

Organoiden en Personalized Medicine



Clevers Lab|Digizyme

Hans Clevers 2016

Veroudering.
Onze cellen lopen schade op en verslijten



Dit gebeurt in alle
weefsels, bijvoorbeeld
ook in onze spieren

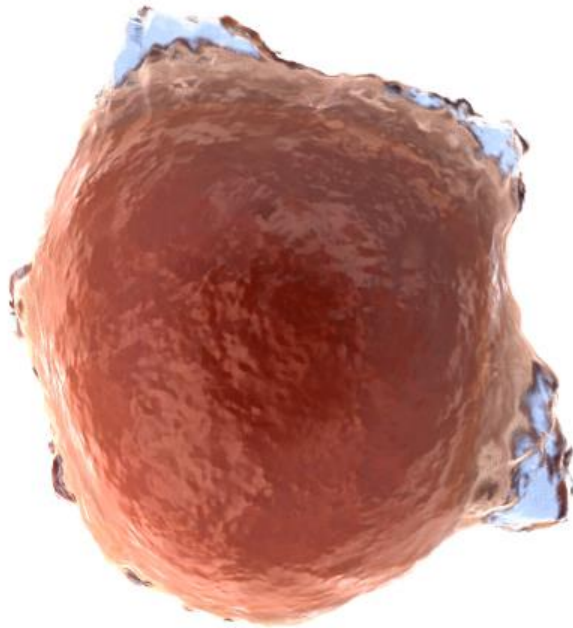
THEN



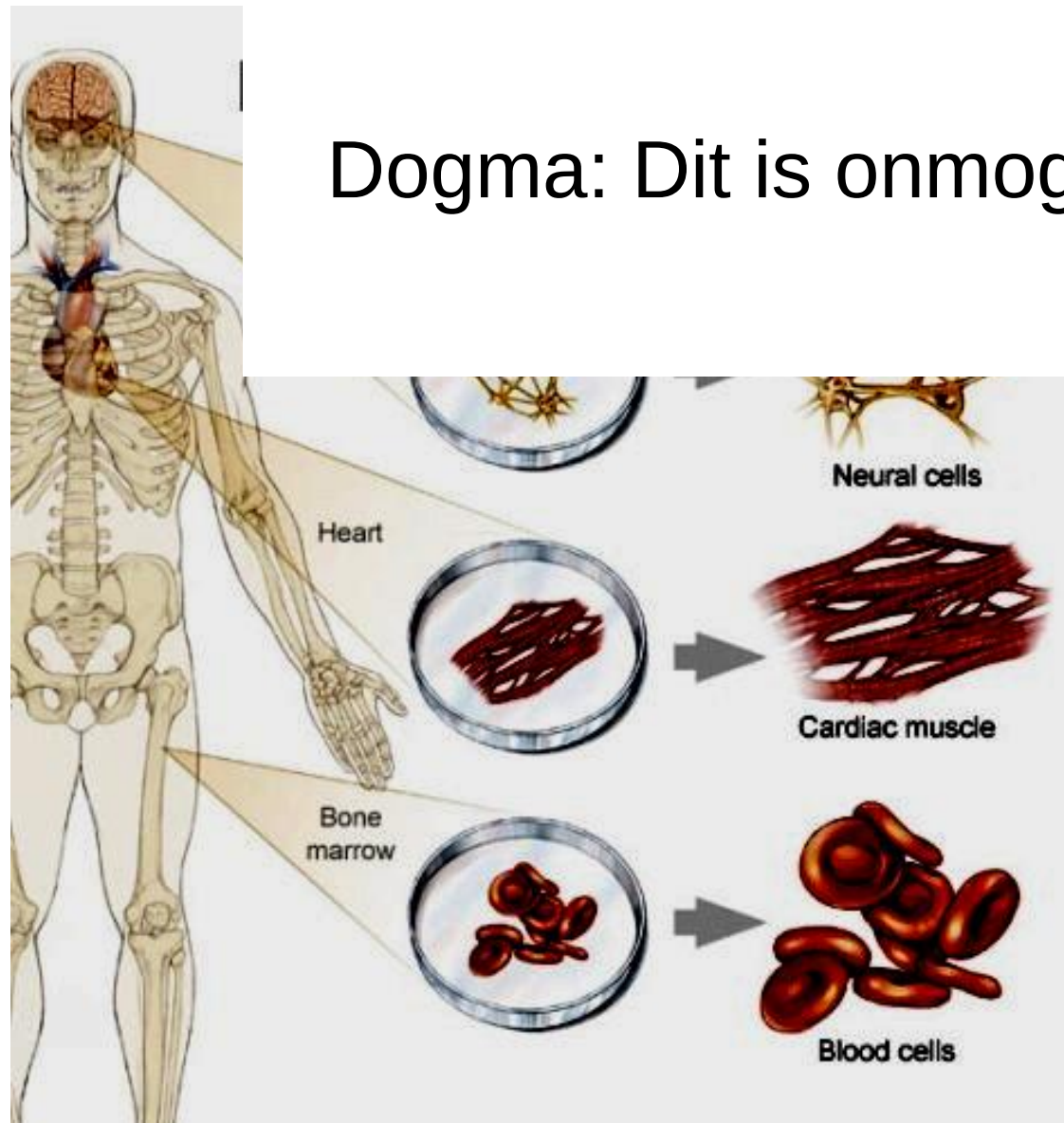
NOW

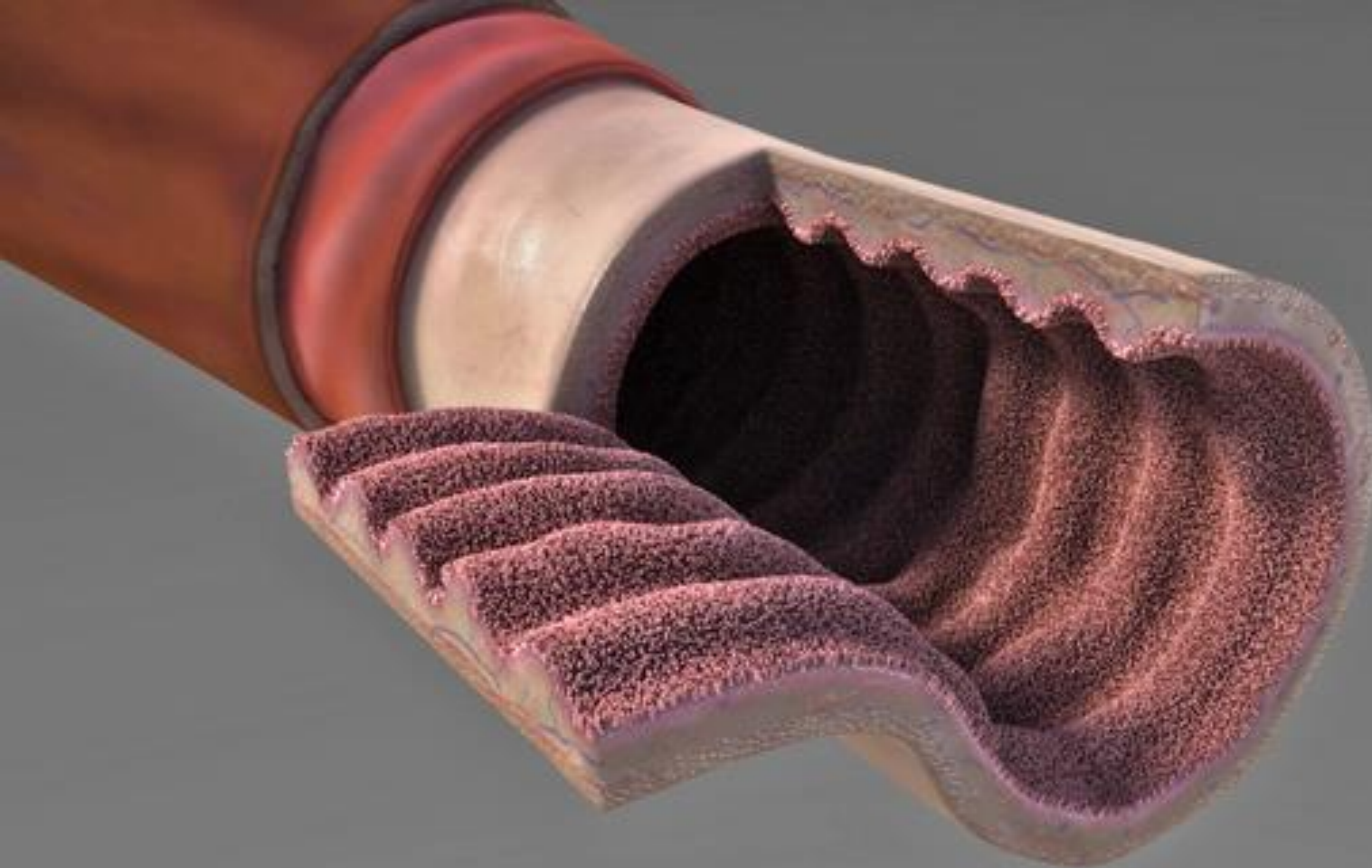


De natuur heeft hier wat op gevonden:
Versleten of beschadigde cellen worden vervangen
door jonge cellen, geproduceerd door stamcellen.



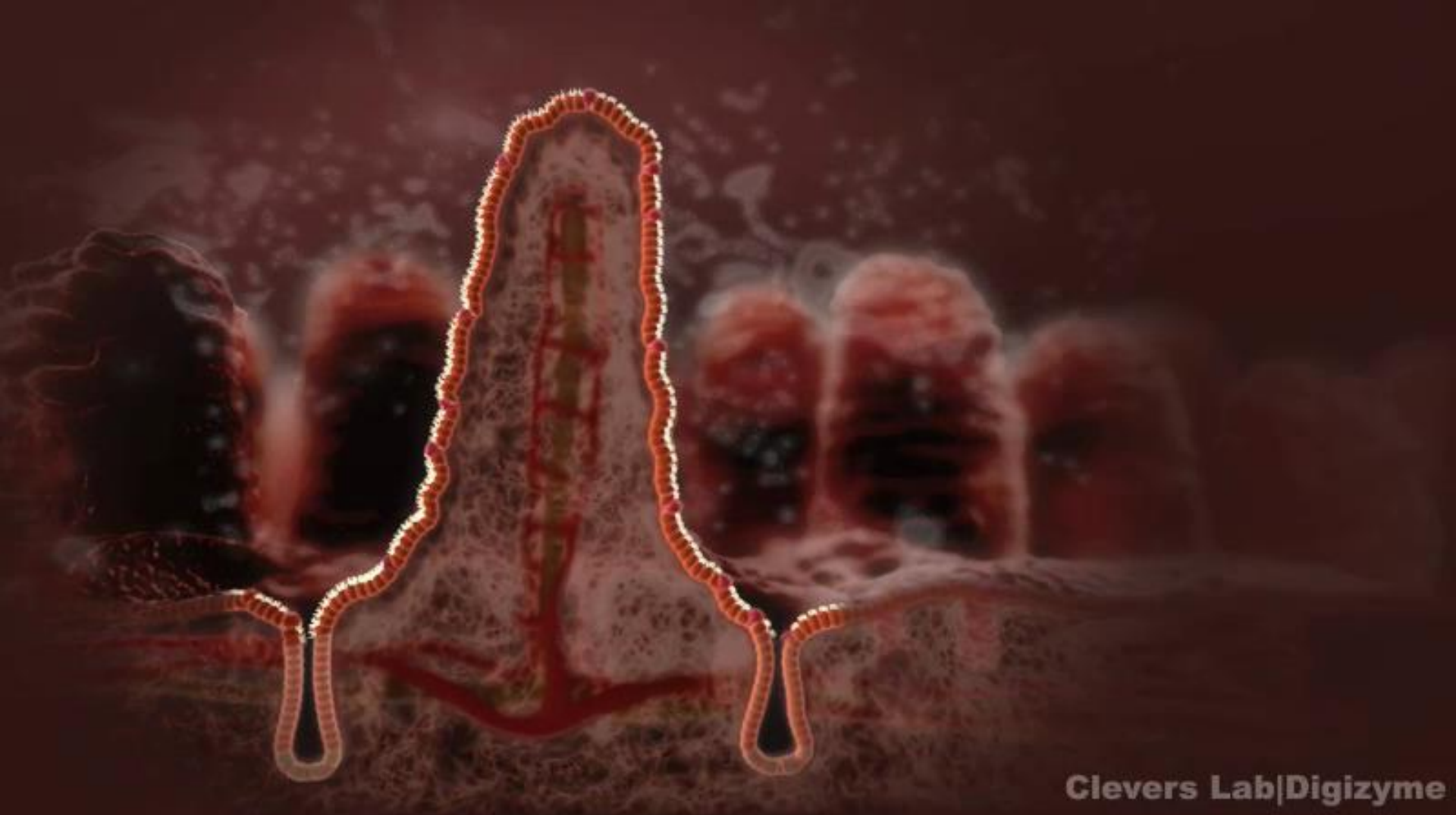
Dogma: Dit is onmogelijk





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De kampioen van alle stamcellen zit in de darm



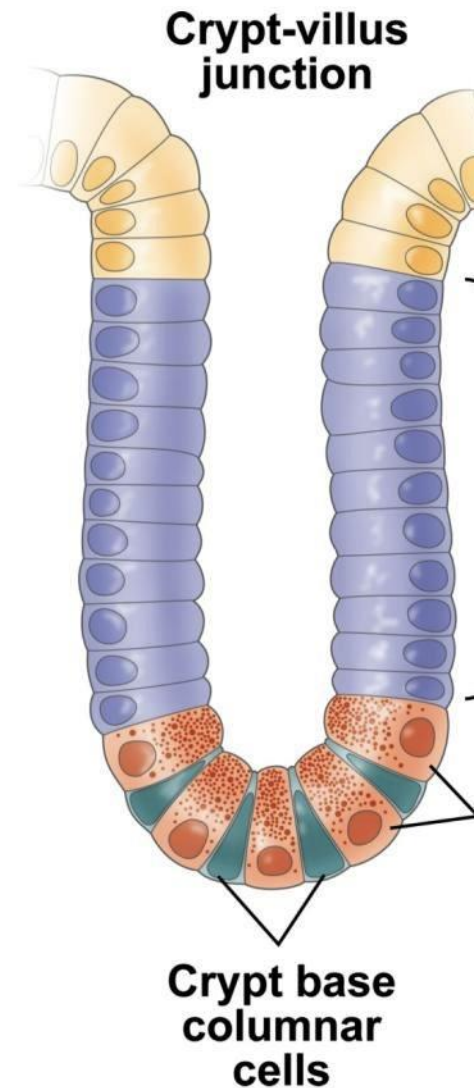
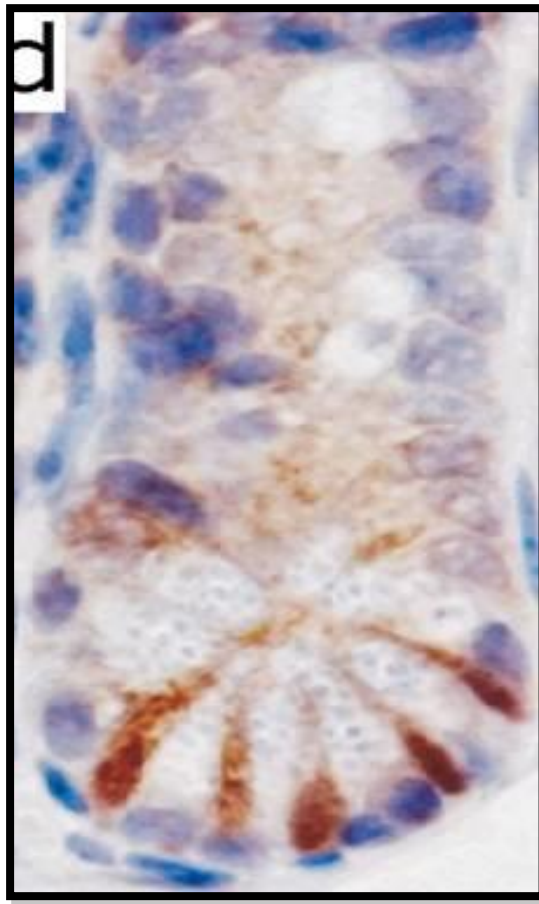
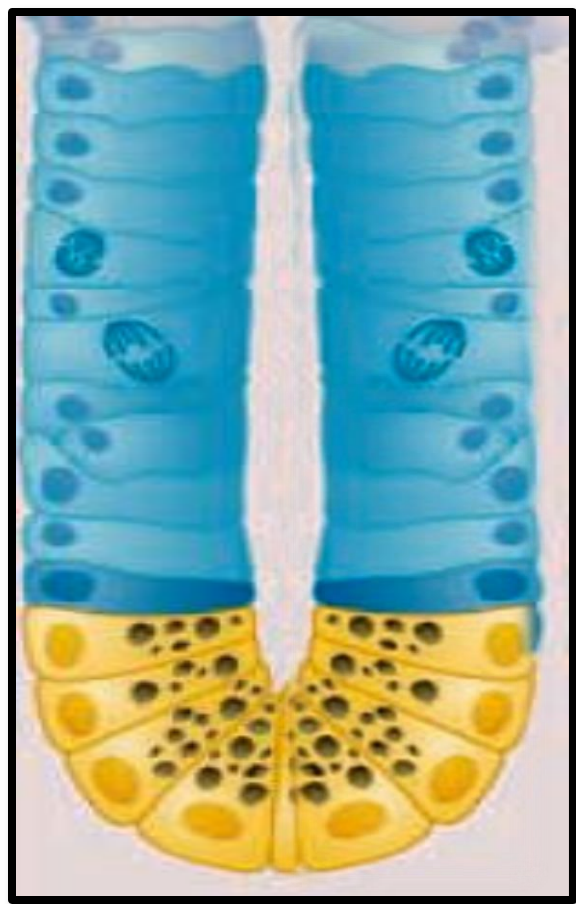
De kampioen der stamcellen aan het werk
Dochtercellen kruipen vanuit de crypt op de
darmvlok

Op zoek naar de darmstamcel

Nick Barker



“Onze” moleculaire vlag: Lgr5
Herontdekking van de “Crypt Base Columnar Cell”
van C.P. Leblond

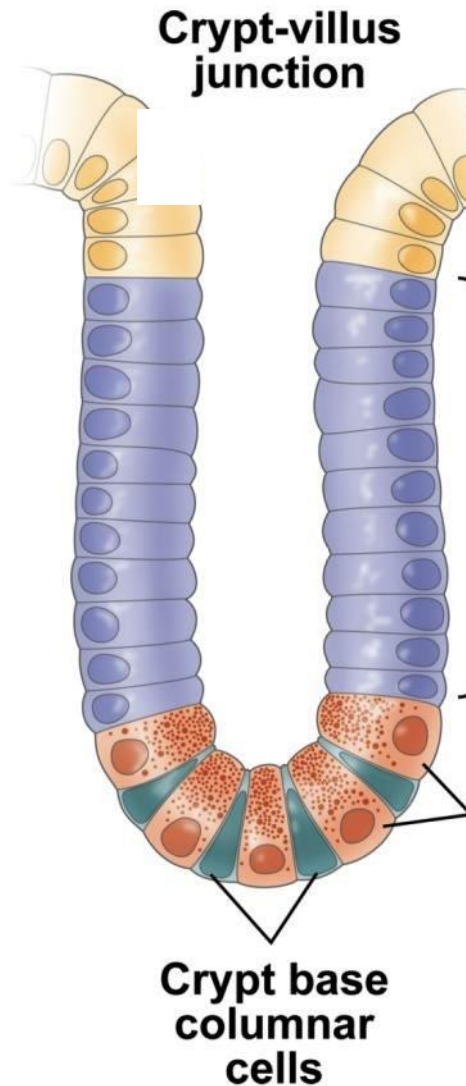


Charles Philippe Leblond (1910 – 2007)

Stamcel pionier



2004: "A month ago, I thought Power Point was a tool for sharpening pencils."

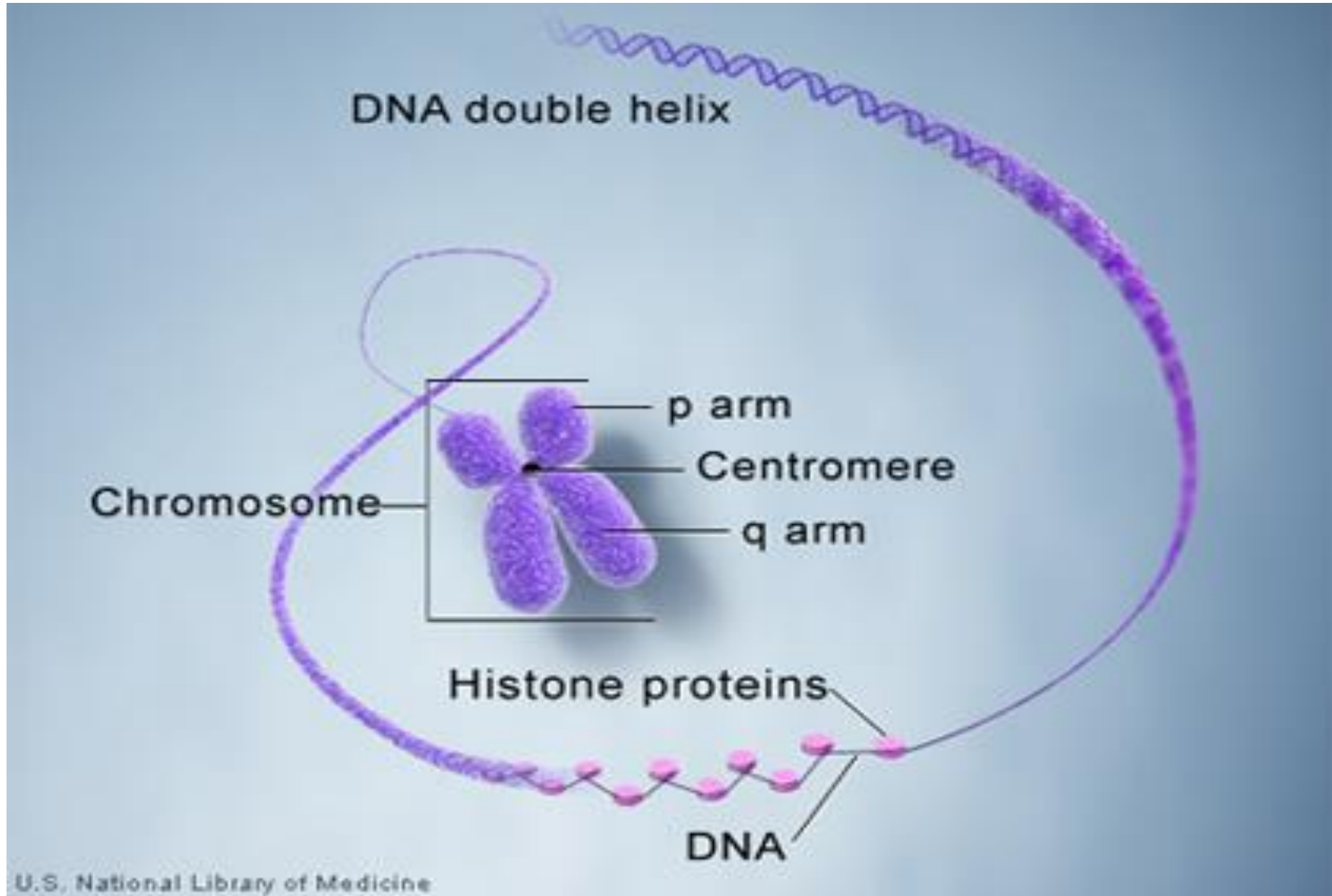


Is de Crypt Base Columnar Cell
de ongrijpbare stamcel?

= Een stamcel gaat een leven lang mee

= Een stamcel maakt alle andere
celtypen van een orgaan

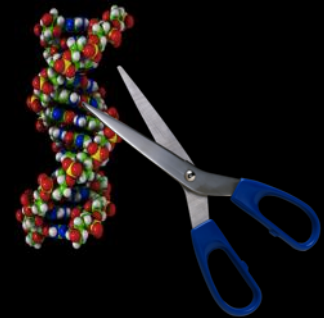
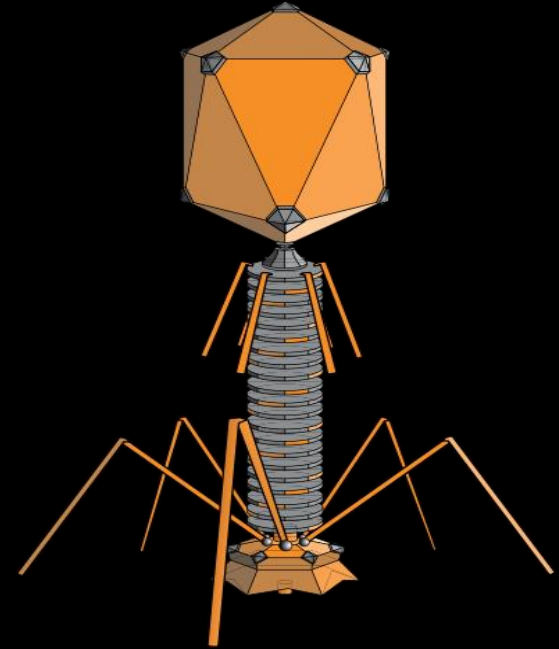
Nick Barker maakt een knockout muis(1)



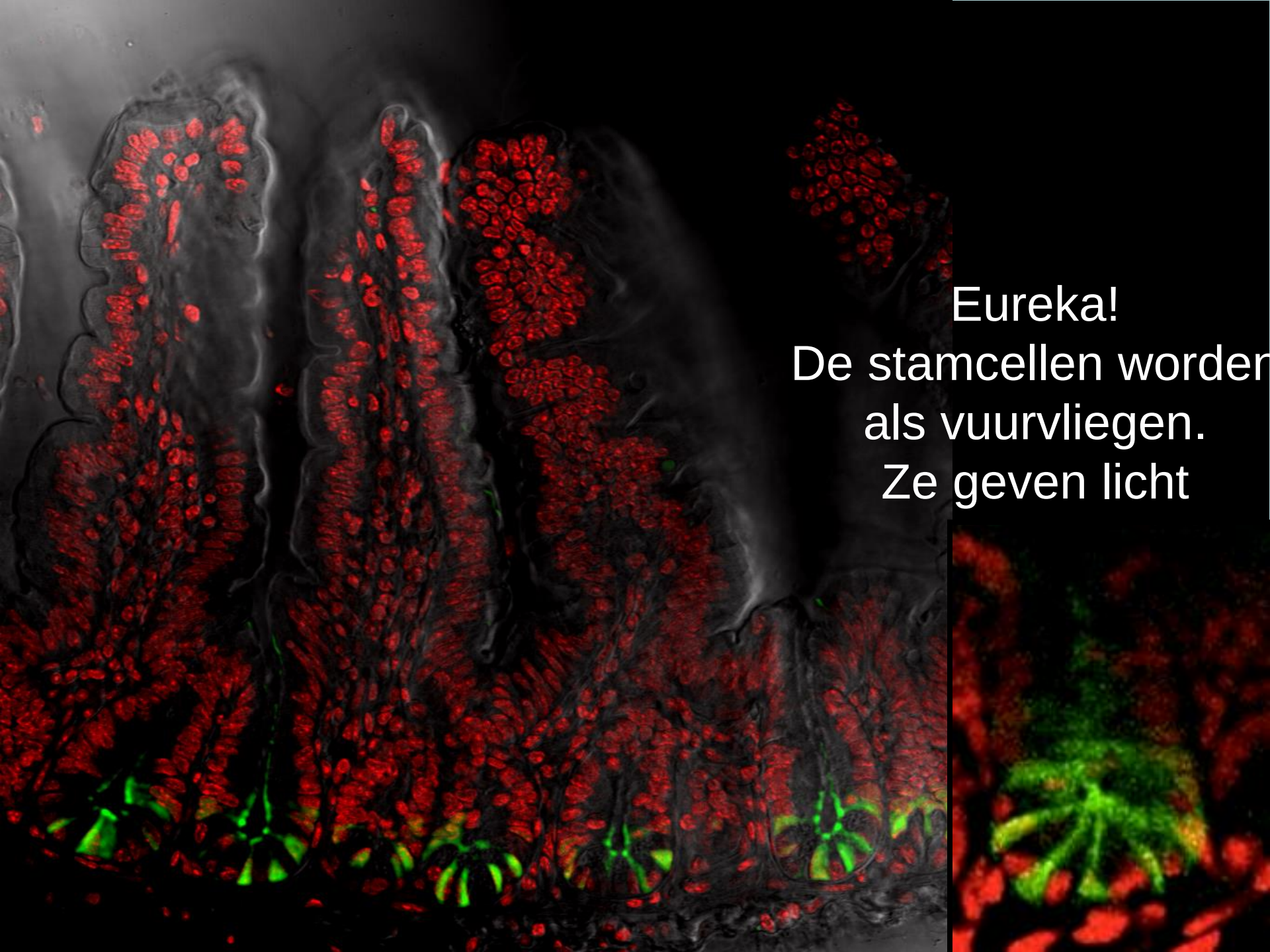
Nick Barker maakt een Knockout muis (2)



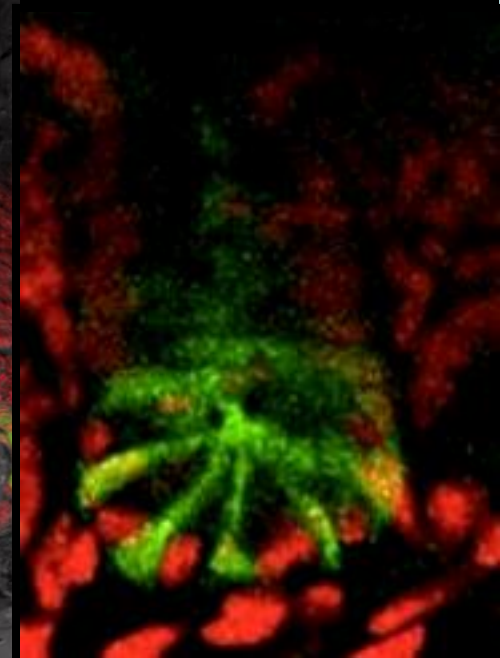
Green fluorescent
protein



Cre recombinase



Eureka!
De stamcellen worden
als vuurvliegen.
Ze geven licht

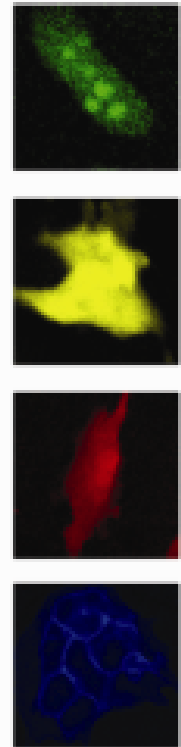
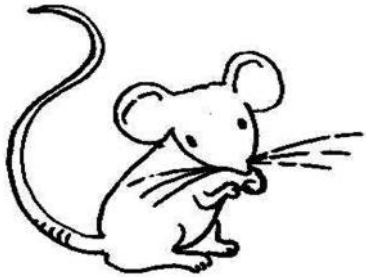




Als we een stamcel in blauw markeren, dan zien we
diens blauwe dochters vanzelf verschijnen

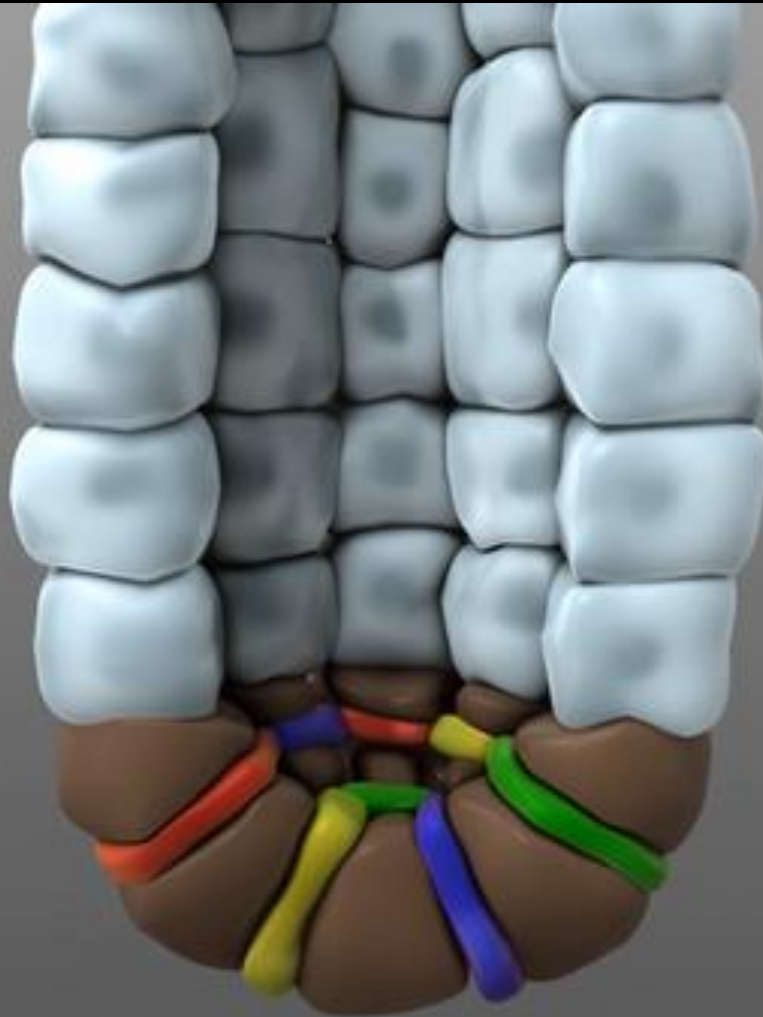
De Confetti-mouse

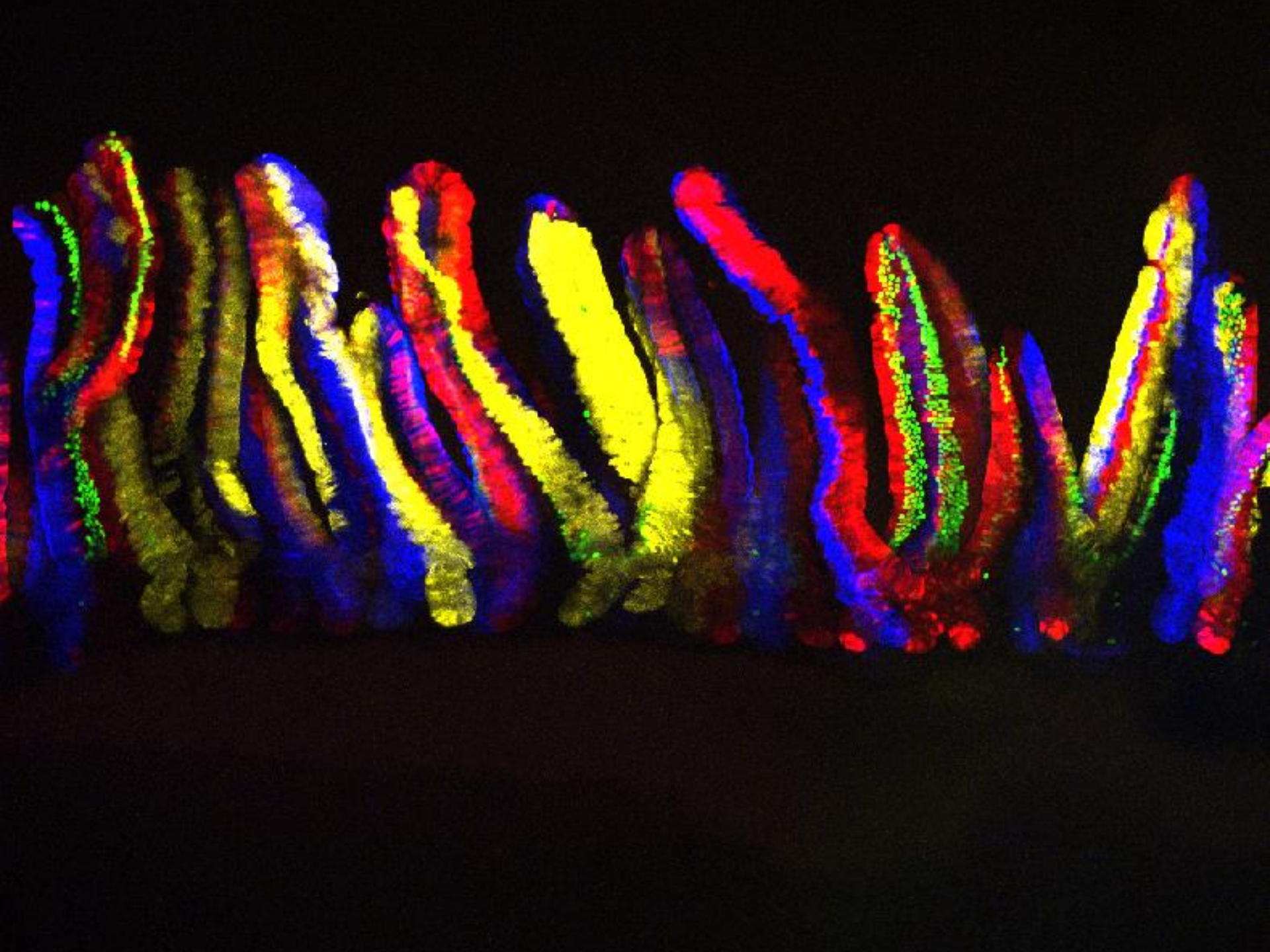
Iedere stem cell een eigen fluorescente kleur

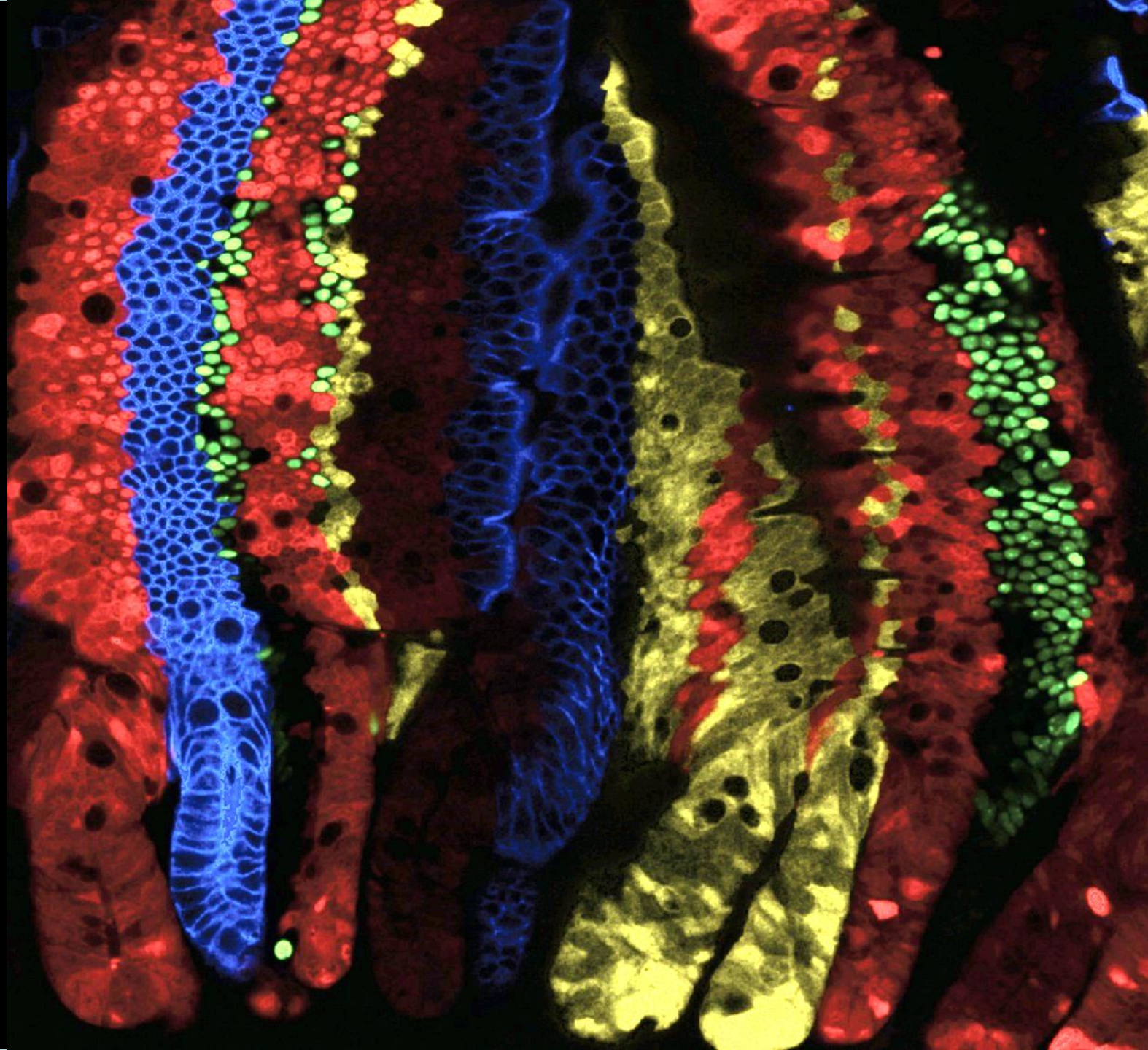


Hugo Snippert
Laurens van der Flier

Veertien veelkleurige stamcellen in iedere crypt

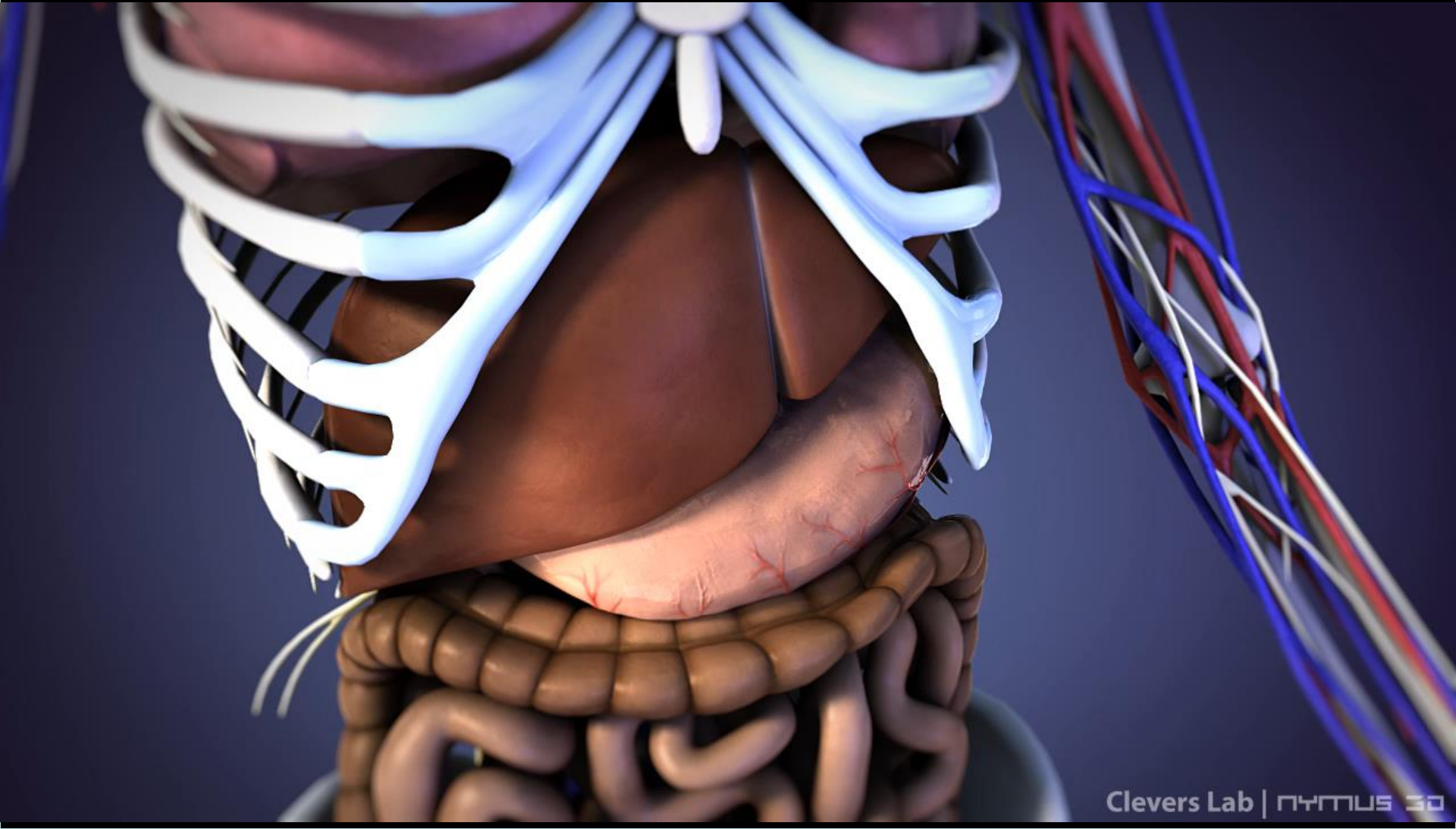






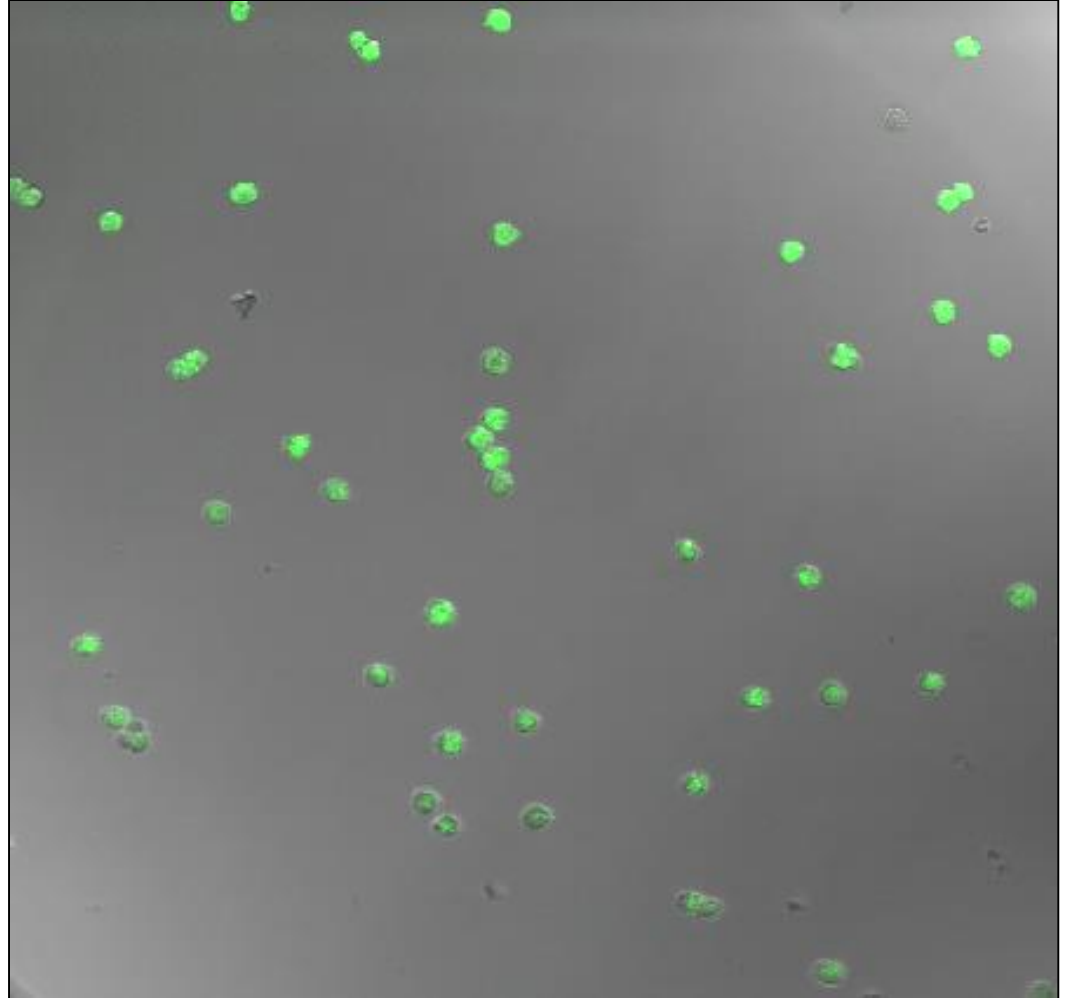
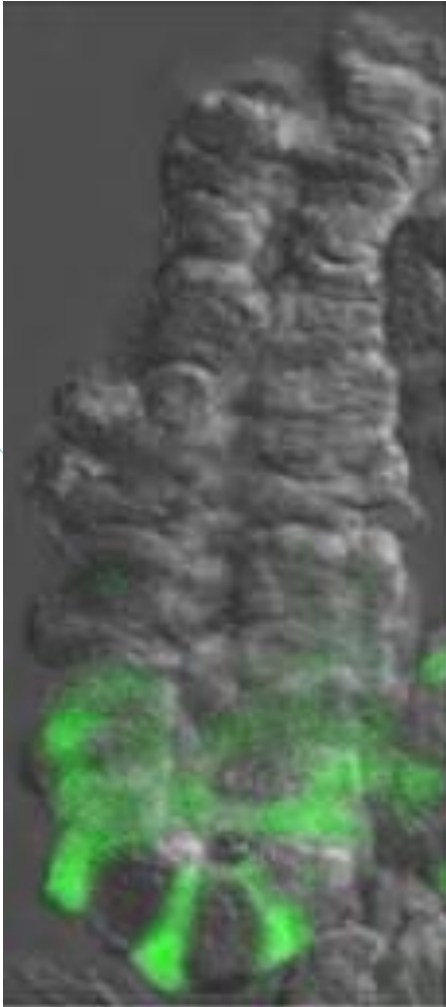
Stamcellen in de maag

(Bon-Kyoung Koo, Daniel Stange, Greg Sibbel, Jason Mills)



Nu onze stamcellen lichtgeven,
kunnen we ze vangen?

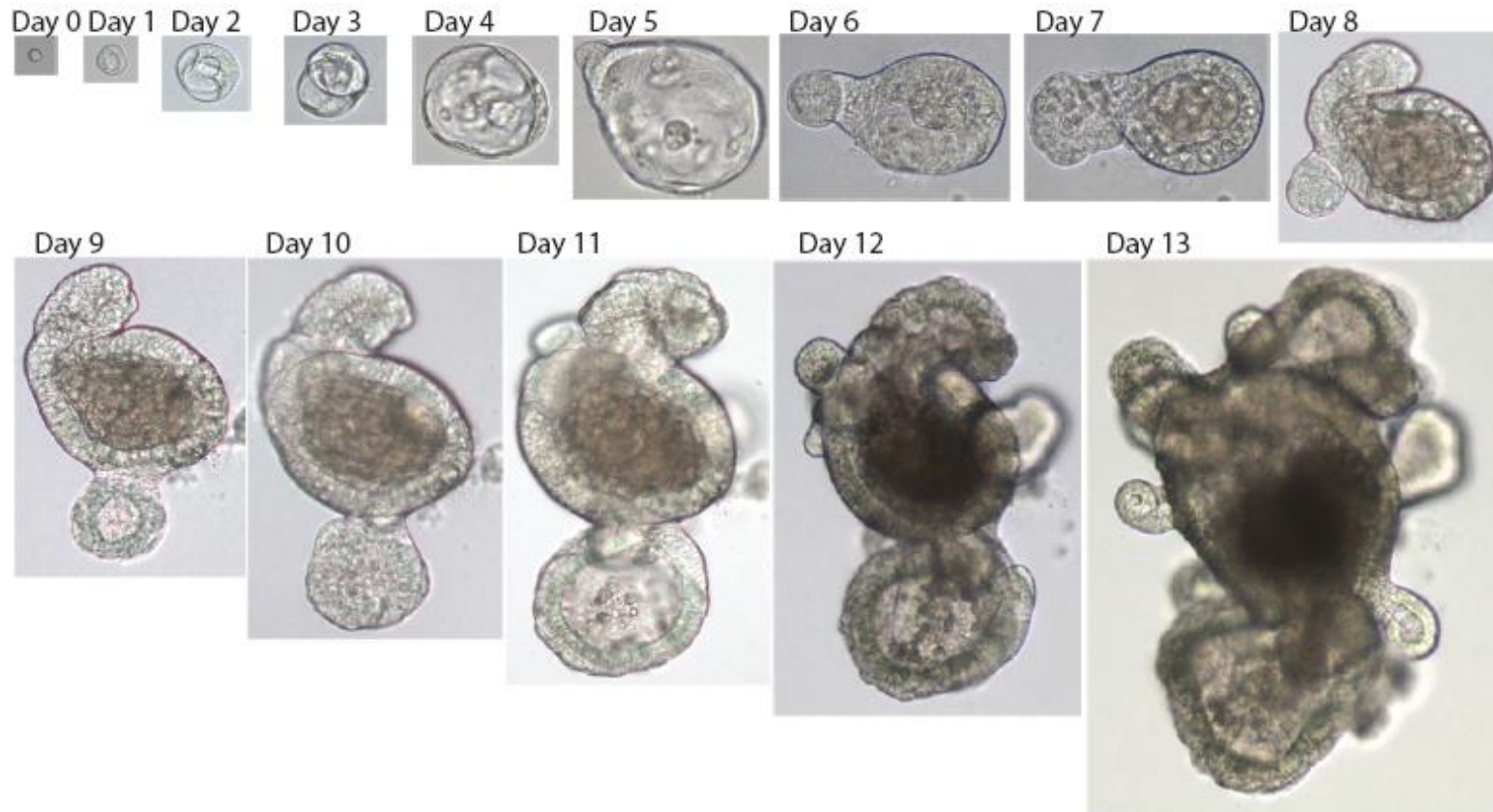
Het 'oogsten' van zuivere stamcellen met een Cell Sorter machine

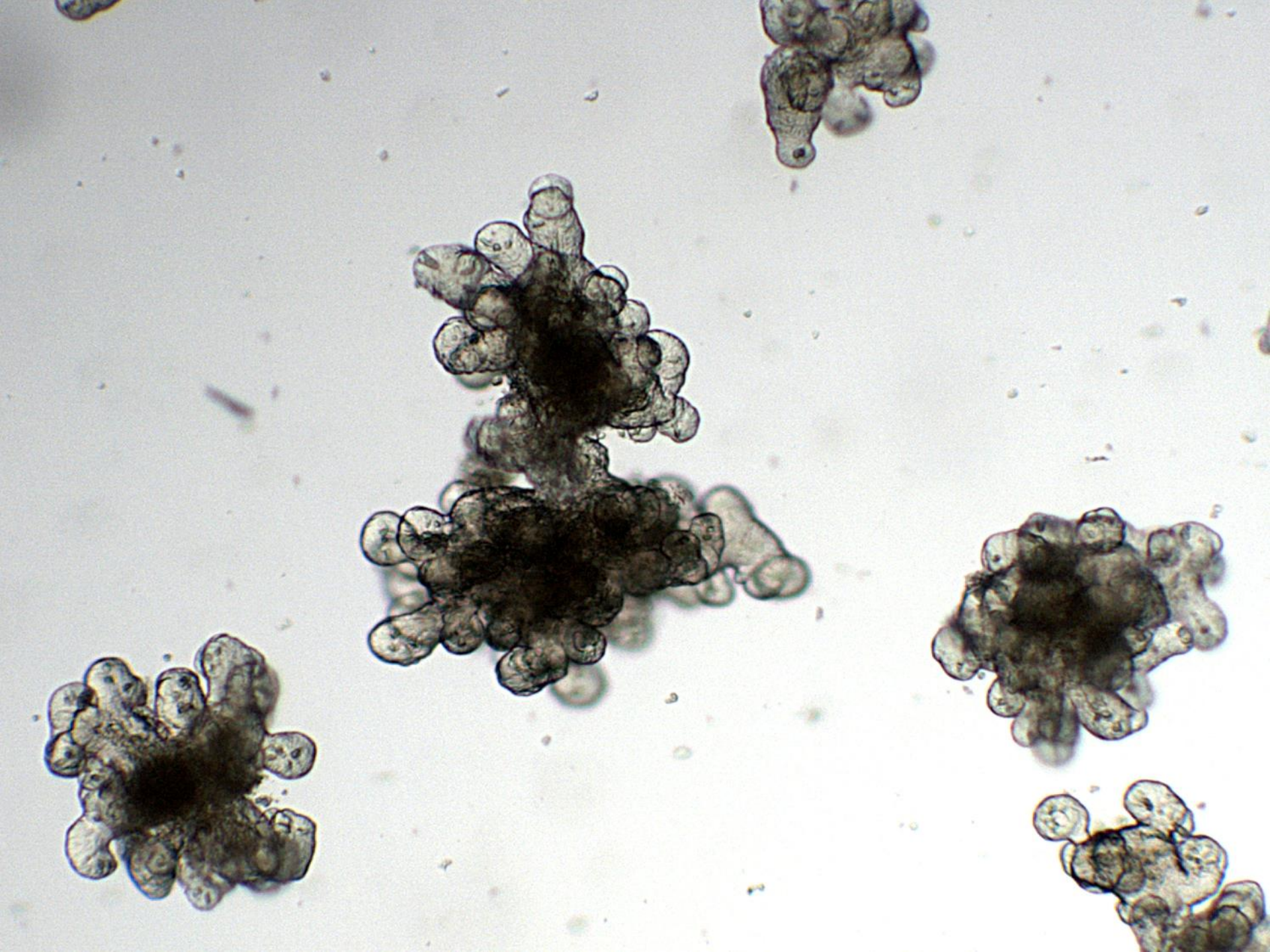


Kunnen we ze nu temmen?

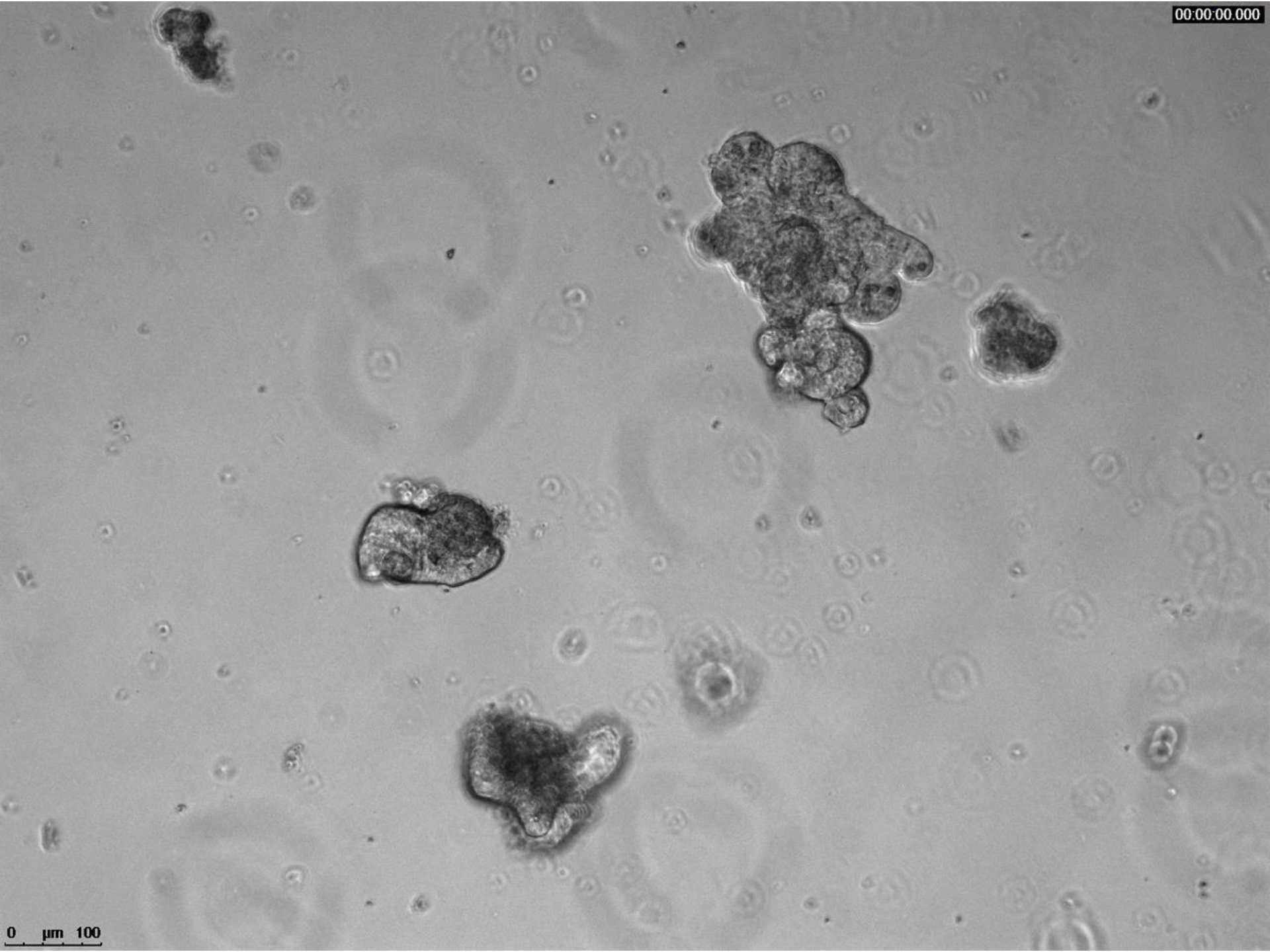
Met andere woorden:
kunnen we veel gezond
weefsel maken
van een enkele stamcel?

De mini-darm, gegroeid uit een enkele darmstamcel (Toshiro Sato).

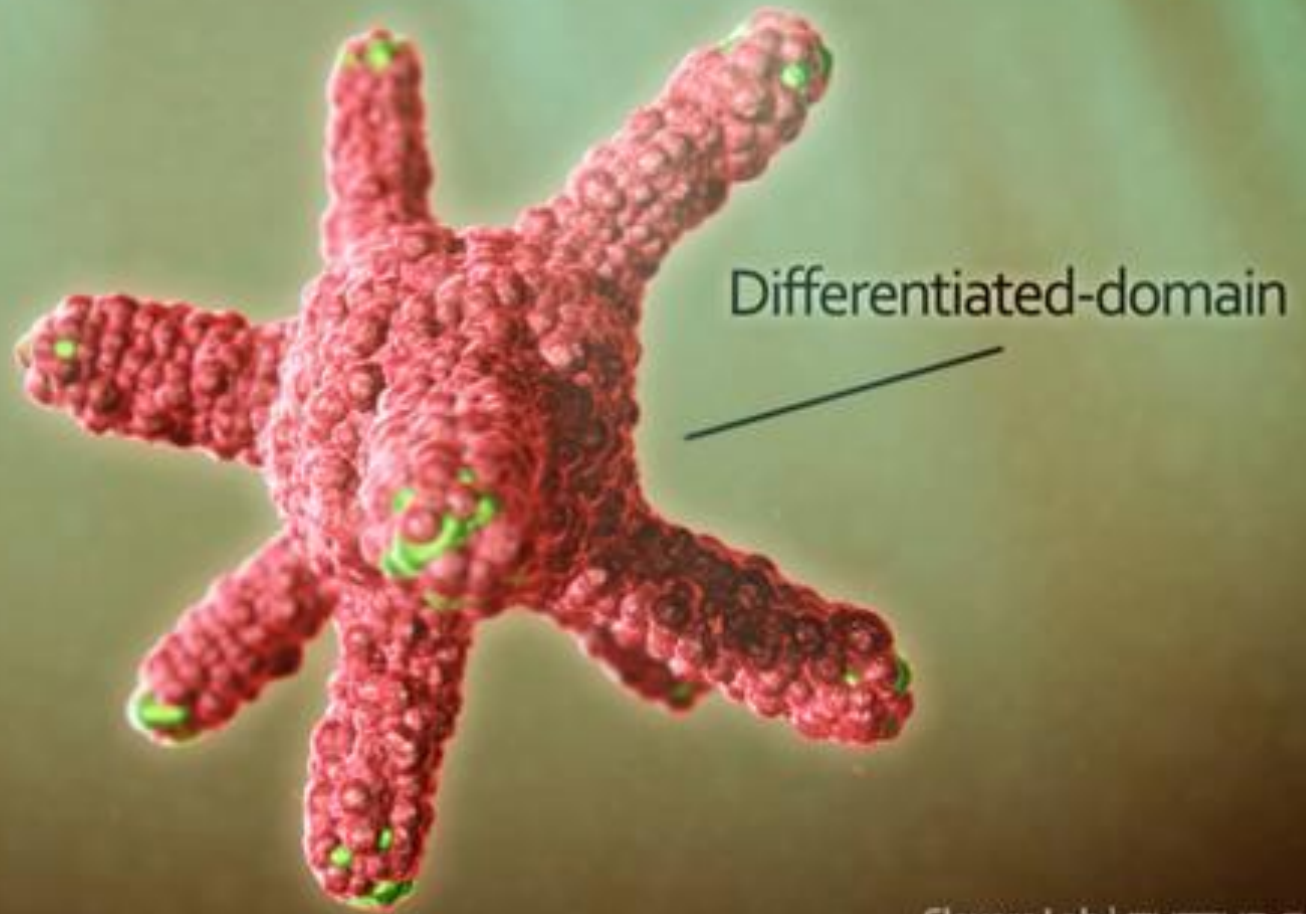




00:00:00.000

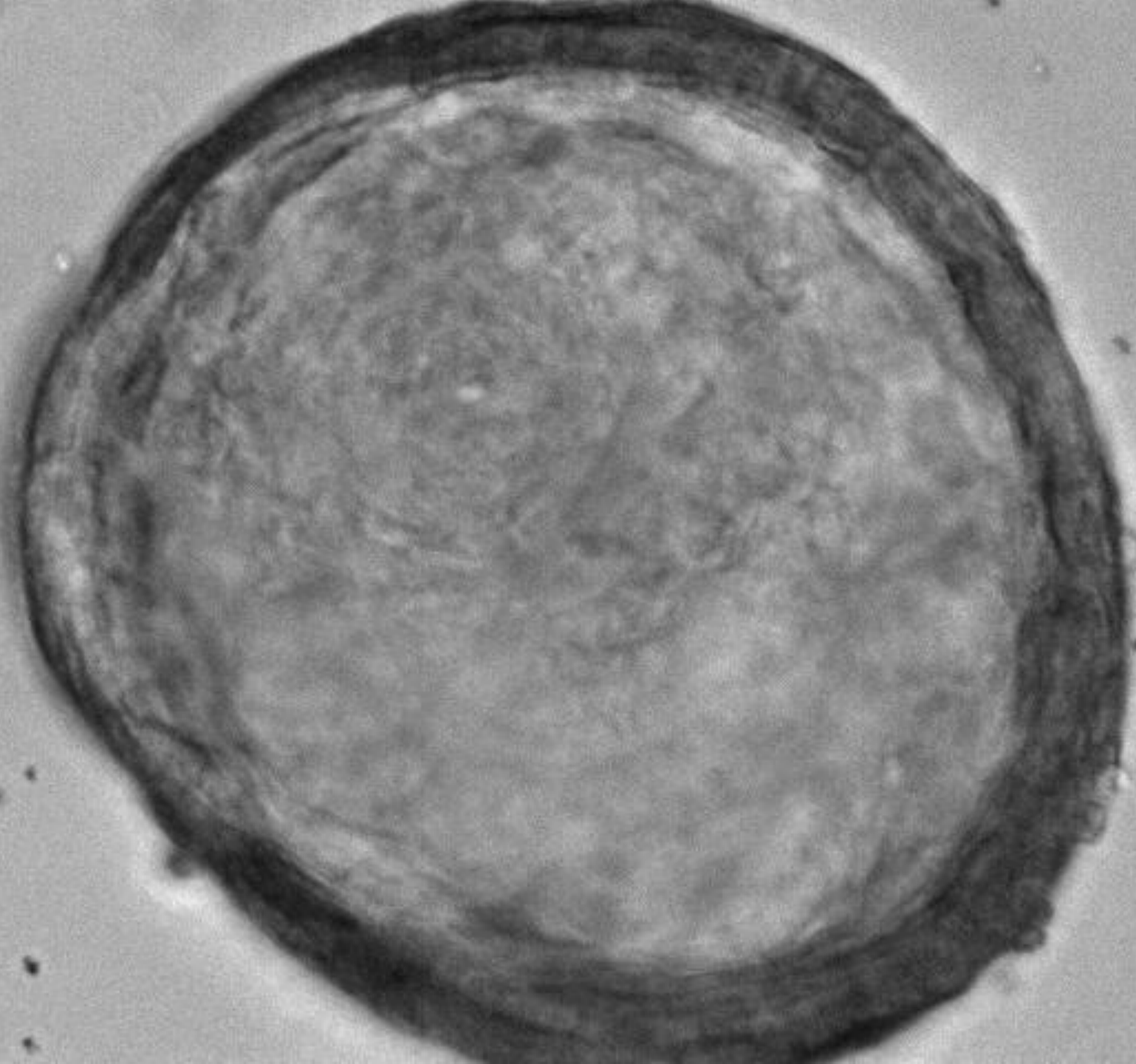


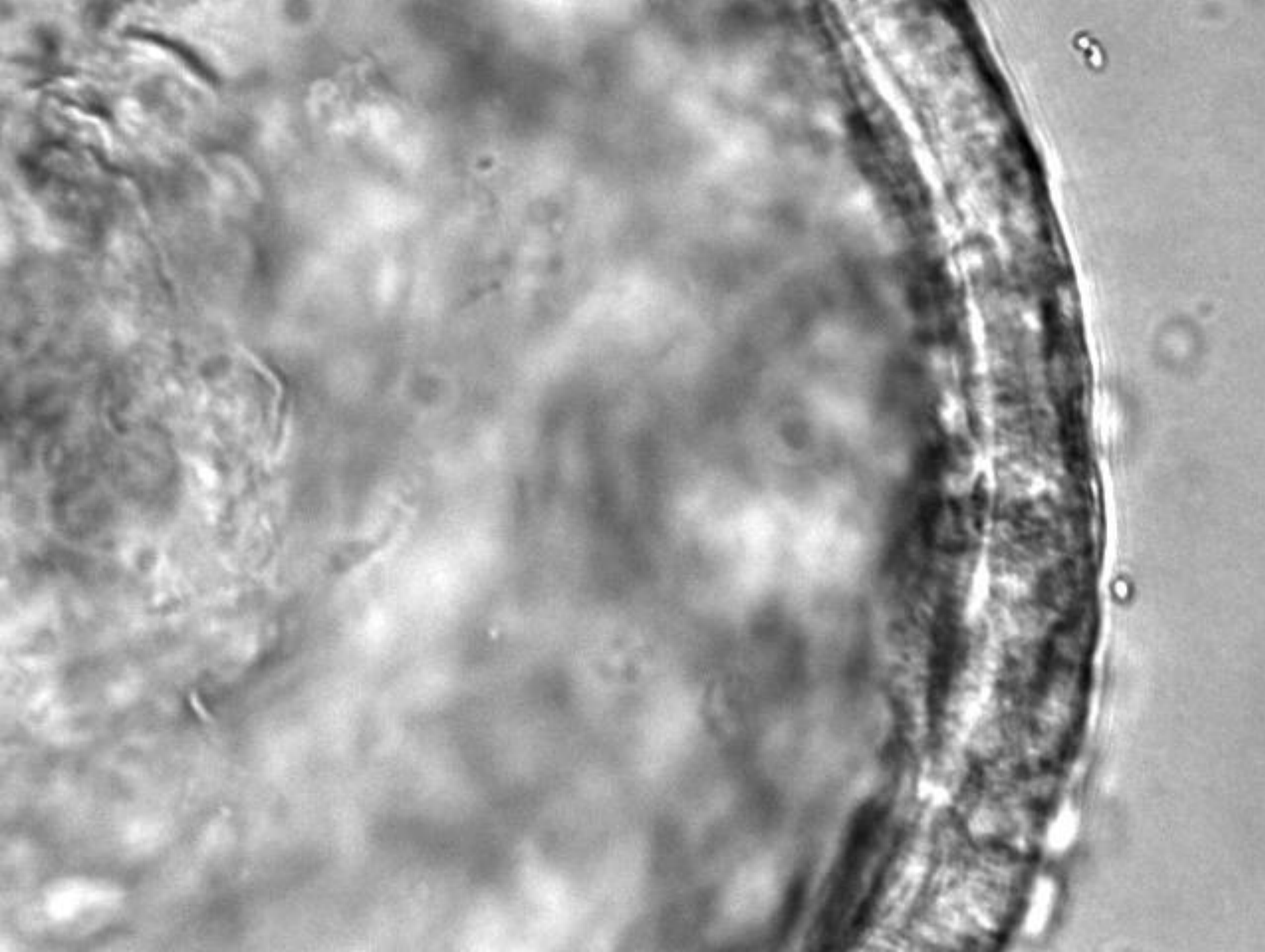
0 μm 100

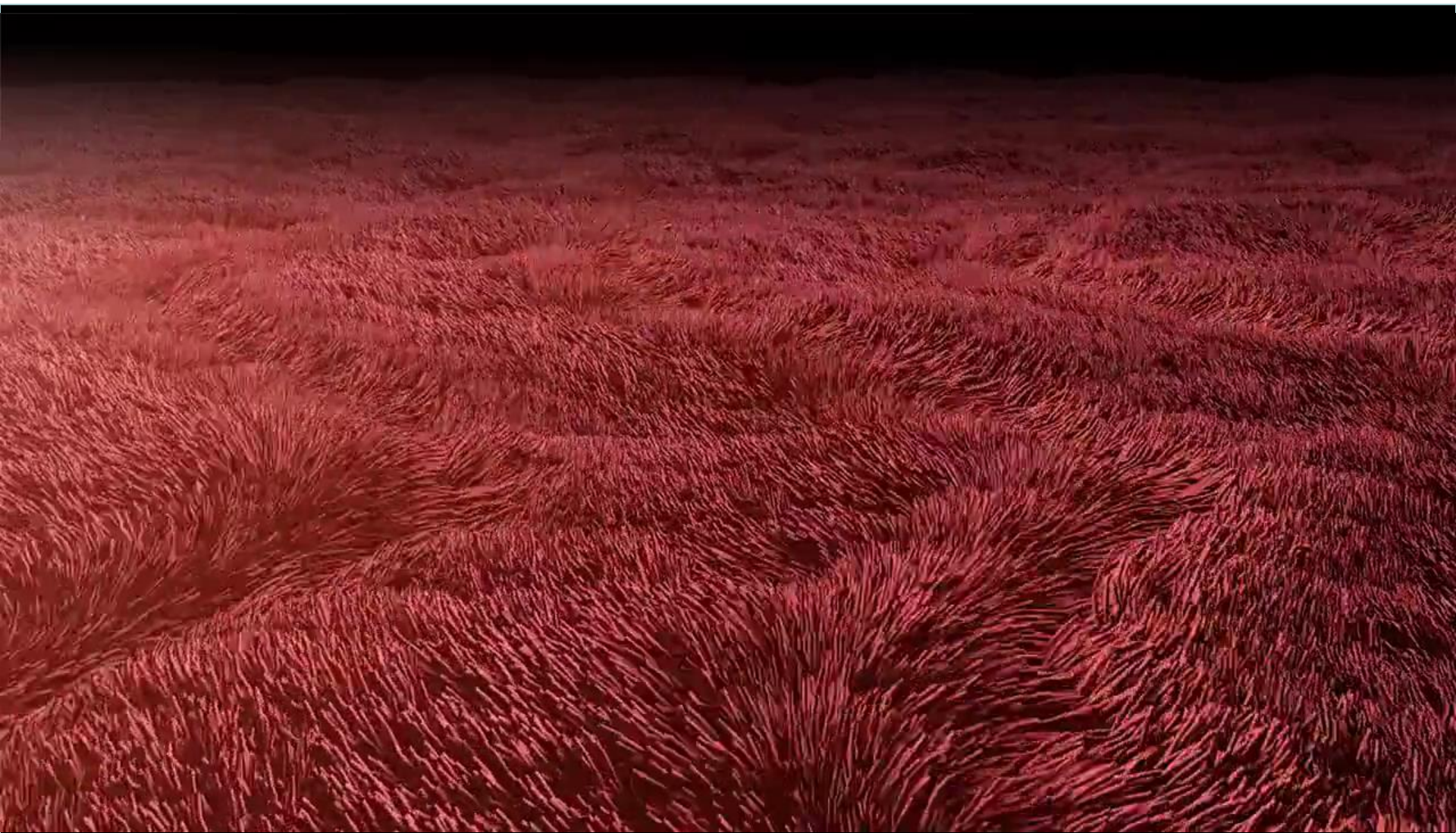


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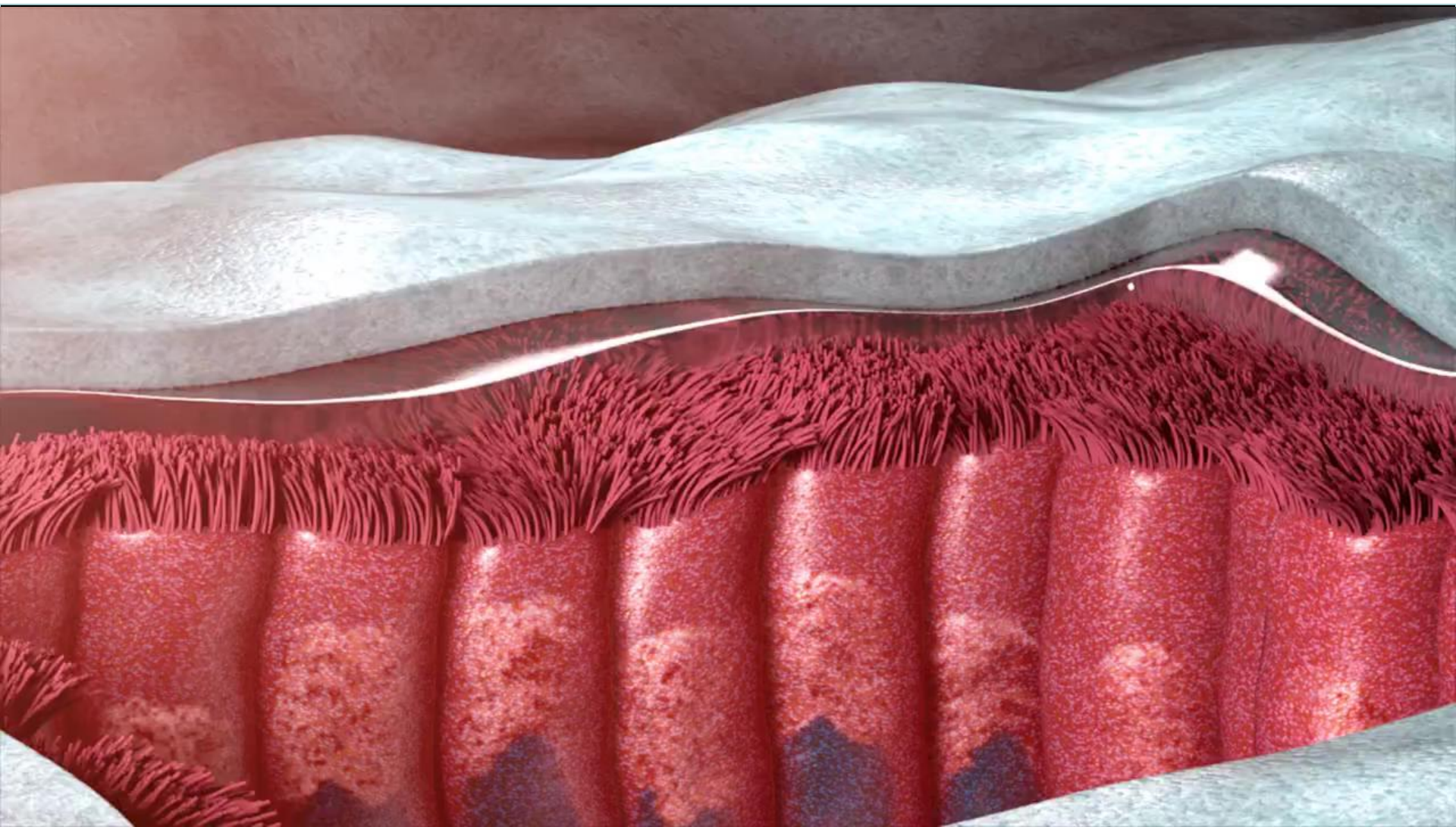
Mini-darmen kunnen getransplanteerd worden



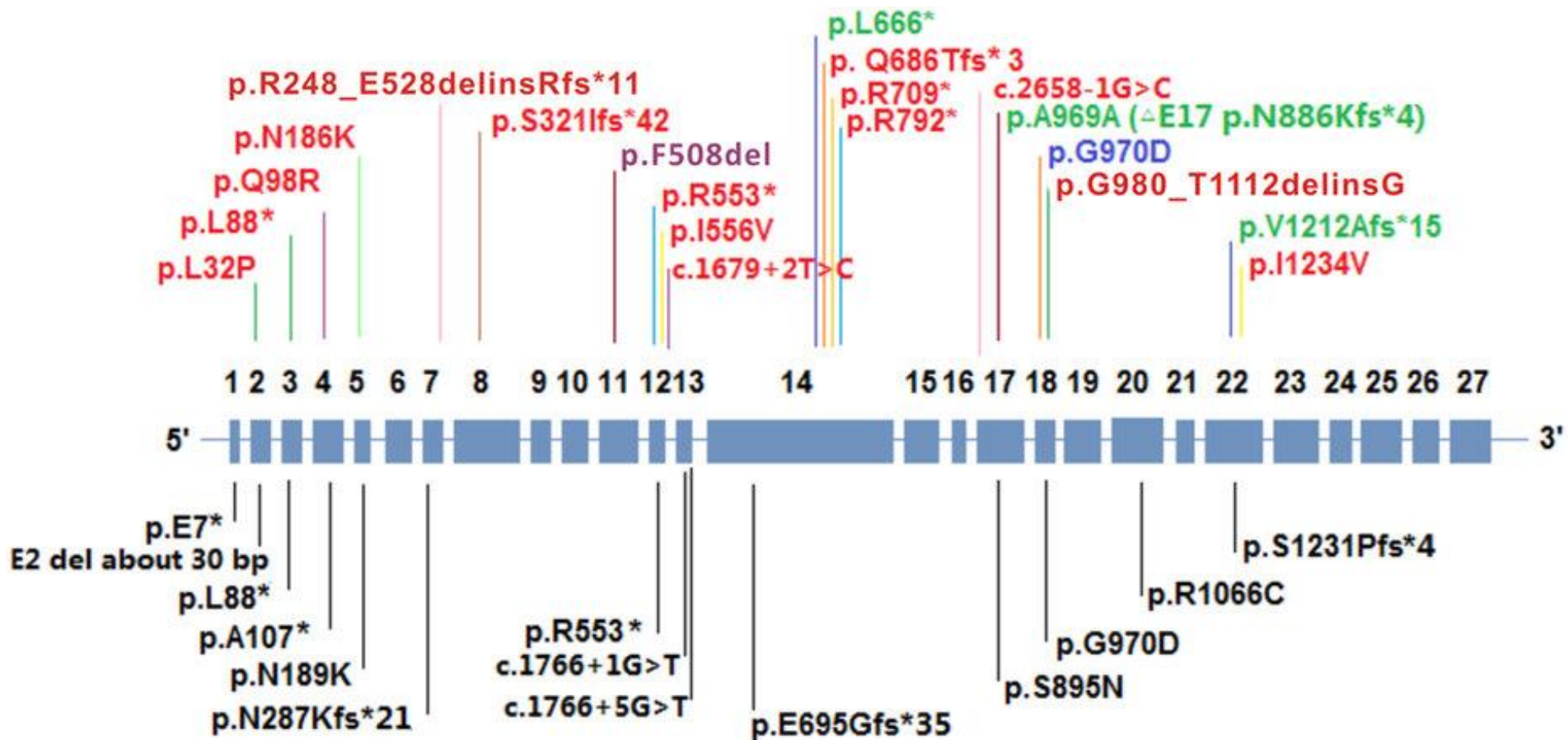




Personalized medicine bij taaislijmziekte
Cystic Fibrosis of CF



Personalized medicine bij taaislijmziekte

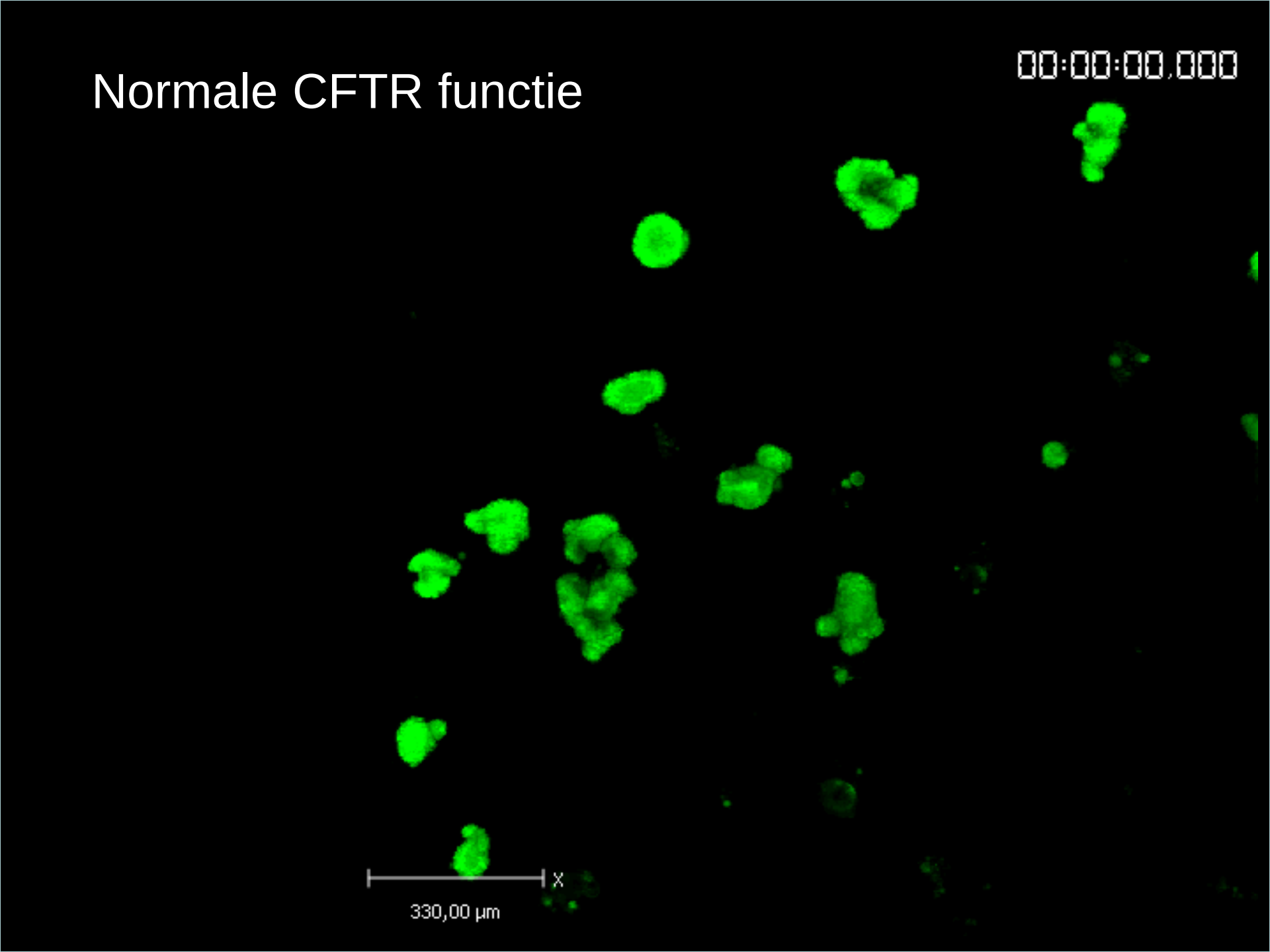


CF wordt veroorzaakt door mutaties in het CFTR gen.
De CF geneesmiddelen zijn mutatie-specifiek

Normale CFTR functie

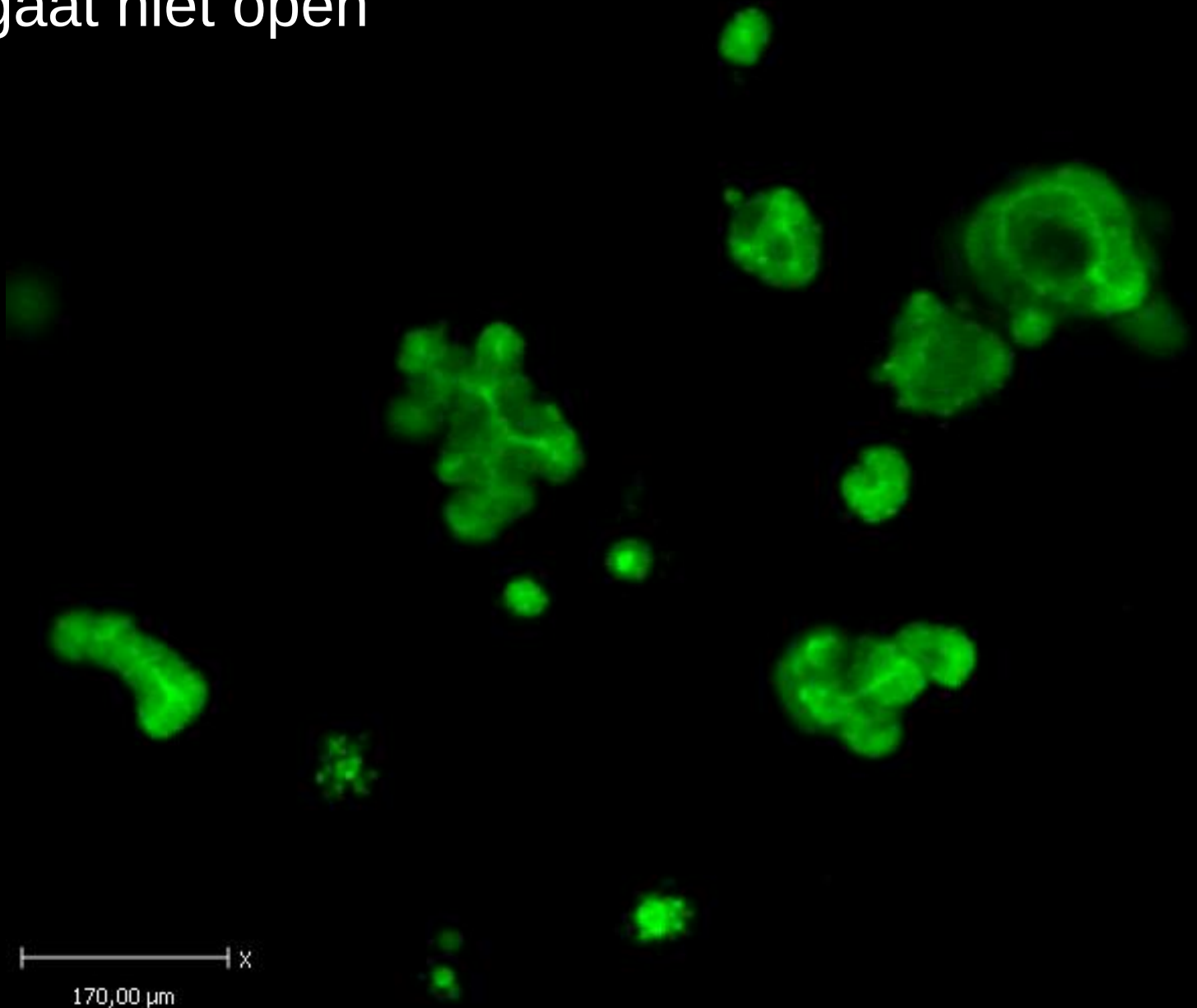
00:00:00,000

330,00 μm



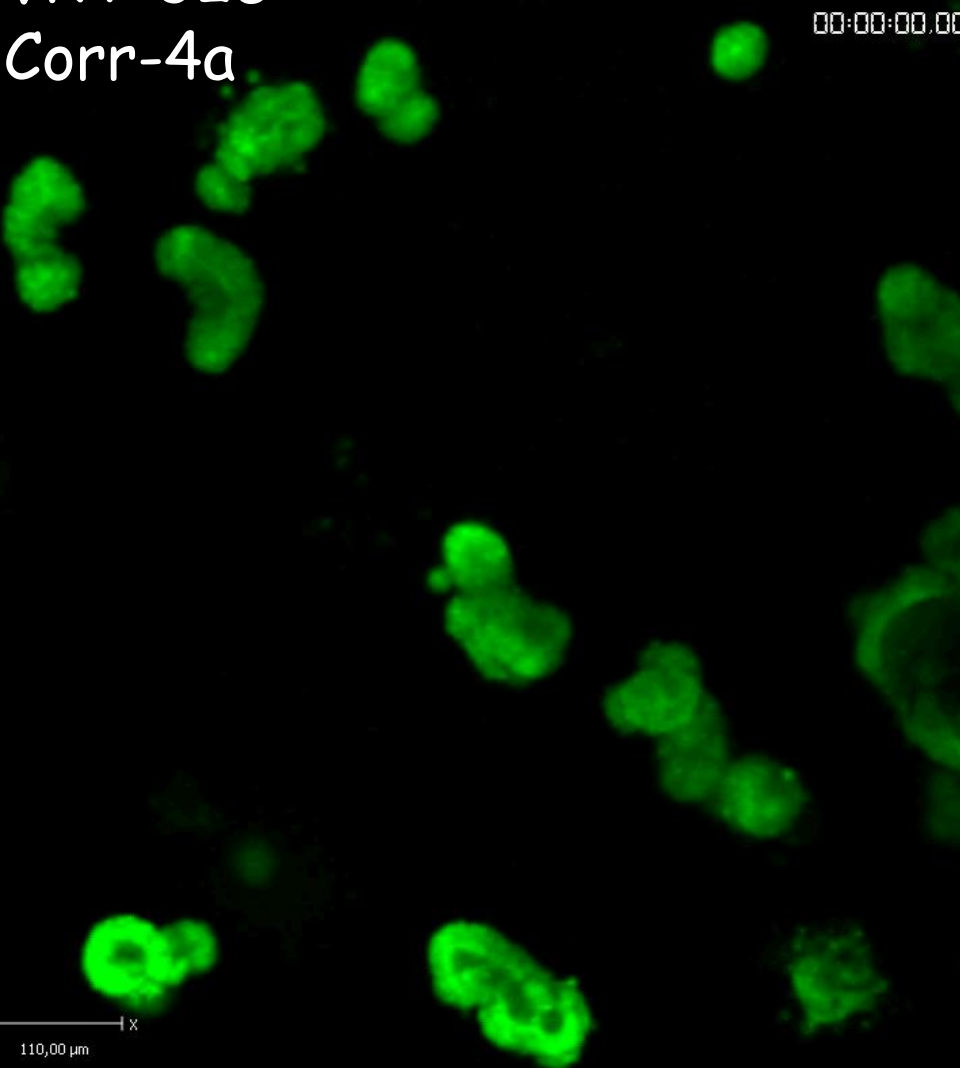
00:00:00,000

mutant CFTR
Kanaal gaat niet open

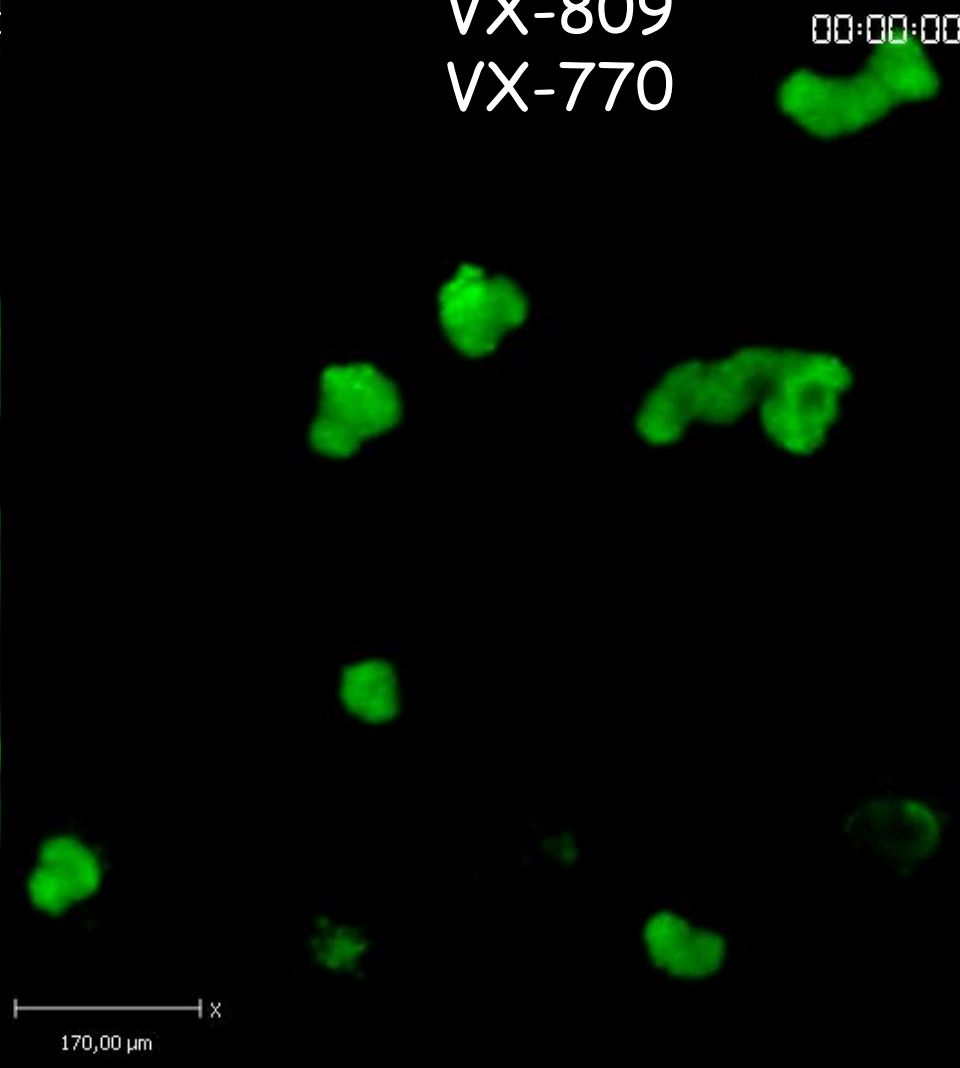


Experimentele geneesmidelen getest op CF organoiden

VRT-325
Corr-4a



VX-809
VX-770





Aanpassen Geneesmiddel Vergoeding Systeem

VX-770/ivacaftor/Kalydeco

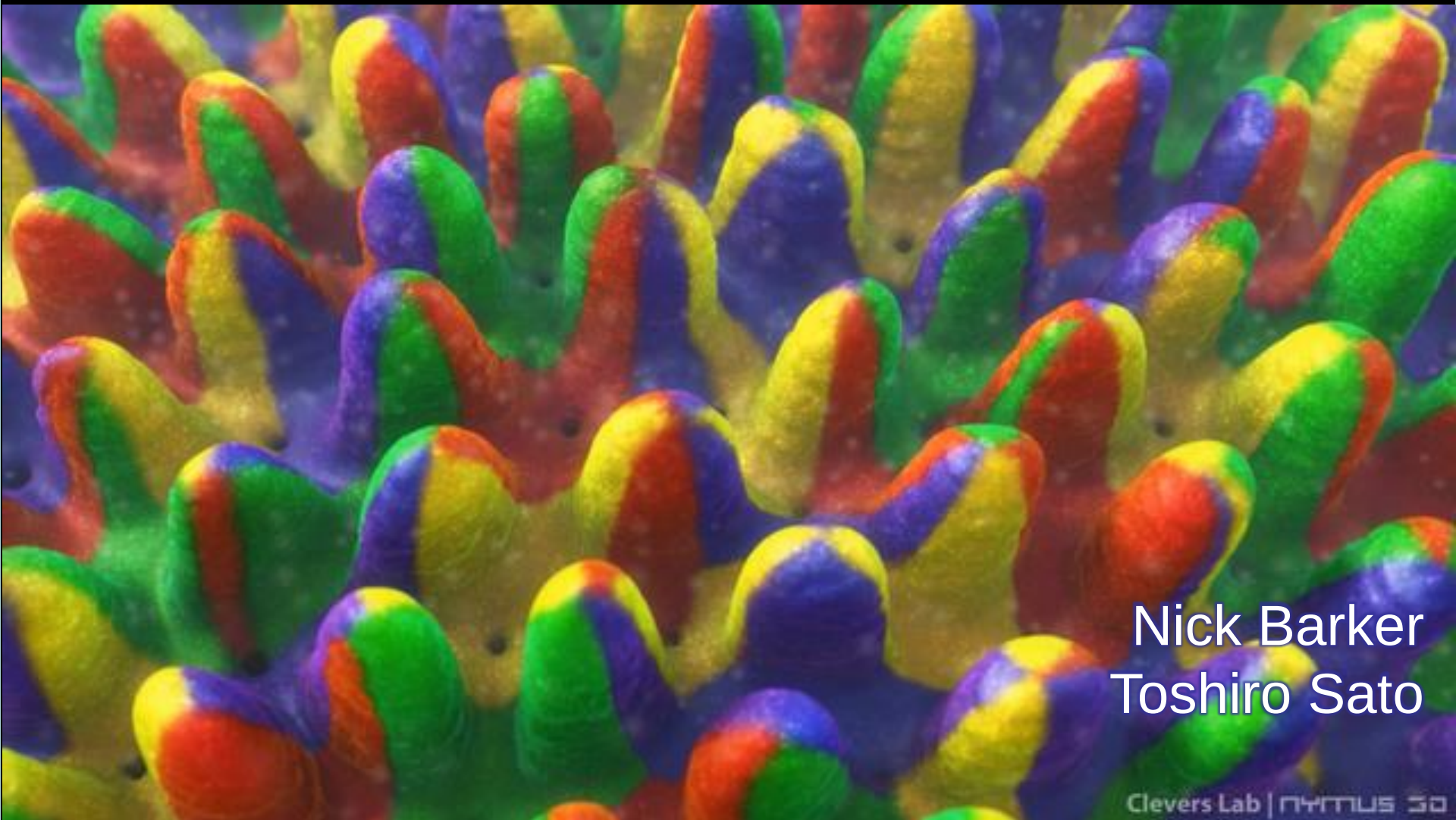
Kanker is een staps-gewijs proces van DNA mutaties, startend in stamcellen





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Personalized medicine voor kanker



Nick Barker
Toshiro Sato