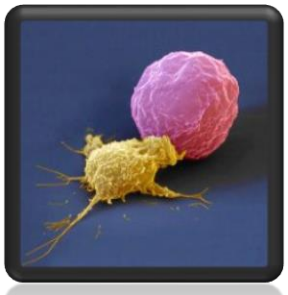
Op weg naar een betere genezing voor kanker!

3 oktober 2016

Gerard MJ Bos, MD, PhD
Professor Immunotherapy of Cancer
MUMC+ , Maastricht

De oplossing…?



Het immuunsysteem bevecht vijanden van buiten, maar kan ook helpen om vijanden binnen te bestrijden:

kanker cellen

Hoe behandelden we kanker nu / tot voor kort?

Operaties

Chemotherapie

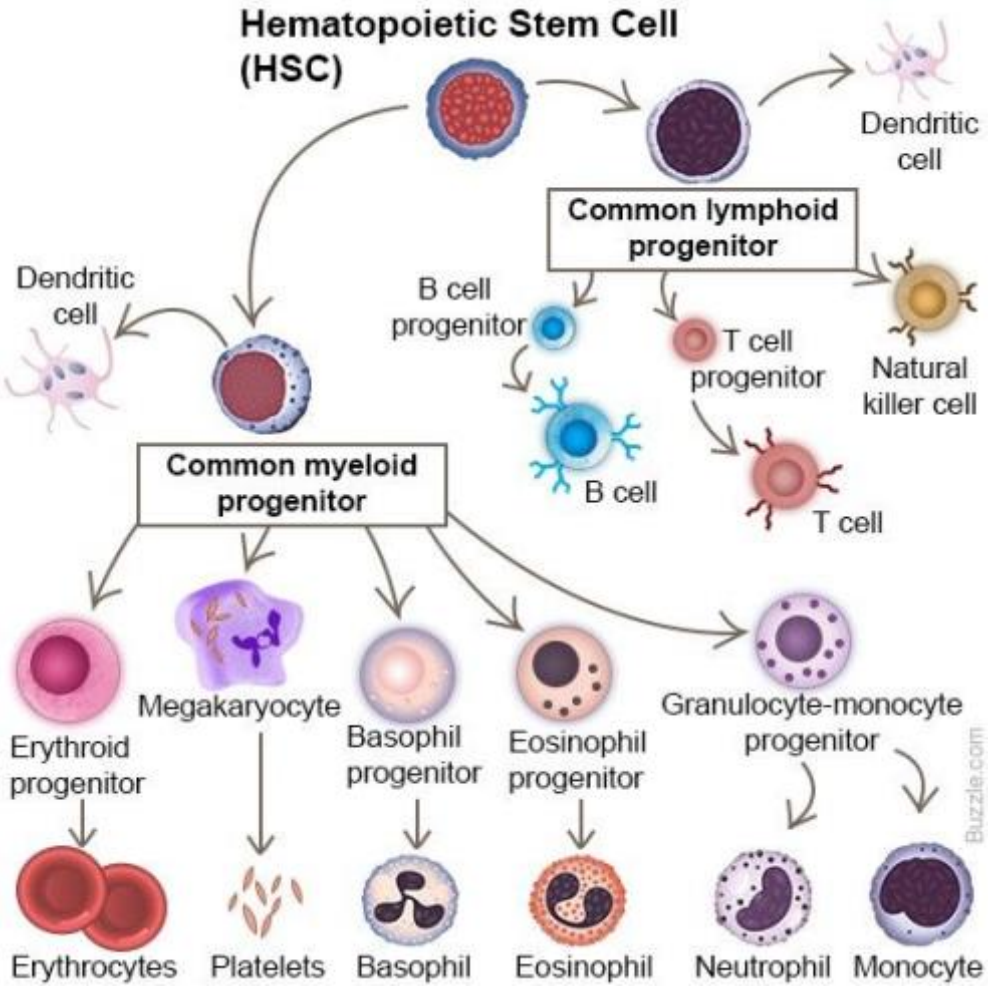
Bestraling

Meer specifieke therapievormen

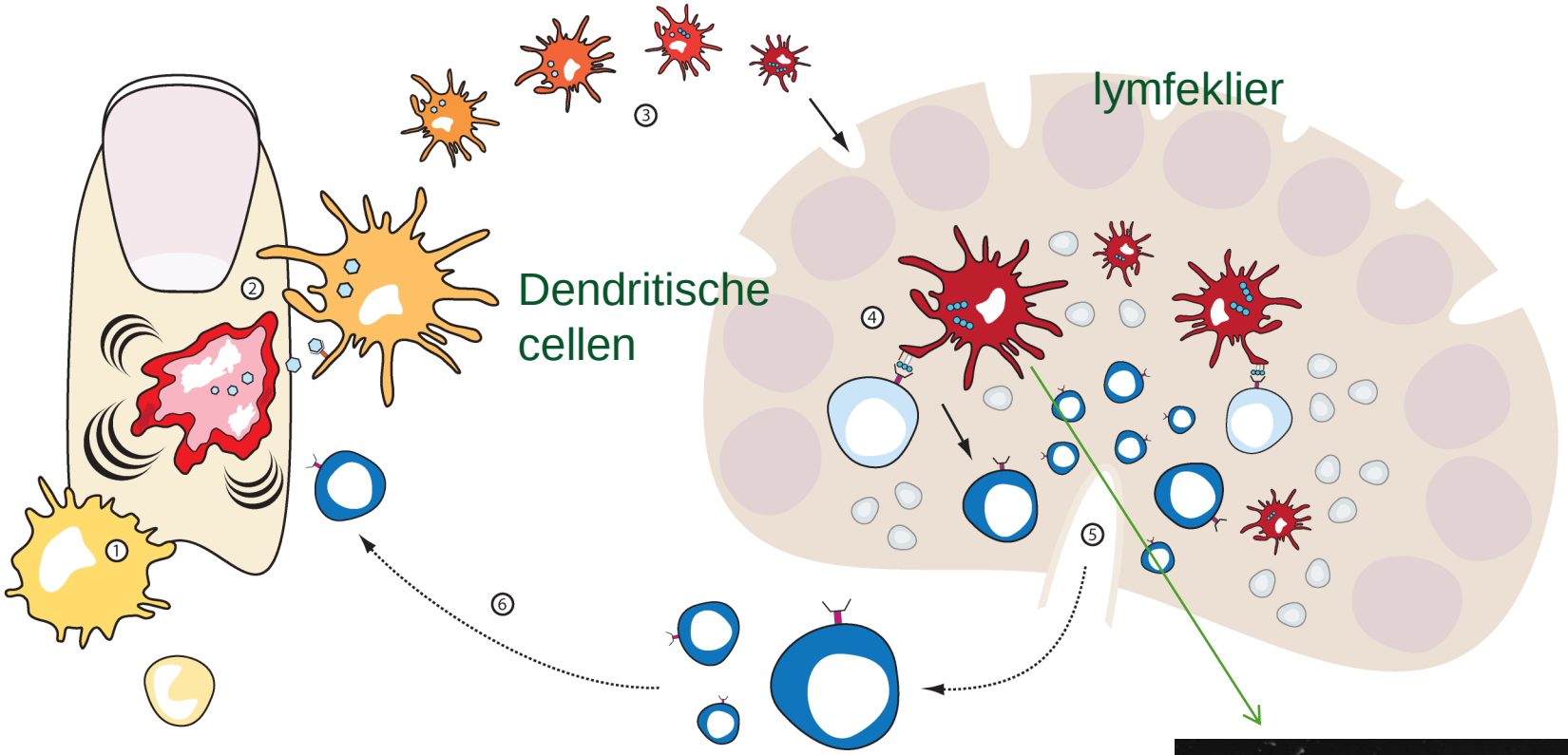
Immunotherapie

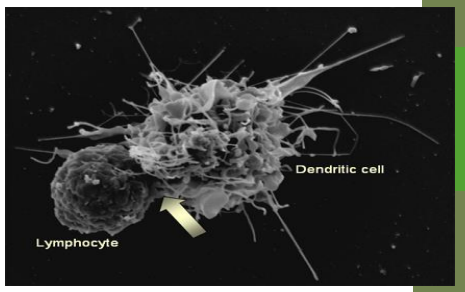
……

Wat is immunotherapie?

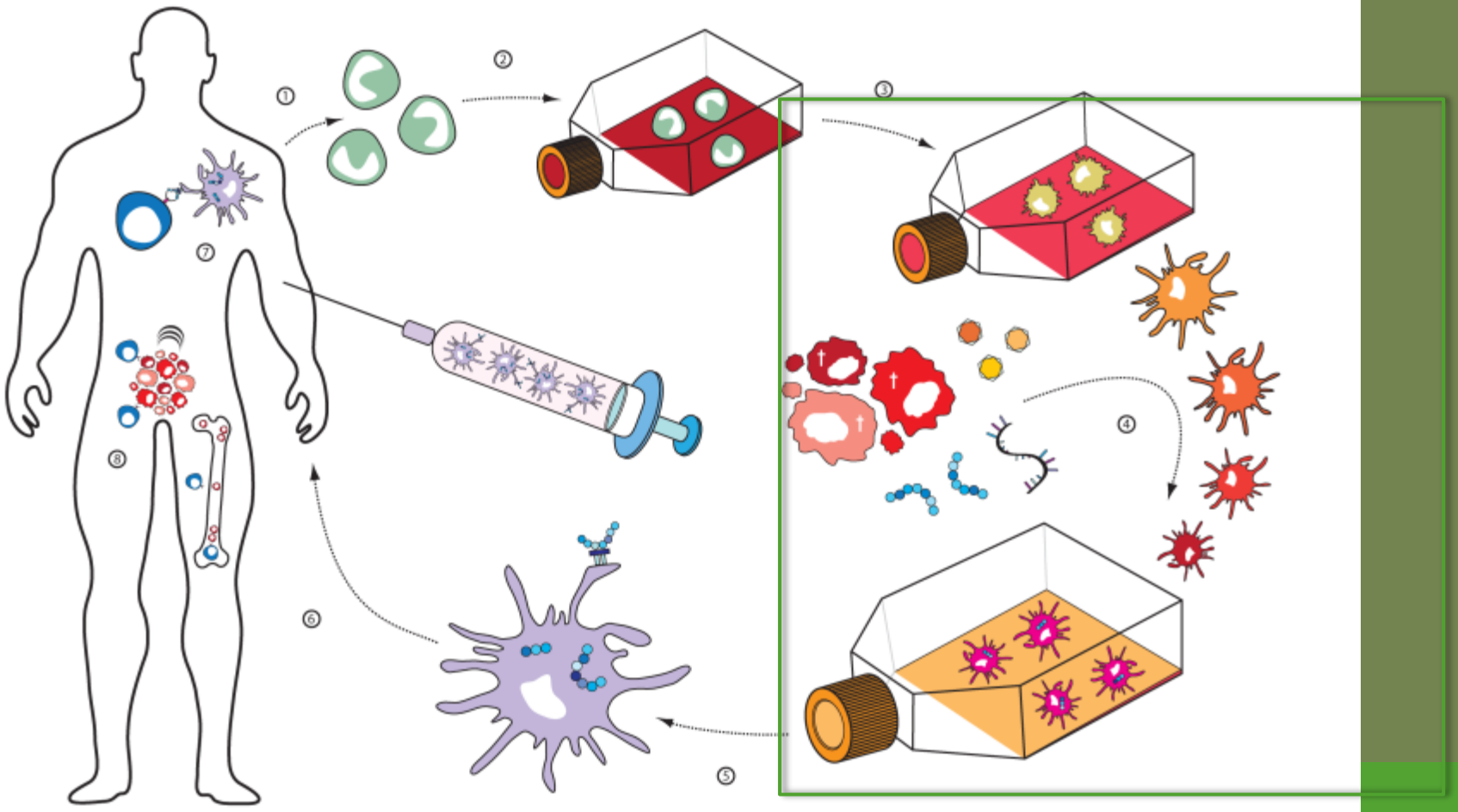


Wat gebeurt er bij een wondje?



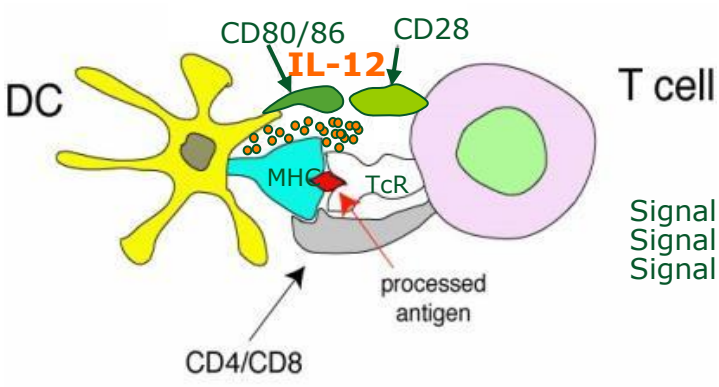


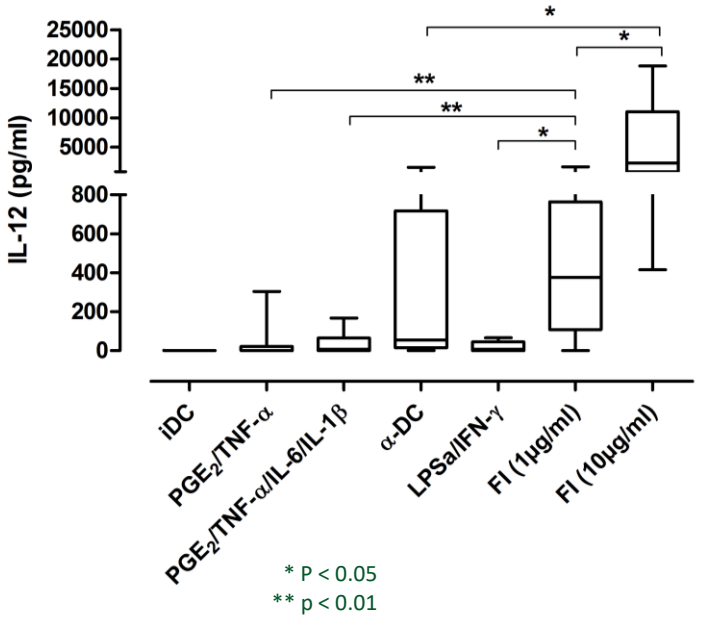
Het immuunsysteem kan ook gebruikt worden om een vaccin te maken (Wilfred Germeraad et al)



Laboratorium

Superieure activiteit (I)

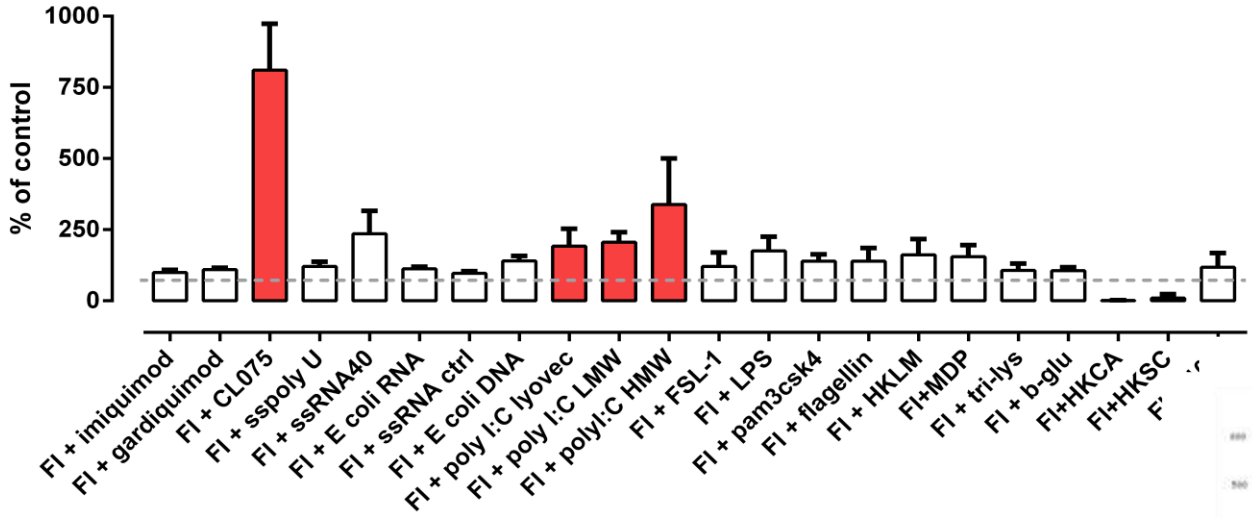




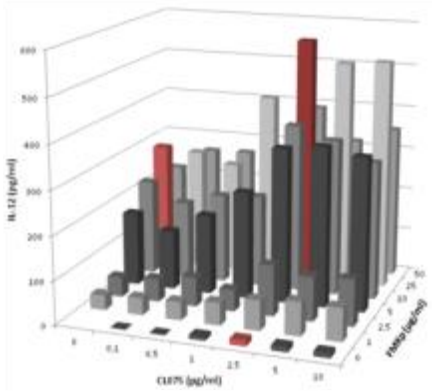
Activatie van de DC is cruciaal!

FI = FMKp + IFN-γ

Enhanced IL-12 production FMKp/IFN-y in combination with CL075

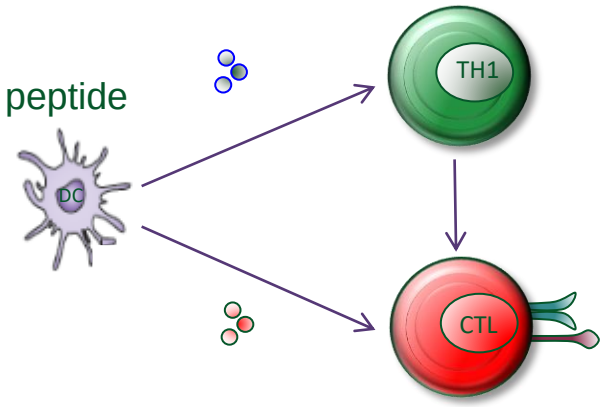


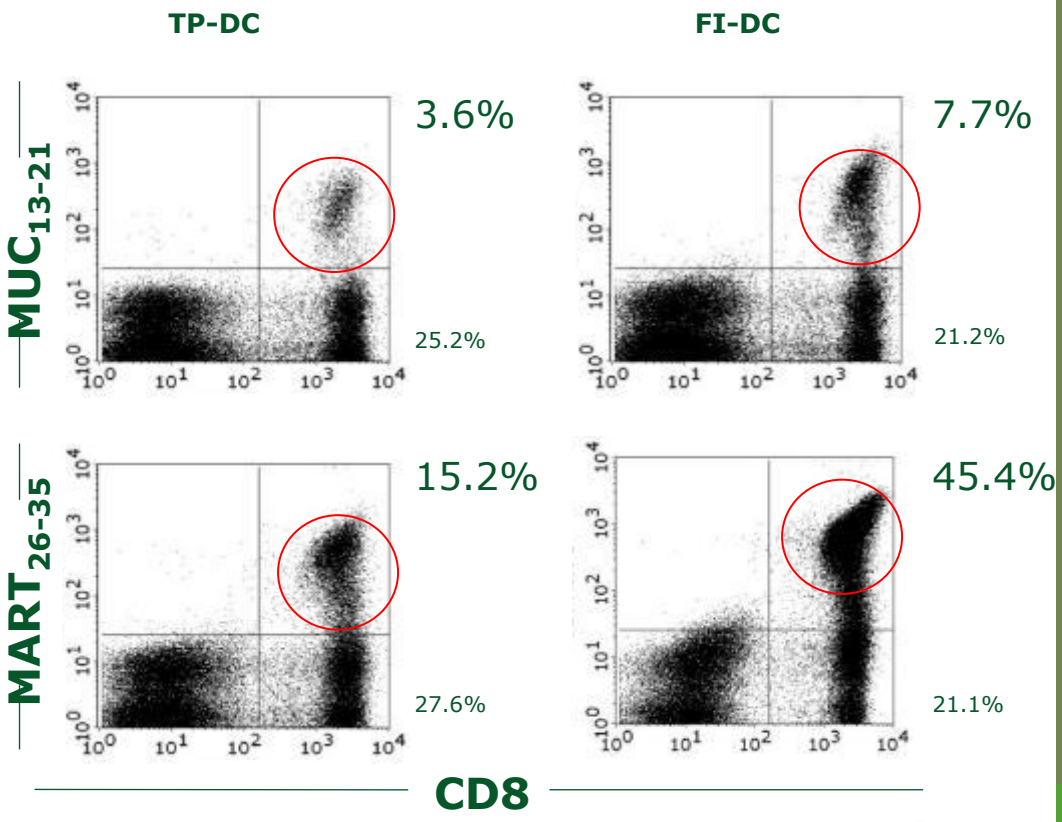
IL-12 production



Oth et al, several published/submitted manuscripts. Bos, Germeraad et al., patent filed

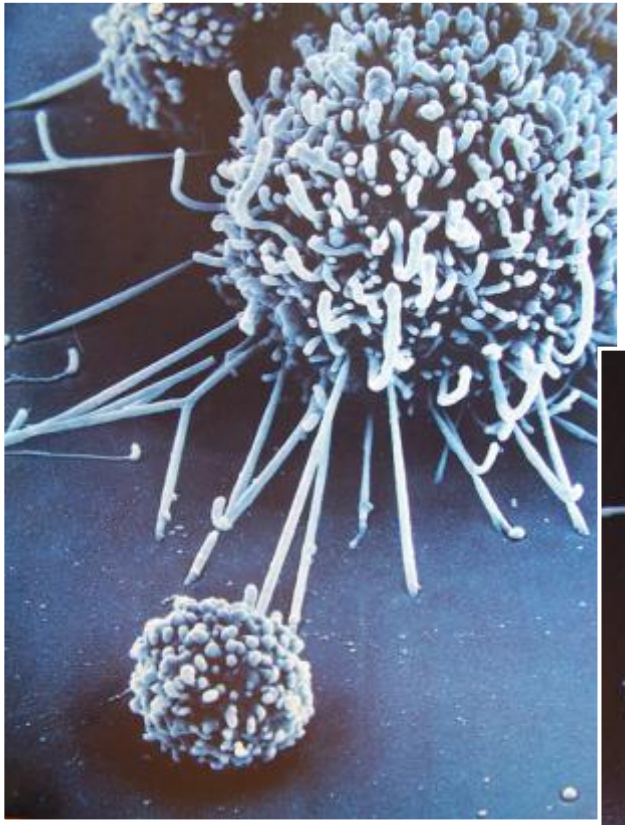
FMKp DC induce more antigen-specific CD8+ T cells

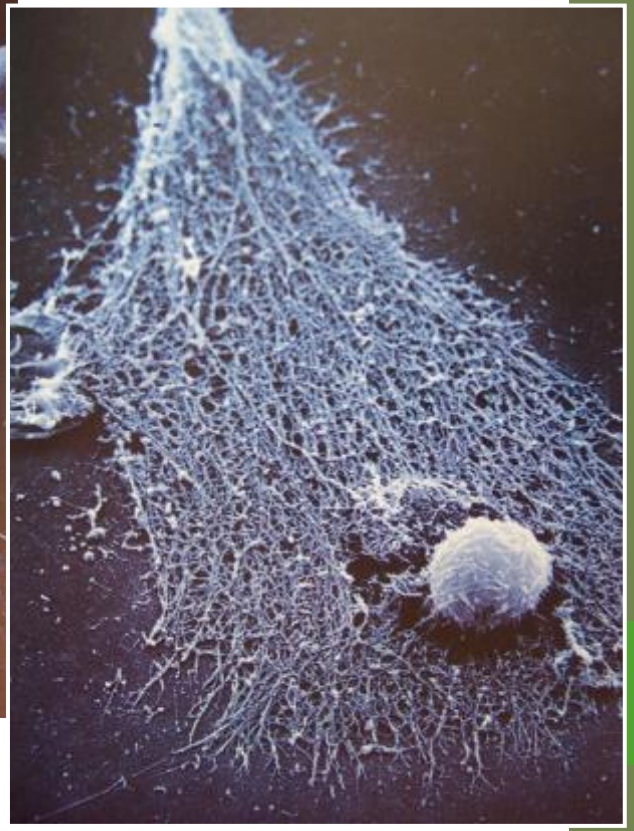


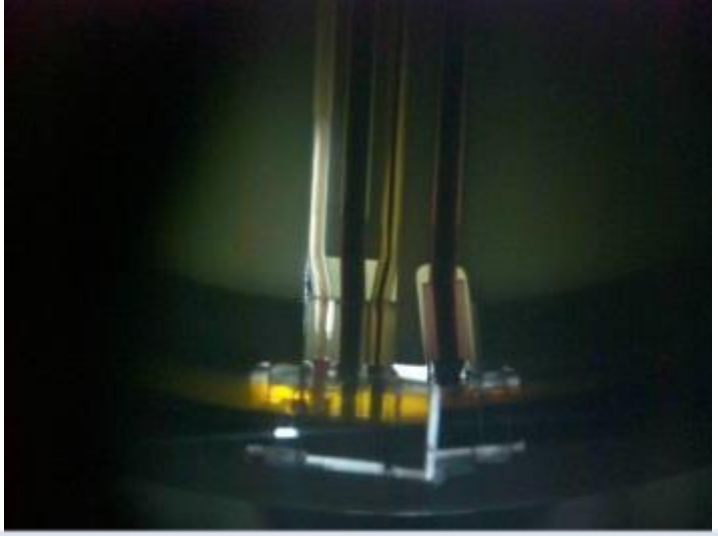


Vanderlocht et al, Int J Immunopathol Pharmacol. 2010;23(1):35-

Killer Cellen

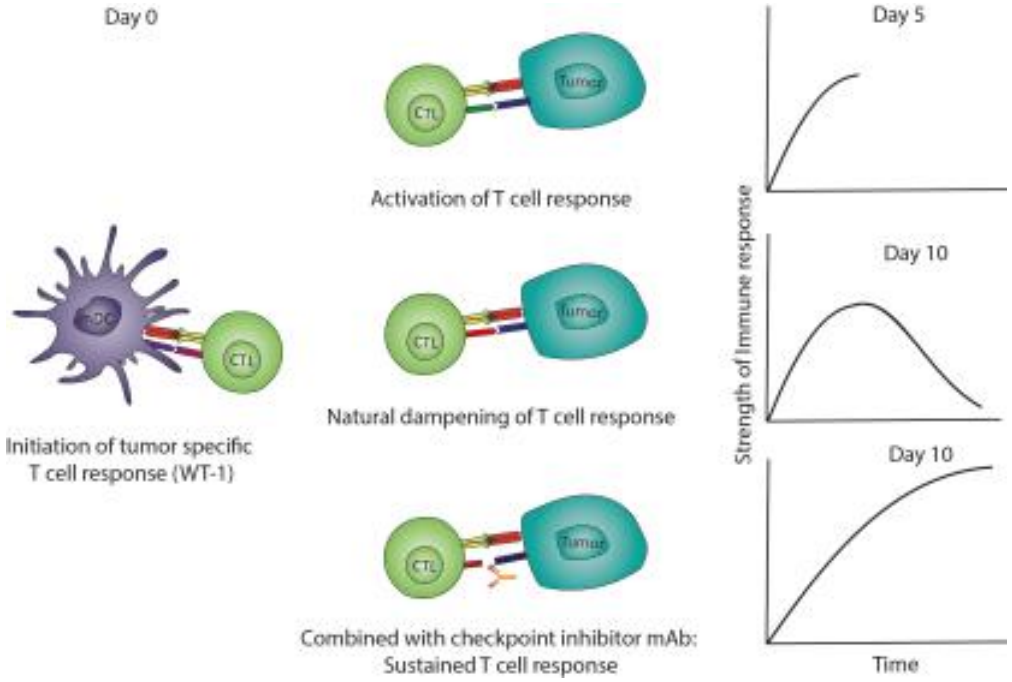




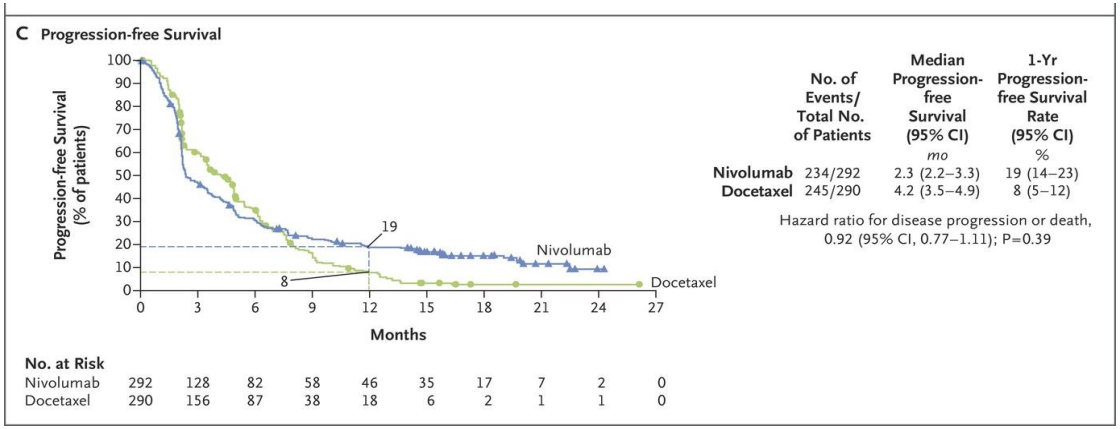



Tubing Set
Roller Pump
Centrifugation/
cell culture
chamber
Touch Screen
Magnet unit for
separation
column
TubeSealer
Bar code reader

Vaccin studie bij longkanker, start 2017



Hypothesis: 1 +1 = 3 for clinical success



Hoe behandelen we kanker nu?

Operaties

Chemotherapie

Bestraling

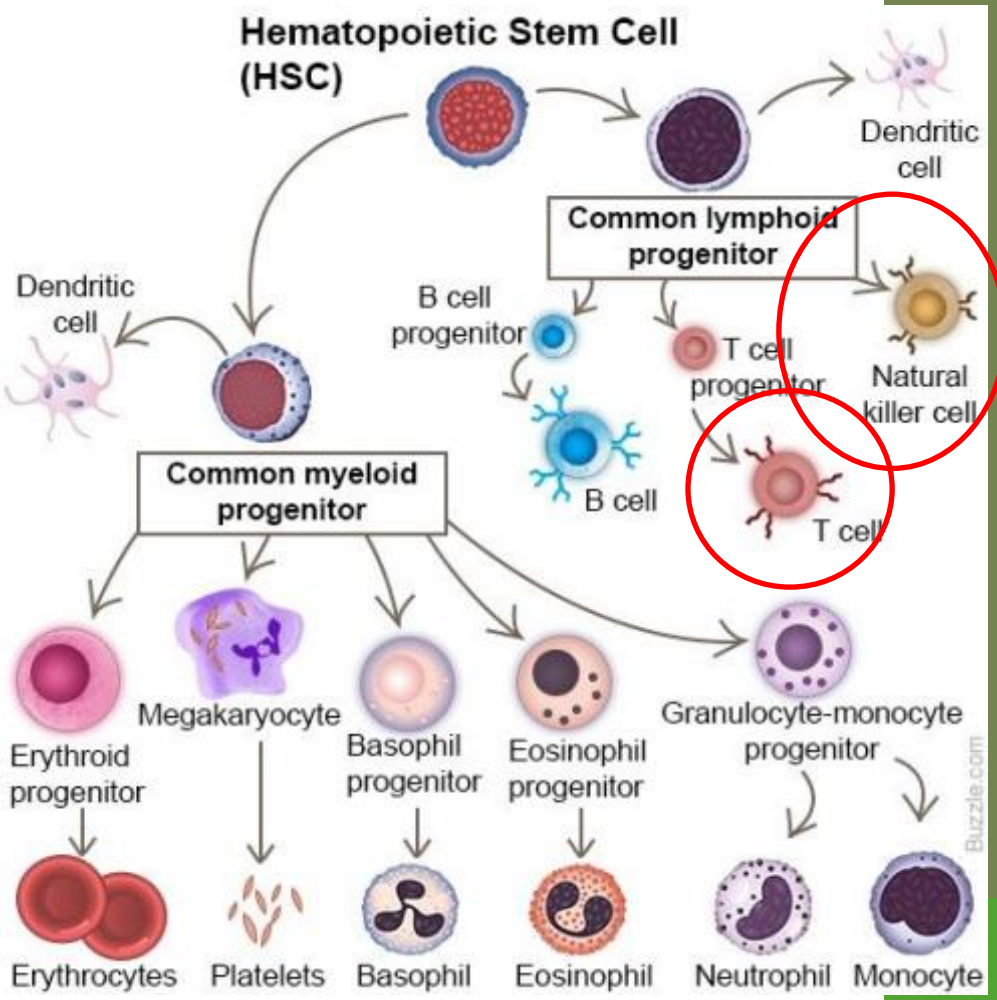
Medicijnen (specifiek)

Immunotherapie

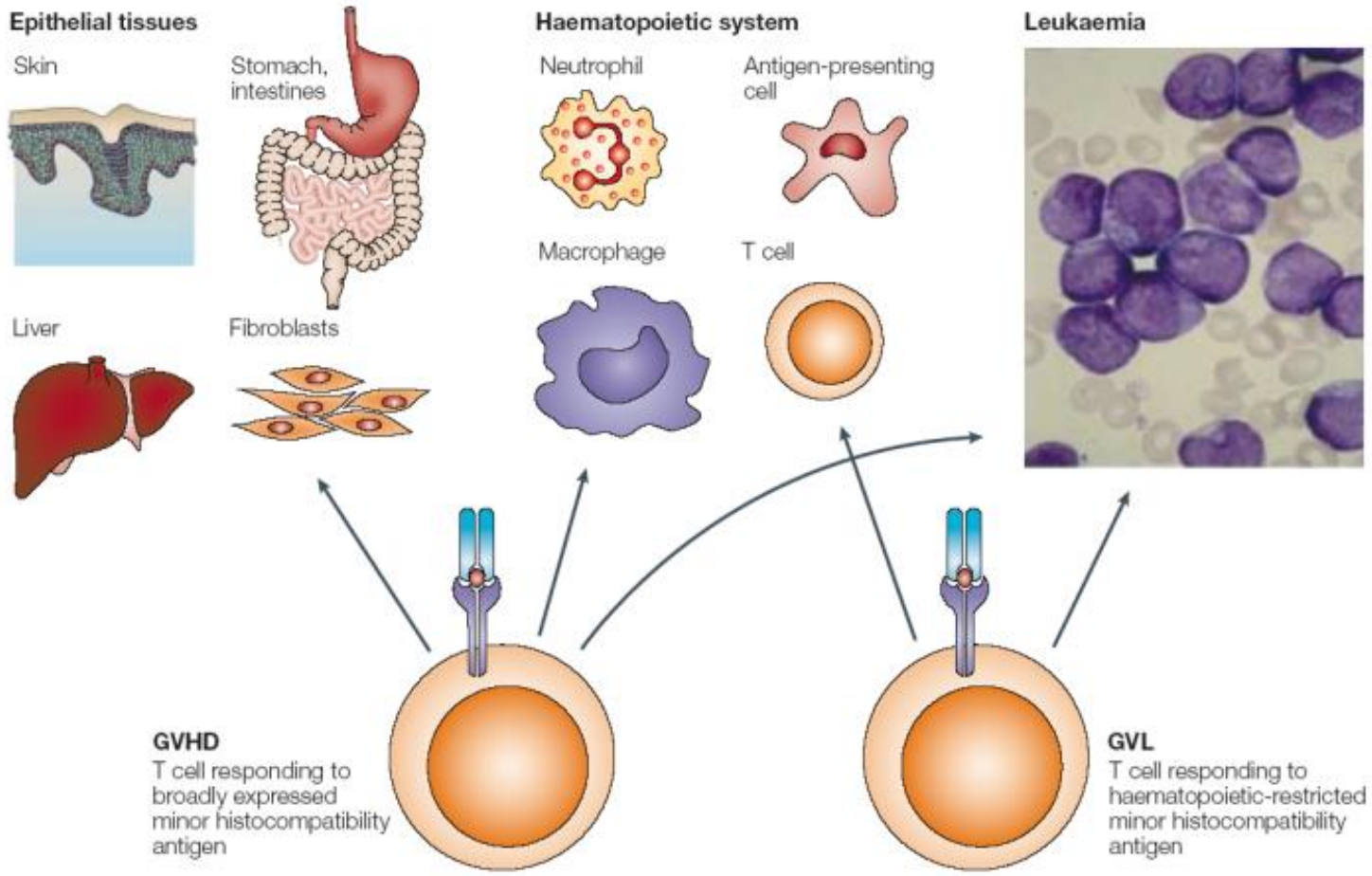
……

Allogene stamcel transplantatie

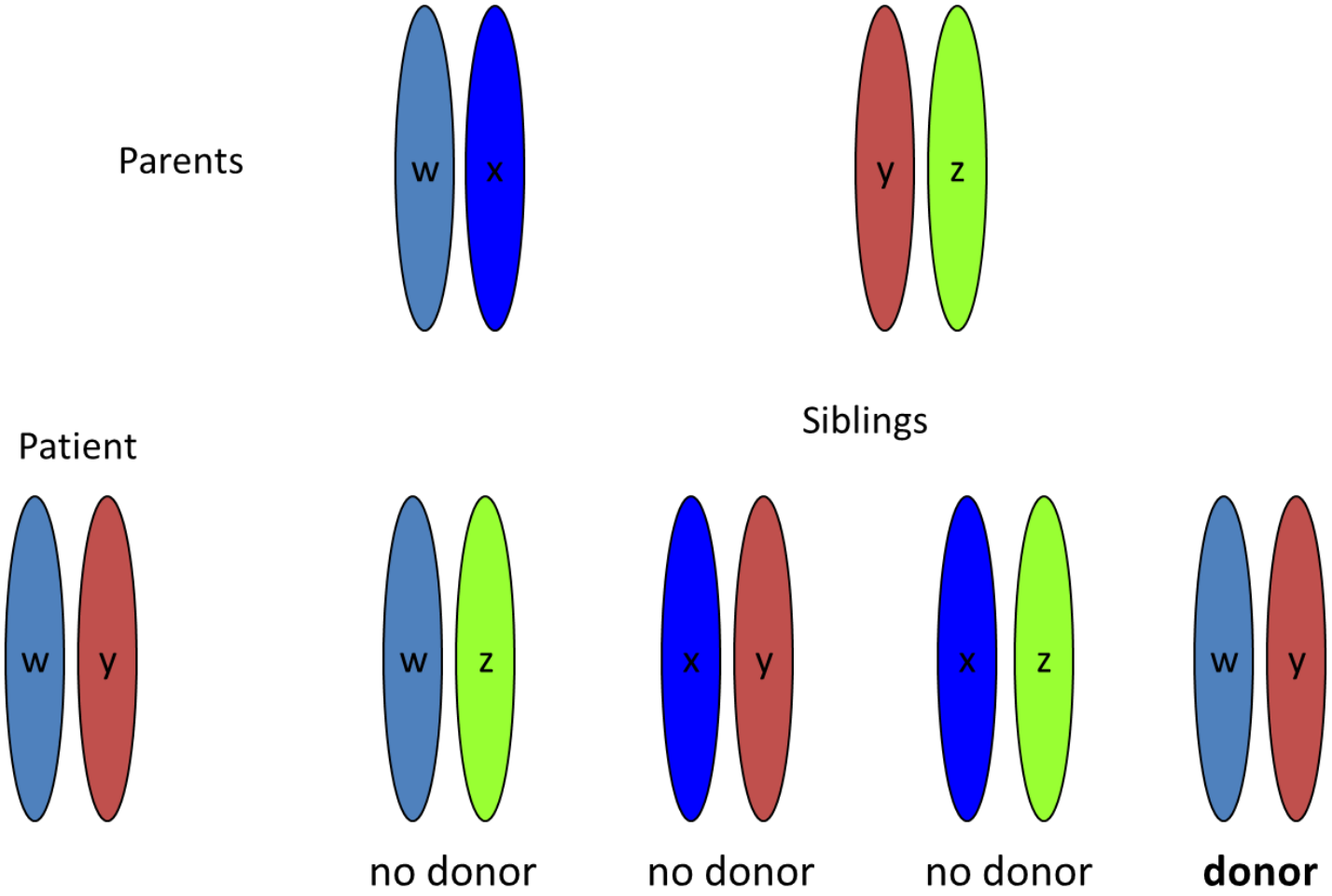
- Chemo- en radiotherapie om de tumor aan te vallen
- Donor stamcellen om het merg te redden
- De immuuncellen in de donor
- Vernietigen de kanker cellen



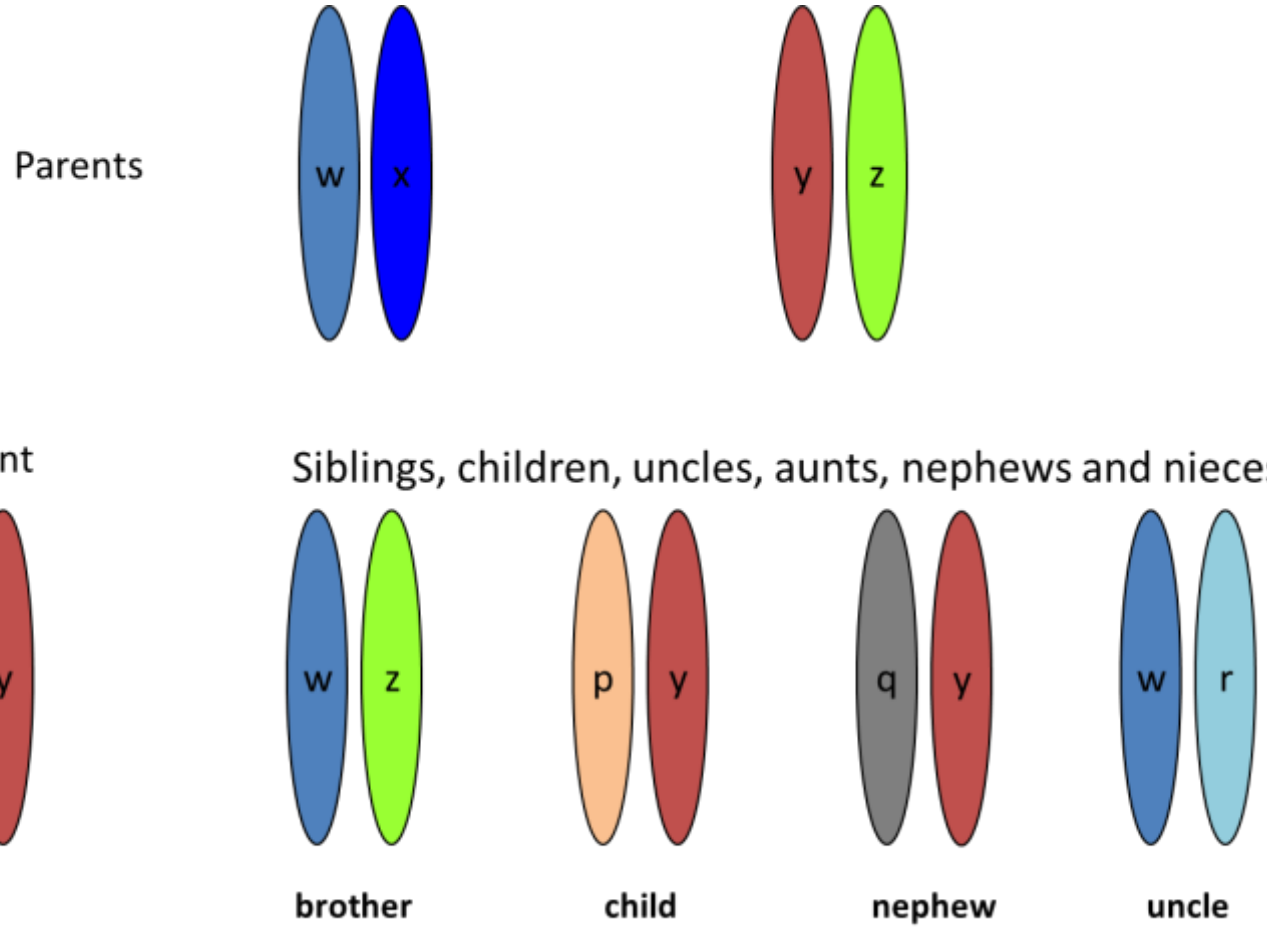
Donor immuuncellen geven graft versus host disease en graft versus tumor effecten



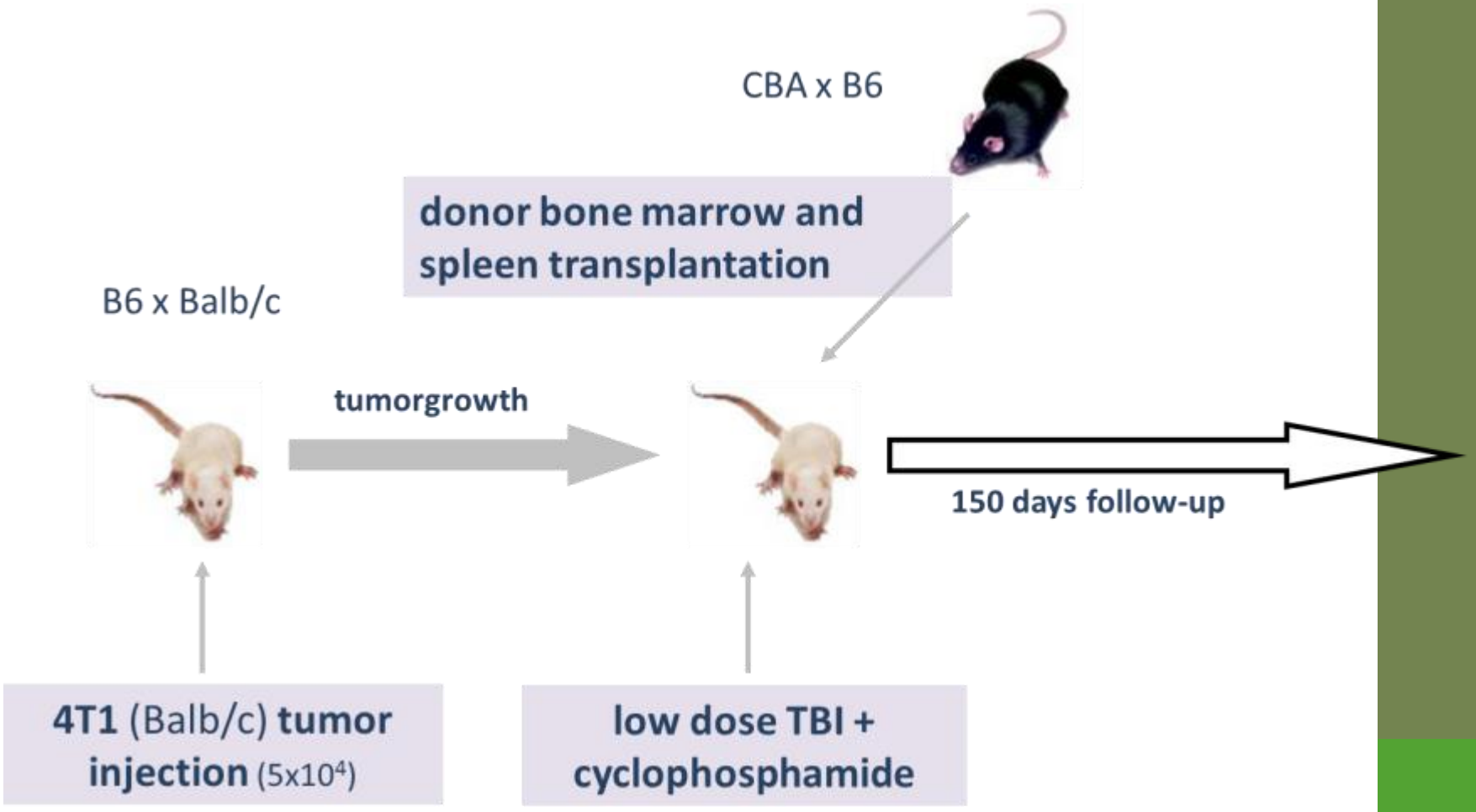
Donor selectie voor HLA-identieke allogene stamcel transplantatie



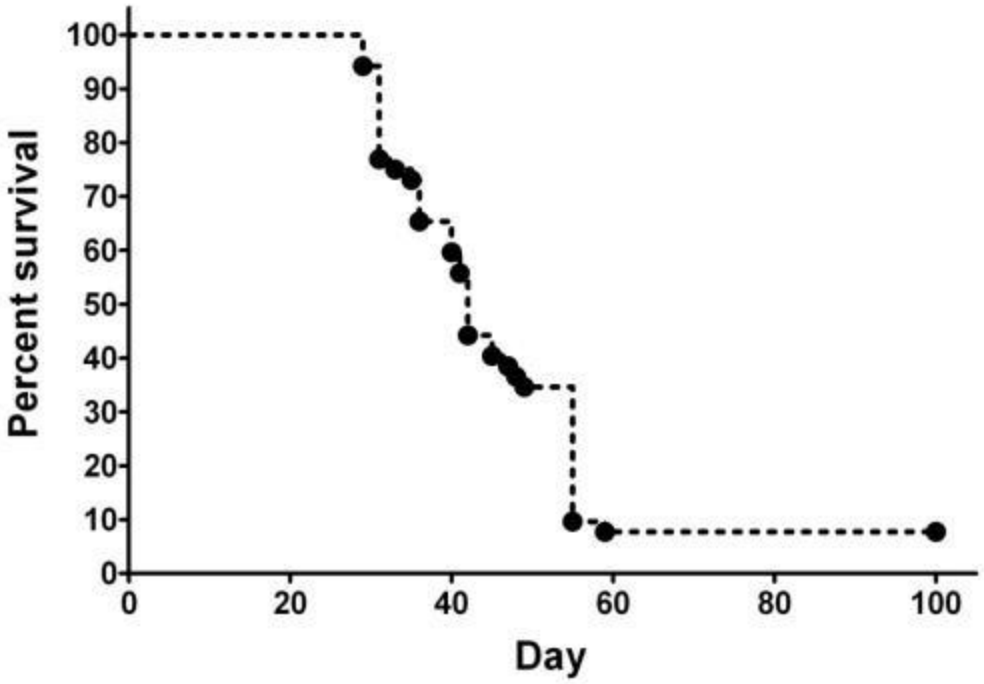
haploidentieke allogene stamcel transplantatie



Haploidentieke beenmerg en immuuncel transplantatie in muizen met borstkanker



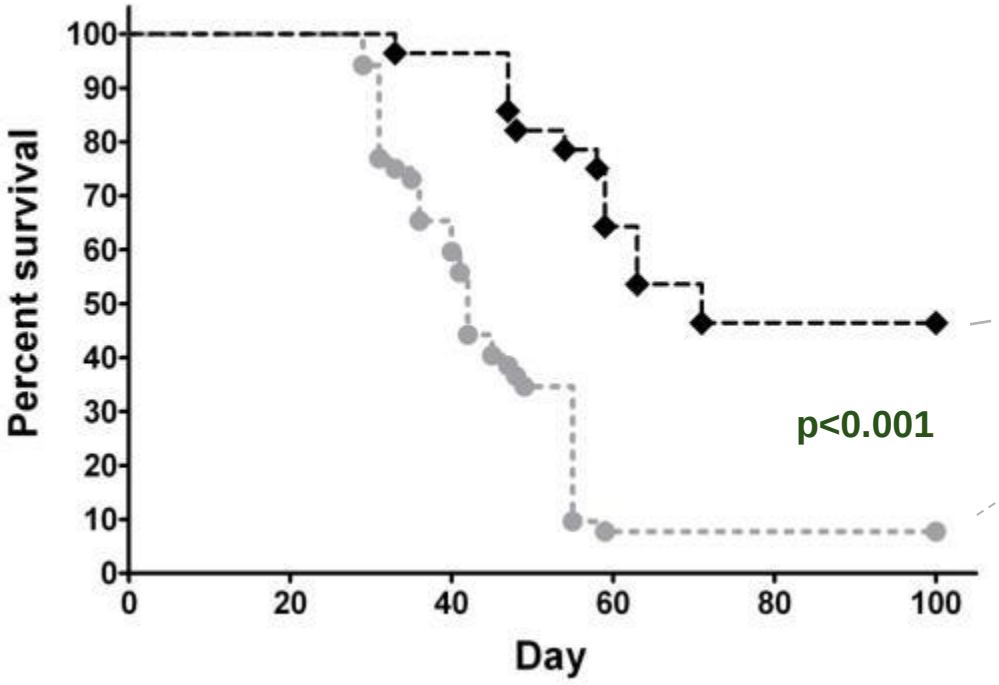
Haploidentieke beenmerg en immuuncel transplantatie genezen muizen met borstkanker



Syngeneic SPL + BMT
(n=40)

CY + TBI+ Transplant

immuuncel transplantatie genezen muizen met borstkanker



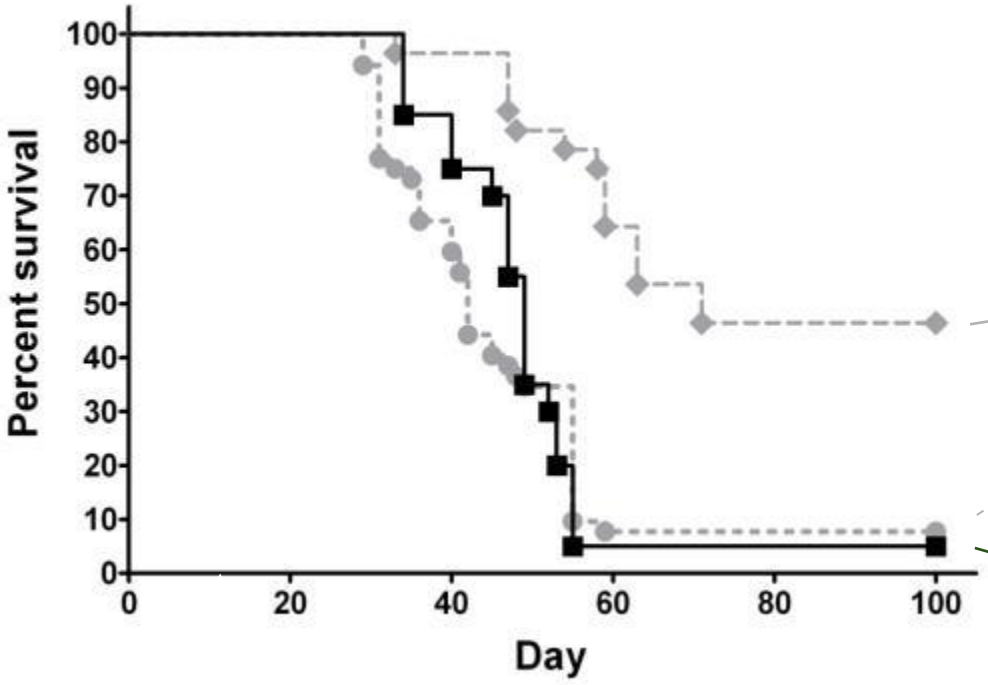
Haplo SPL + BMT (n=20)

Syngeneic SPL + BMT (n=40)

CY + TBI+ Transplant

(2 experiments summarized)

Haploidentieke beenmerg en immuuncel transplantatie genezen muizen met borstkanker



Haplo SPL + BMT (n=20)

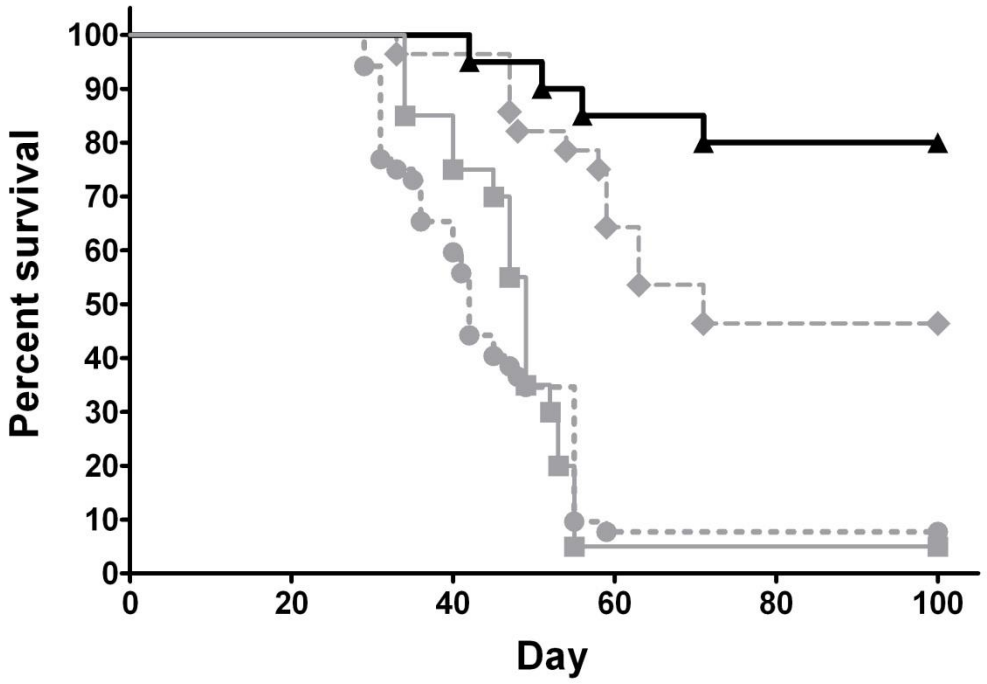
Syngeneic SPL + BMT (n=40)

Haplo "no NK" + BMT (n=20)

CY + TBI+ Transplant

(2 experiments summarized)

Haploidentieke beenmerg en immuuncel transplantatie genezen muizen met borstkanker



Sorted Haplo NK + BMT (n=20)

Haplo SPL + BMT (n=20)

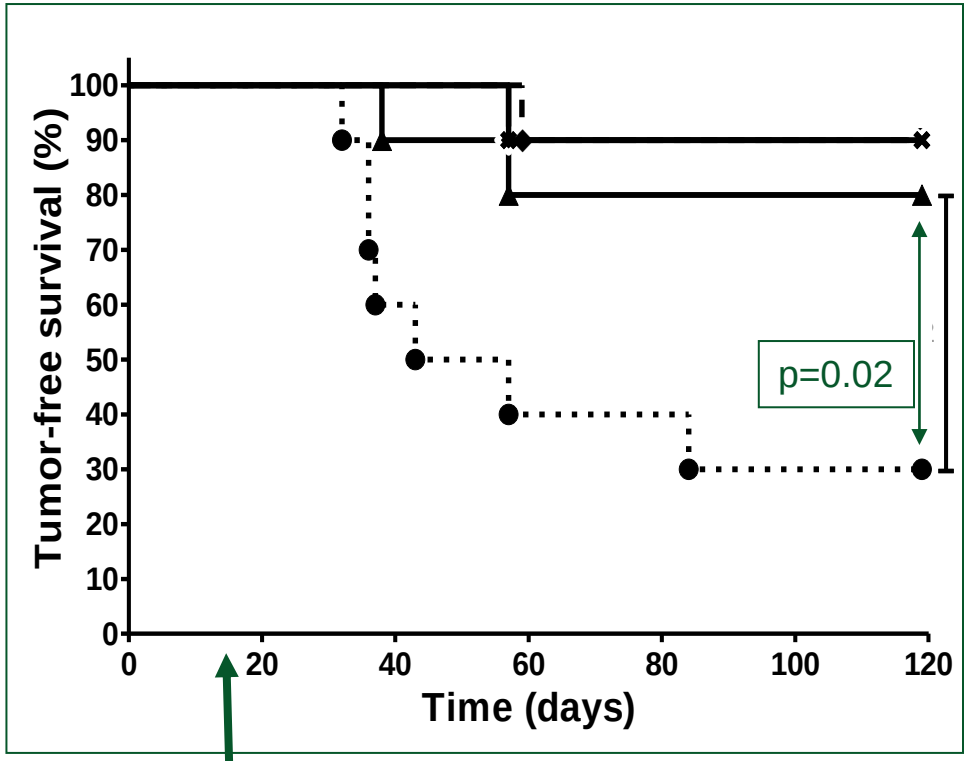
Syngeneic SPL + BMT (n=40)

Haplo “no NK” + BMT (n=20)

CY + TBI+ Transplant

zed)

Donor NK cellen zijn genoeg voor genezing



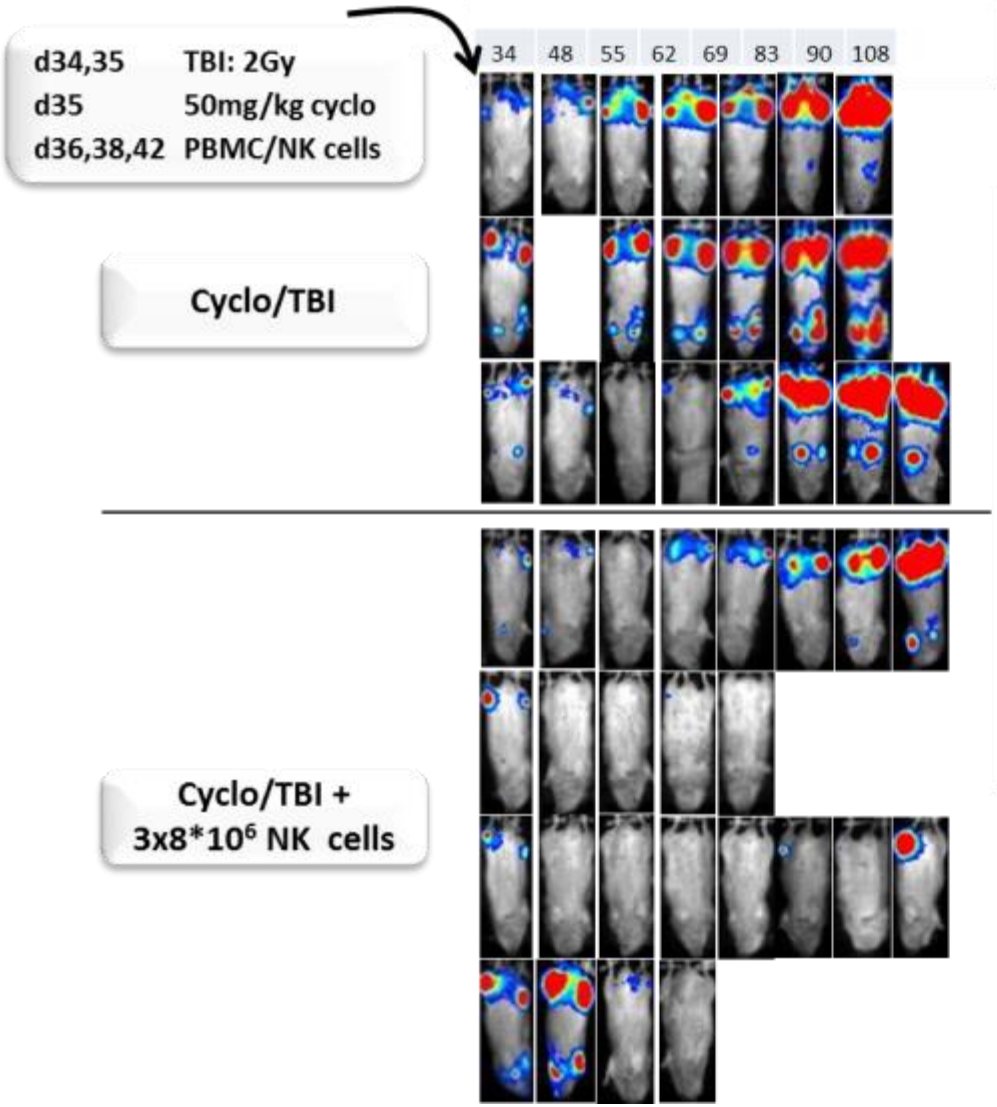
donor NK + beenmerg cellen

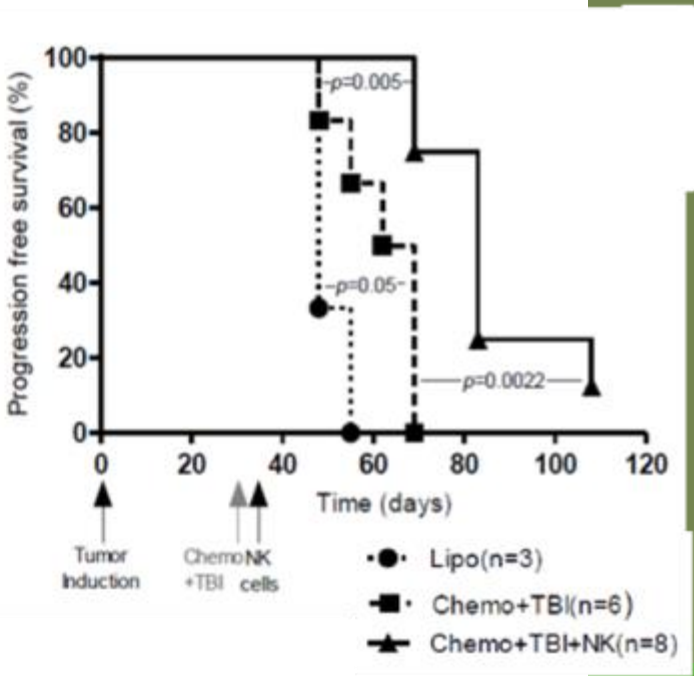
alleen donor NK cellen

eigen NK cellen

NK cel toediening

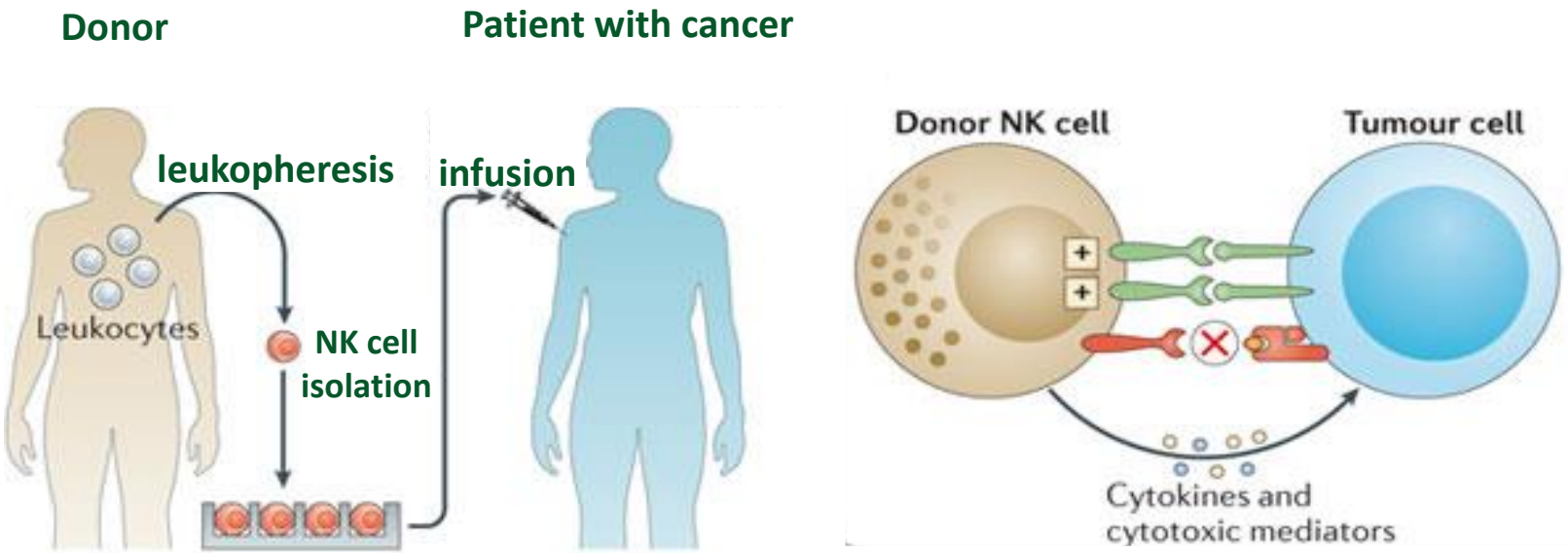
Chemo/radiotherapie en alloreactieve NK cellen vertragen multipel myeloom progressie





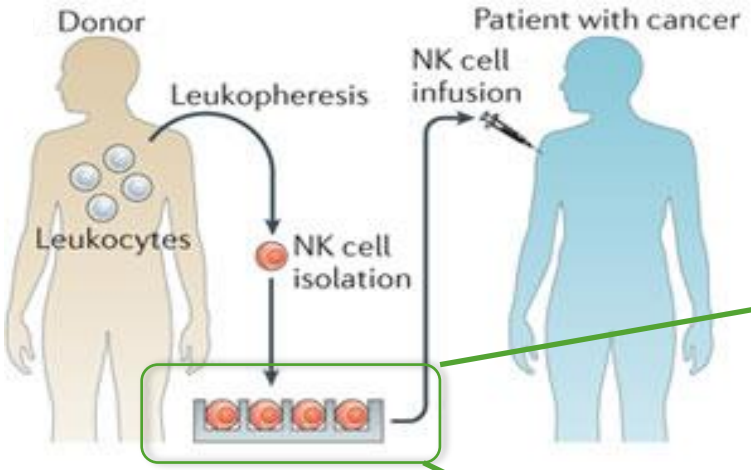
Sarkar *et al,* J. Molecular Cytotherapy 2015

Natural killer cel therapie in kanker

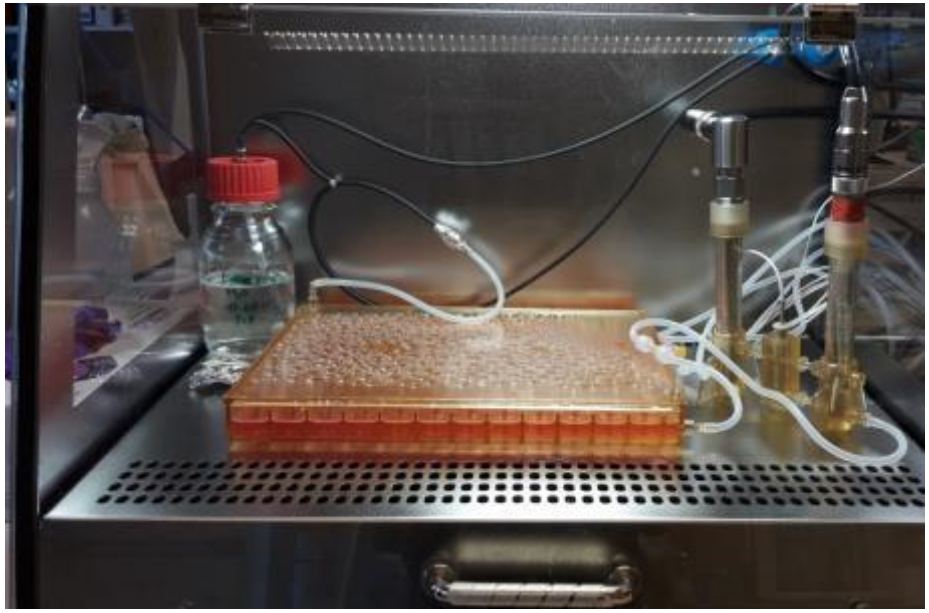


Vivier et al., Nat Rev Immunol 2012

Kweken van NK cellen voor klinische applicatie

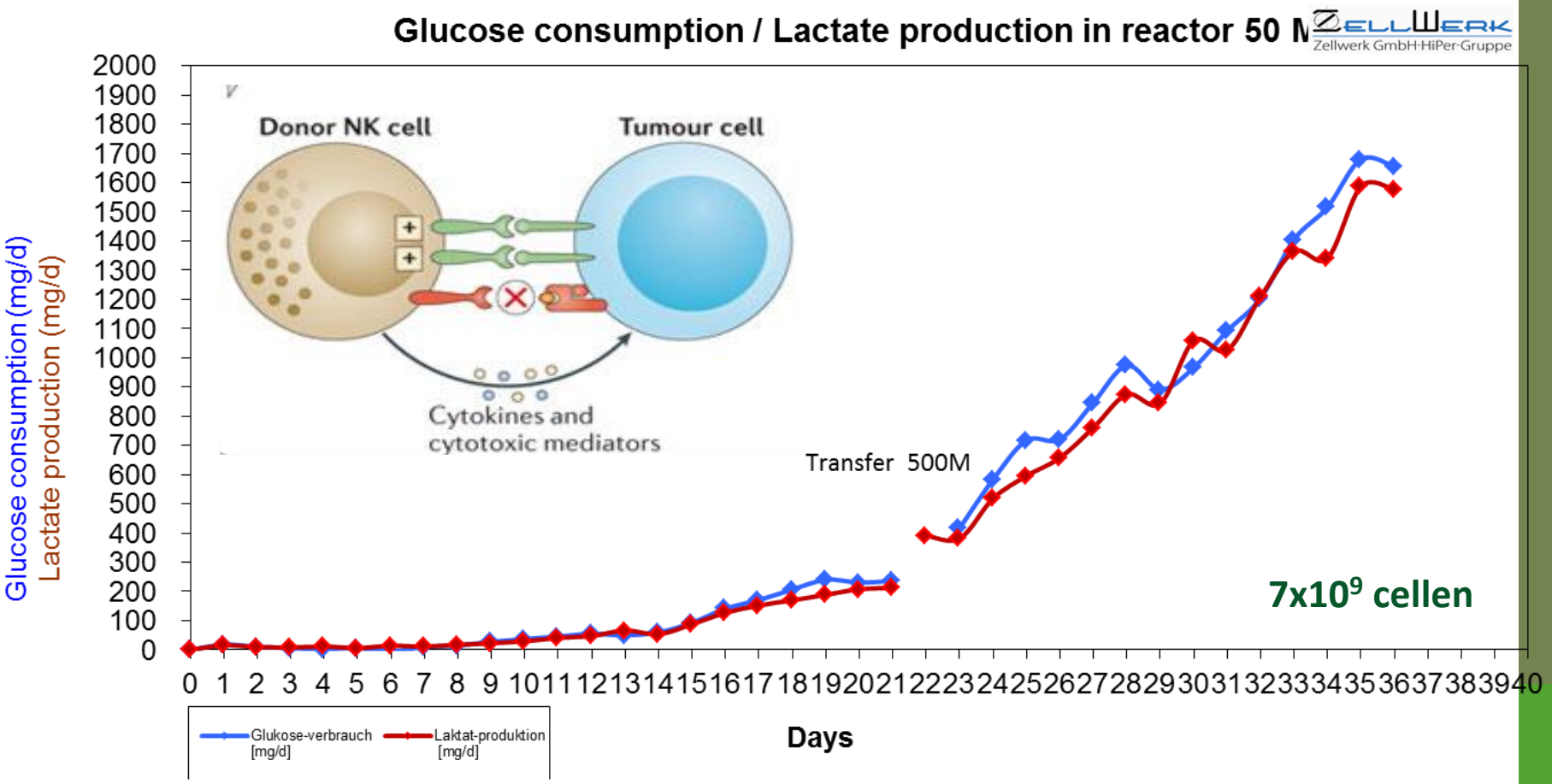


Kweken van NK cellen voor klinische applicatie

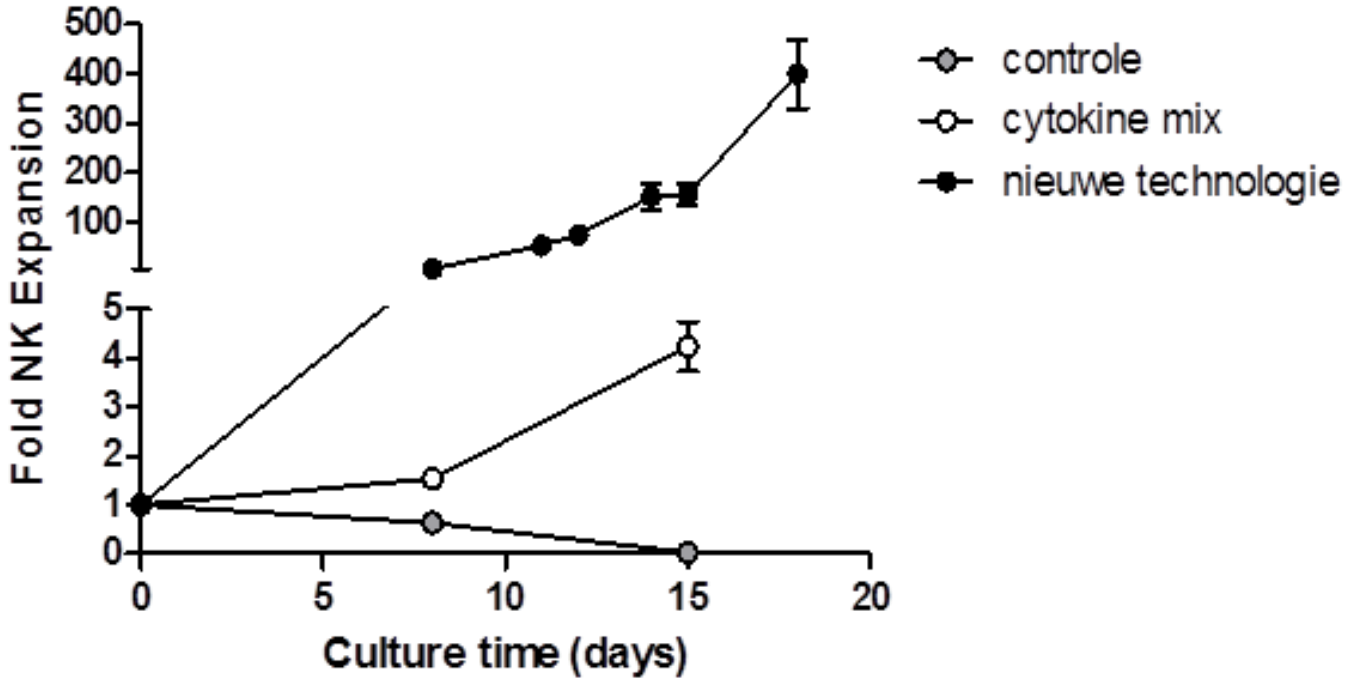


$10x10^9$ NK cellen

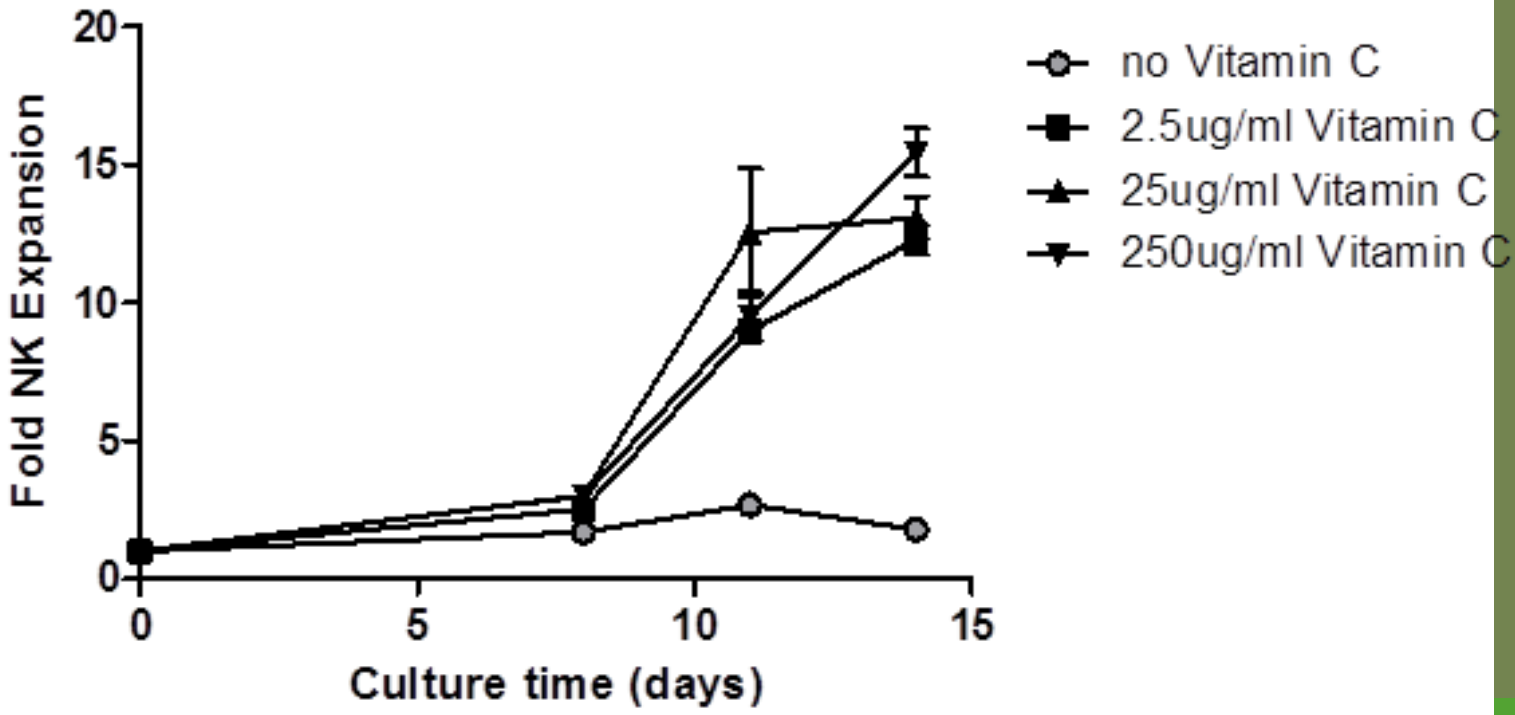
NK cellen kunnen vermeerderd worden in de 500M bioreactor



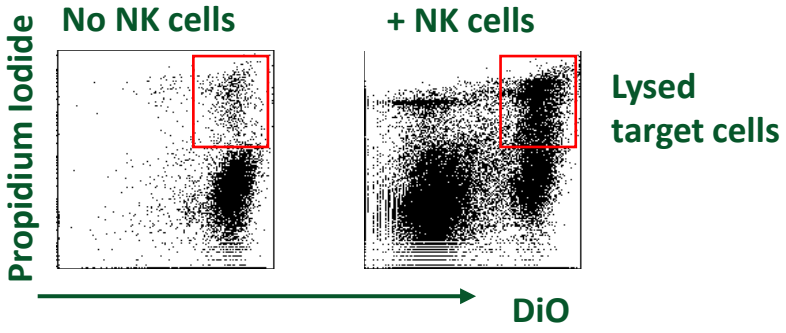
Toevoegen van extra factoren helpt om de NK cellen te vermeerderen

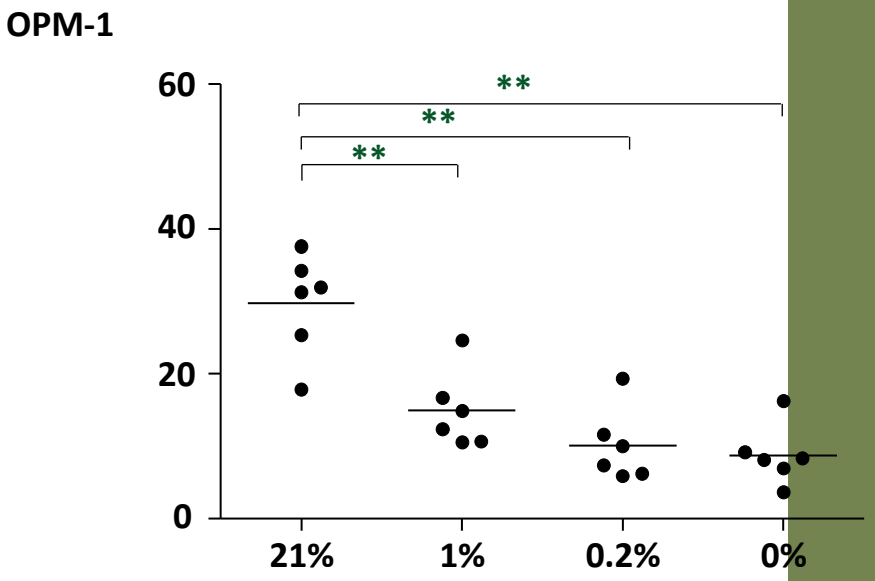


Toevoegen van Vitamine C helpt om de NK cellen te vermeerderen



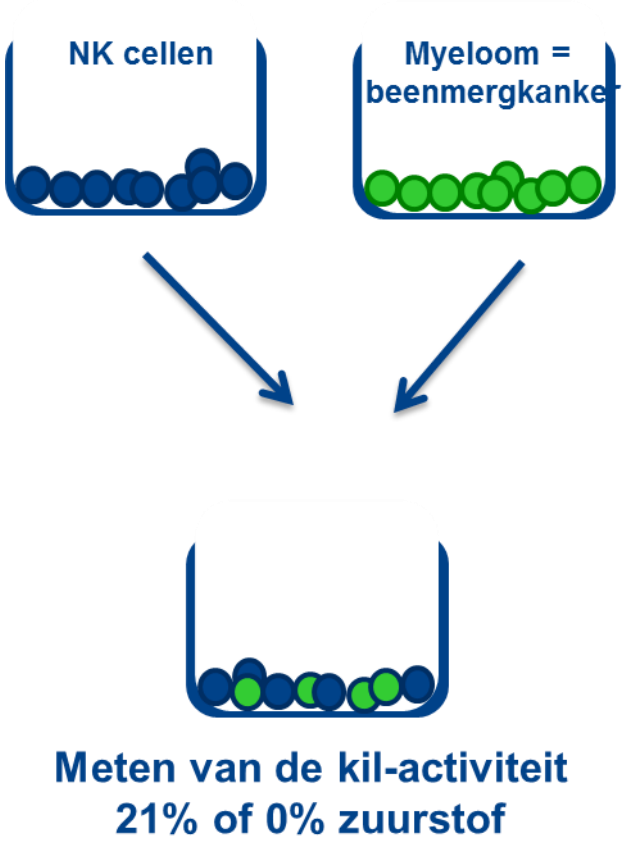
Weinig zuurstof remt killer cellen

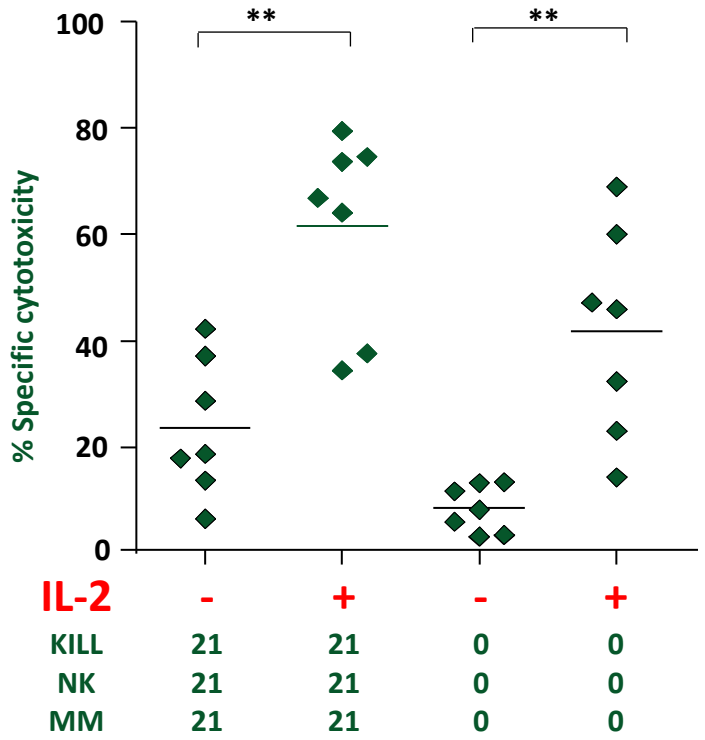




Sarkar *et al* Plos One 2013

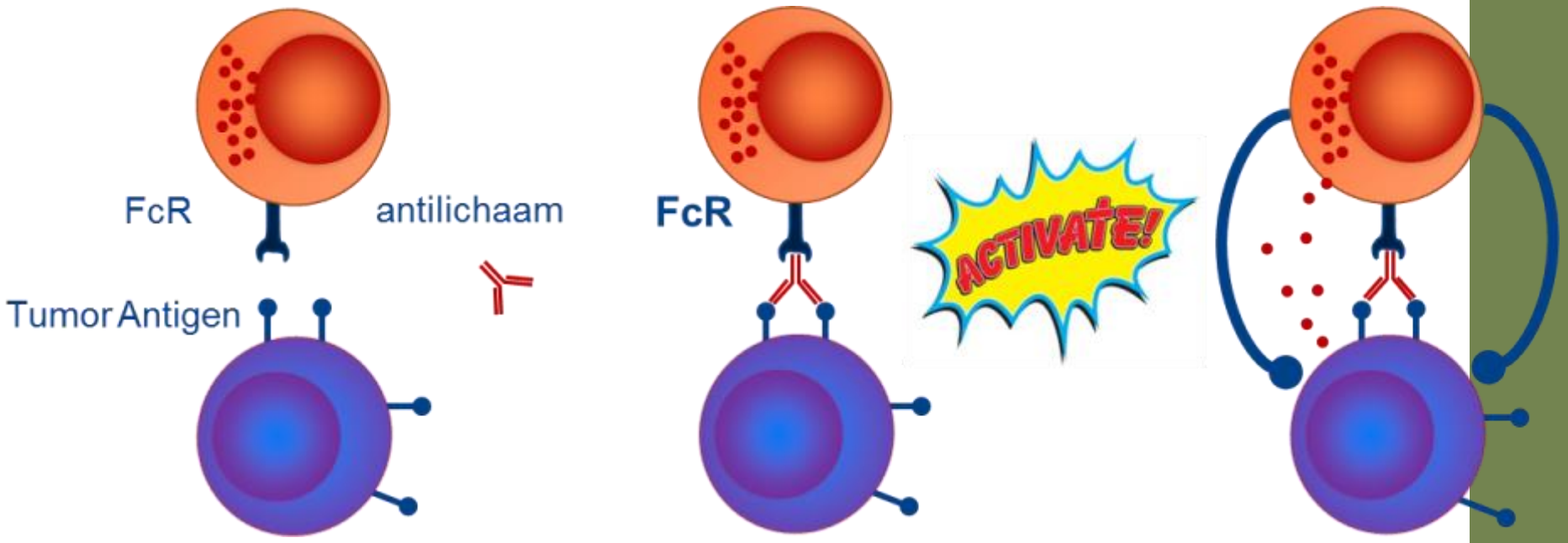
Het negatieve effect van weinig zuurstof kan worden opgelost!



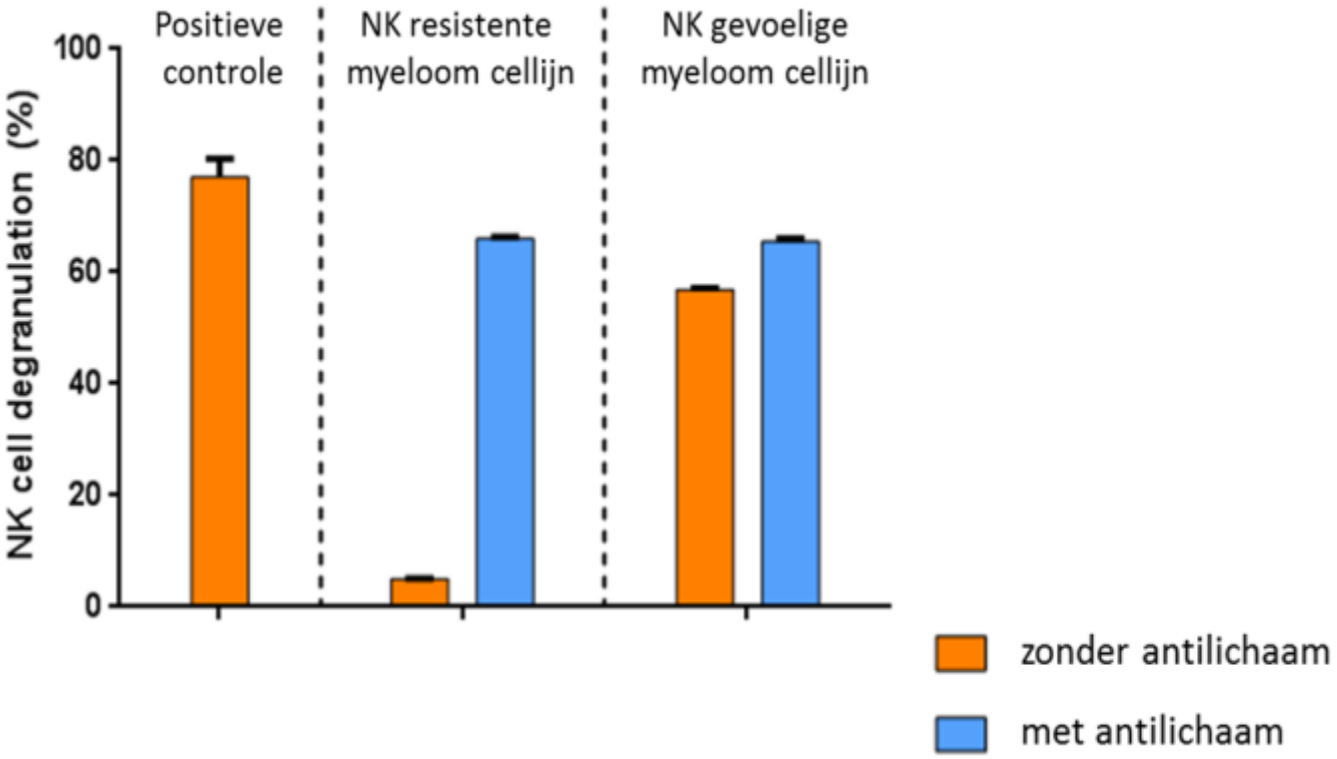


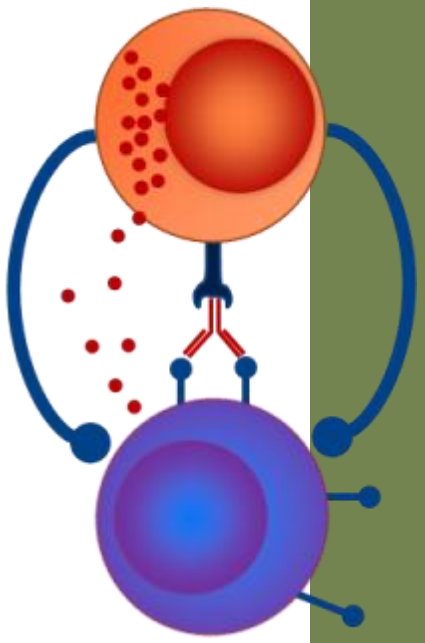
Sarkar *et al* Plos One 2013

Antilichamen gebruiken om NK cel functie te verbeteren



Antilichamen gebruiken om NK cel functie te verbeteren



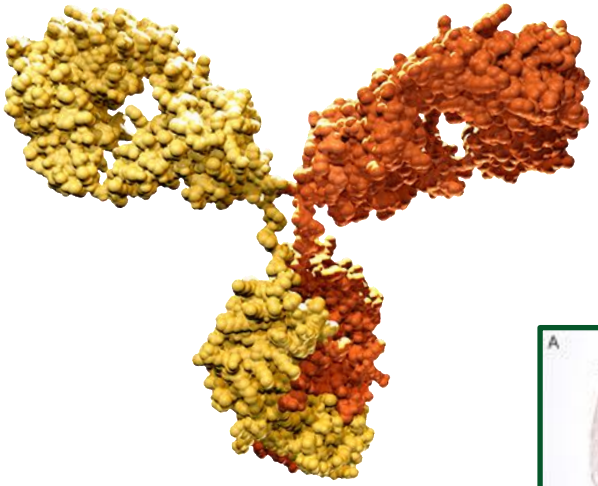


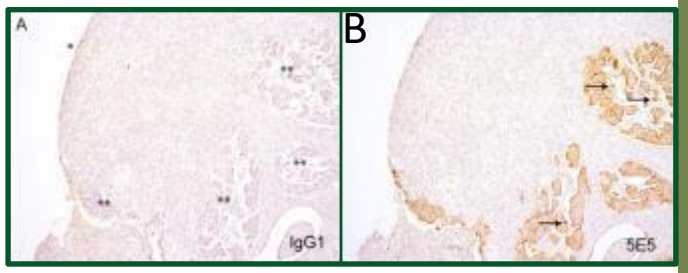
NK-Ngage

Tumor specific NK engaging antibodies

NK activating receptor

Tumor specific binding





- ✓ Exclusive license to tumor binding Ab
- ✓ DuoBody™ technology partnership

CiMaas

Financiele middelen nodig:

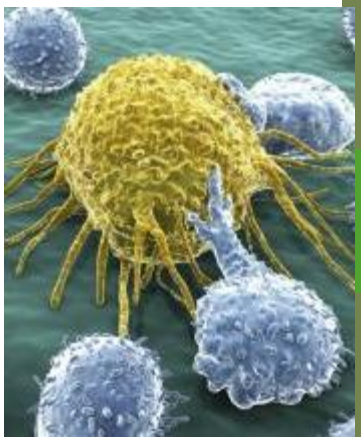
- 1,5 M€
  - phase I DC Vaccin
    - preclinical work NK
    - antibody preclinical
- 7 M€ (1,5 +5,5)
  - phase II DC Vaccine
  - Phase I NK cells
- 10 M € (2+8)
  - phase II NK

- PM M€ antibody development (Licentie fee upfront)

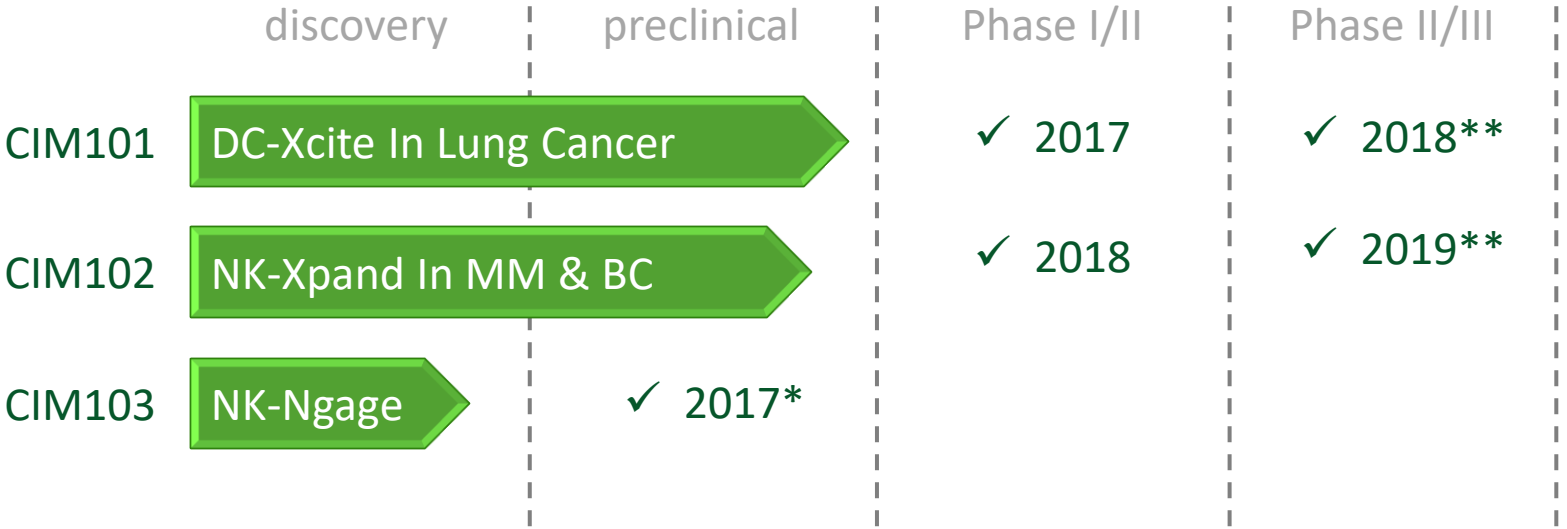
Achieving a better cure for Cancer!

Maart 2015

Gerard MJ Bos, MD, PhD
CEO CiMaas + Professor Immunotherapy of Cancer MUMC+

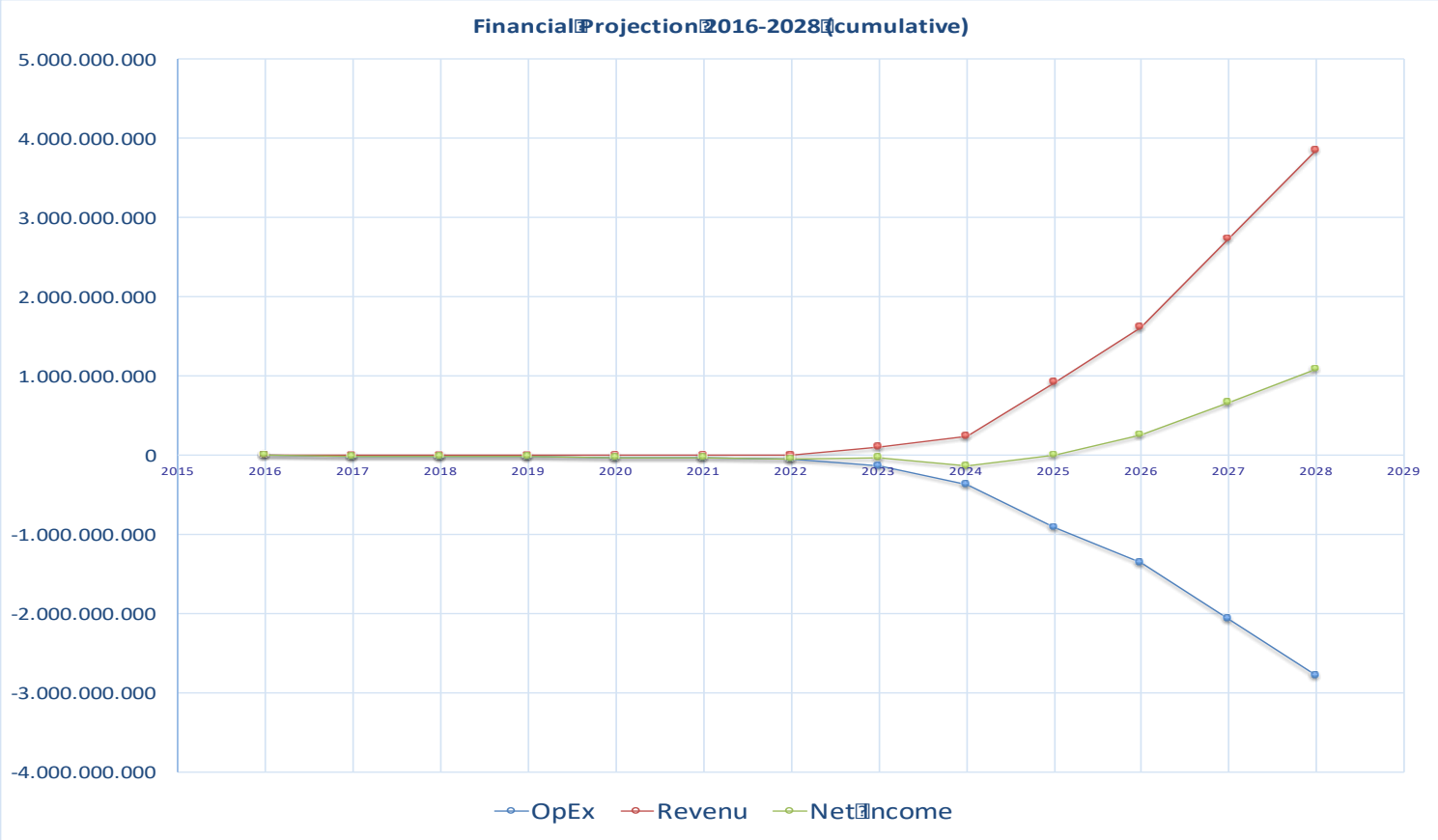


Traject CiMaas



*Potential out-license/partnership ** Strategic partnership

Financiele projectie:
Productprijs per Qualy < 80.000 €



Tumor Immunology

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Harry Schouten
Wilfred Germeraad
Michel van Gelder
Gerard Bos

Transplantation Immunology

Mathijs Groeneweg
Timo Olieslagers
Christien Voorter
Marcel Tilanus

Maastro lab

Kasper Rouschop
Ludwig Dubois

Zellwerk, Berlin

Anne Reichardt
Hans Hoffmeister Jr
Hans Hoffmeister Sr

VUMC

Willy Noort
Richard Groen
Anton Martens

DFCI/Harvard med school

Constantine Mitsiades
Michal Scheffer

US Florida: Robert Igarashi

MD Anderson: D. Lee

KWF KANKER BESTRIJDING

Kankeronderzoekfonds LIMBURG

Fonds Stimulans

Is een bedrijf een noodzakelijk kwaad?

Mogen we de patiënt vragen zelf te betalen voor participatie aan klinische studies?