

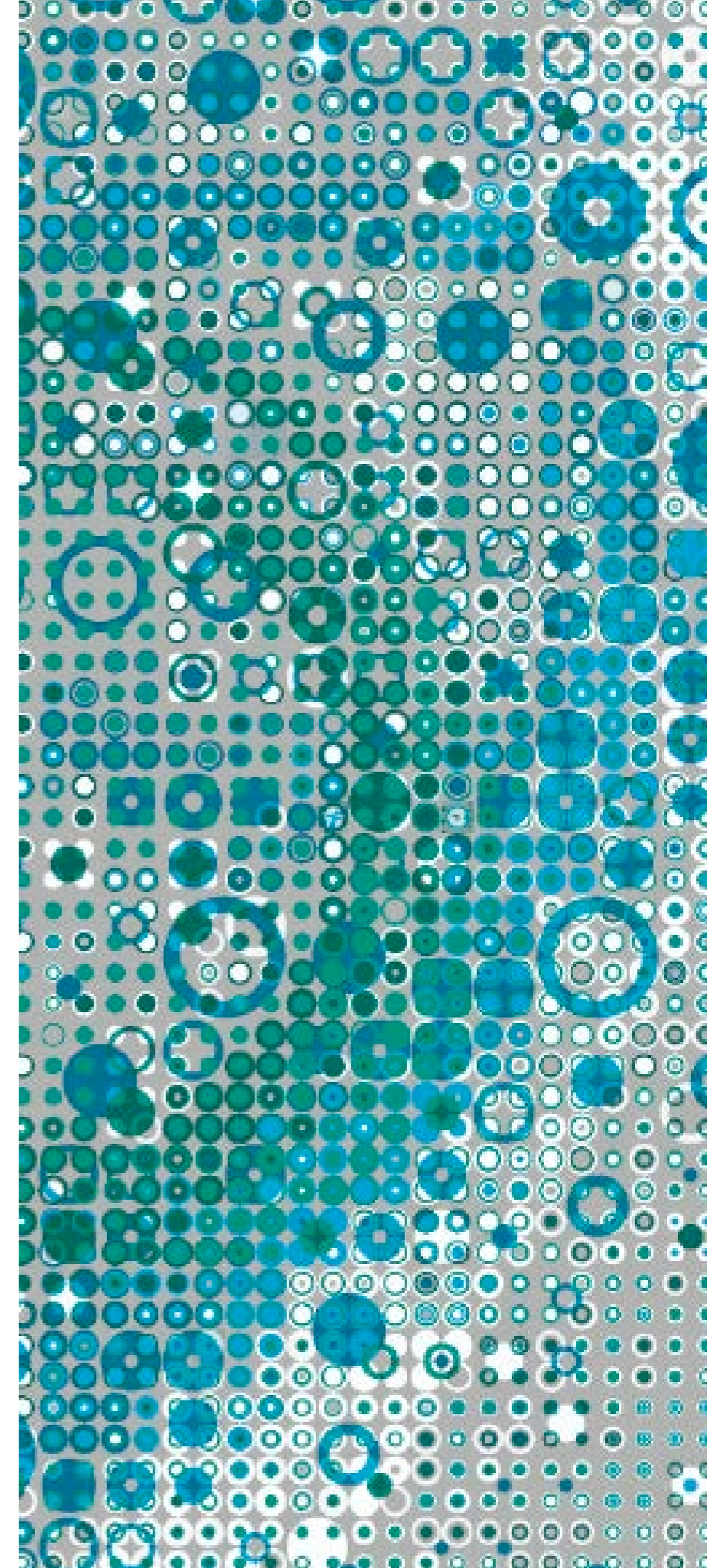


# Hubrecht Institute

Developmental Biology  
and Stem Cell Research

## **Het Hubrecht Instituut in een notendop**

Jeroen den Hertog  
*Deputy Director Research  
& Groupleader*



# Koninklijke Nederlandse Akademie van Wetenschappen







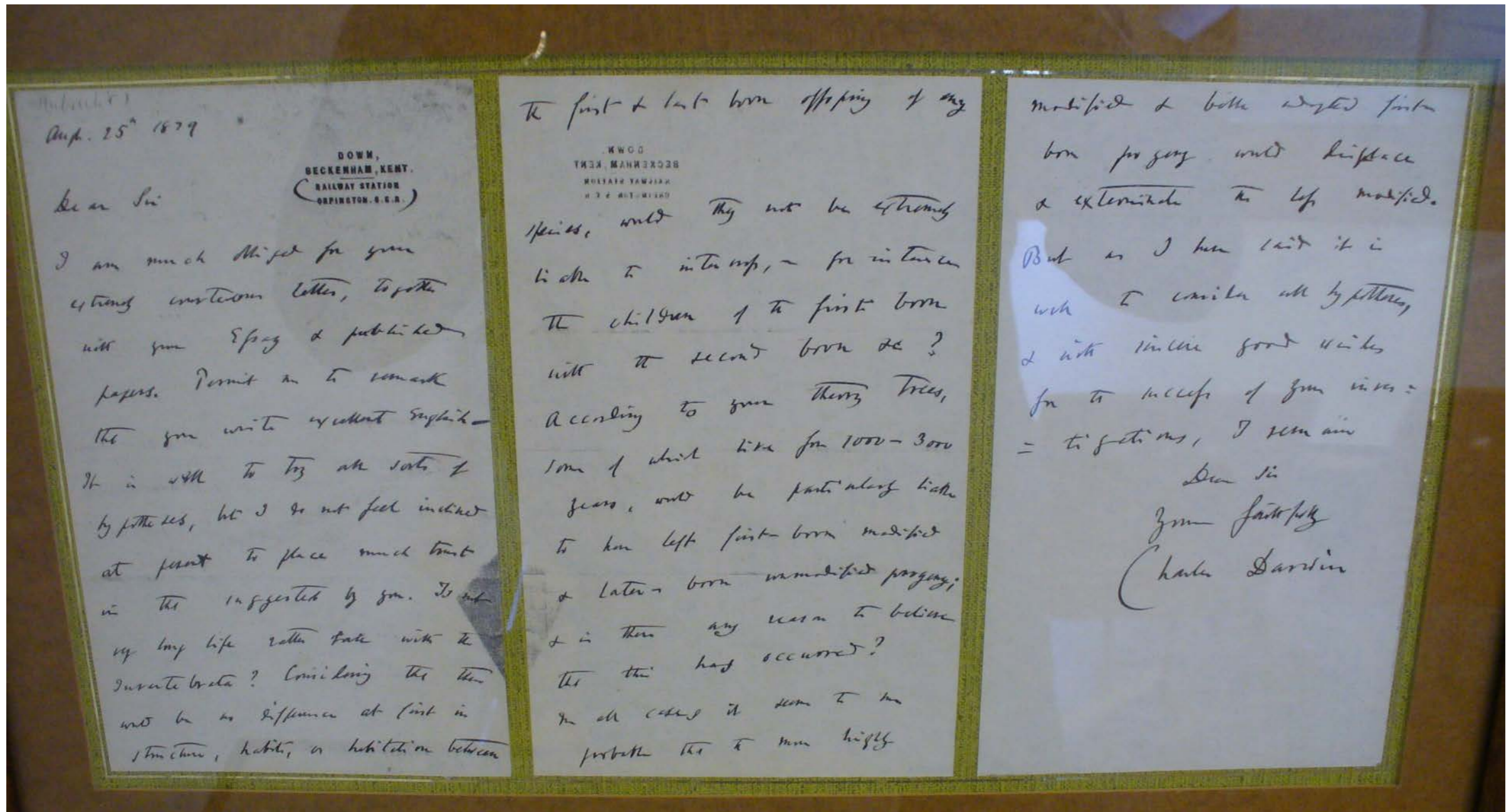
Ambrosius A.W. Hubrecht  
1853 - 1915





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Ambrosius Hubrecht correspondeerde met Charles Darwin





Brief d.d. 25/8/1879 van Charles Darwin  
aan A.A.W. Hubrecht.

Dear Sir,

I am much obliged for your extremely courteous letter, together with your essay and published papers. Permit me to remark that you write excellent English. It is well to toss all sorts of hypotheses, but I do not feel inclined at present to place much trust in that suggested by you. Is not

very long live rather rare with the Invertebrata? Considering that there would be no difference at first in structure, habits, or habilitation between the first and last born offspring of any species, would they not be extremely liable to intercross for instance the children of the first born with the second born etc.?

According to your theory trees, some of which live from 1000-3000 years, would be particularly liable to have first born modified and later on born unmodified progeny; and is there any reason to believe that this has occurred?

In all cases it seems to me probable that the more highly modified and better adapted first born progeny would displace and exterminate the less modified. But as I have said it is well to consider all hypotheses, and with sincere good wishes for the success of your investigations I remain

dear Sir  
your faithfully

CHARLES DARWIN

*“I am much obliged for your extremely courteous letter, together with your essay and published papers. Permit me to remark that you write excellent English”*

*“It is well to toss all sorts of hypotheses, but I do not feel inclined at present to place much trust in that suggested by you.”*



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Hubrecht Institute is opgericht 1916,  
KNAW instituut sinds 1917

- Beschrijvende embryologie: Hubrecht collectie (nu in Berlijn)
- In de 1950's: Experimentele embryologie: Nieuwkoop Center
- Late 1980s: Moleculaire basis van embryonale ontwikkeling
- 2000s: focus op (volwassen) stamcellen

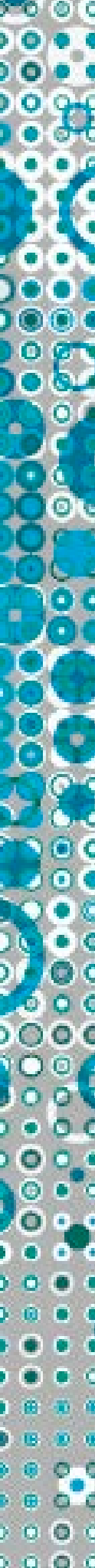




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Van het centrum van Utrecht...



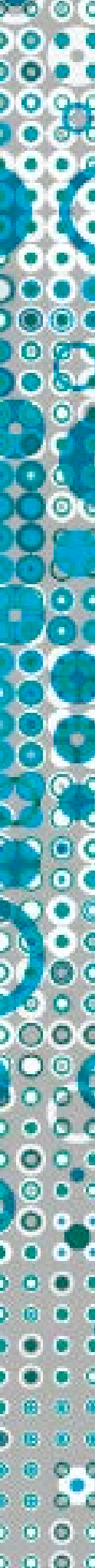
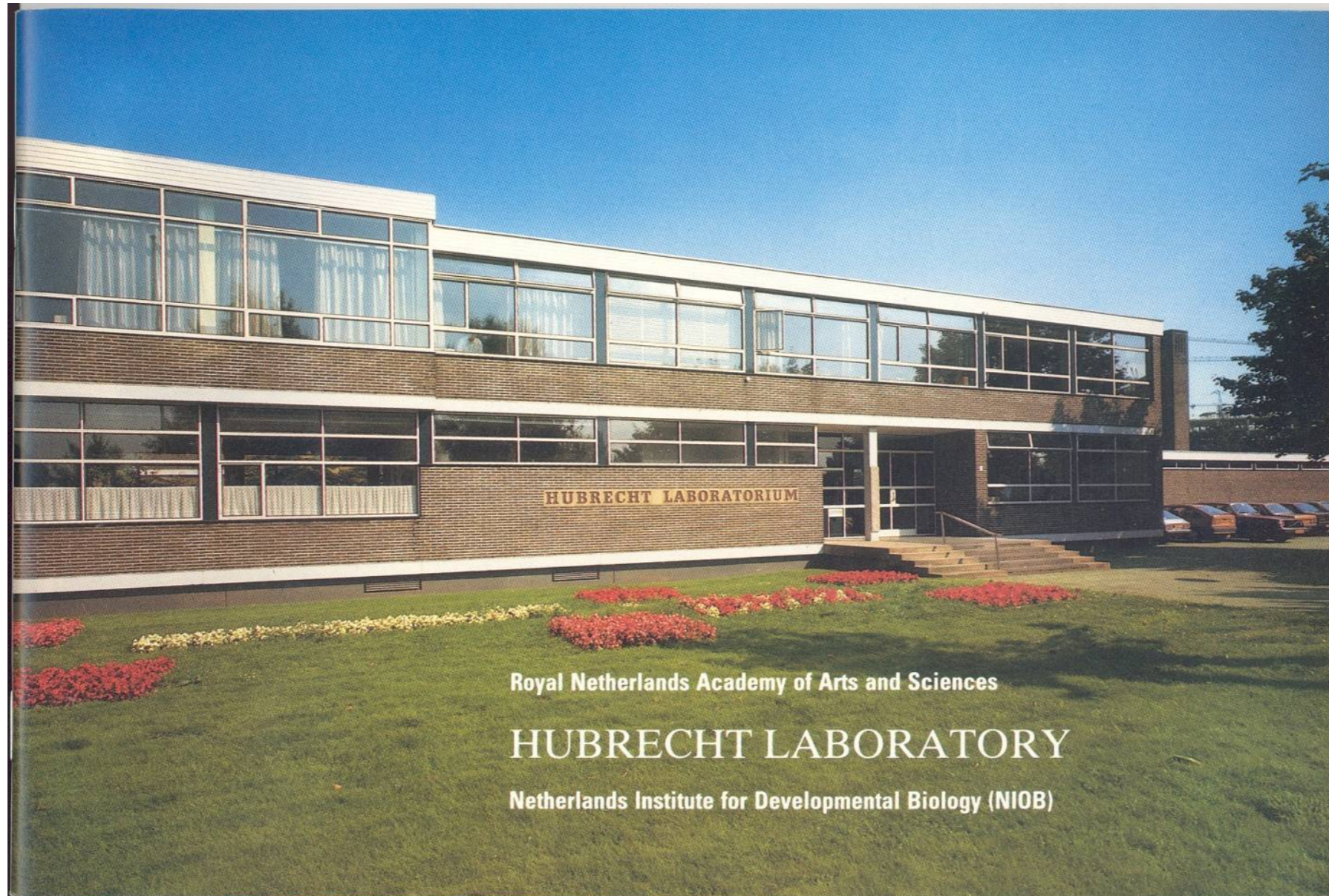




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... naar de campus van de universiteit in de  
jaren 60, “de Uithof”, nu Utrecht Science Park



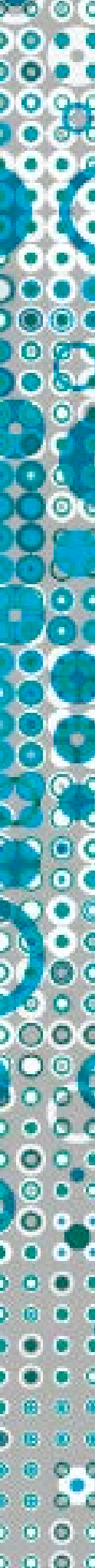




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...naar een nieuw gebouw in 2000...



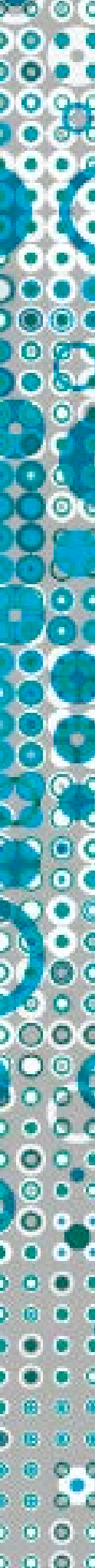




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...en de laatste uitbreiding,  
in gebruik sinds September 2015







# Hubrecht Institute

Developmental Biology  
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Anno 2017

- 18 onderzoeksgroepen (6 junior tenure-track, 12 senior)
- 250 medewerkers (180 wetenschappers, ~40% buitenlands, 30 landen)
- Affiliatie met UMC Utrecht sinds 2008
- Totaal budget: ~20 M€ per jaar (> 50% extern geld)
- Fundamenteel onderzoek met oog voor klinische toepassingen (kanker, regeneratieve geneeskunde, diabetes)
- Model systemen:  
cellen, organoïden, wormen, vliegen, vissen, kikkers, muizen, ratten

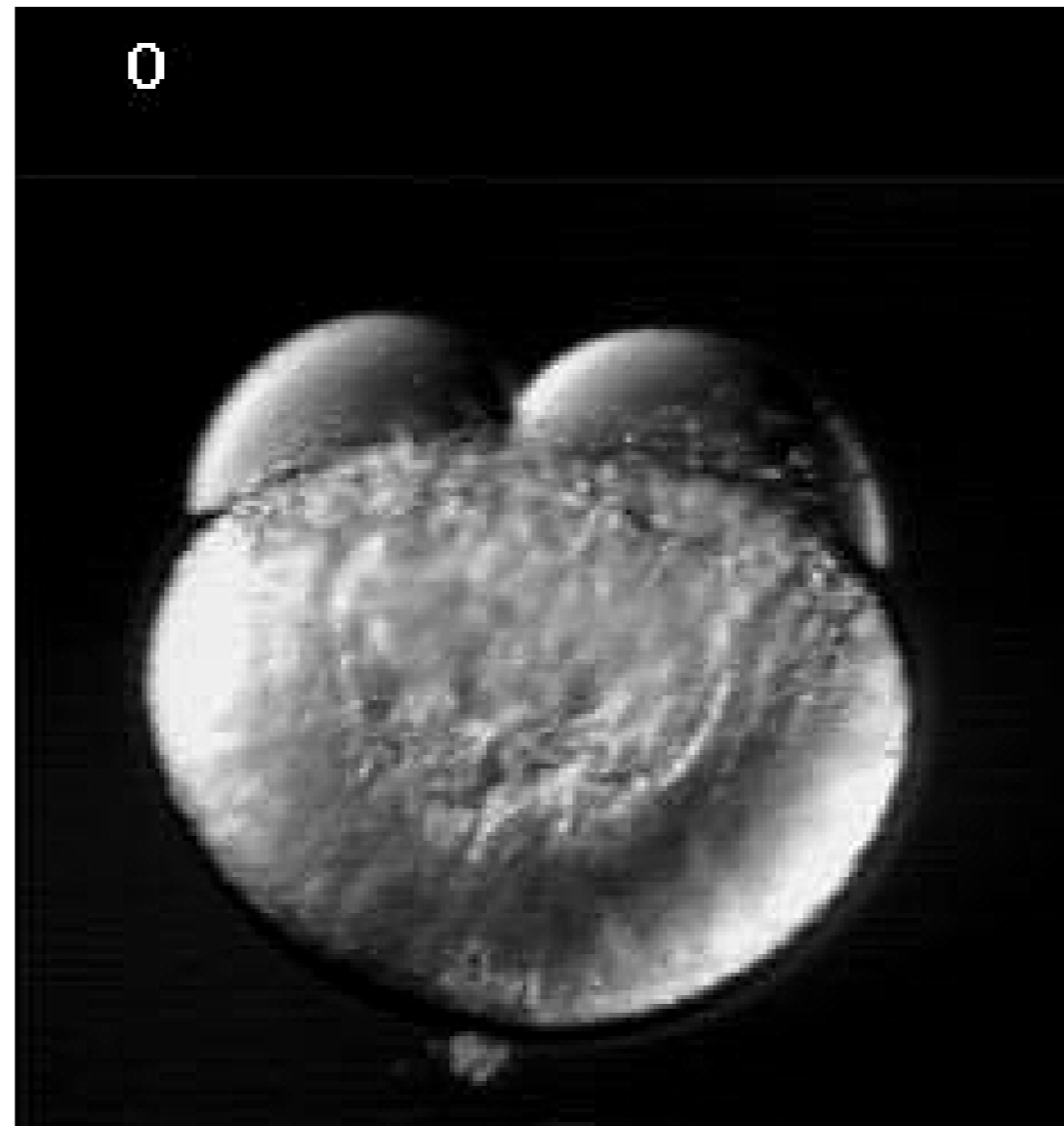




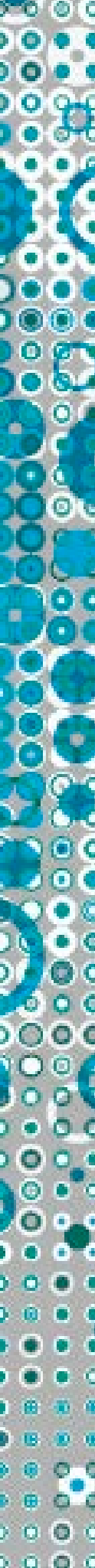
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# Zebravis ontwikkeling *time-lapse*

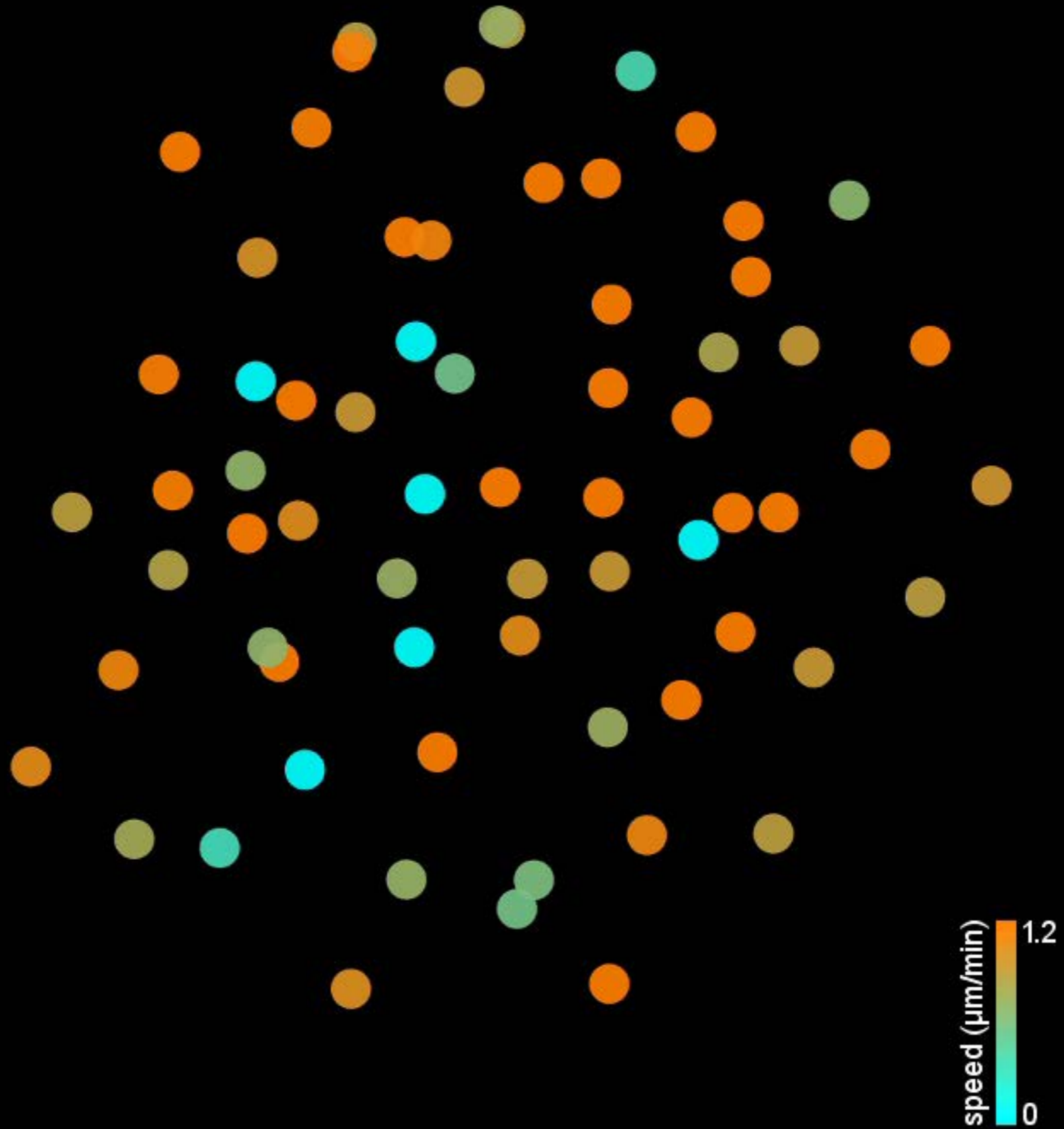


0 - 16 uur na fertilisatie





100 min



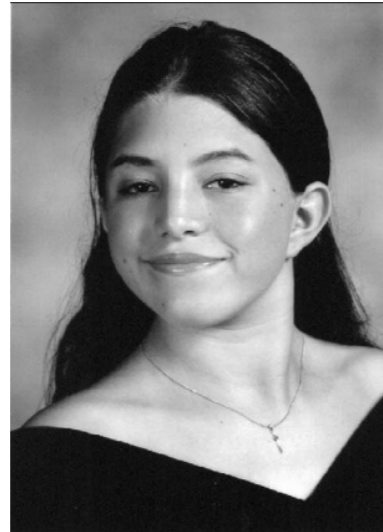
# Zebravissen als modelsysteem





# Noonan syndroom en LEOPARD syndroom

## Symptomen



### Noonan Syndrome (NS):

klein van stuk  
hypertelorisme  
hartafwijkingen

~1:2000 aangedaan

50% veroorzaakt door  
activerende mutatie  
in *PTPN11*



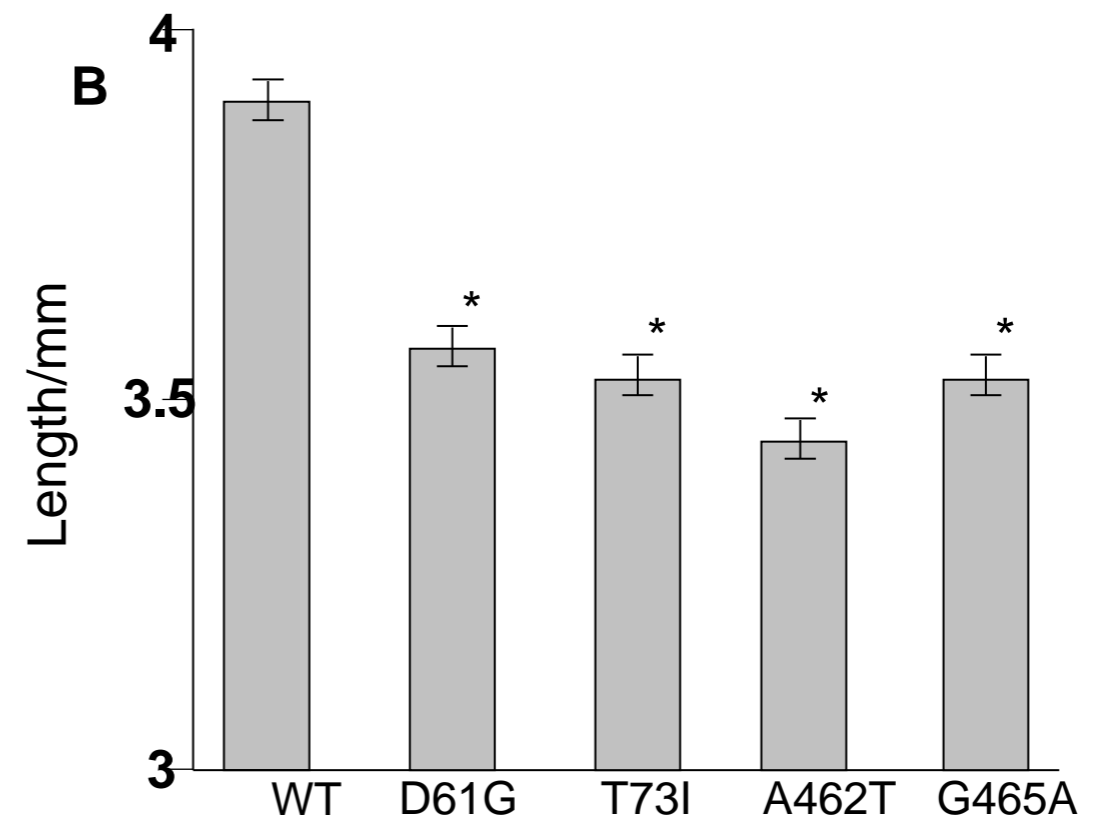
### LEOPARD syndrome (LS):

Lentiginosities  
Electrocardiographic defects  
Ocular hypertelorism  
Pulmonary stenosis  
Abnormal genitals  
Retarded growth  
Deafness

sporadisch

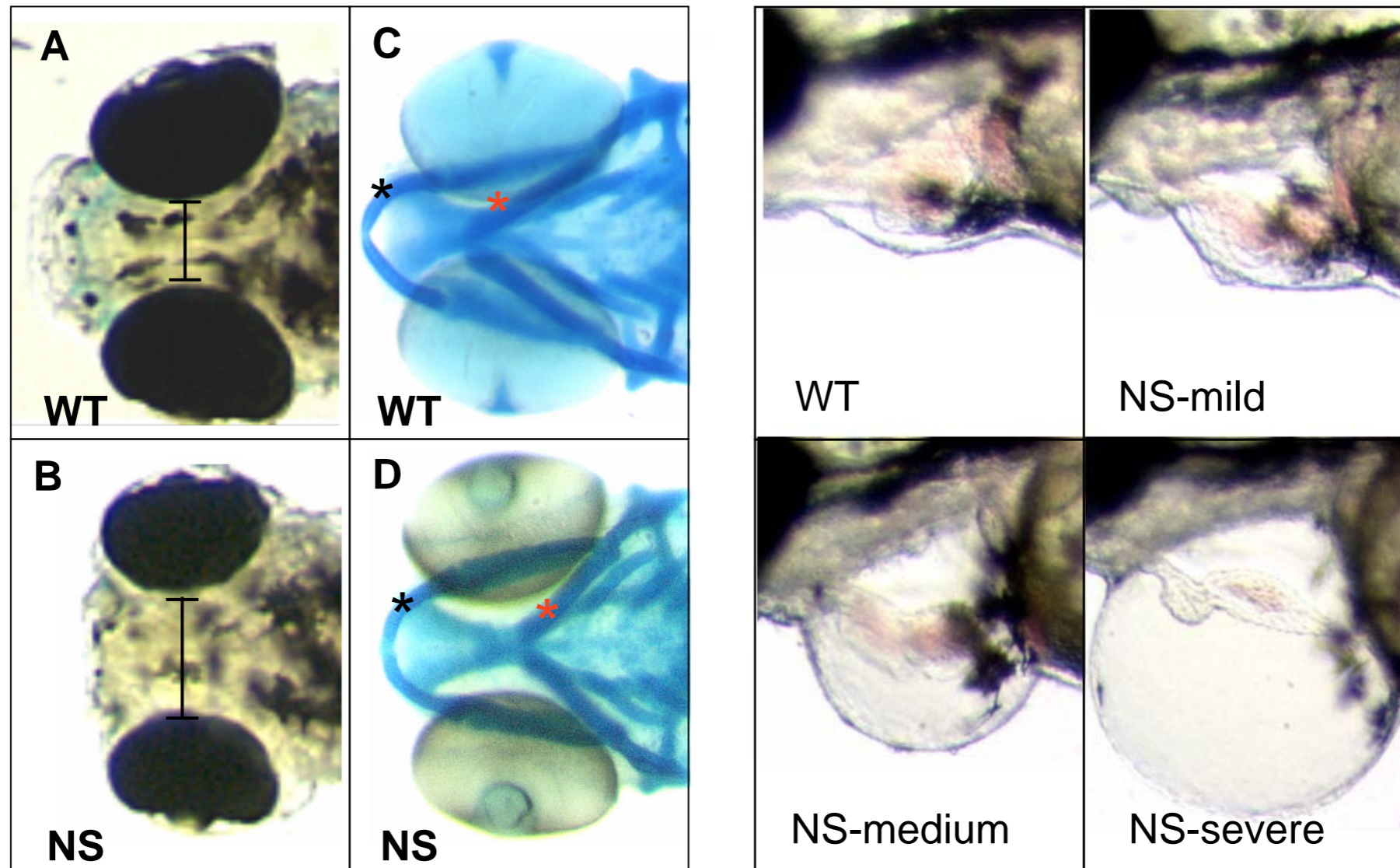
90% veroorzaakt door  
inactiverende mutaties  
in *PTPN11*

# Noonan and LEOPARD varianten van *ptpn11* induceren defecten in zebravis embryos

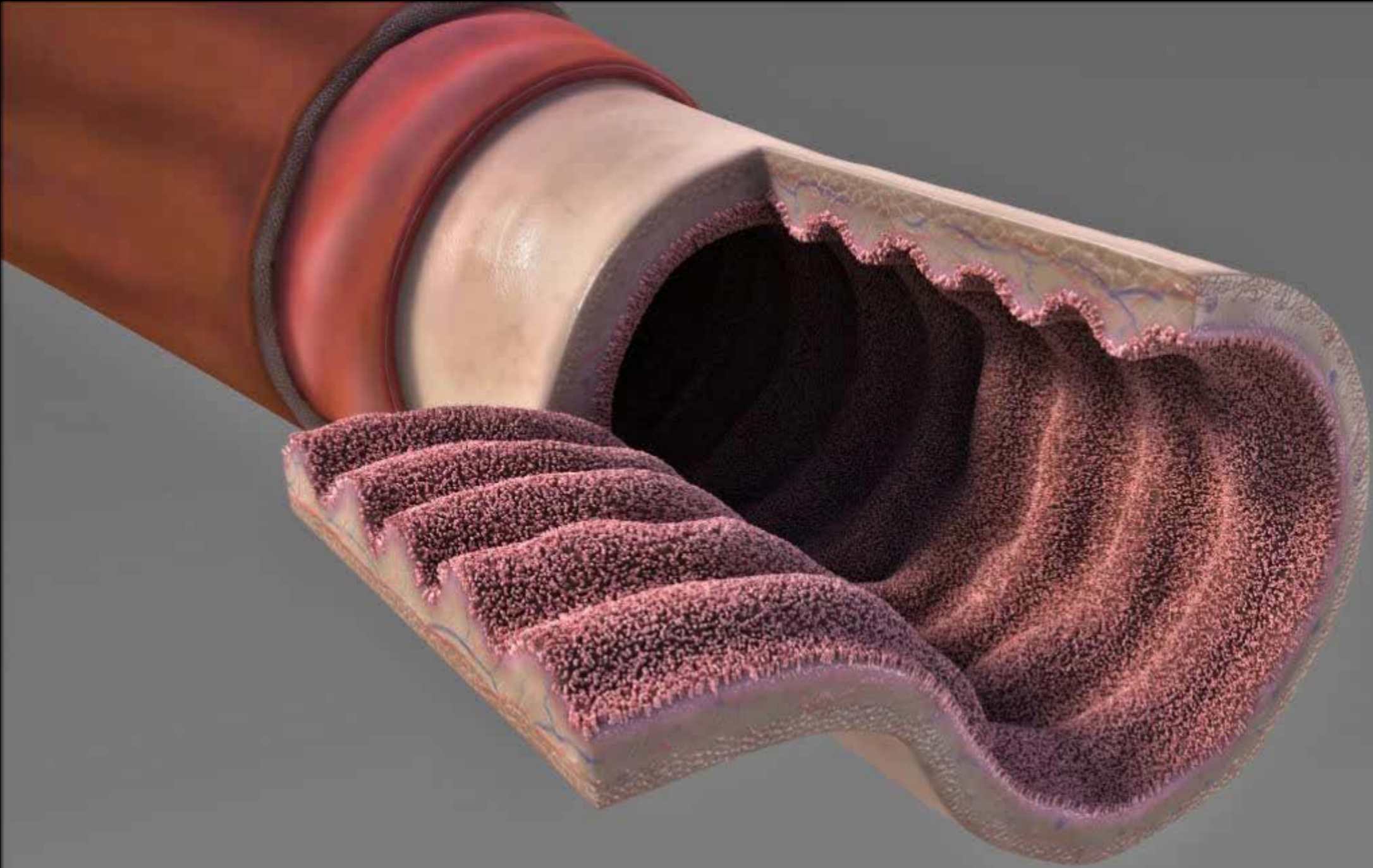




# Noonan and LEOPARD varianten van *ptpn11* induceren defecten in zebravis embryos



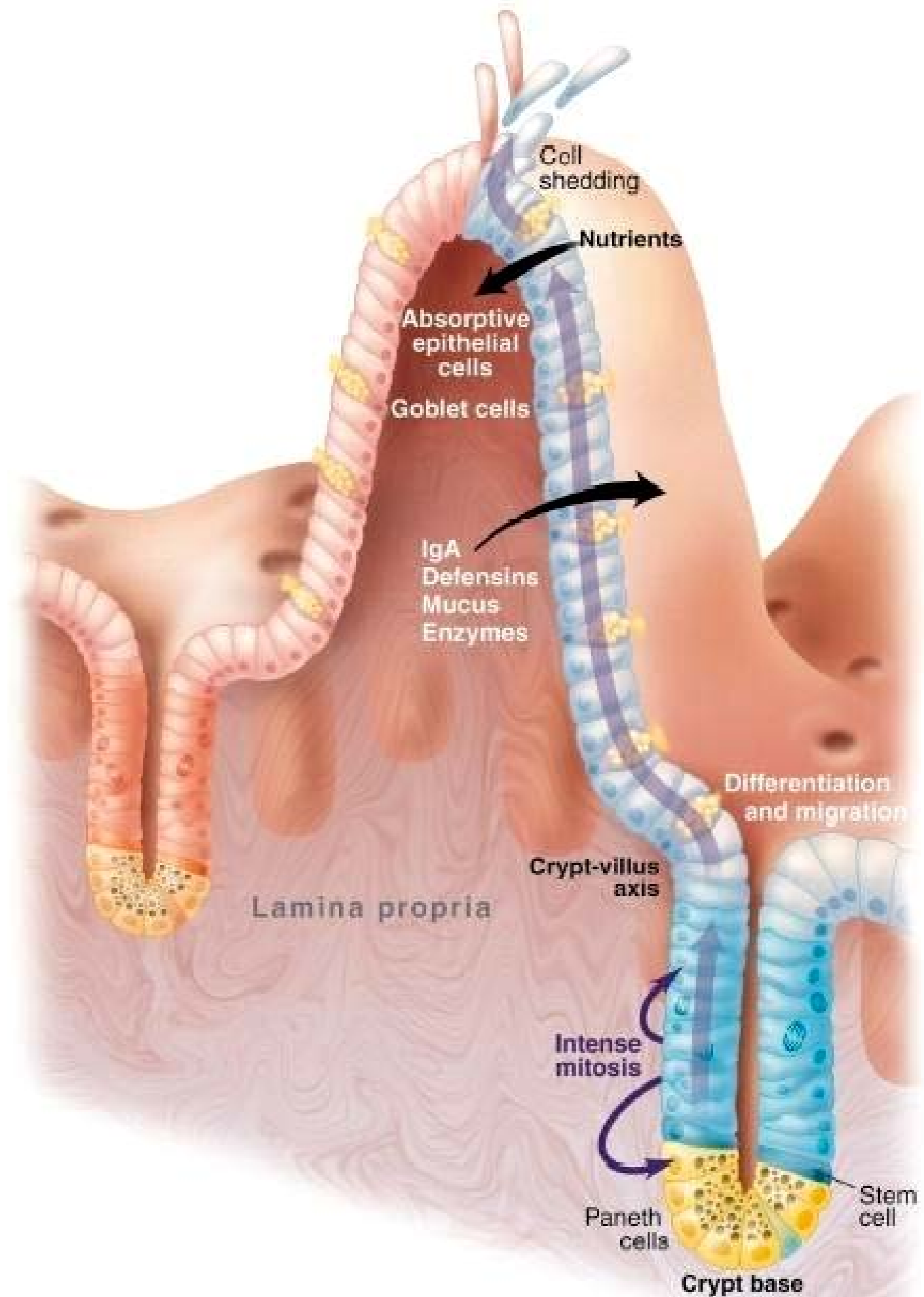
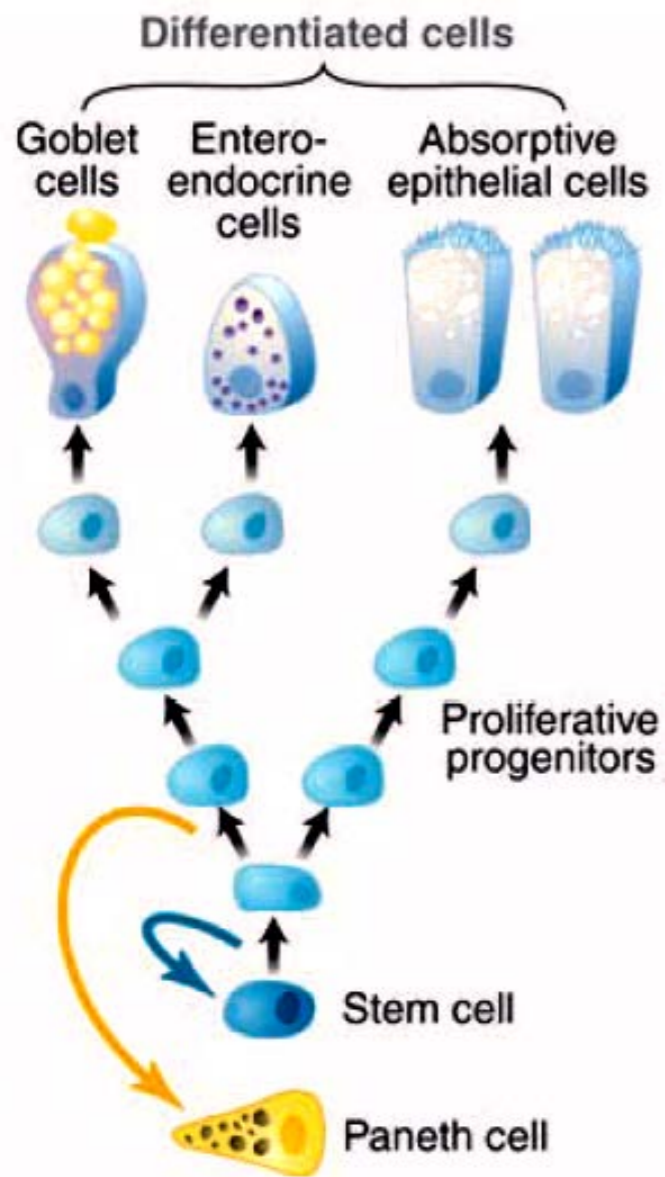
Defecten lijken veel op symptomen bij mensen



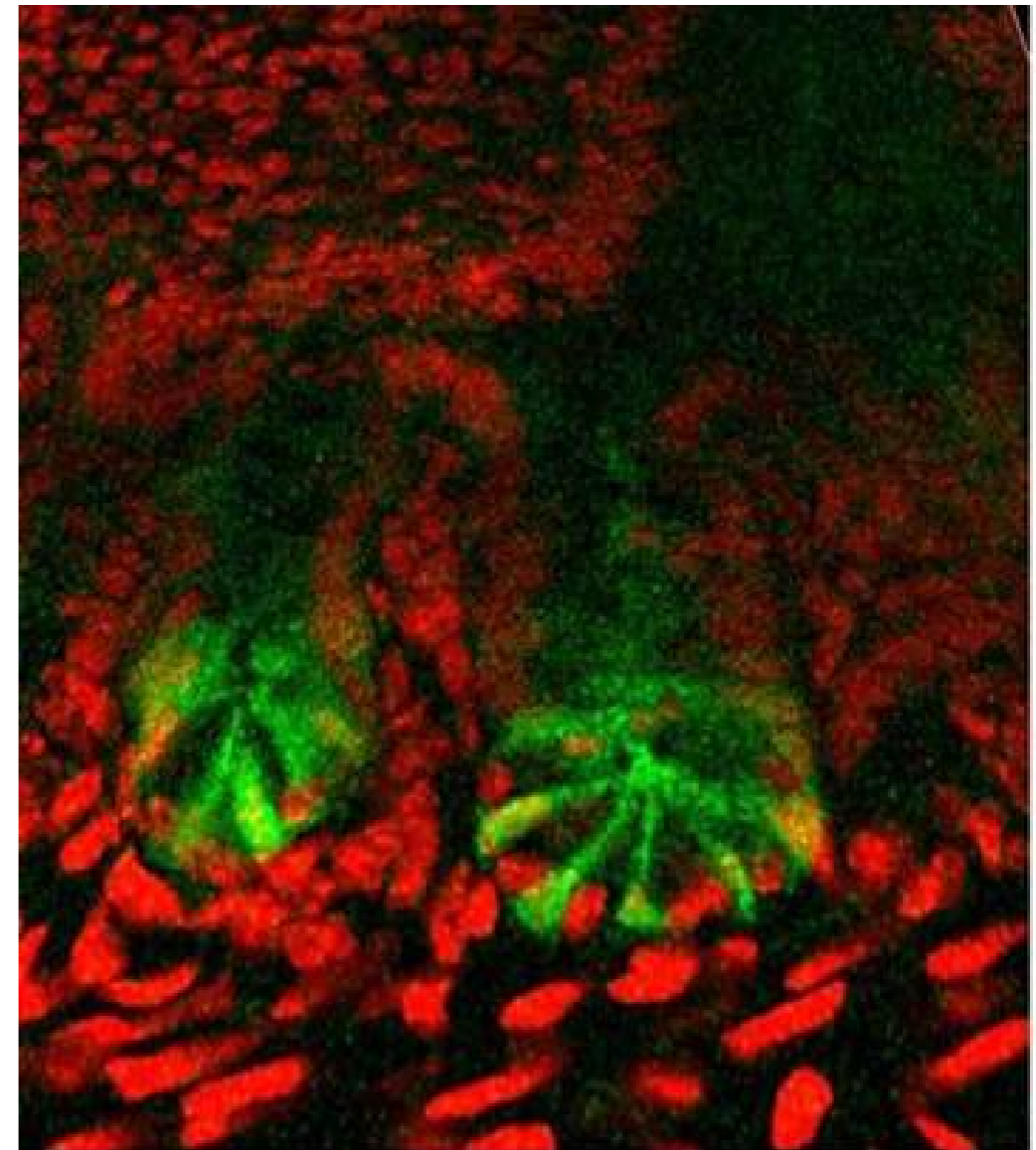
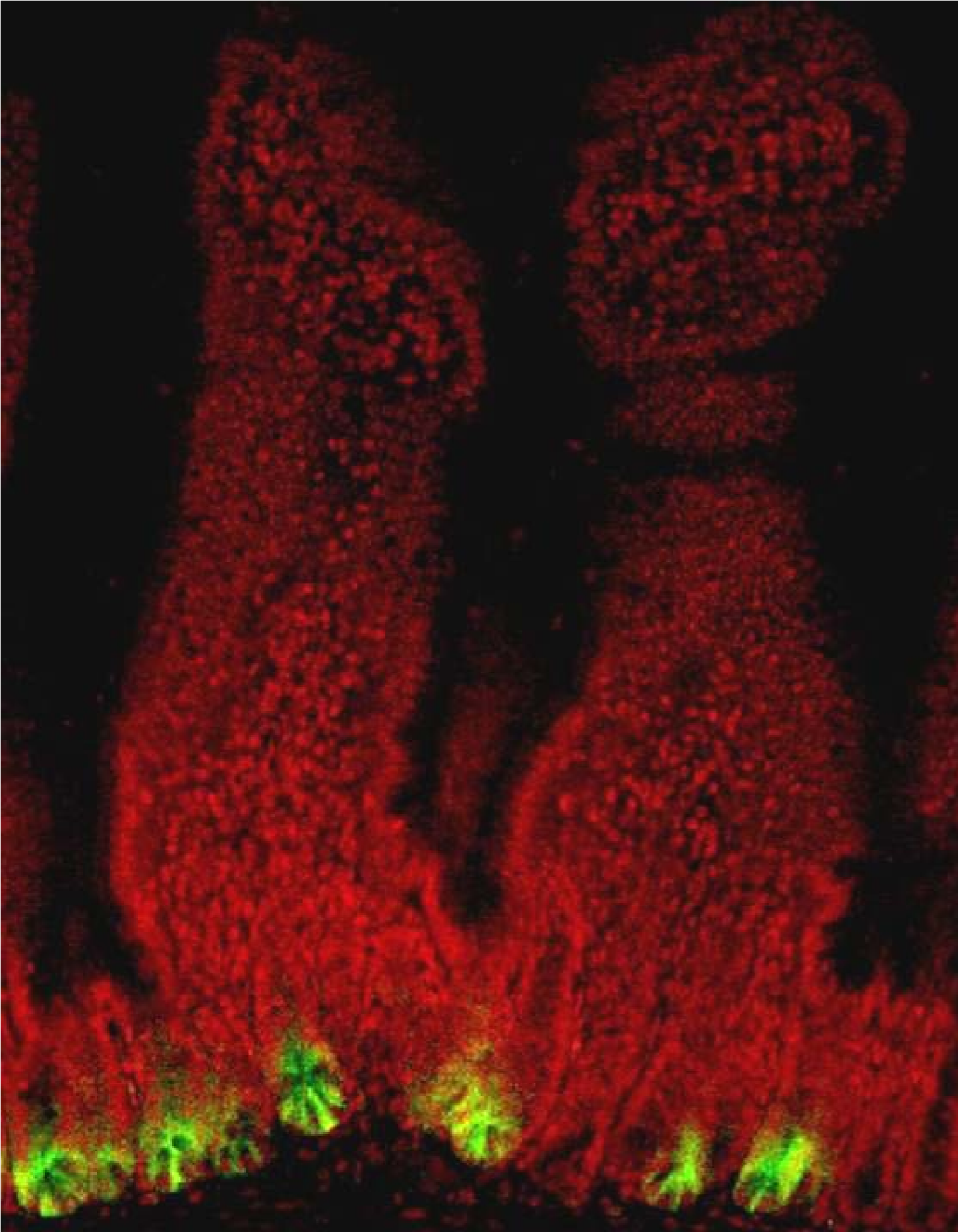




# Epithelial self-renewal in the small intestine

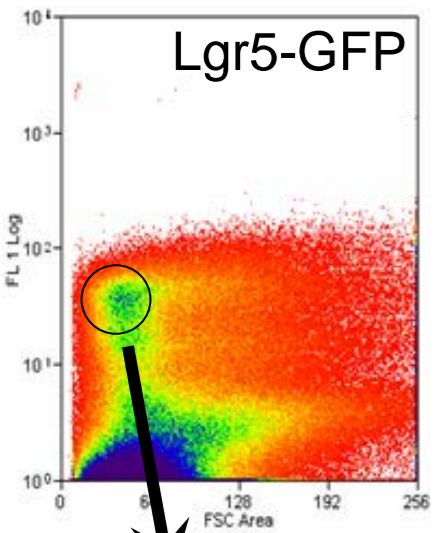


Lgr5-Driven GFP  
Expression in Crypt  
Base Columnar Cells





# Enkele Lgr5+ cellen vormen crypt structuren in Matrigel *in vitro*



Day 0 Day 1 Day 2



Day 3



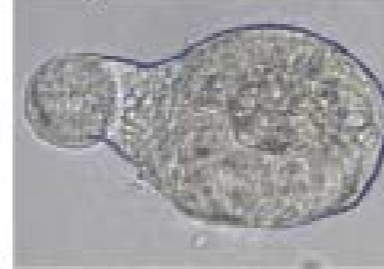
Day 4



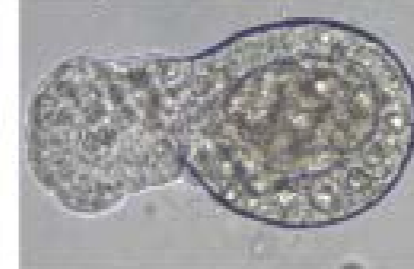
Day 5



Day 6



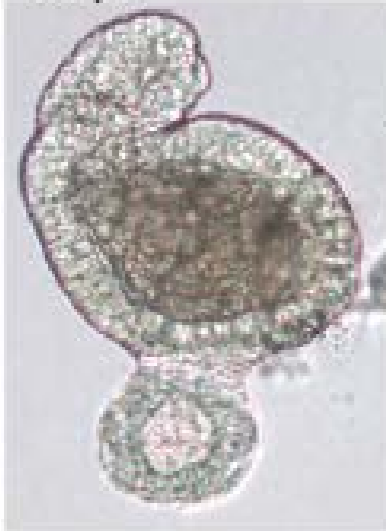
Day 7



Day 8



Day 9



Day 10



Day 11



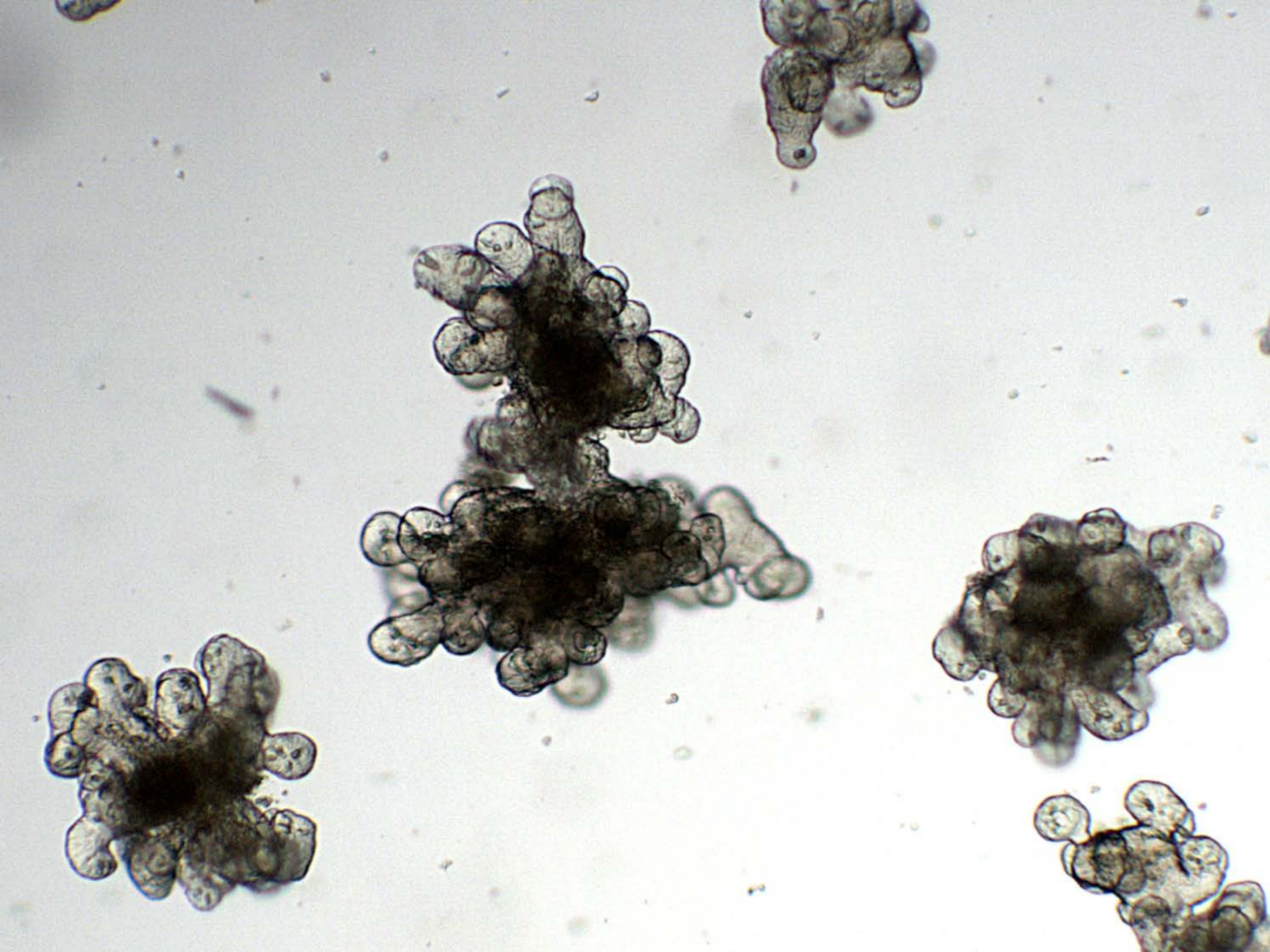
Day 12



Day 13







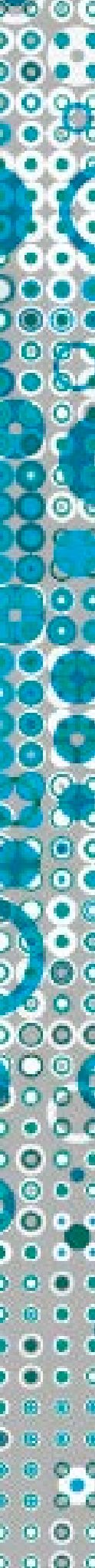
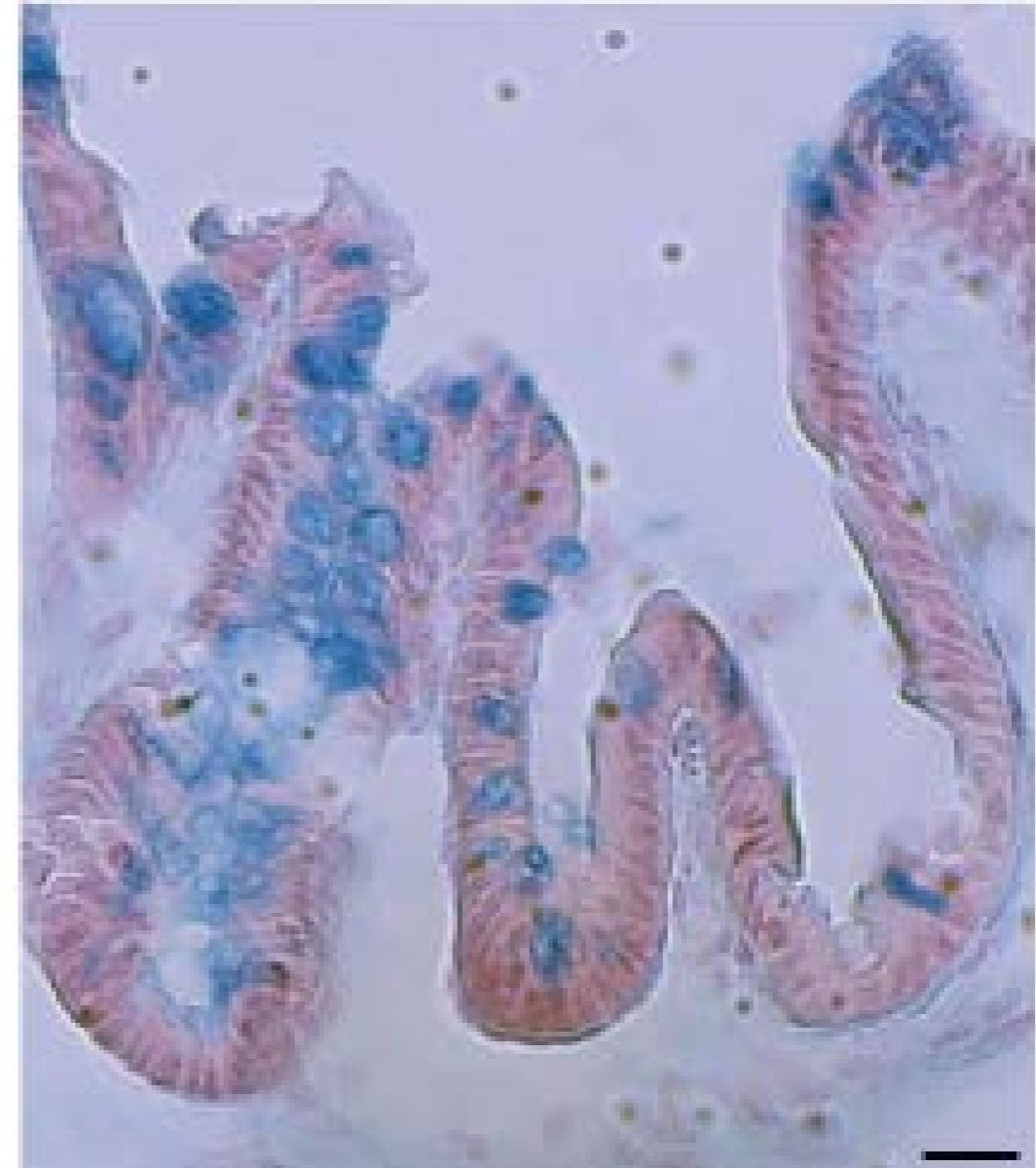
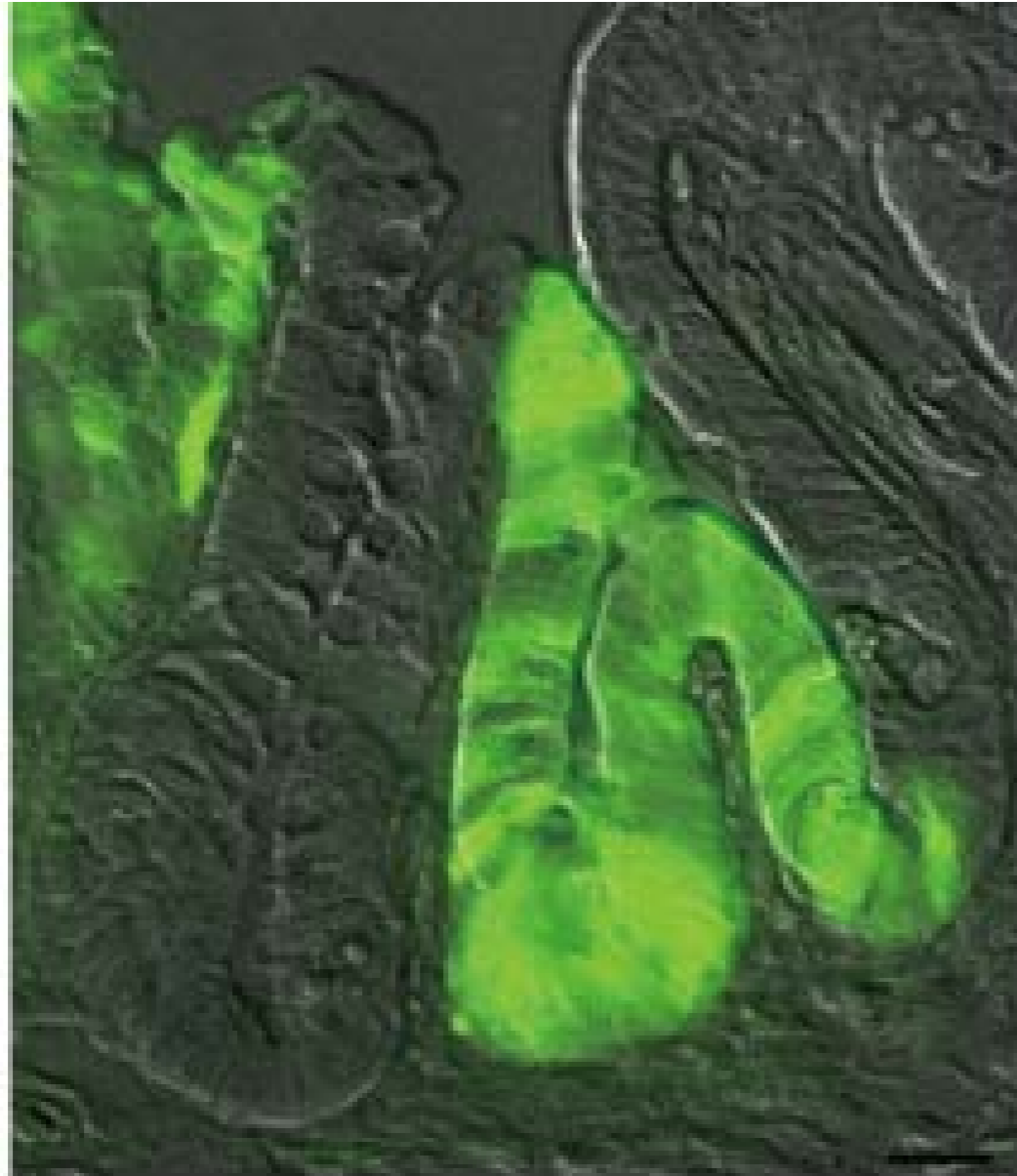




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# Succesvolle transplantatie van *in vitro* organen (muis)

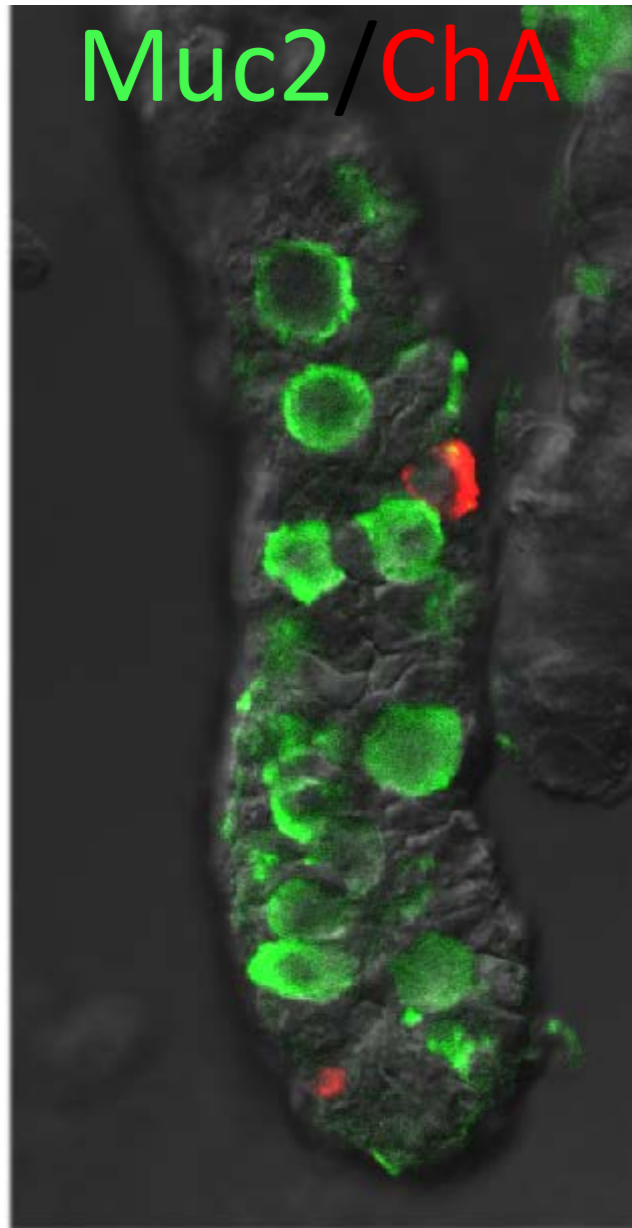




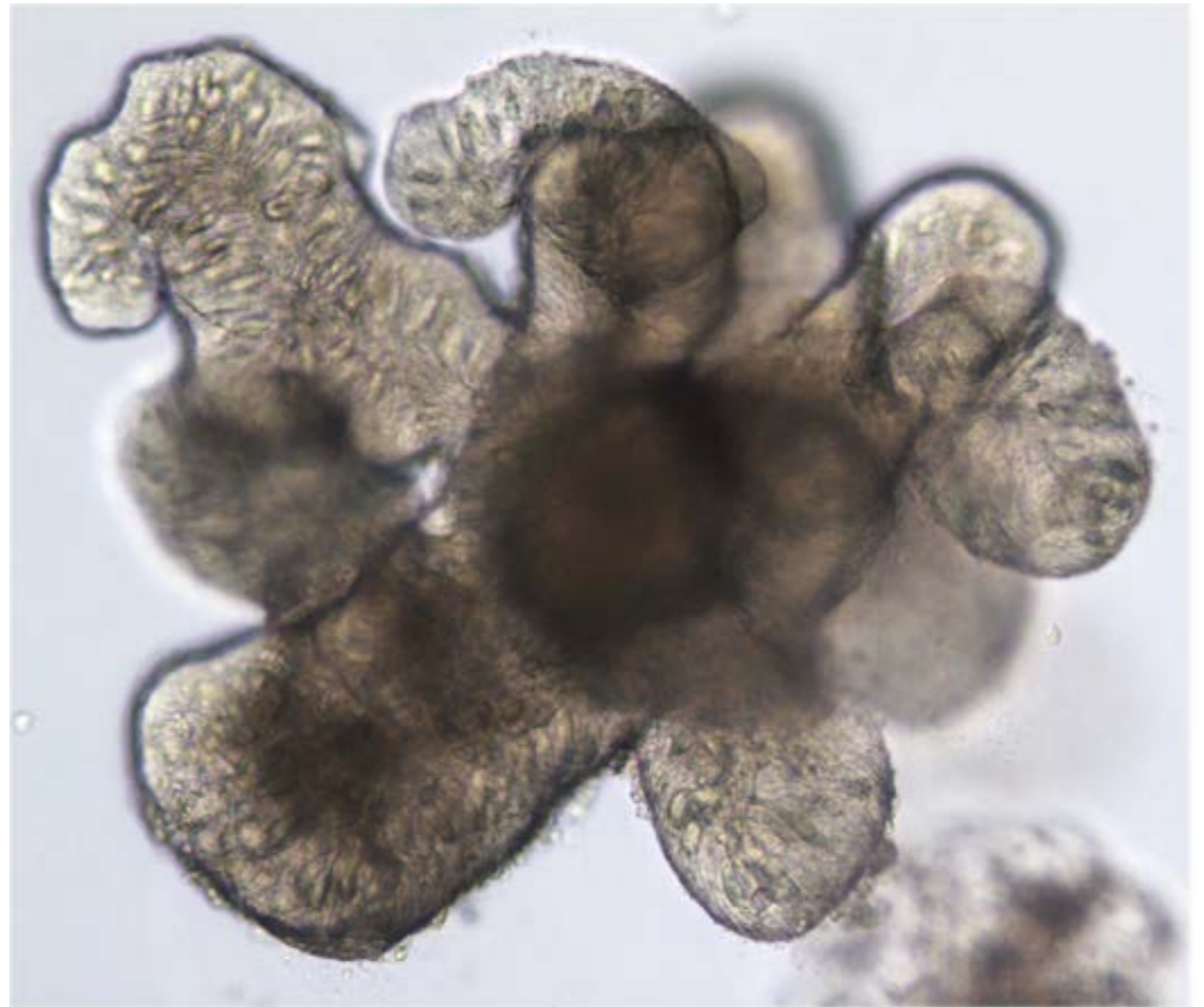
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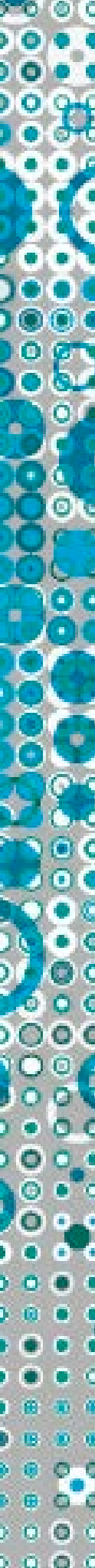
# Groeien van menselijke dikke darm *in vitro*



Freshly isolated crypt



Cultured organoids







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## Normalized impact

MIT

2.4 

Harvard University

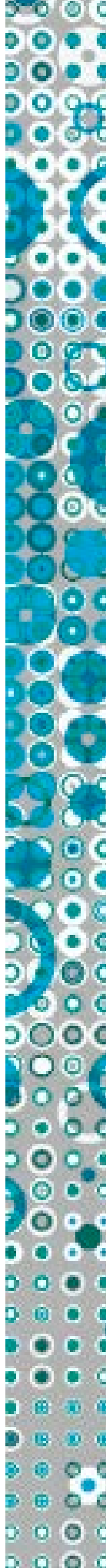
2.4 

Stanford University

2.3 

CalTech

2.0 





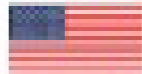
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## Institute

## Normalized impact

MIT  
Harvard University  
Stanford University  
CalTech  
Max Planck Institutes

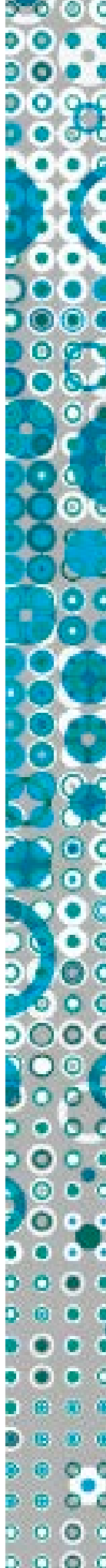
2.4 

2.4 

2.3 

2.0 

1.8 







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and Stem Cell Research

## Institute

## Normalized impact

MIT

2.4 

Harvard University

2.4 

Stanford University

2.3 

KNMI

2.1 


CalTech

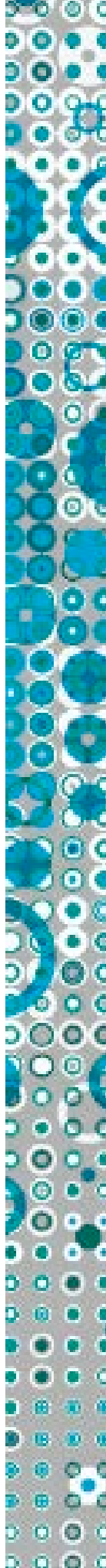
2.0 

NKI

1.9 

Max Planck Institutes

1.8 





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and Stem Cell Research

## Institute

## Normalized impact

Hubrecht

2.6 

MIT

2.4 


Harvard University

2.4 

Stanford University

2.3 


KNMI

2.1 


CalTech

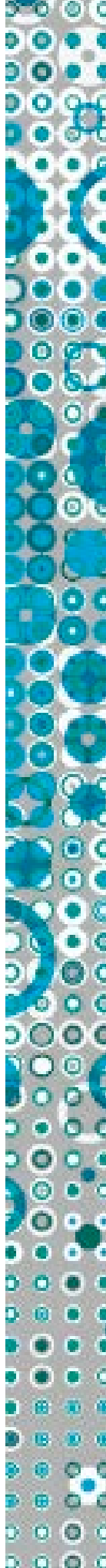
2.0 

NKI

1.9 

Max Planck Institutes

1.8 







## Samengevat

- Het Hubrecht Institute heeft een rijke historie
- Het Hubrecht Institute doet excellent onderzoek, vergelijkbaar met top universiteiten in de VS zoals MIT en Harvard
- Het Hubrecht Institute heeft een top positie in biomedisch onderzoek met directe toepassingen in de kliniek (regeneratieve geneeskunde, kanker, diabetes)



 Hubrecht Institute

