

Wetenschapsdag 11 oktober 2019

De toekomst van regeneratieve geneeskunde voor nierziekte

Martin Hoogduijn

Geen disclosures

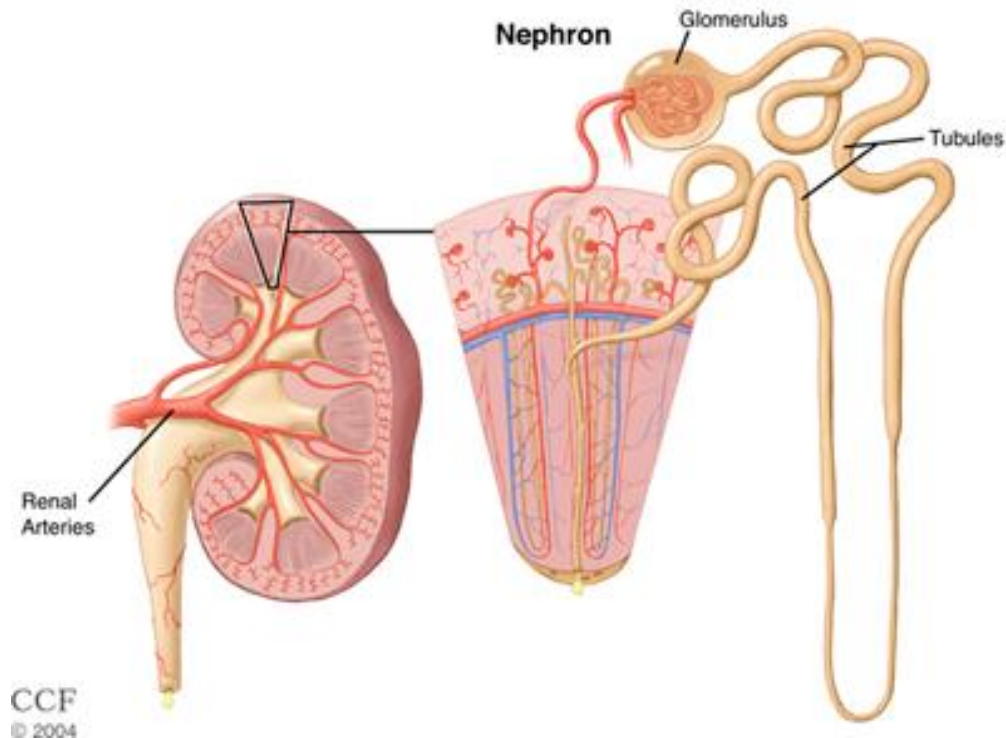
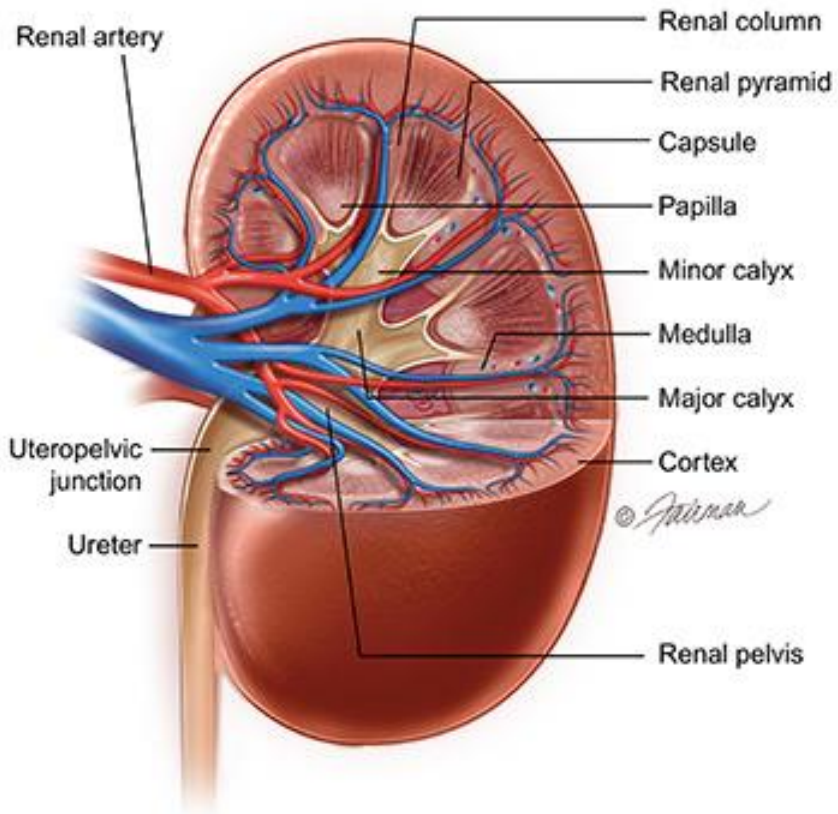
De toekomst van regeneratieve geneeskunde voor nierziekte



Het probleem

- Nierziekte ☐ toenemend probleem
 - Dialyse ☐ kwaliteit van leven ☐
 - Transplantatie ☐ wachtlijst
 - Donor nieren ☐ steeds ouder wordende donoren
 - Levensduur transplant nieren gemiddeld 12-15 jaar
-
- Herstellen zieke nier?
 - Verbeteren van de kwaliteit van de donor nier?
 - Bouwen van nieren in het laboratorium?

De Nier



Regeneratie

Herstel van weefsels



Stamcellen

Embryonale stamcellen

- Afkomstig uit 7 dagen oude embryo's
- Kunnen 200 cel types worden



Carnegie Stages of Human Development

Dr Mark Hill, Cell Biology Lab, School of Medical Sciences (Anatomy), UNSW



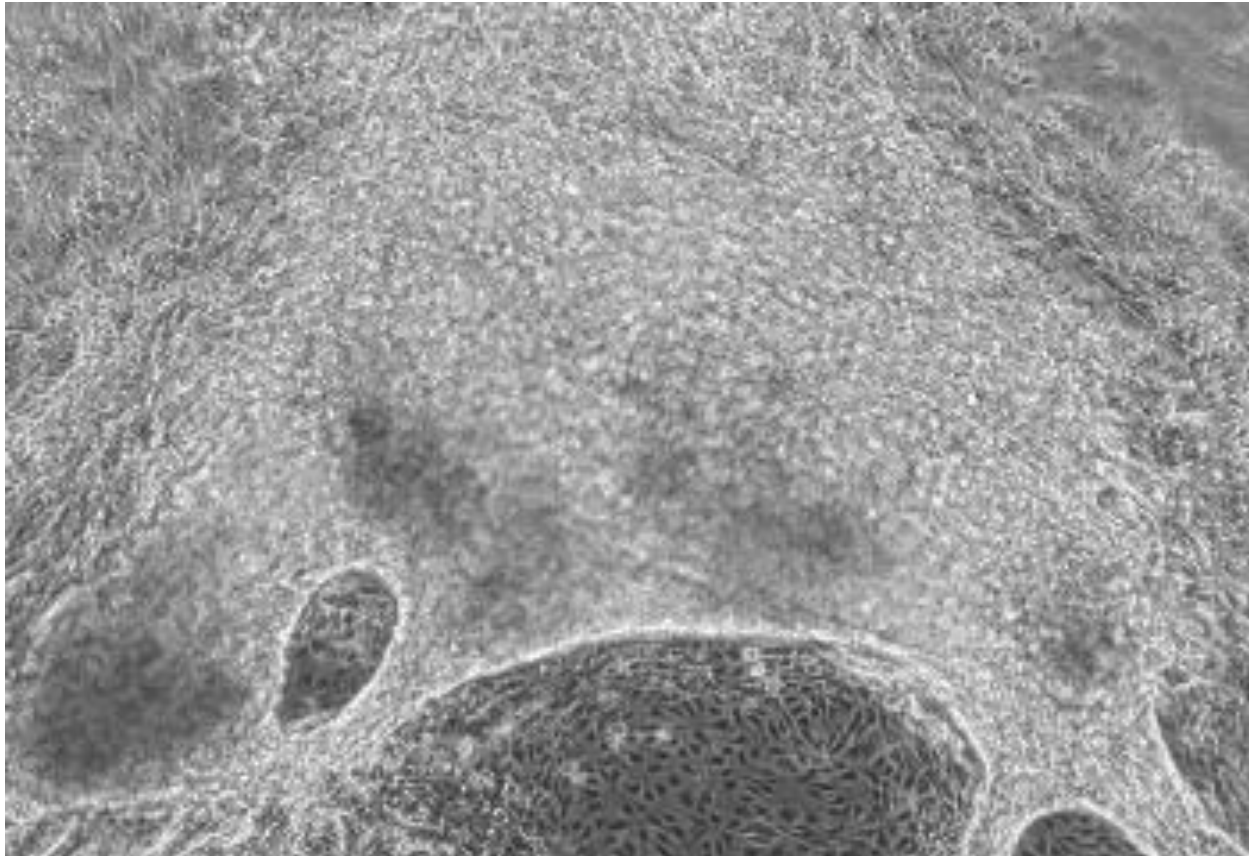
Acknowledgements

Special thanks to Dr S. J. DiMarzo and Prof. Kohel Shiota for allowing reproduction of their research images and material from the Kyoto Collection and Ms B. Hill for image preparation.

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Vorming van hartspiercellen uit embryonale stamcellen



Stamcellen

Embryonale stamcellen

- Afkomstig uit 7 dagen oude embryo's
- Kunnen 200 cel types worden

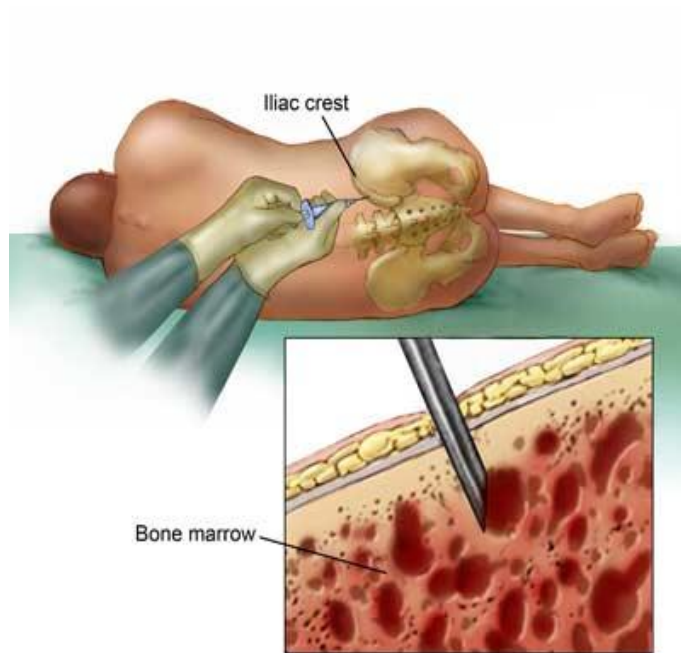


Volwassen stamcellen

- Aanwezig in jong en oud
- Kunnen een aantal cel types vormen
- Afweeronderdrukkende werking



Isolatie van stamcellen

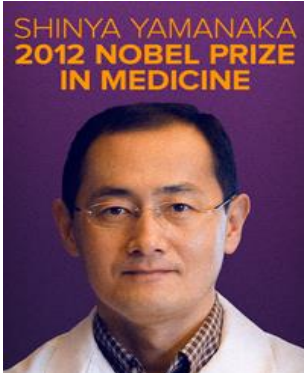


Beenmerg aspiratie

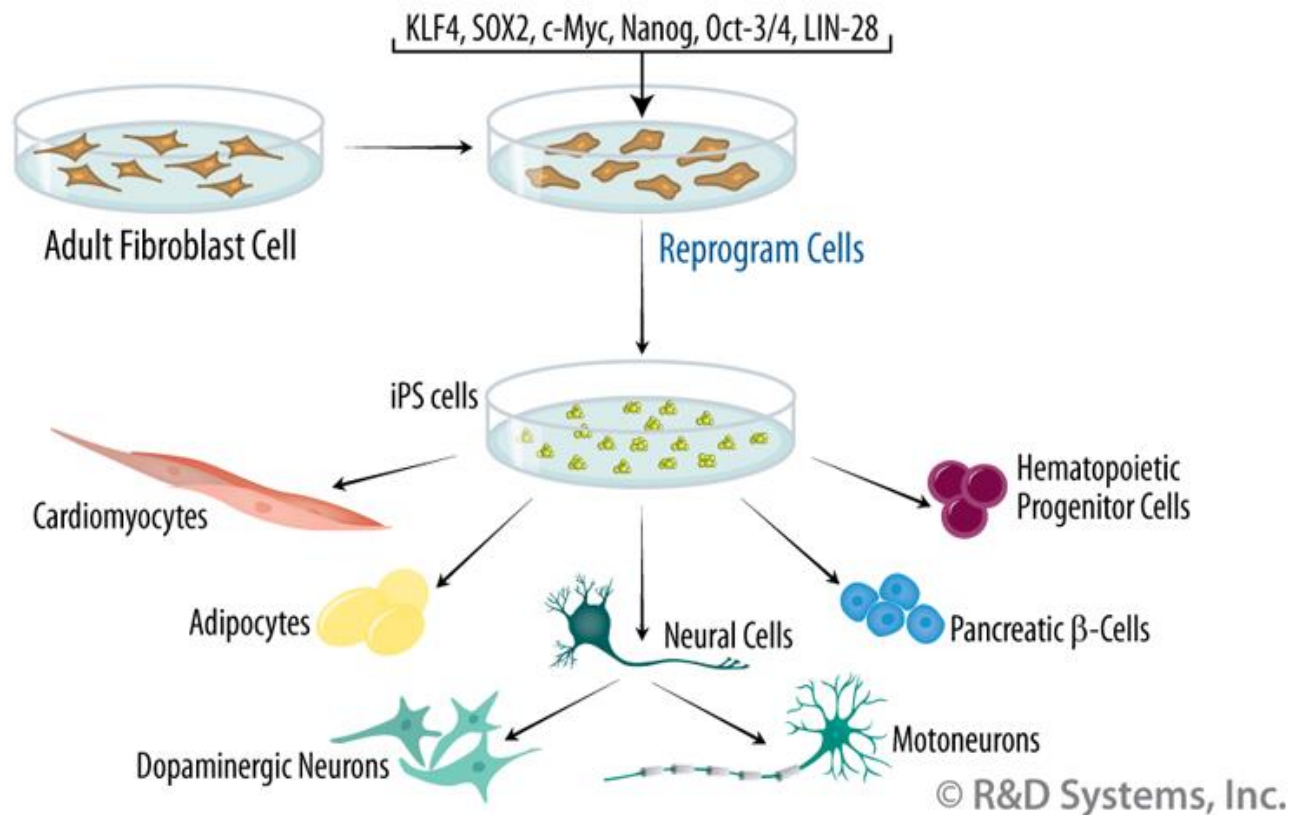


Liposuctie

Geïnduceerde Pluripotente Stamcellen (iPSC)



Shinya Yamanaka



Stamcellen voor nierziekte

- Reparatie van beschadigde (transplantatie) nieren
- Onderdrukken afweer tegen getransplanteerde nieren
- Bouwen van nieuwe nieren

Toediening van stamcellen aan transplantatie nieren



Vroeger:
nier bewaard op ijs

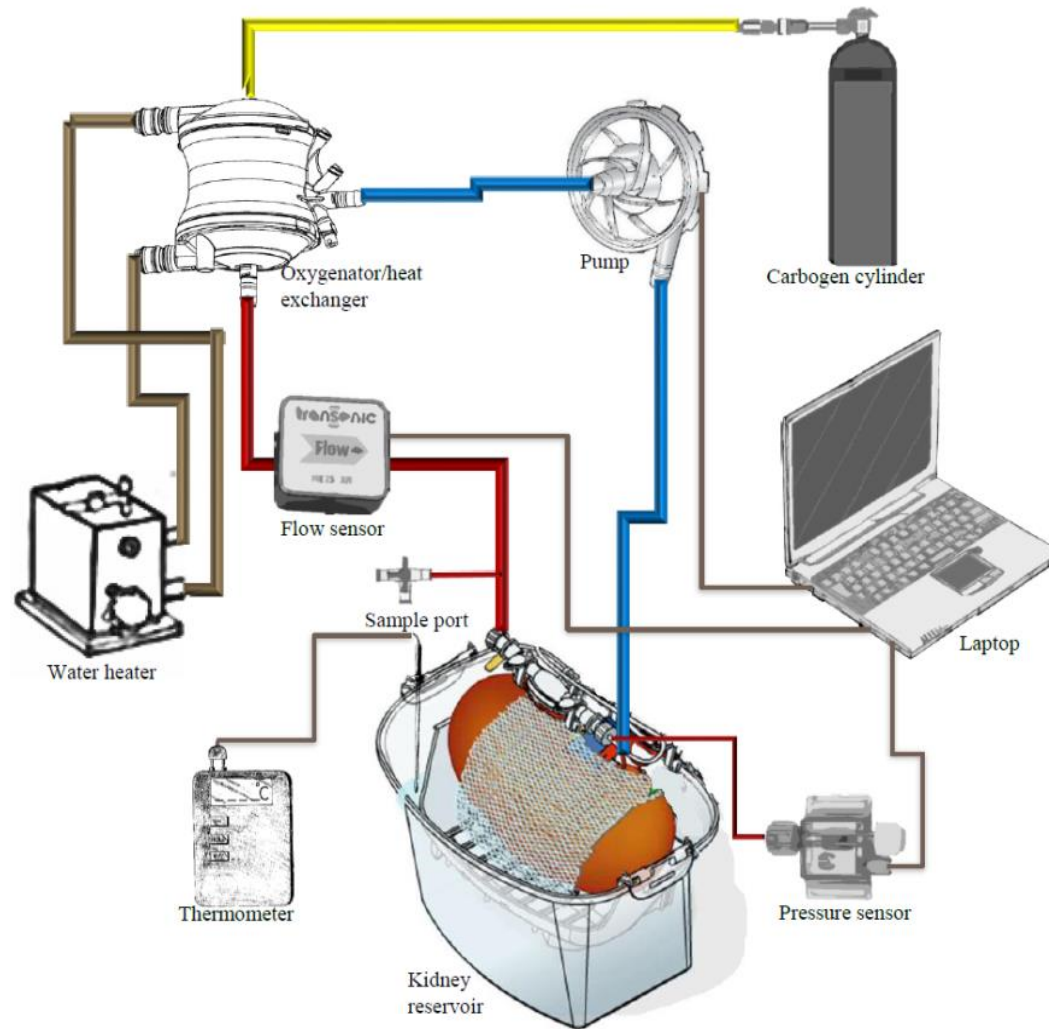


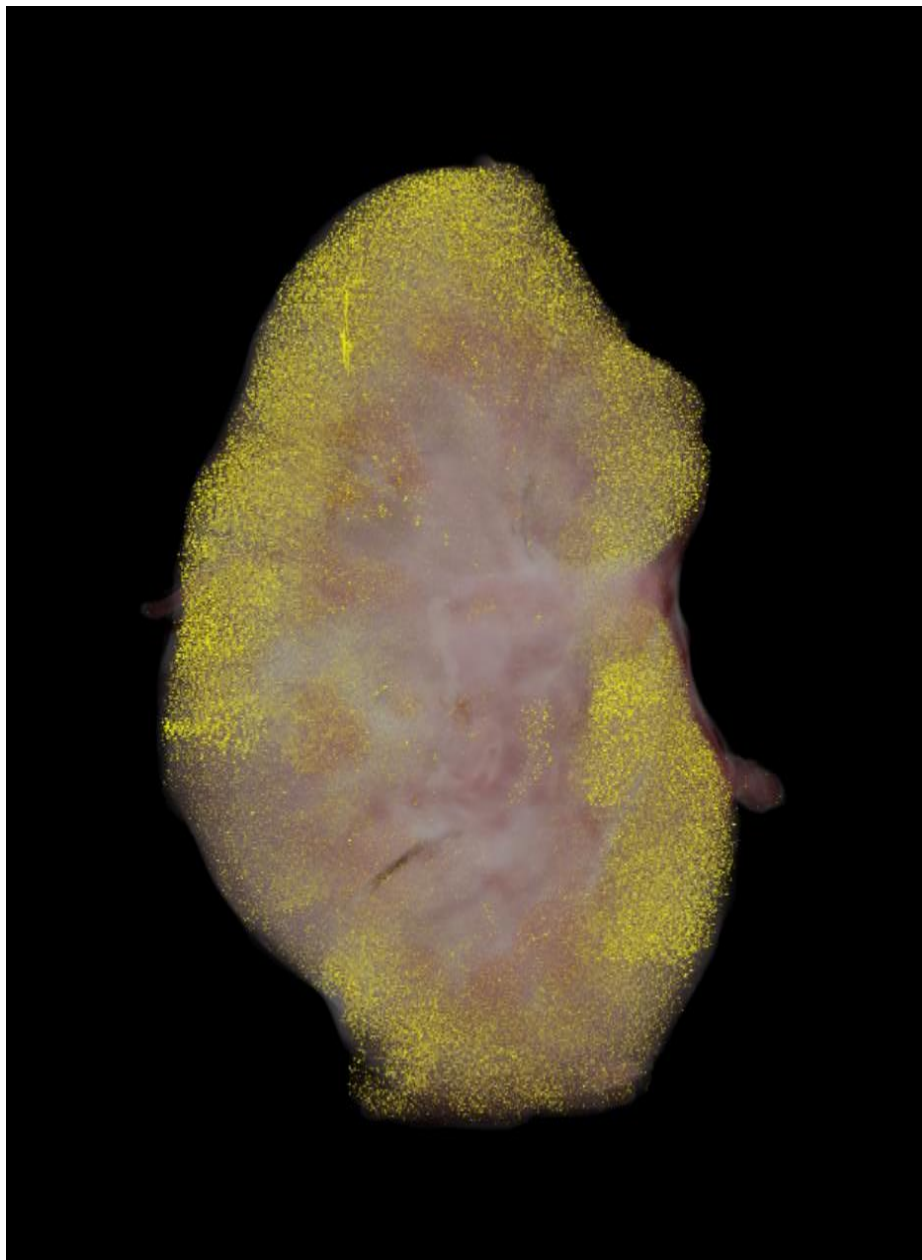
Nu:
nier bewaard in machine

Erasmus MC

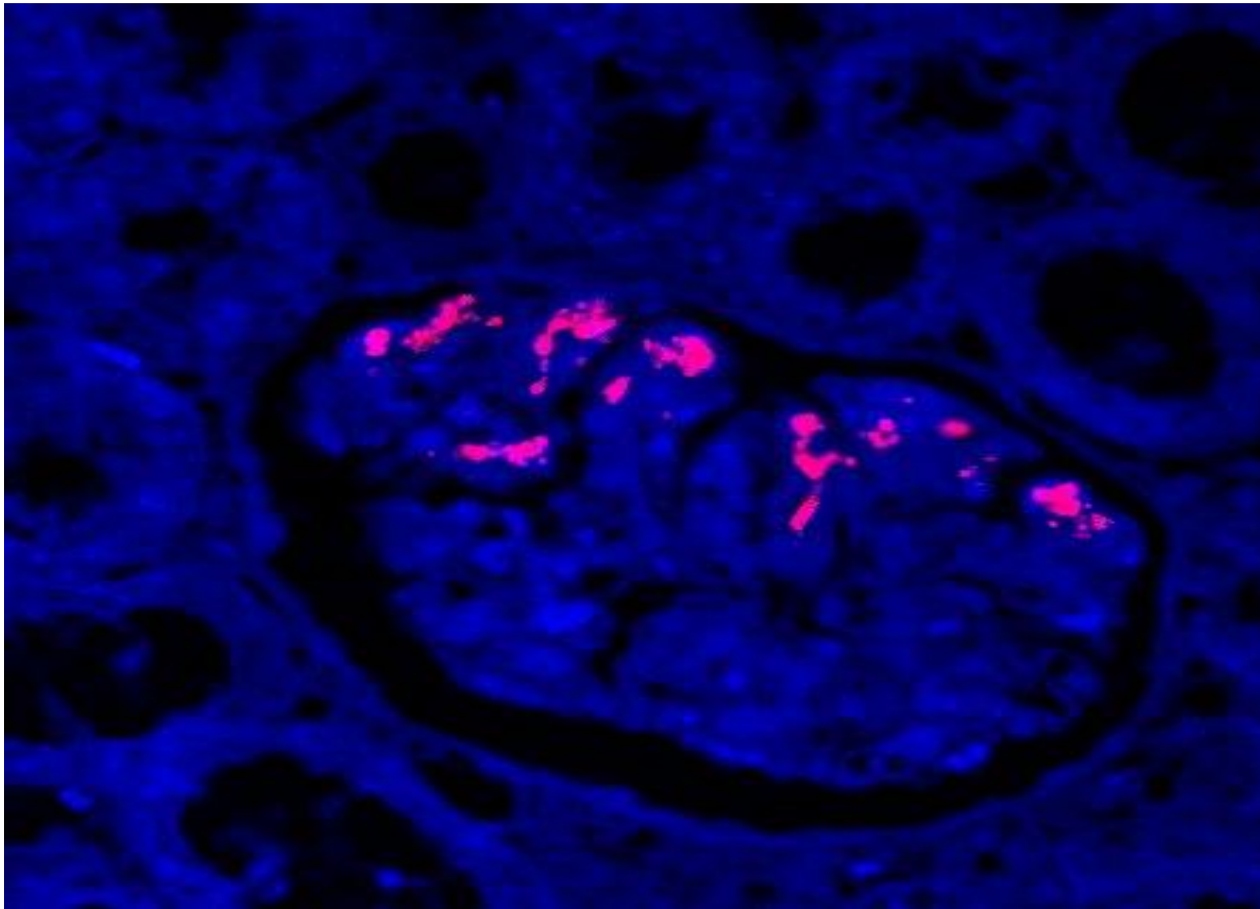


Toediening van stamcellen aan transplantatie nieren





Toegediende stamcellen verzamelen zich in de filtratie units van de nier



Klinische trial met stamcellen in niertransplantatie patienten

GOALS

- Reduction of IRI
- Prevention and/or reversal of acute rejection
- Improvement of long term graft survival with minimization of immune suppression
- Reversal/stabilization of IFTA

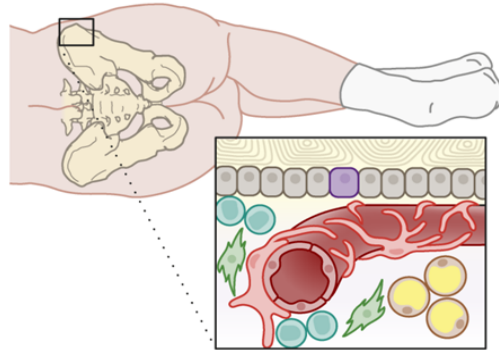
CHALLENGES

- Autologous
- Allogeneic
- Third party
- Dose
- Route
- Timing
- Protocol with concomitant immunosuppression

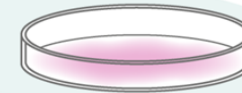
EVALUATION

- Safety/feasibility
- Lab and urinary markers
- Histology
- Immune monitoring
- Biomarkers

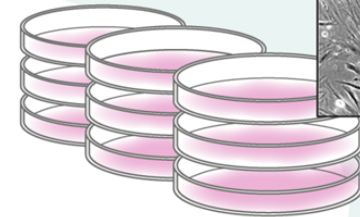
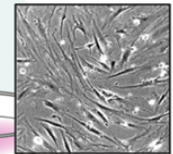
Bone marrow aspiration from spina iliaca



Density gradient



MSCs expansion



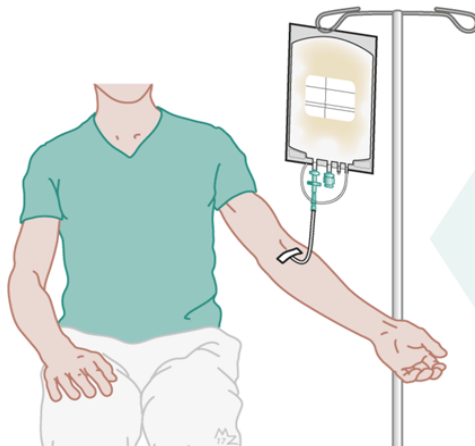
RELEASE CRITERIA
Checked



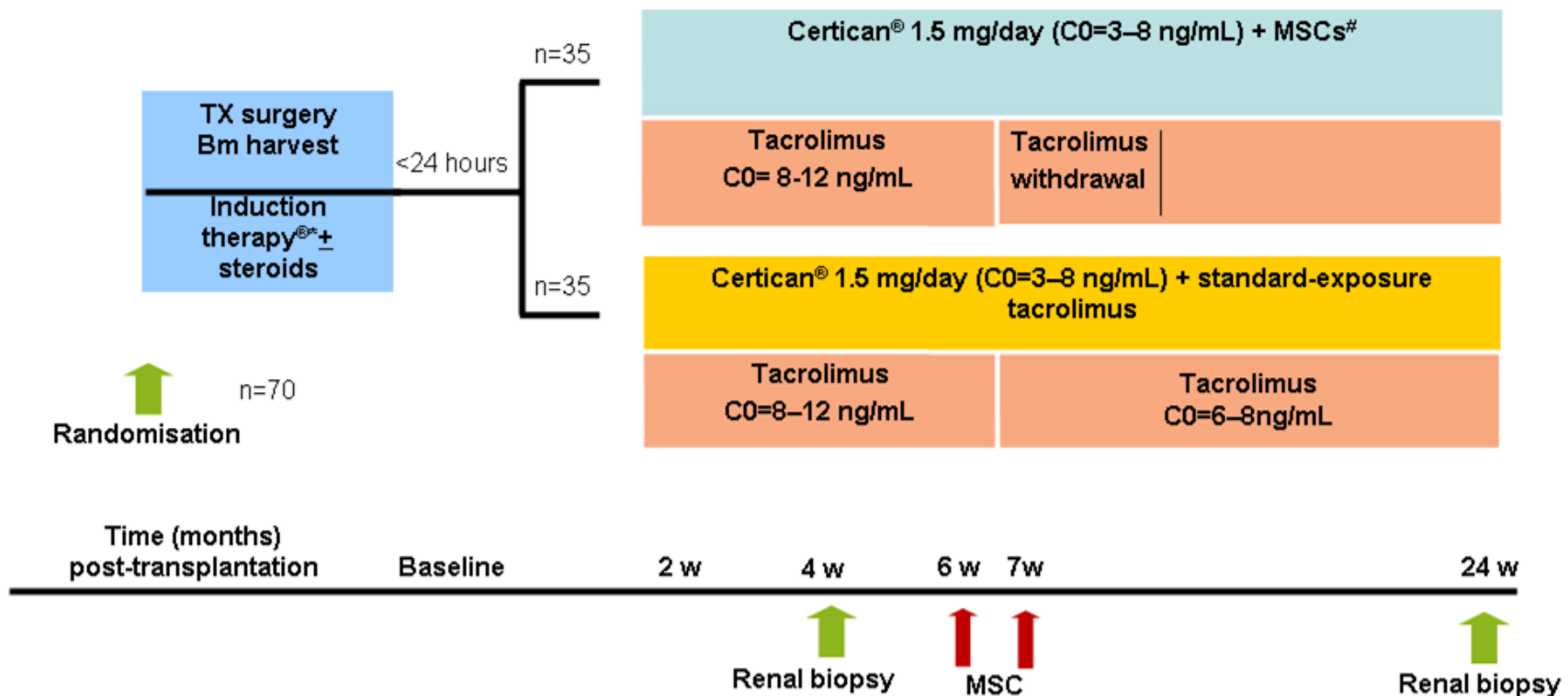
Nitrogen



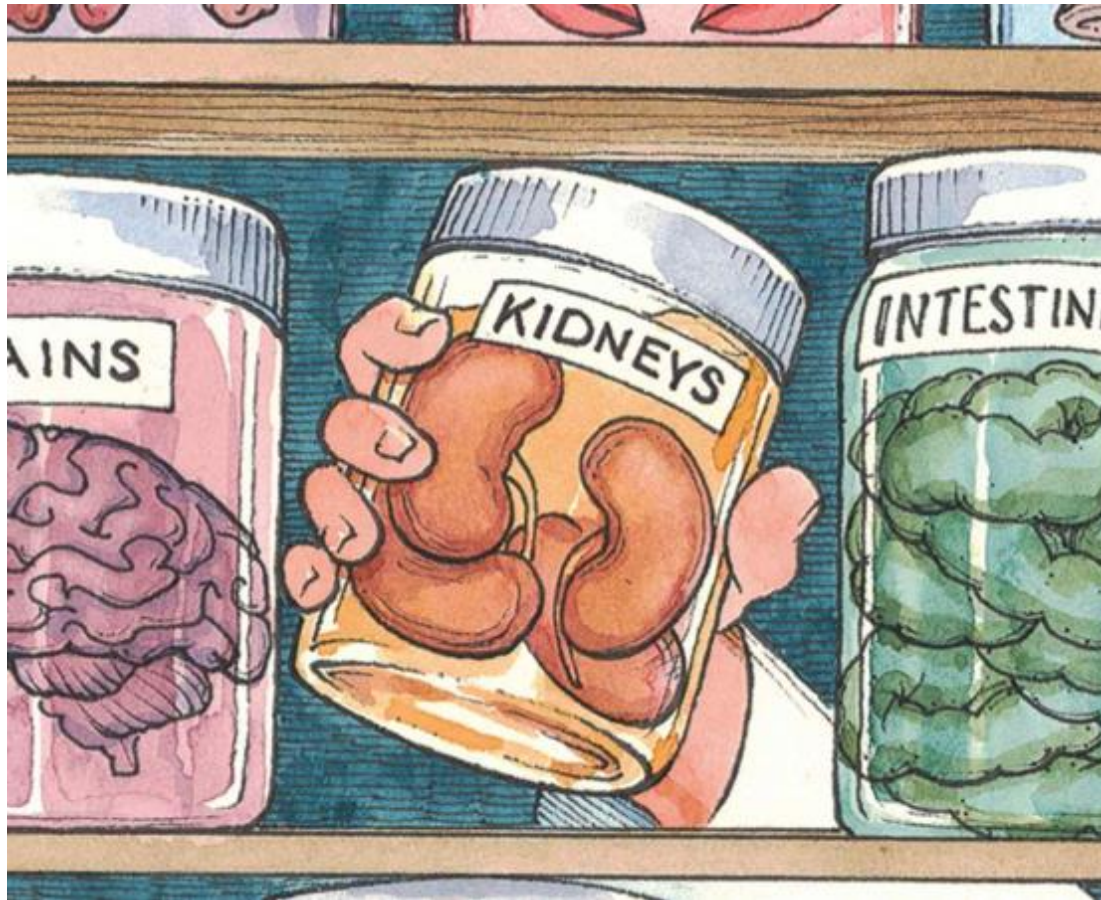
Thawed



Klinische trial met stamcellen in niertransplantatie patienten



Bouwen van nieuwe nieren



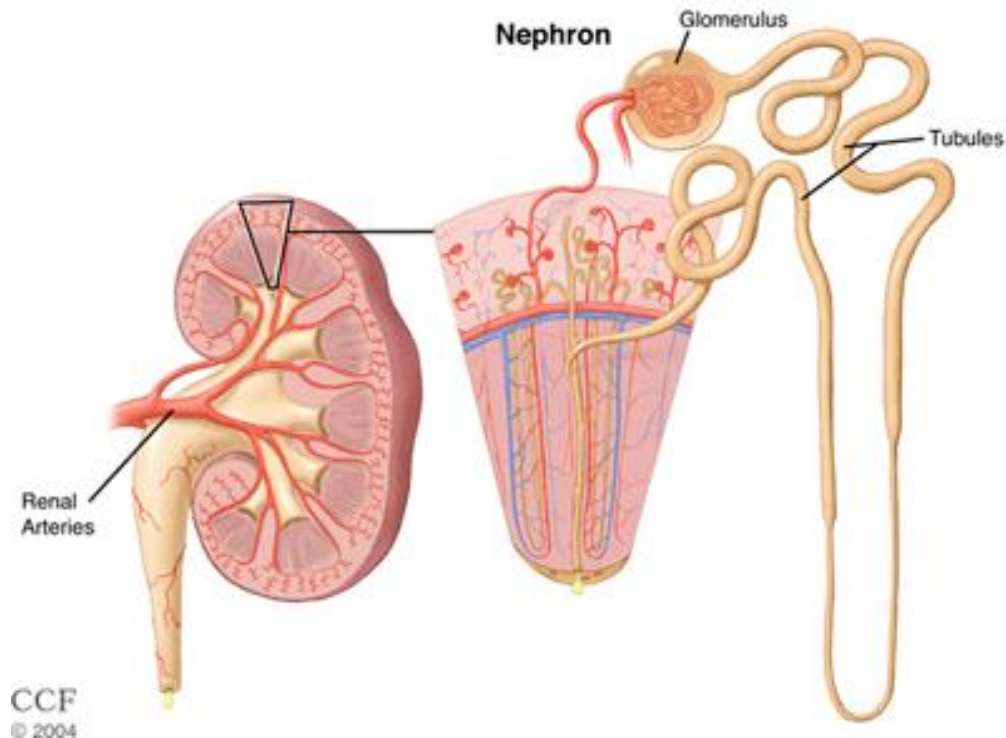
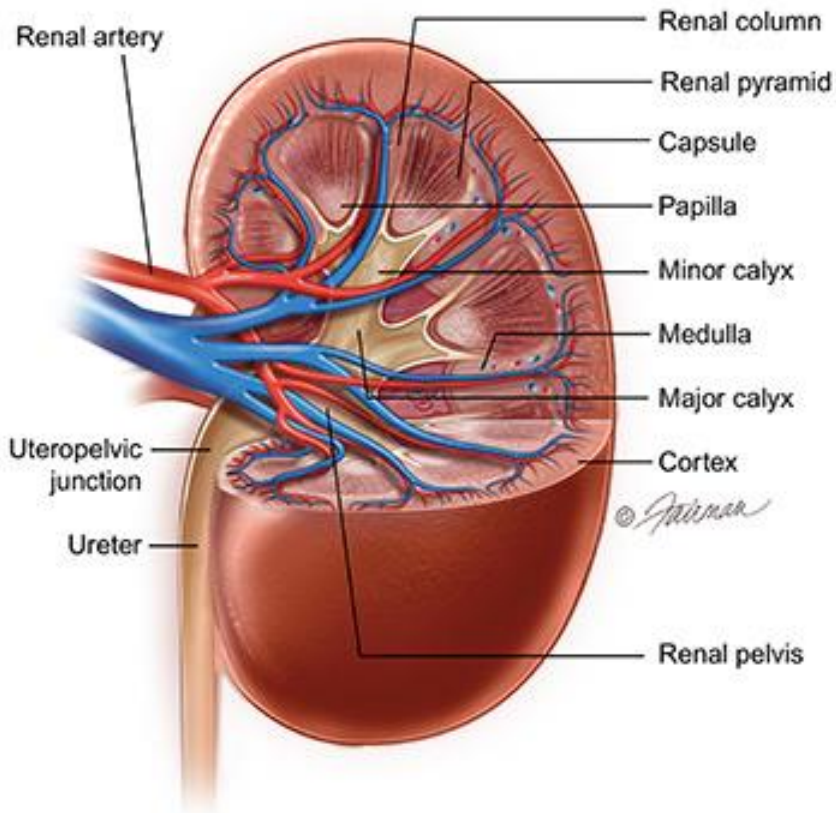
Organoiden

‘Orgaanachtig lichaam’

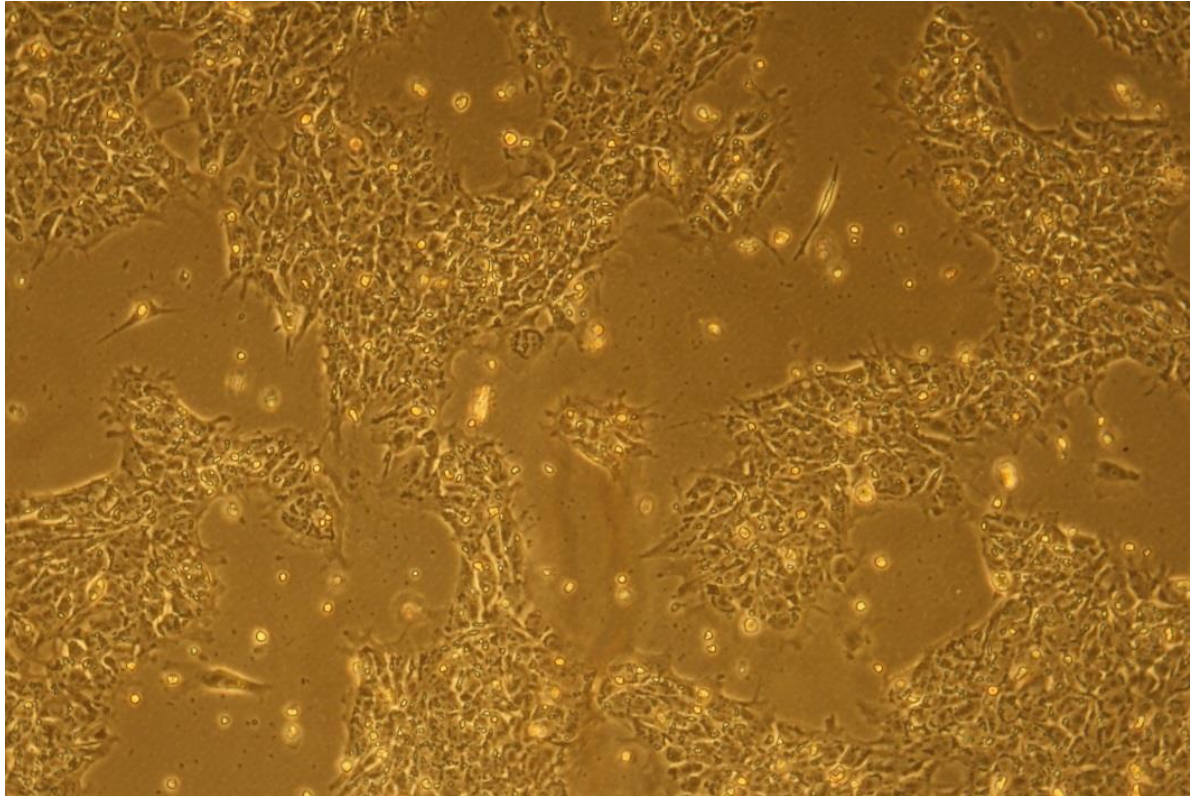
‘Kunstmatig gegroeide op organ lijkende cel massa’



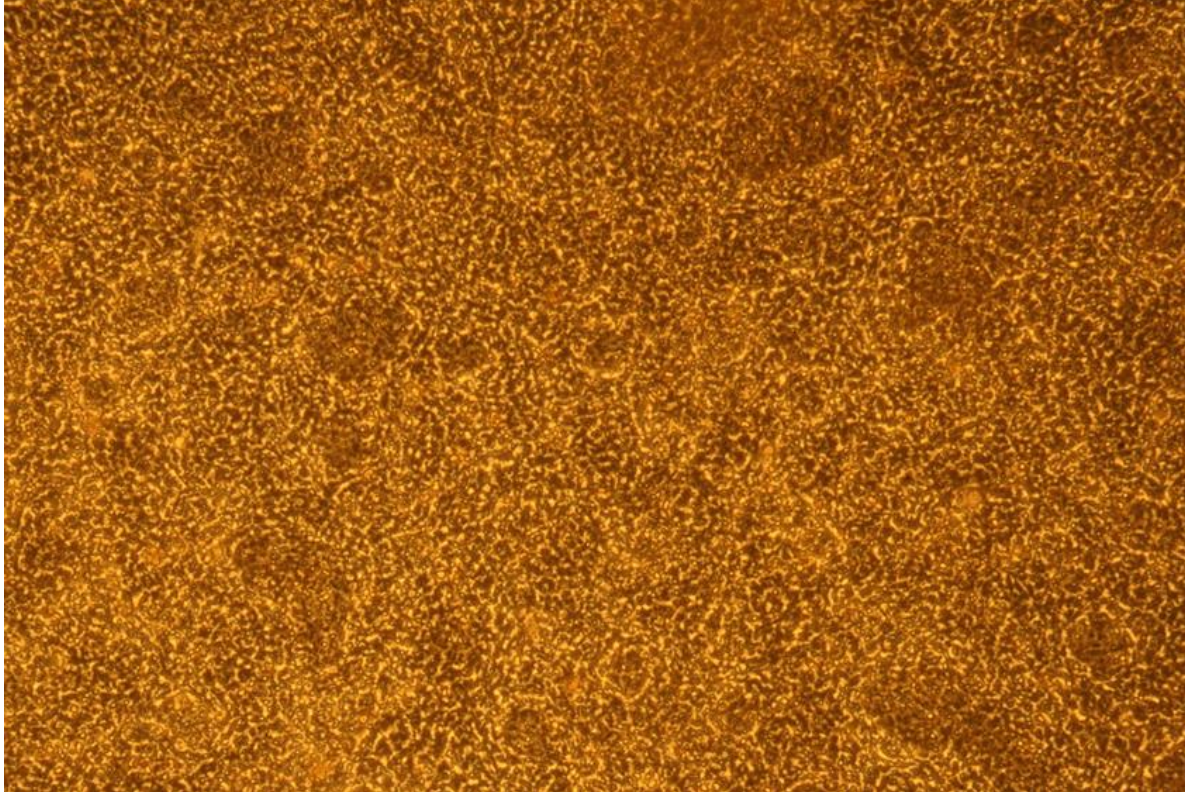
De Nier



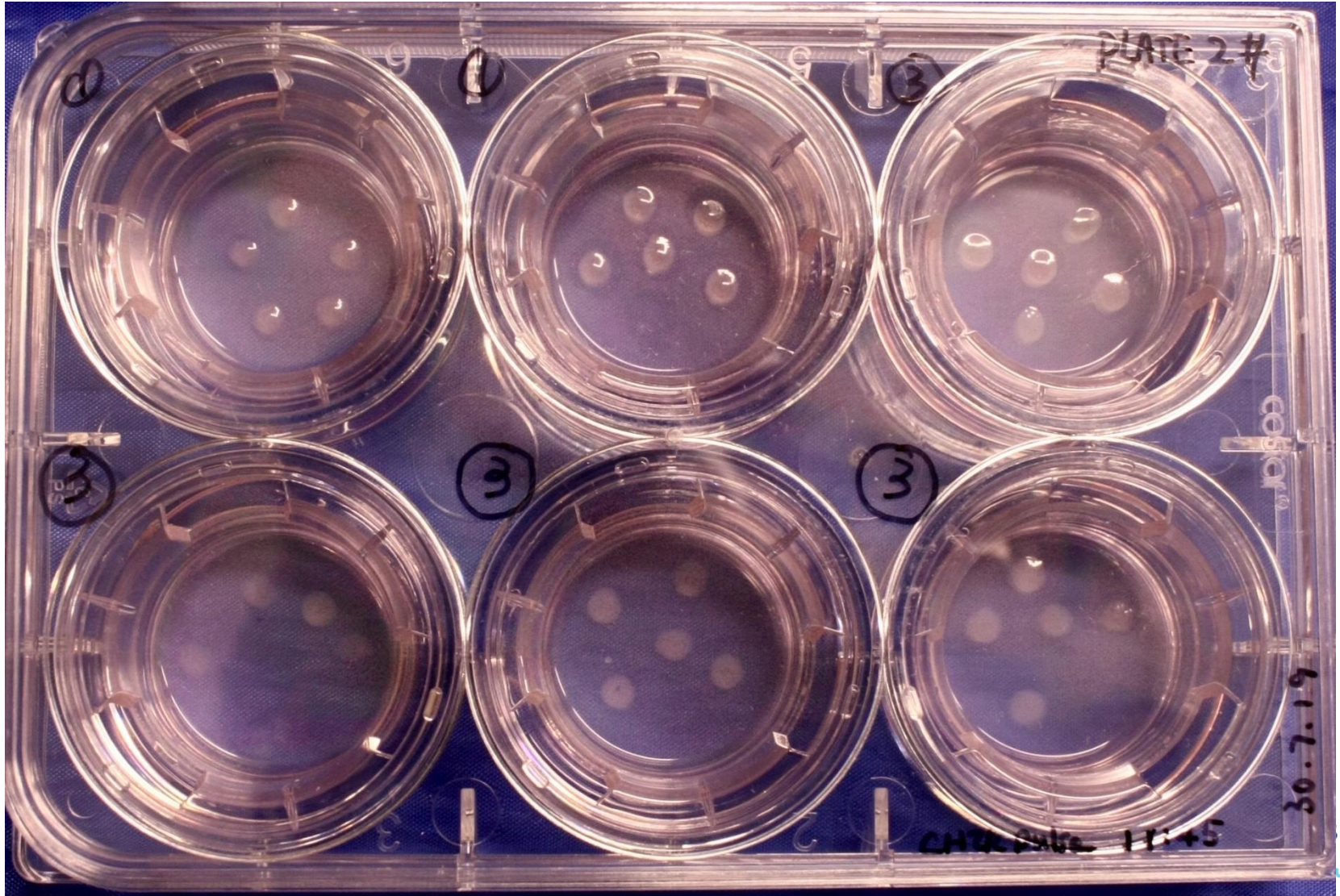
Bouwen van nier organoiden; dag 0



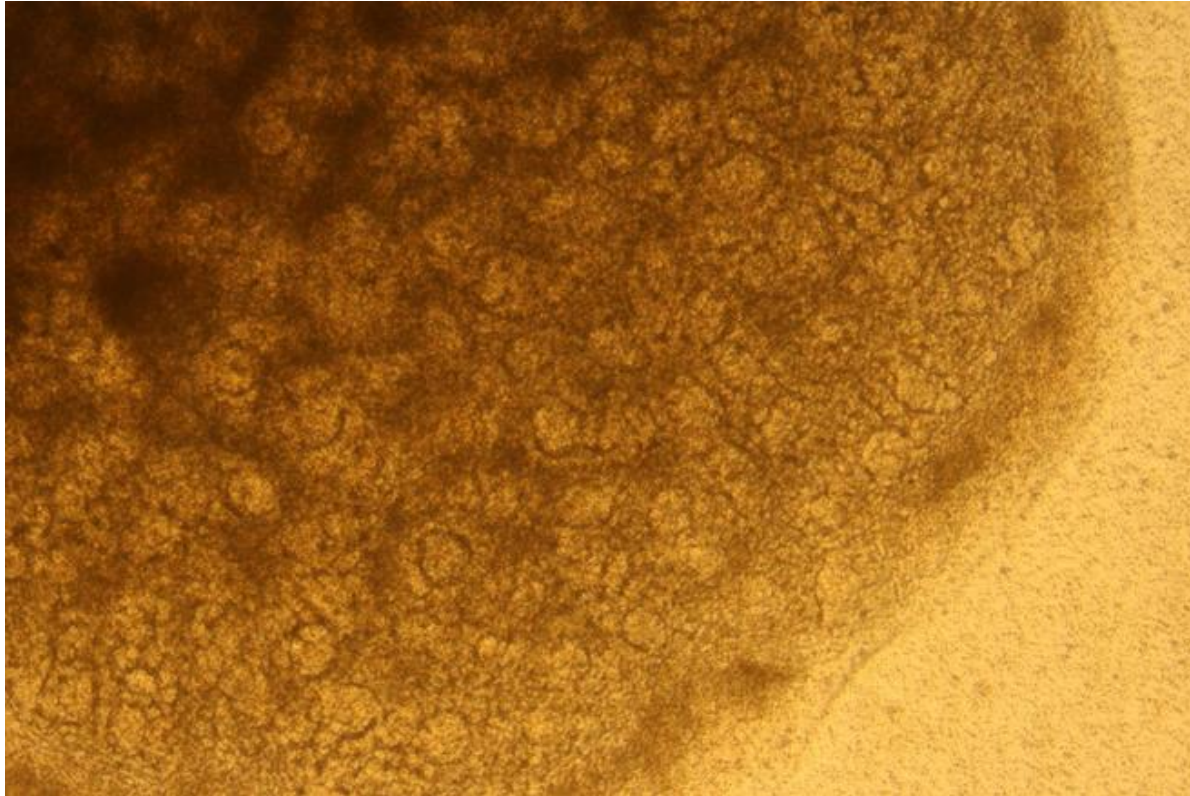
Bouwen van nier organoiden; dag 7



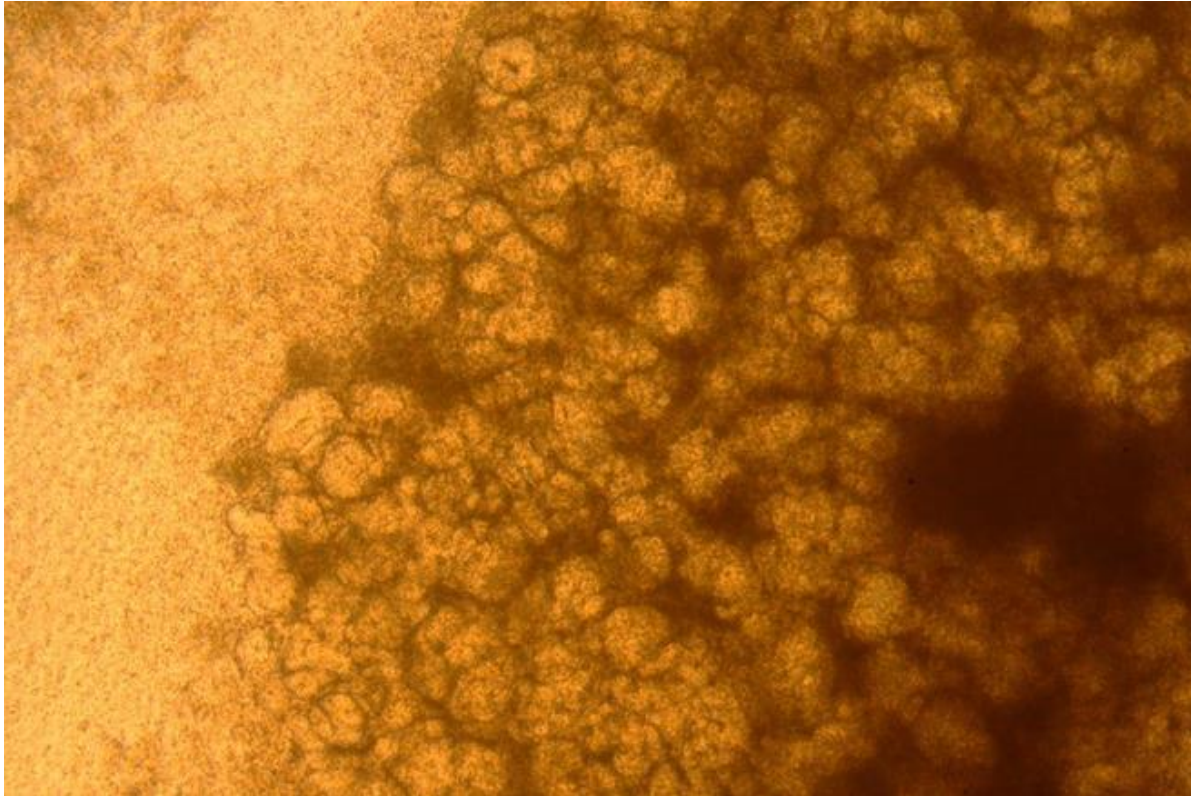
Bouwen van nier organoiden; dag 8



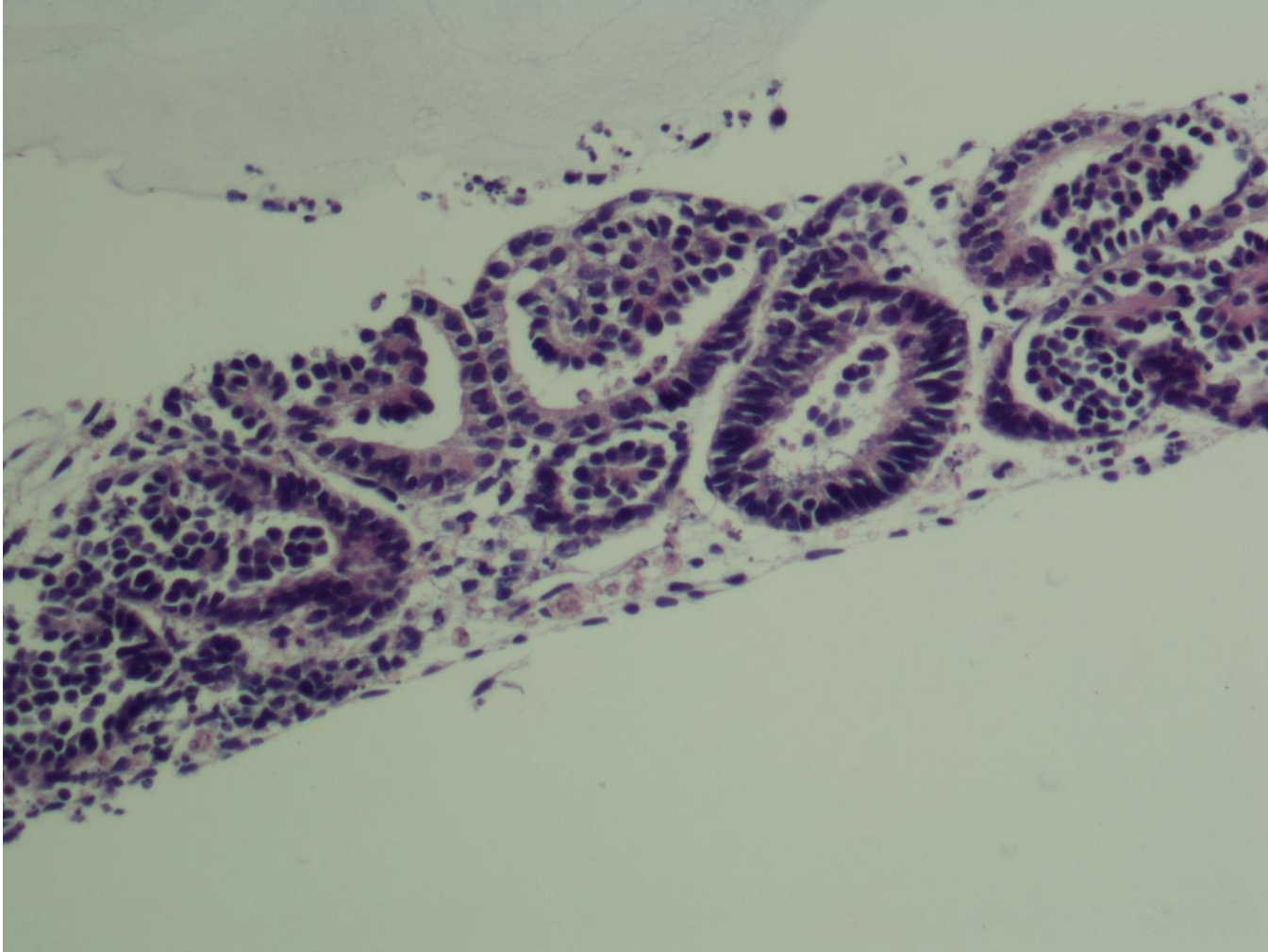
Bouwen van nier organoiden; dag 13



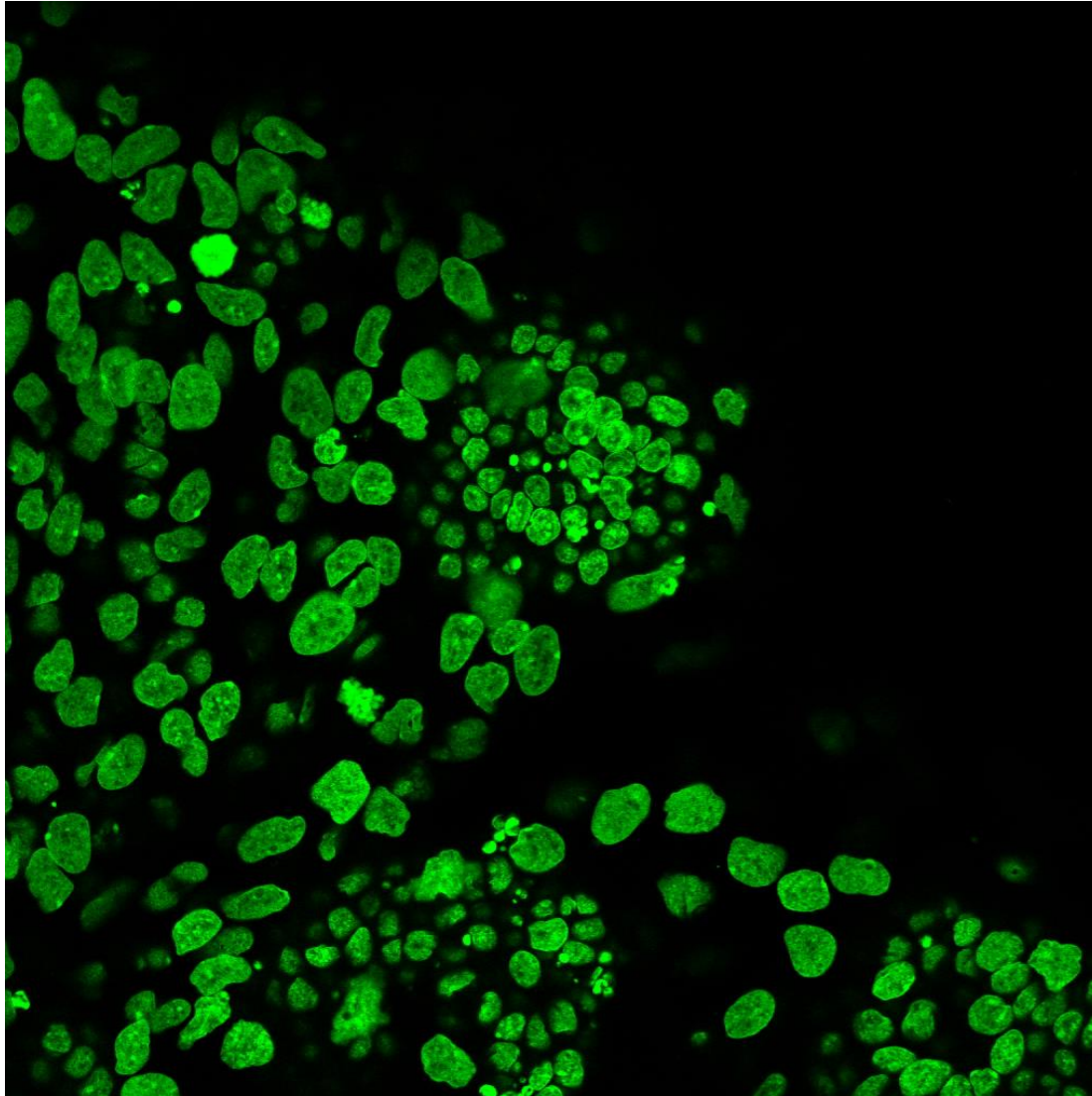
Bouwen van nier organoiden; dag 18



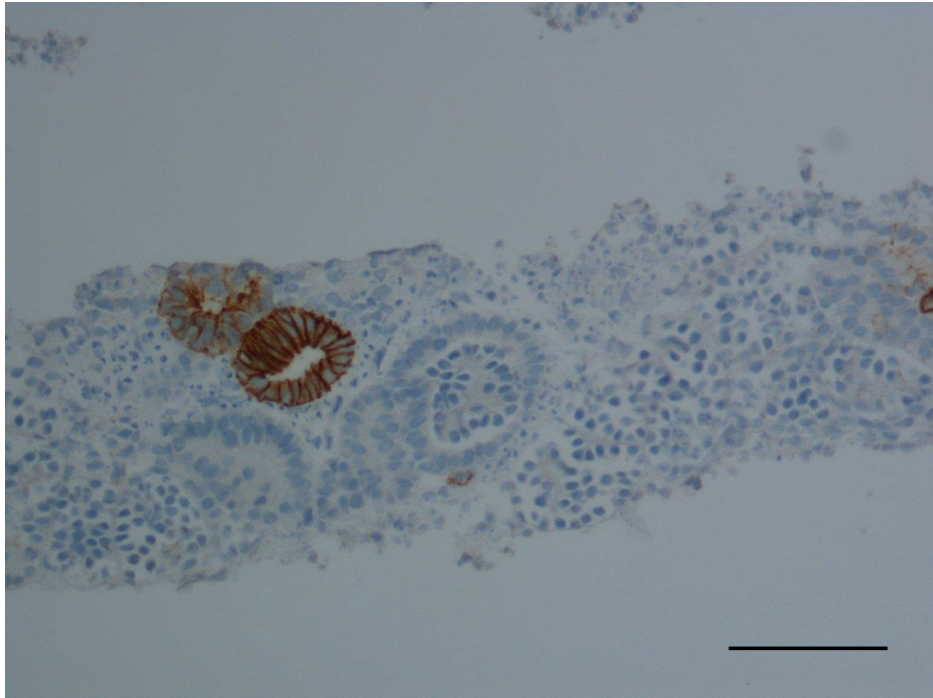
Bouwen van nier organoiden; dag 22



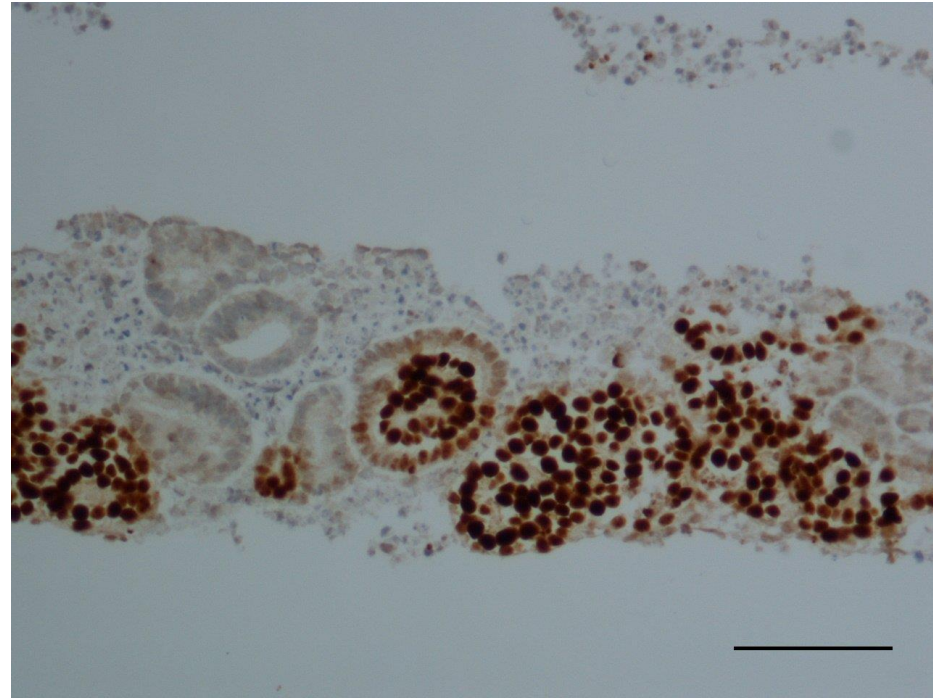
Nier organoide 3D



Filtratie units in nier organoiden

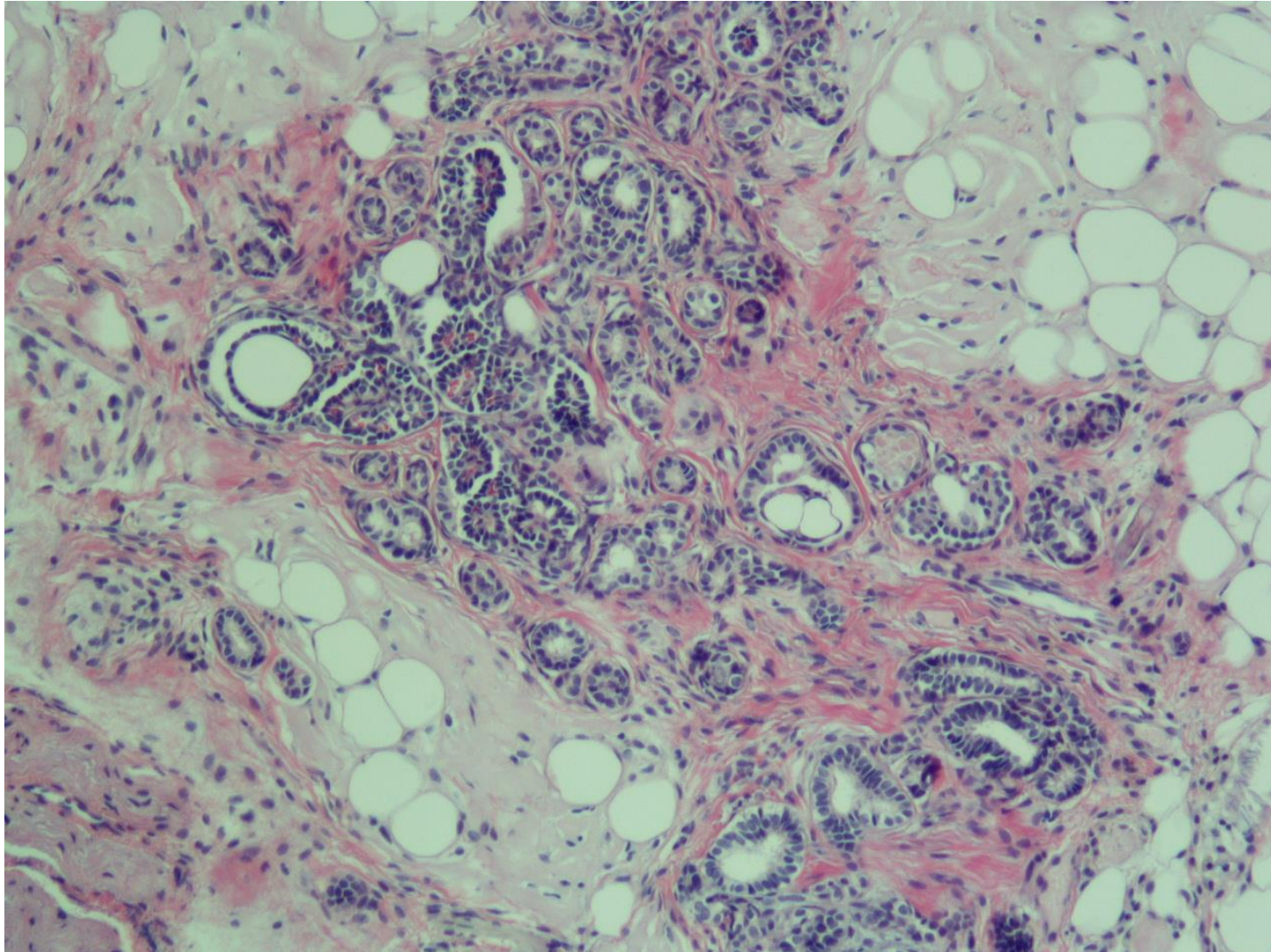


ECAD proximal tubular staining

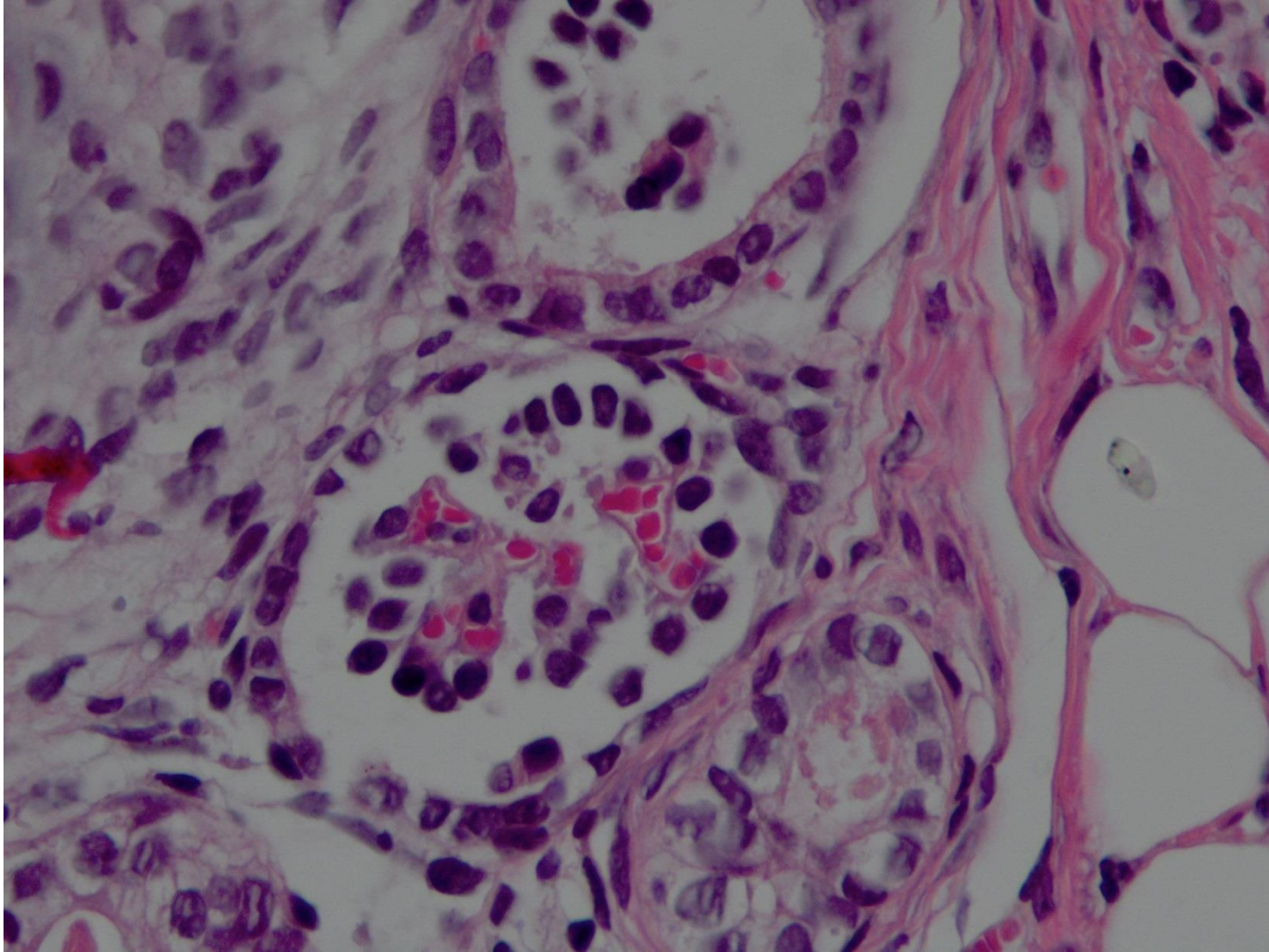


WT1 glomerular staining

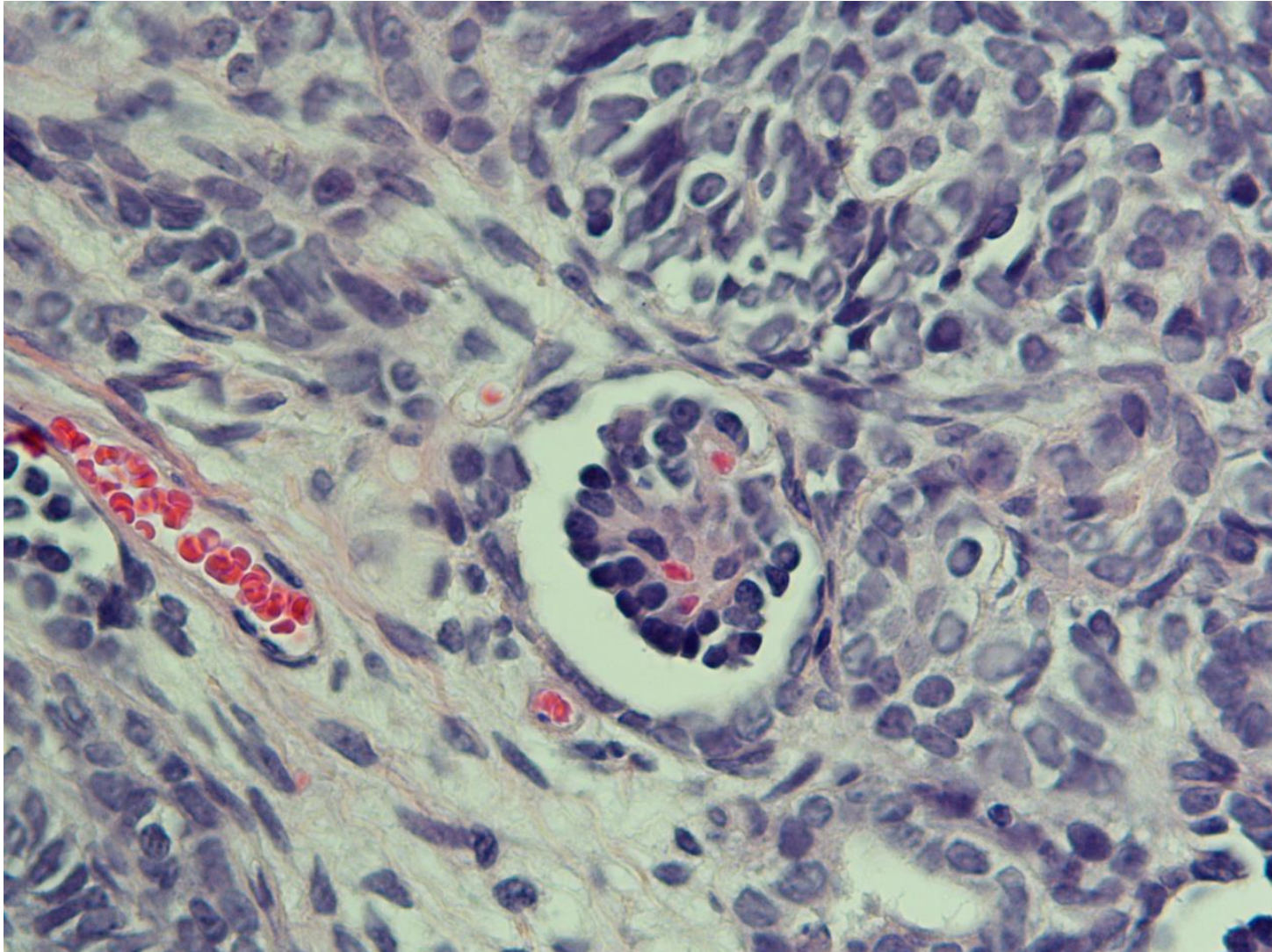
Implantatie van nier organoiden



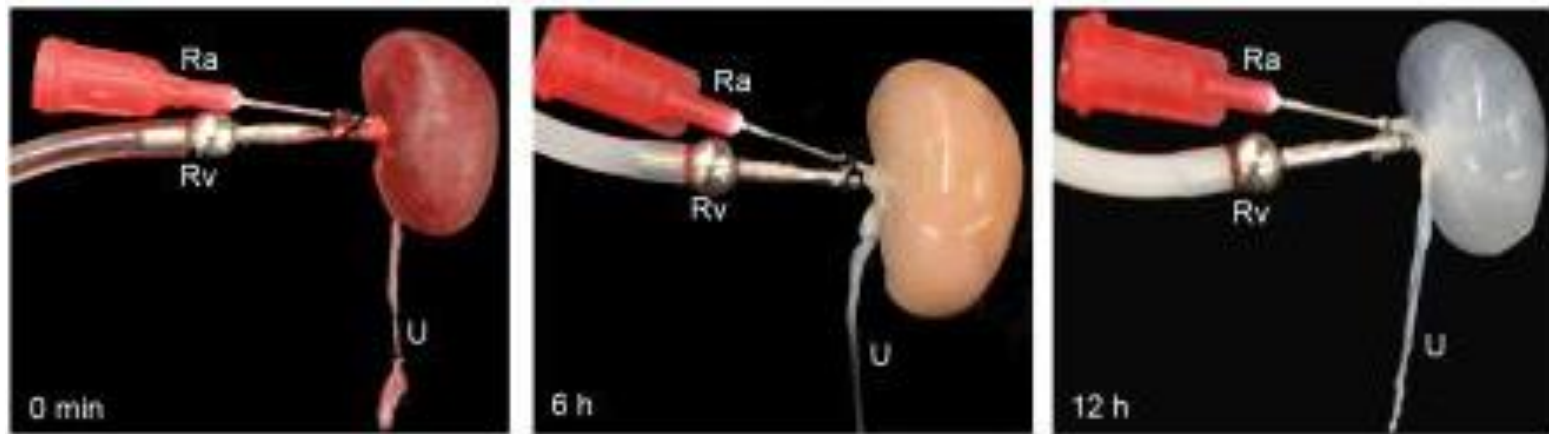
Implantatie van nier organoiden



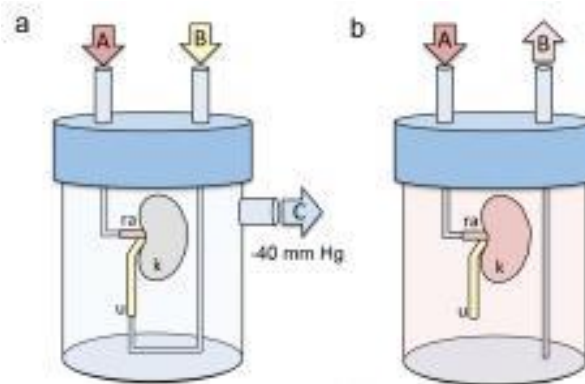
Implantatie van nier organoiden



Oude nier als 'mal' voor stamcellen



Decellularisatie en recellularisatie van de nier



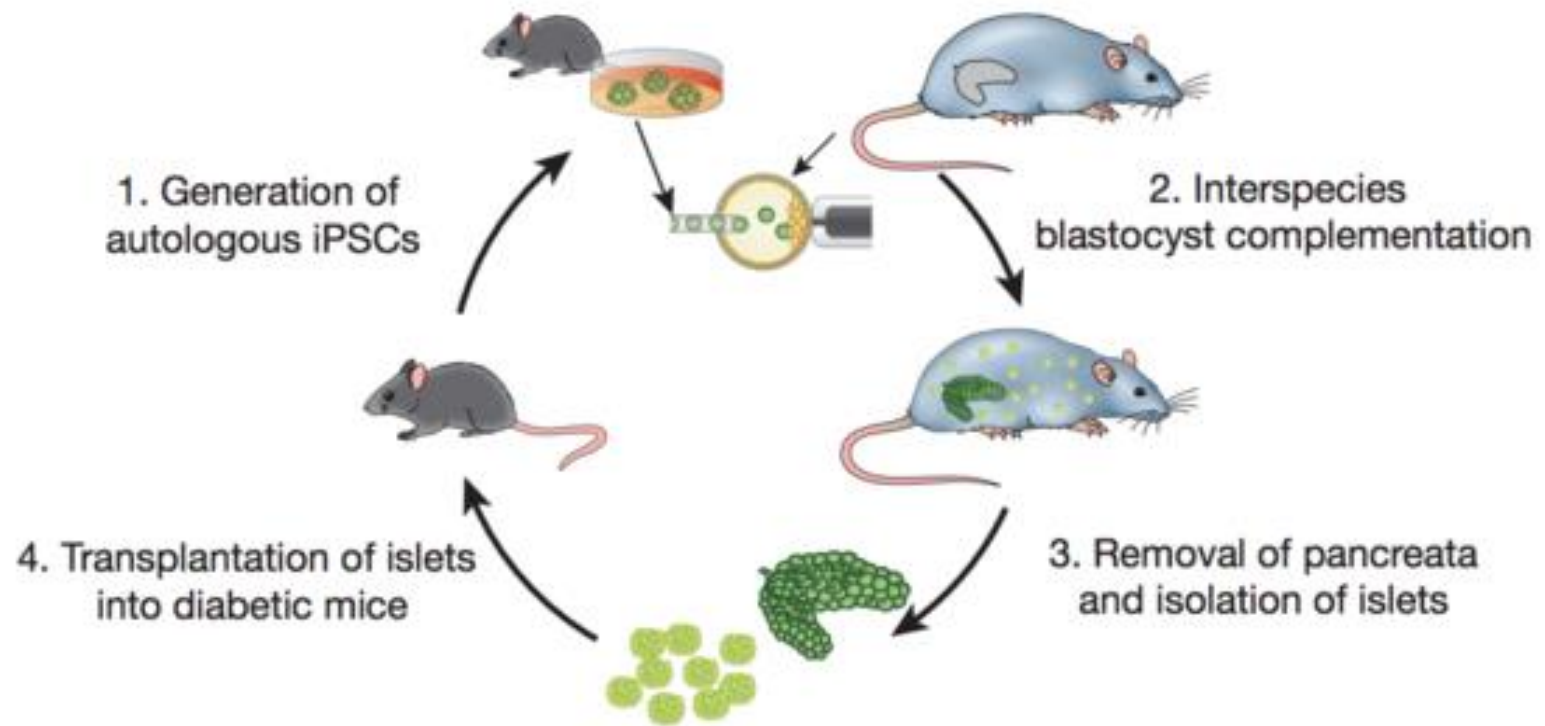
Scientists Grow Mouse Organs Inside Rats, Then Transplant Them Into Mice

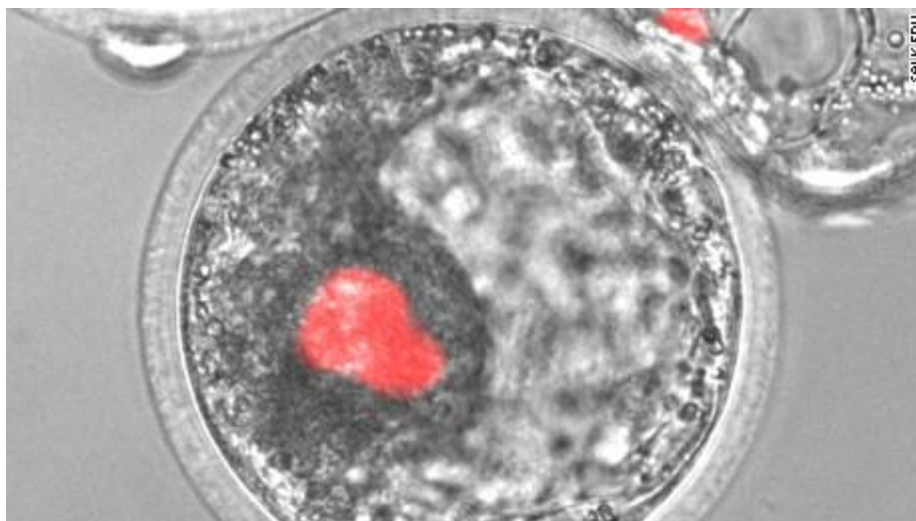
BY KATE HOROWITZ

JANUARY 25, 2017

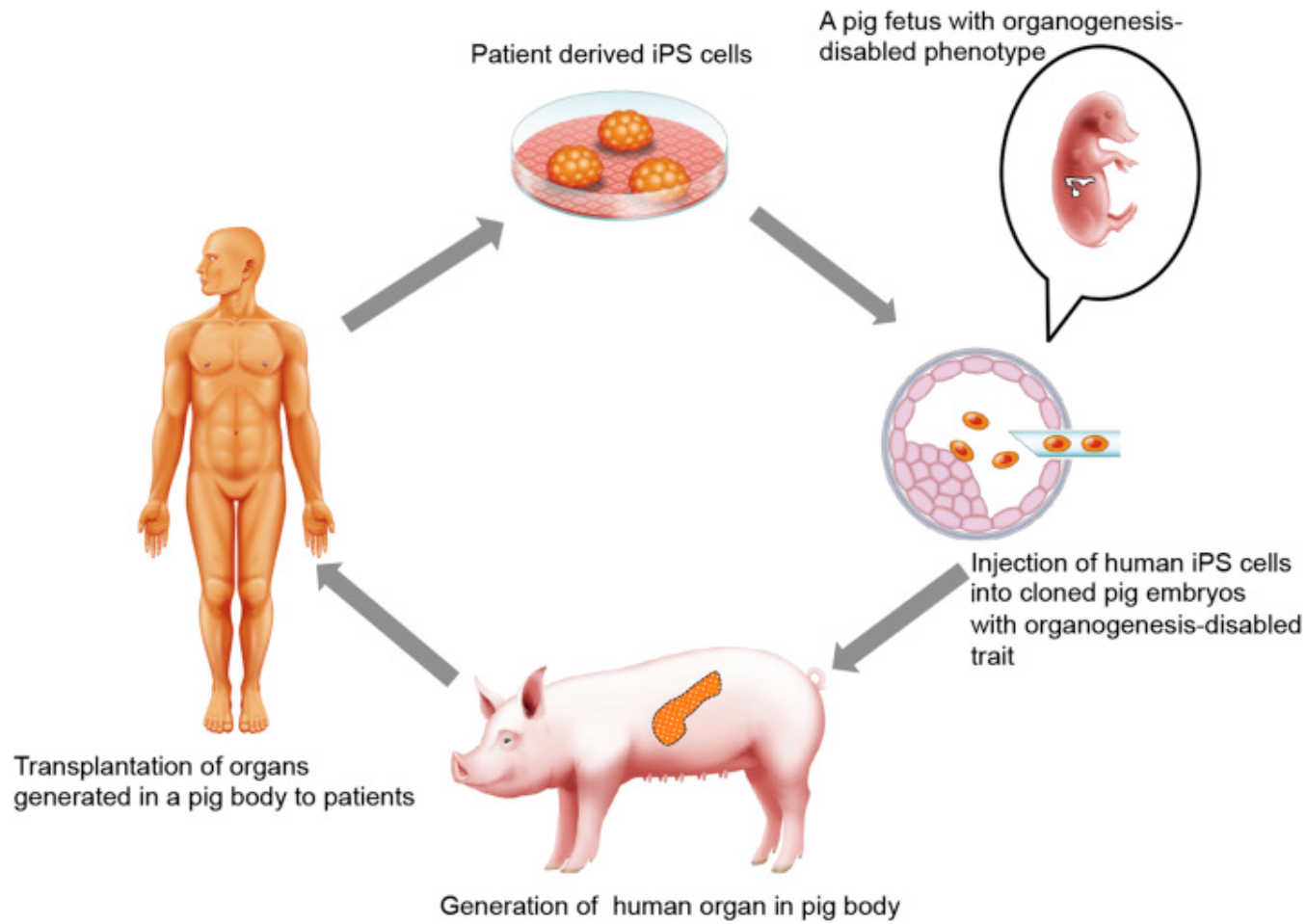


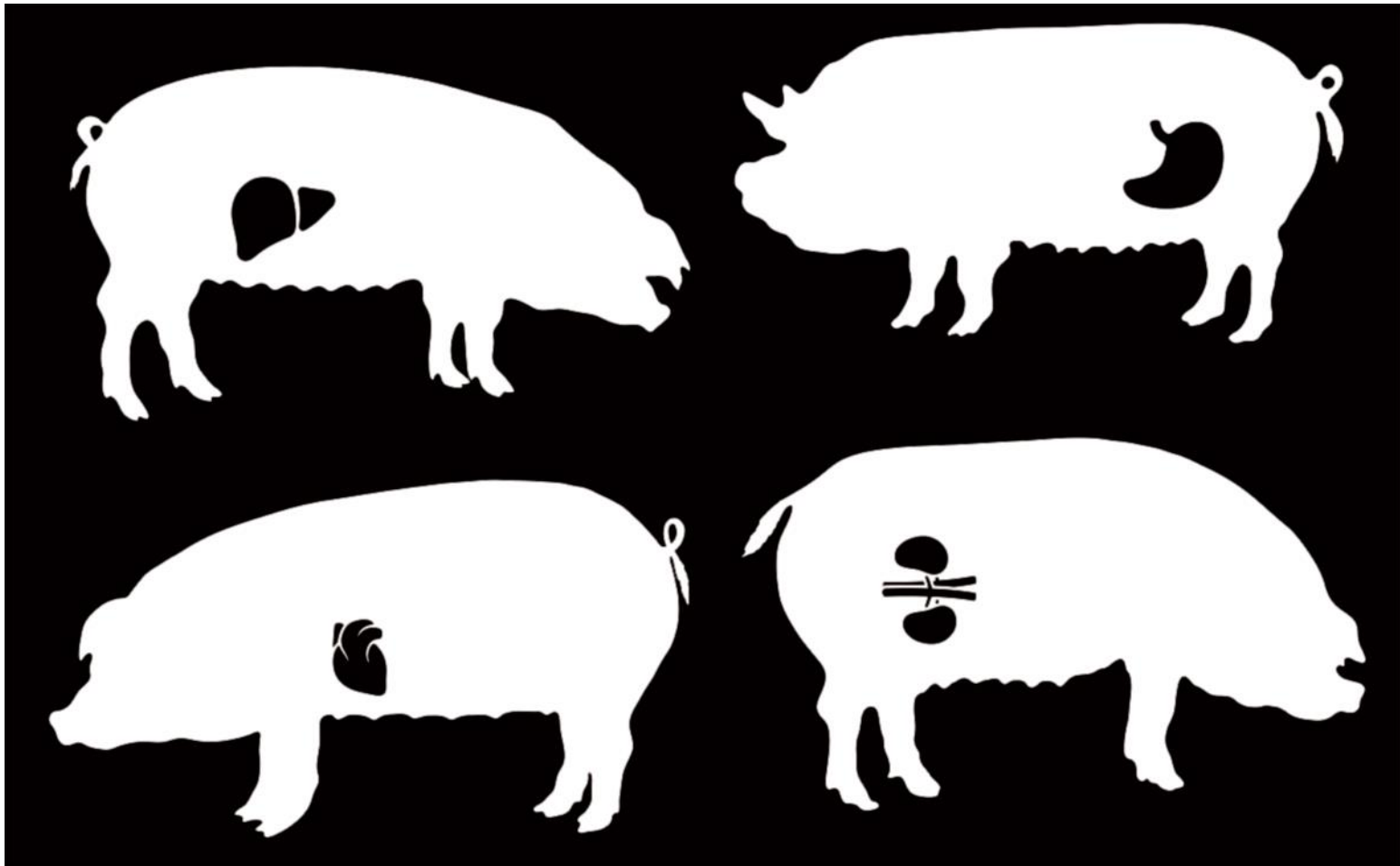






Bouwen van menselijke nieren in varken





De toekomst

Herstel van slechte kwaliteit donor nieren

Behandeling van patiënten met stamcel toediening

Ontwikkeling van organoiden voor nier herstel

Creëren van menselijke nieren in varkens

Bouwen van gehele menselijke nieren in het laboratorium