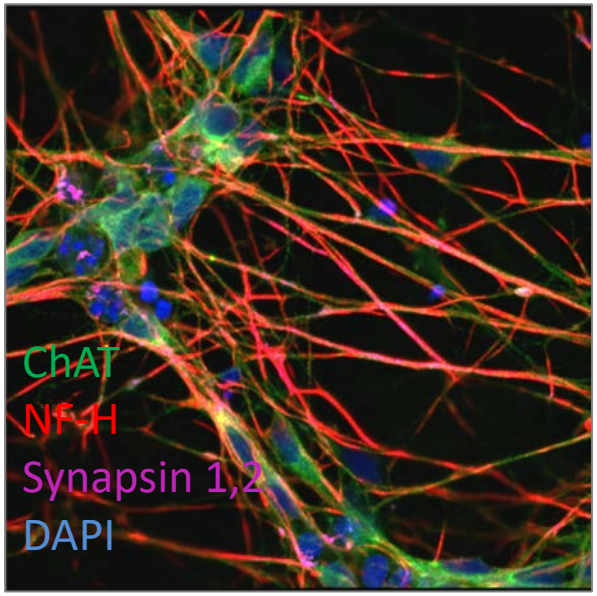
Muskelcellene



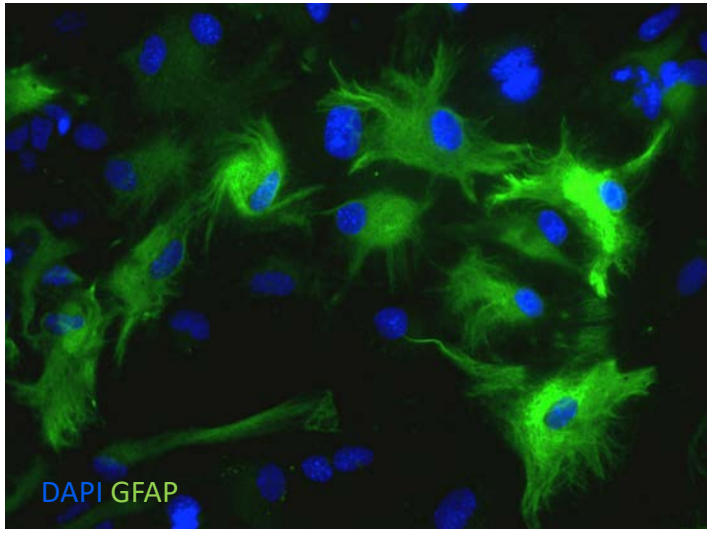
Vår modell: 4-celletype mikrofluidikk plattform



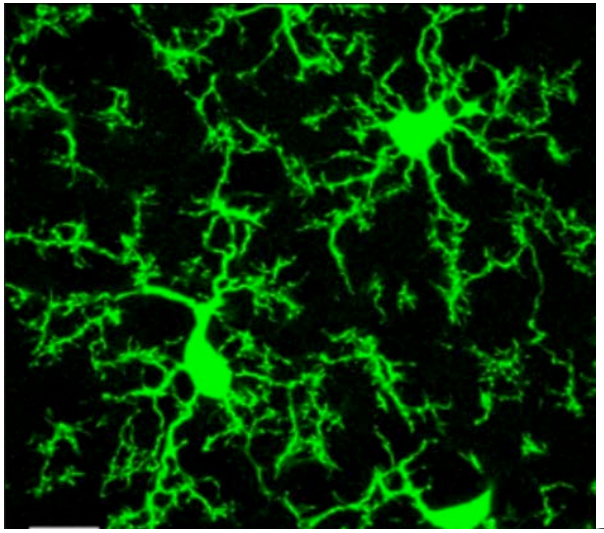




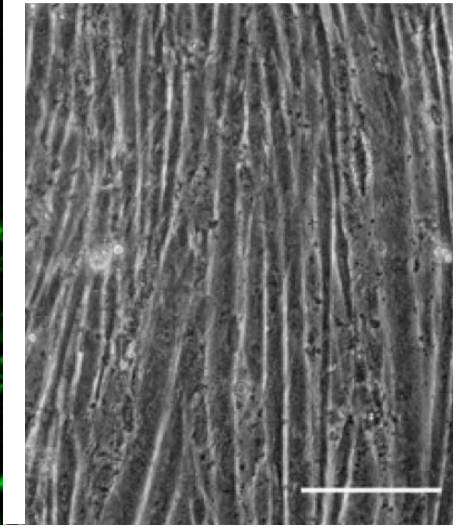
Motoriske nerveceller



Astrocytter



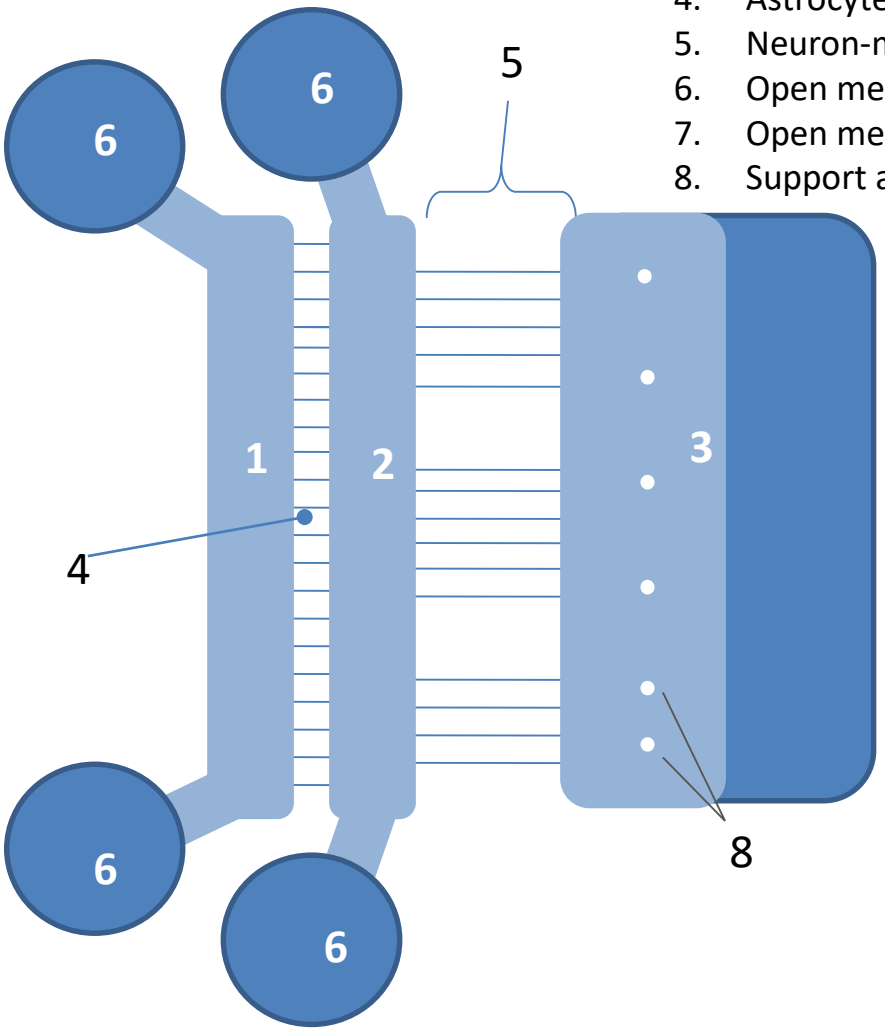
Mikroglia

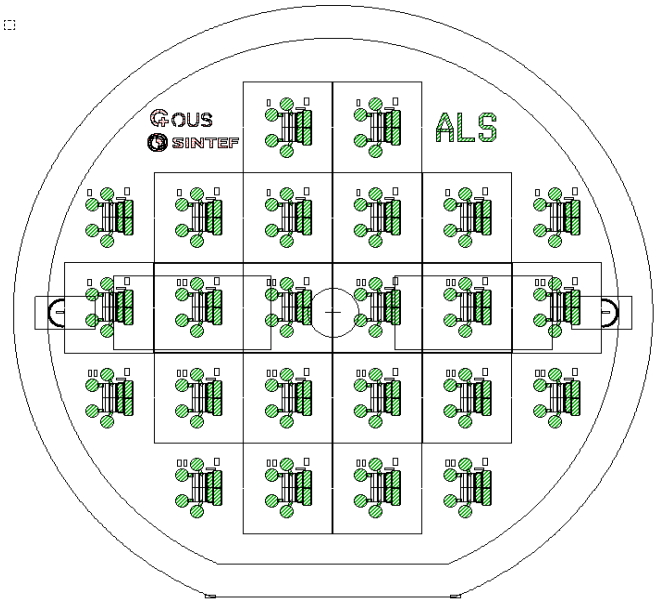


Muskelceller

Vår modell: 4-celletype mikrofluidikk plattform

1. Astrocyte/microglia chamber: 1.5 x 7 mm
2. Motoneuron/presynaptic neuron chamber: 1.5 x 7 mm
3. Muscle/postsynaptic neurons chamber: 2 x 20 mm
4. Astrocyte-neuron microgroove barrier: 50-75 µm
5. Neuron-muscle microgroove barrier: 200-450 µm
6. Open media filling ports for 1 and 2
7. Open media filling ports for 3
8. Support anchors for muscle bundle anchoring





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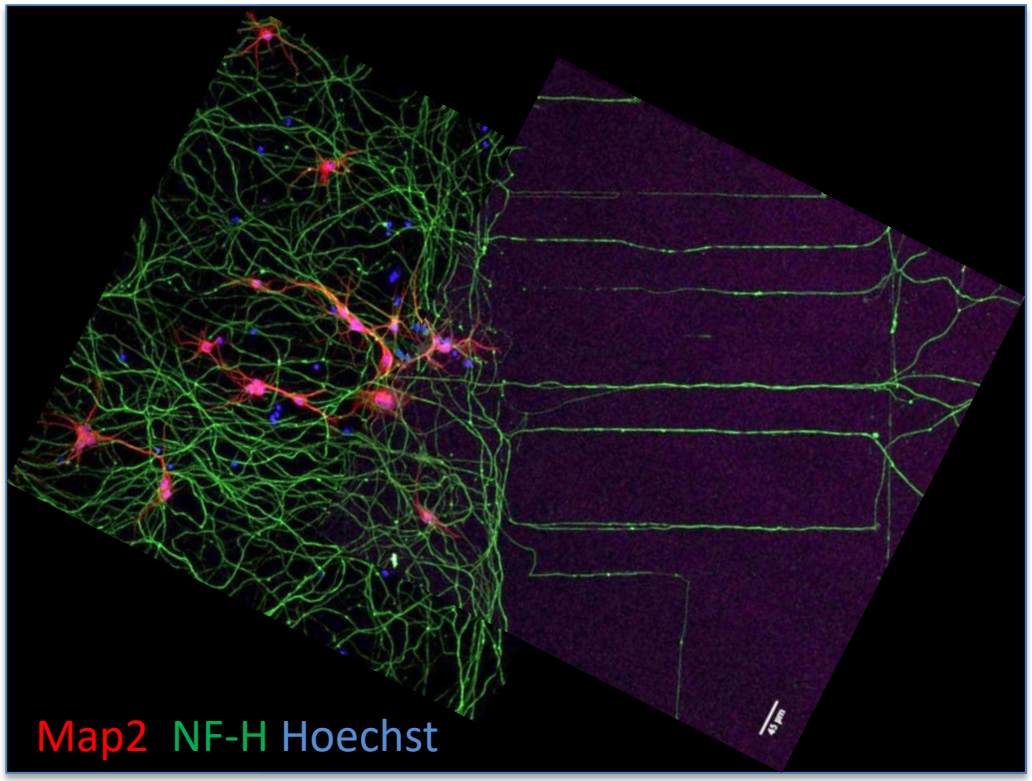
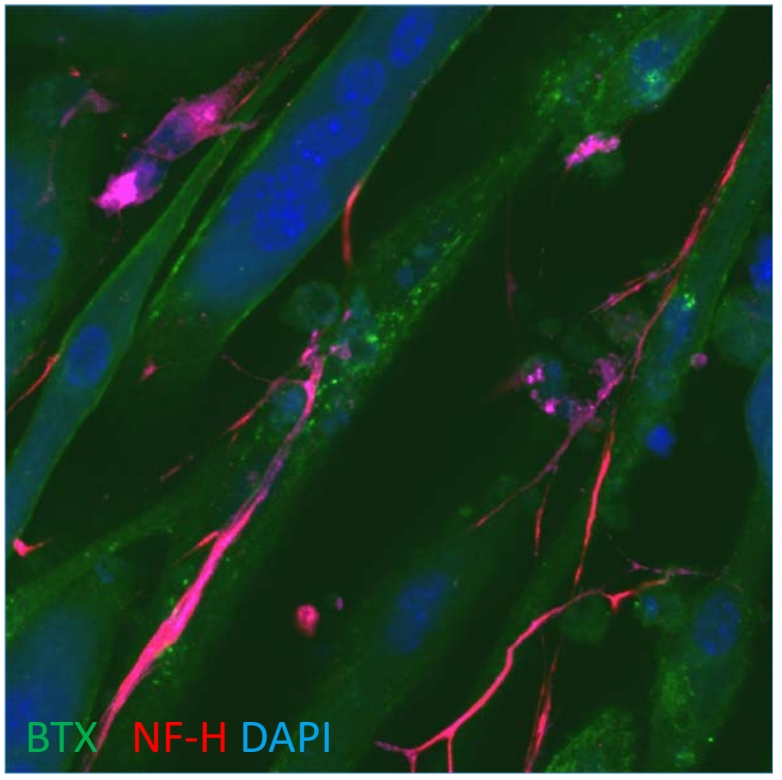
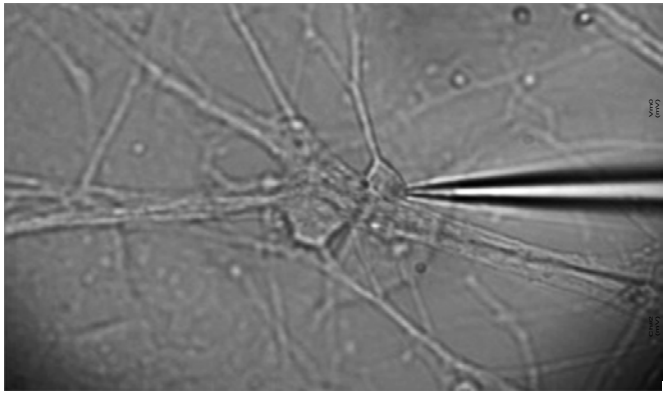
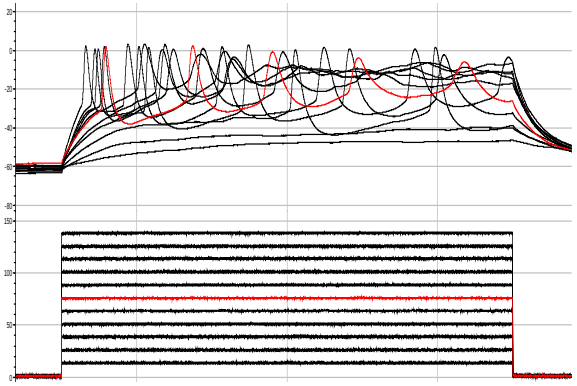
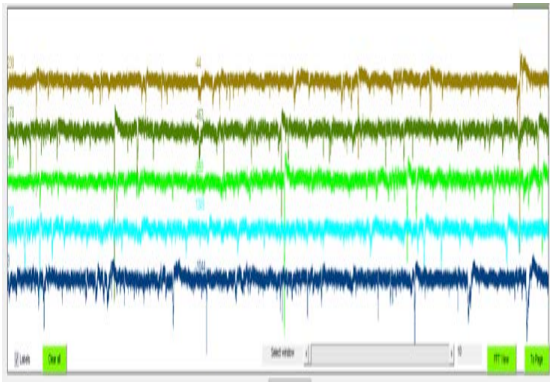
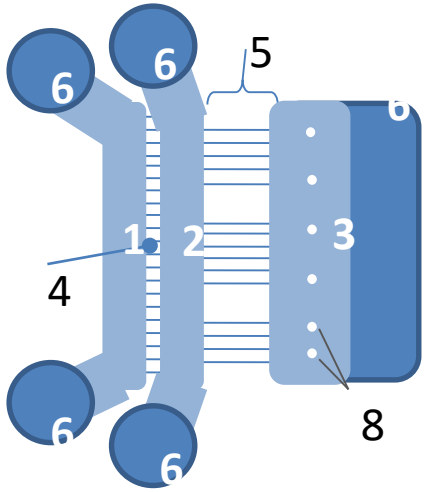












Fordeler ved denne modellen:

1) *Adskilte MNer og muskelbundter, selektiv aktivering og aktivitetsregistrering av de motoriske nervefibre*
2) *+ Astrocytter og mikroglia, adskilte (eller ikke) fra Mner*
3) *Alle 4 celletyper kan skaffes fra ALS-pasient iPS-celler*
4) *Kompatibel med en rekke registreringsmuligheter, bade fysiologiske (elektrofysiologi, optiske) og biokjemiske*
5) *Applisering av medikamenter til bestemte celletyper*
6) *Viktig bidrag til etablering av nye kliniske studier*

Hva kan iPS-celler brukes til?

Forskning på sykdommer

Medikamenttesting/toksikologi

✔**Behandling** (erstatning av syke celler og organer)

Hvorfor en nasjonal bank av iPS-celler?

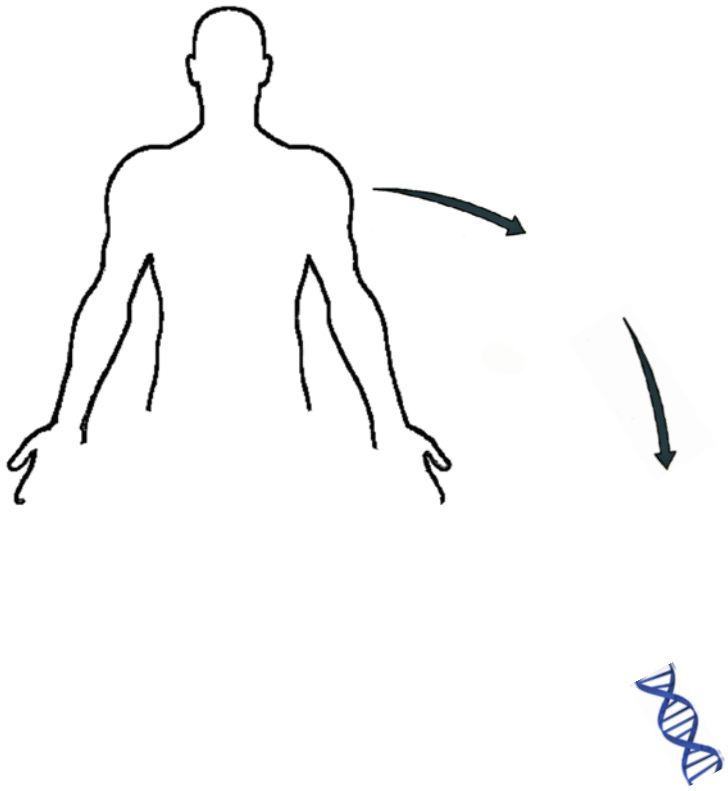
Autologe iPS-celler kontra allogene iPS-celler

(fra pasienten) (fra en donor)

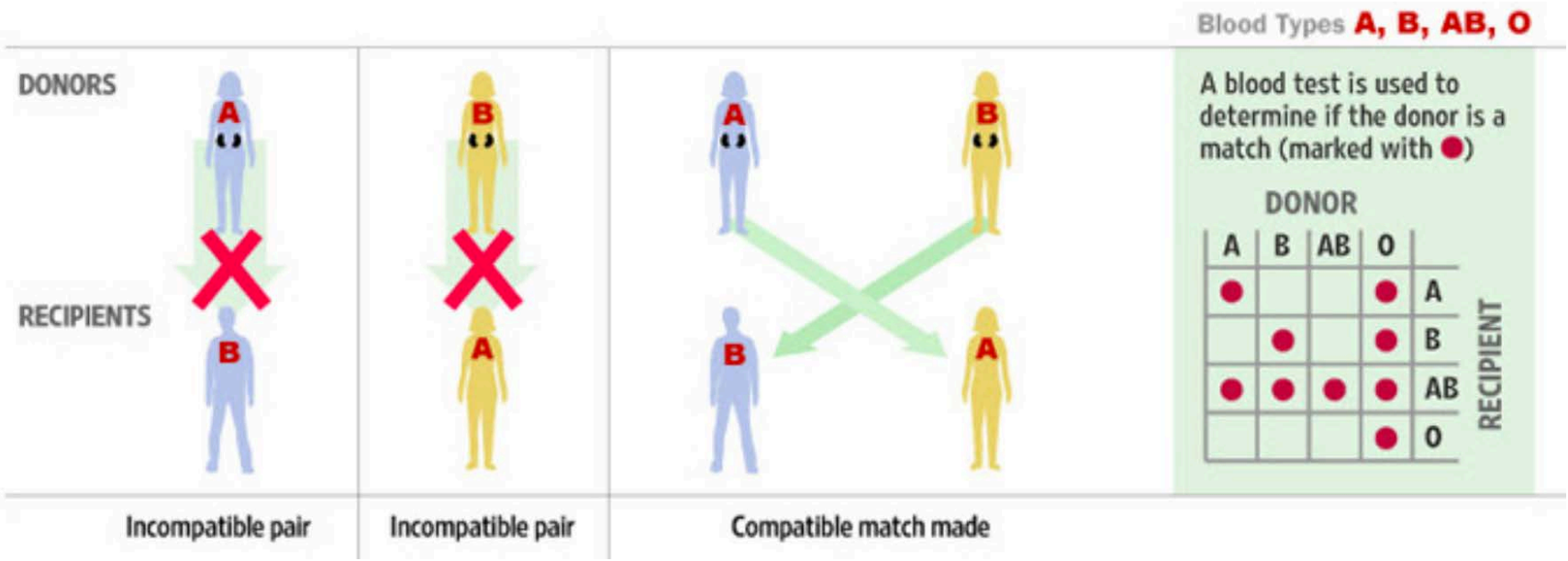
Problemet med autologe: Ting Tar Tid!

Fordeler ved allogene iPS-celler

- kan oppbevares i en bank – varer “evig”
- klar til bruk – sparer tid
- donor og pasient må matches

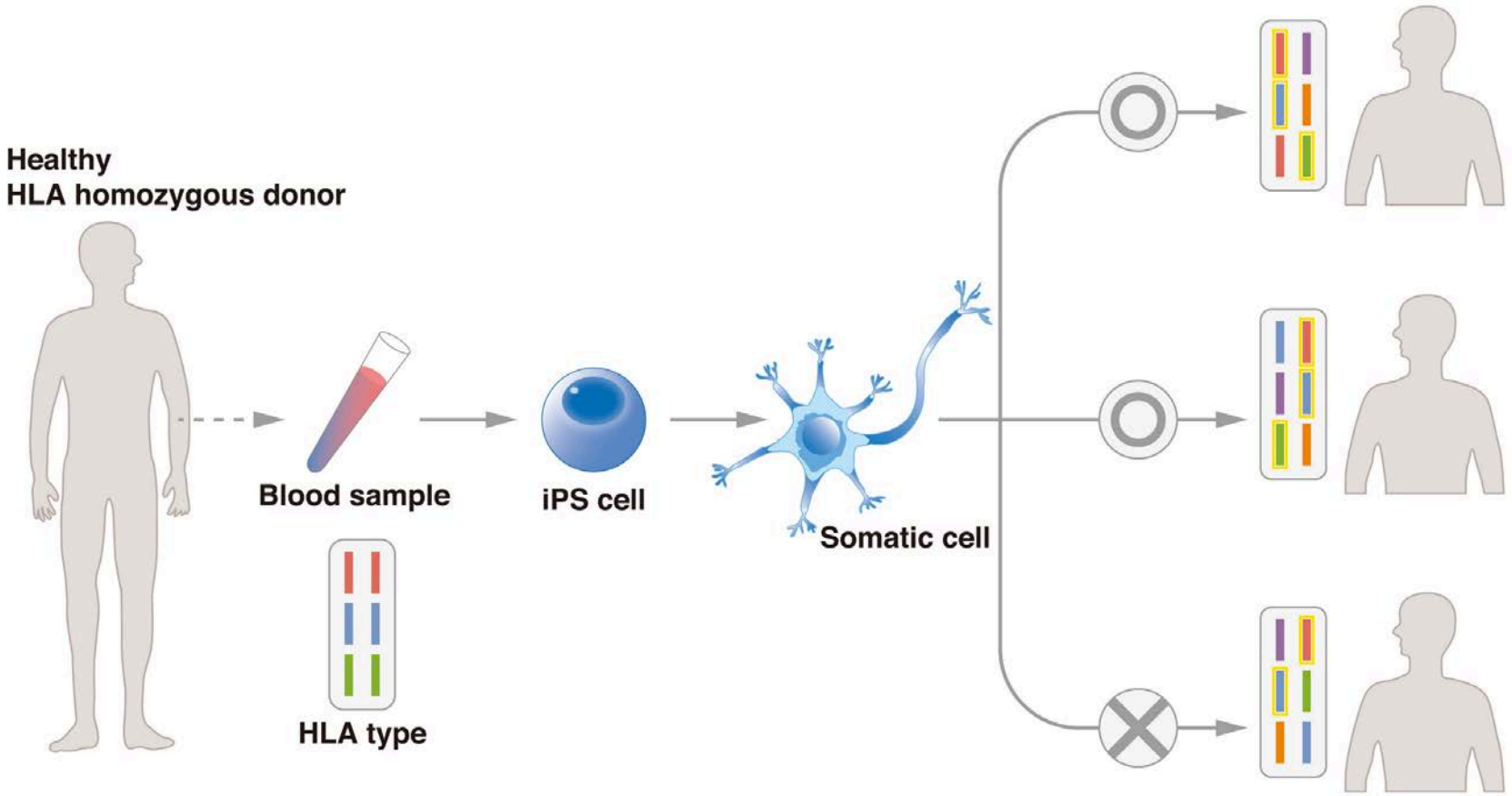


Bloddonasjon – her finnes det "universelle" donorer



ABO-systemet

Stamcelledonasjon – ingen ordentlige “universelle” donorer, men det finnes noen få “super-donorer”



HLA-systemet

Etnisitet er viktig, fordi matchingen er genetisk basert

Japan startet det hele – har satset på en iPS-cellebank der cirka 130 donorer vil kunne dekke behovet til den etnisk japanske befolkningen

USA er også med – men har den utfordringen at befolkningen er genetisk veldig heterogen

Enkelte europeiske land er interesserte

Norge har ypperlige forutsetninger for en iPS-cellebank!

Hva har vi?

9 allerede identifiserte superdonorer som genetisk dekker 70% av den etnisk norske befolkningen

Høy kompetanse innen fremstilling av iPS-celler

Alle fasiliteter som trengs

Hva trenger vi? ***Finansiering***

Takk for oppmerksomheten

Støttet av:

ALS Norge®
Etablert februar 2008

HELSE SØR-ØST

UNIVERSITY OF OSLO
FACULTY OF MEDICINE

Oslo University Hospital

NORWEGIAN CENTER FOR STEM CELL RESEARCH