FACULTEIT GENEESKUNDE EN GEZONDHEIDSWETENSCHAPPEN

DIENST HEMATOLOGIE UZ GENT



IMMUNOTHERAPIE VOOR KANKER

10 MAART 2025

UNIVERSITEIT DERDE LEEFTIJD BRUGGE

Prof. Dr. Tessa Kerre

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CANCER RESEARCH INSTITUTE GHENT

ION
immuno-oncology network Ghent

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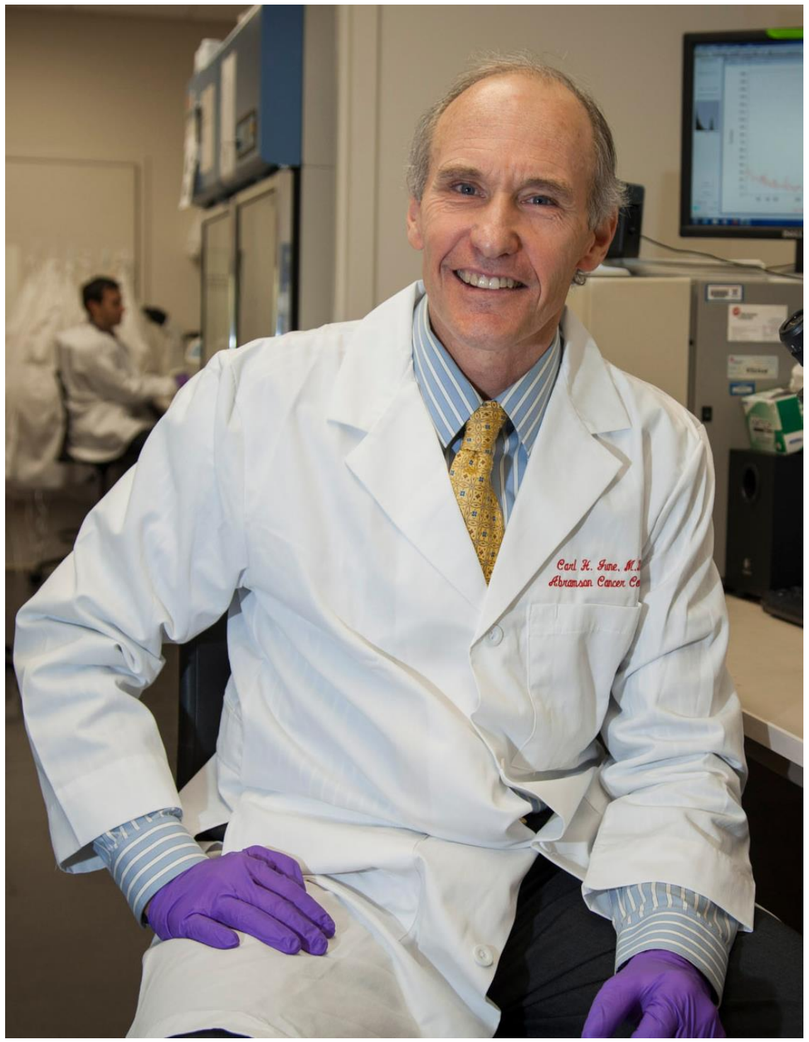
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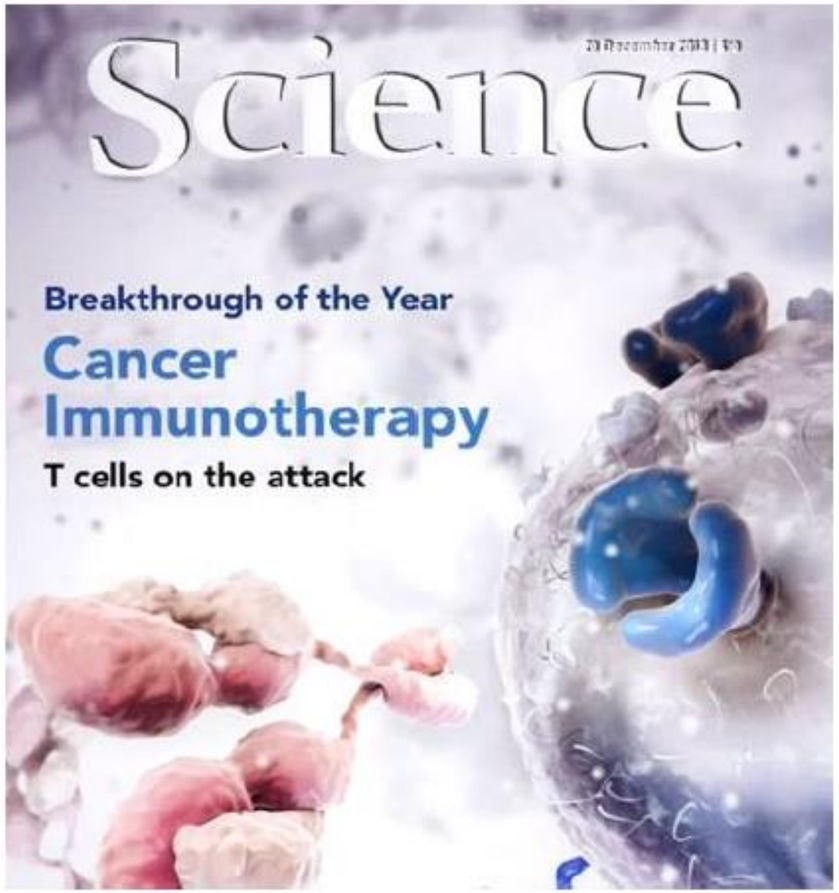
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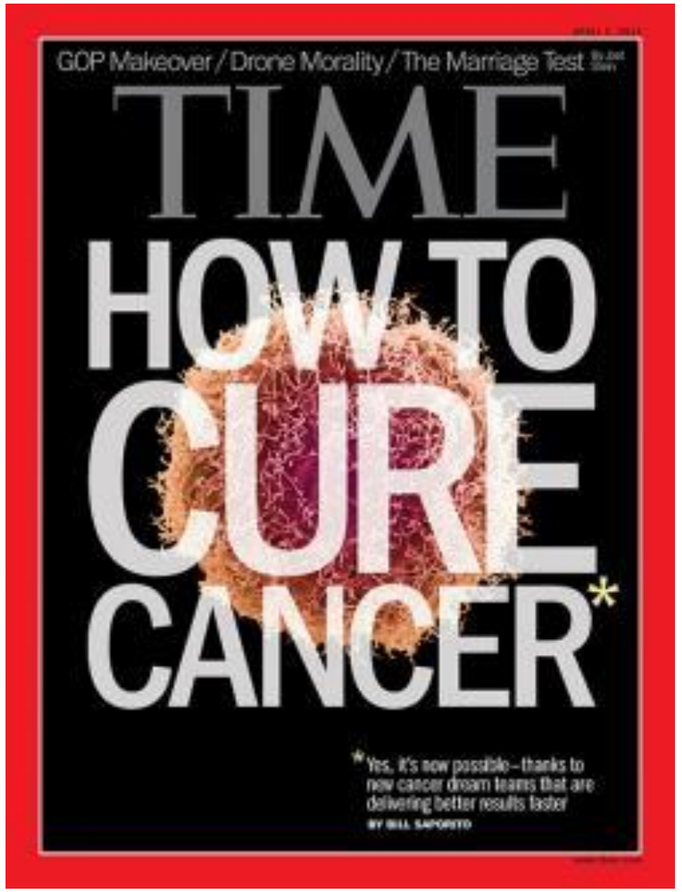


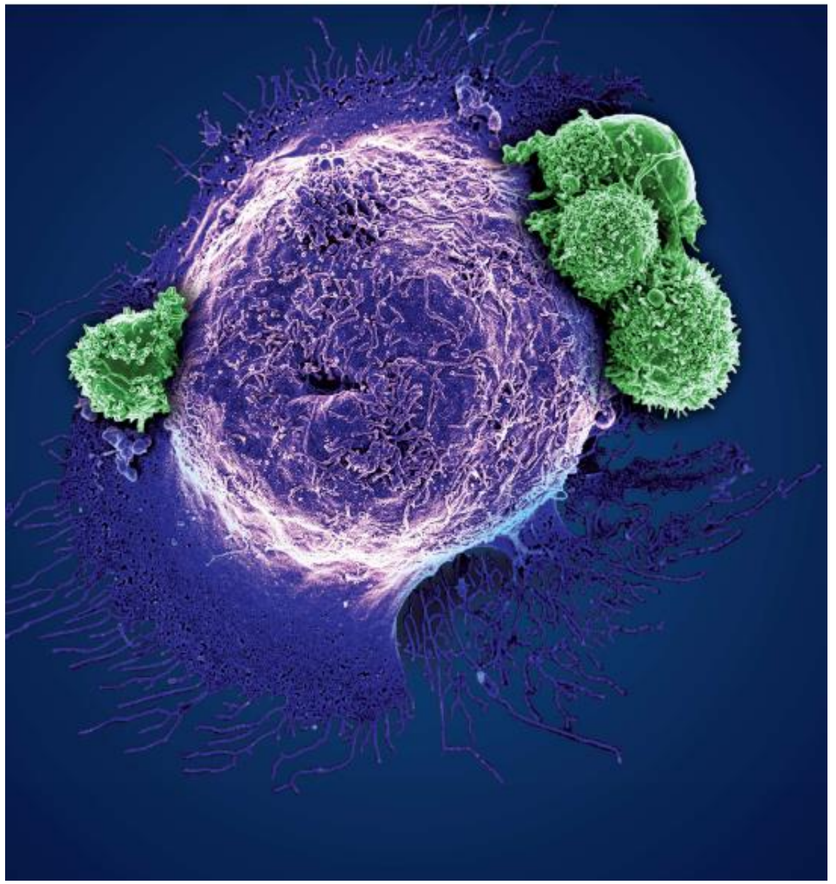


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IMMUNOTHERAPIE



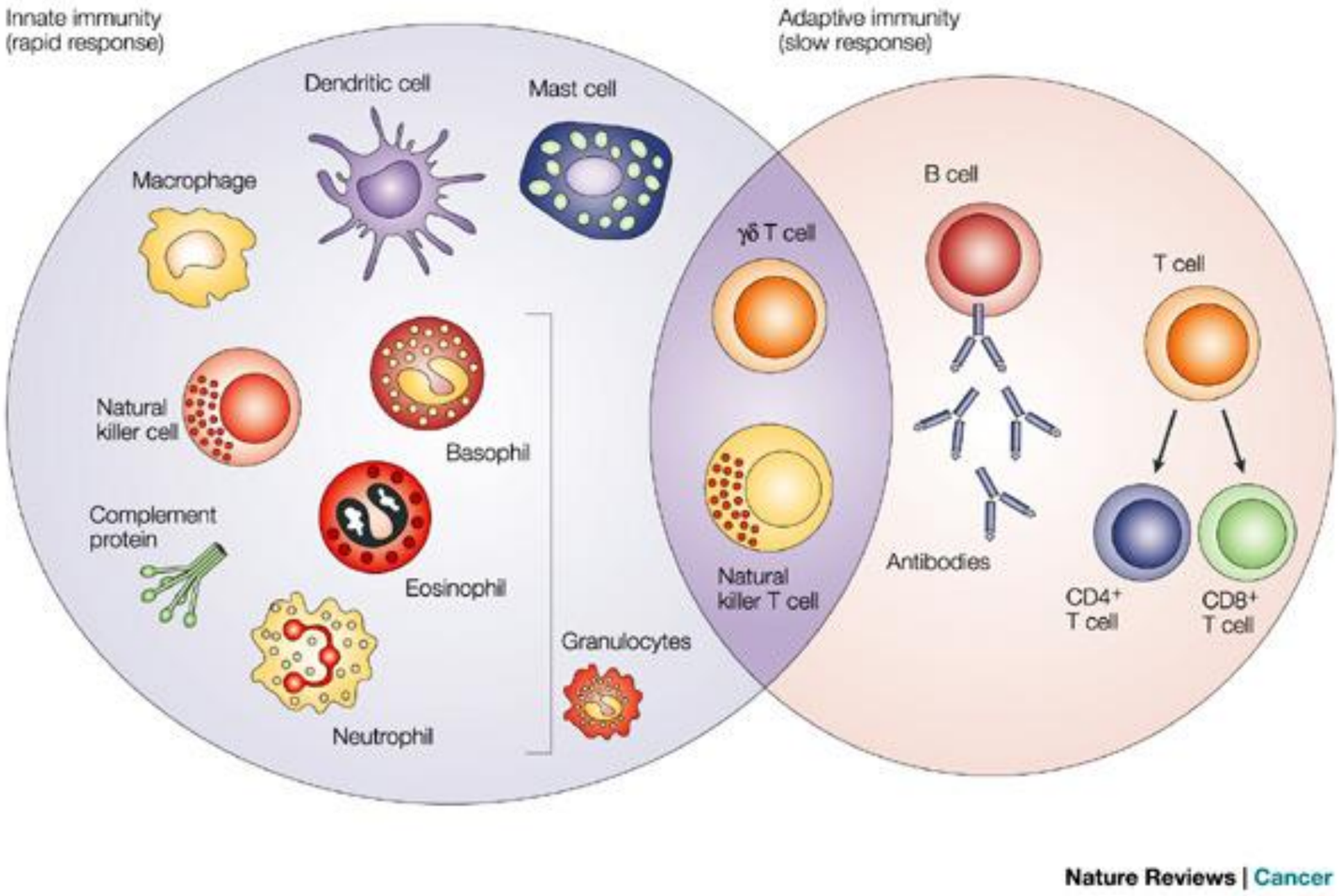




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HET IMMUUNSYSTEEM

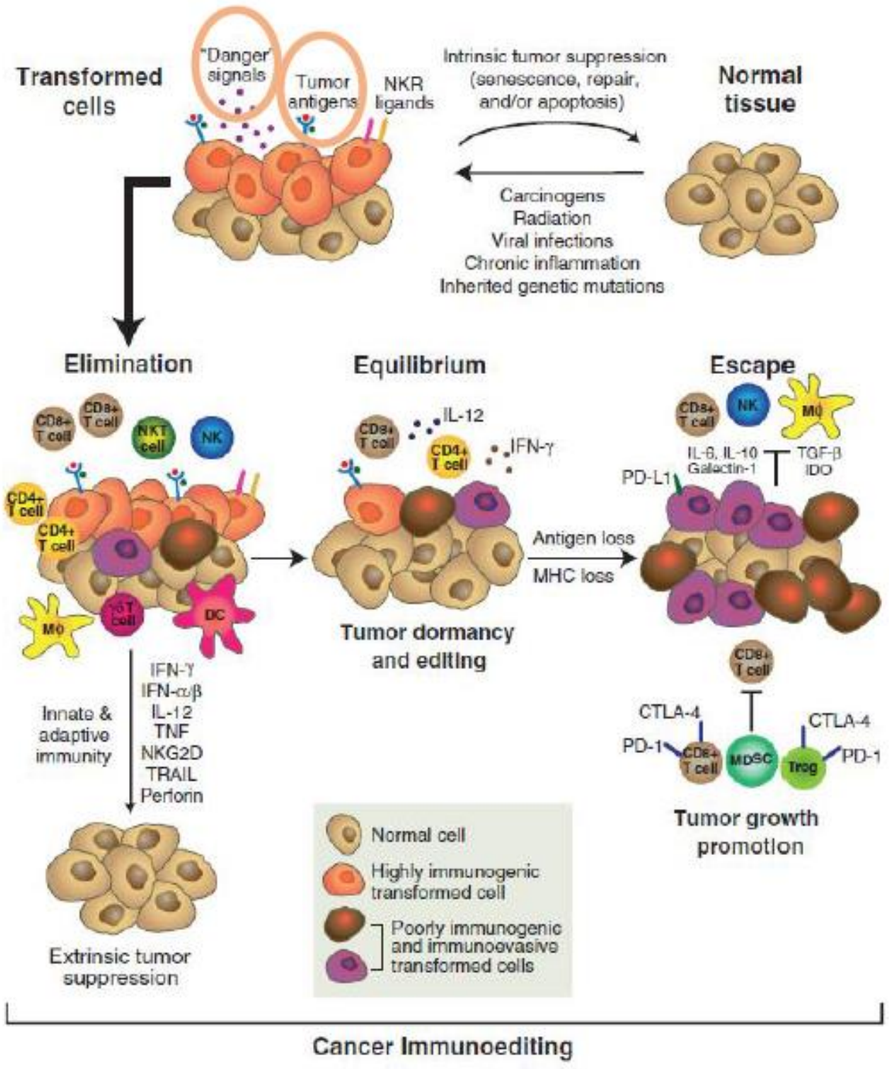


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Dranoff G. Nature Reviews Cancer, 2004

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– Interacties immuunsysteem en kanker

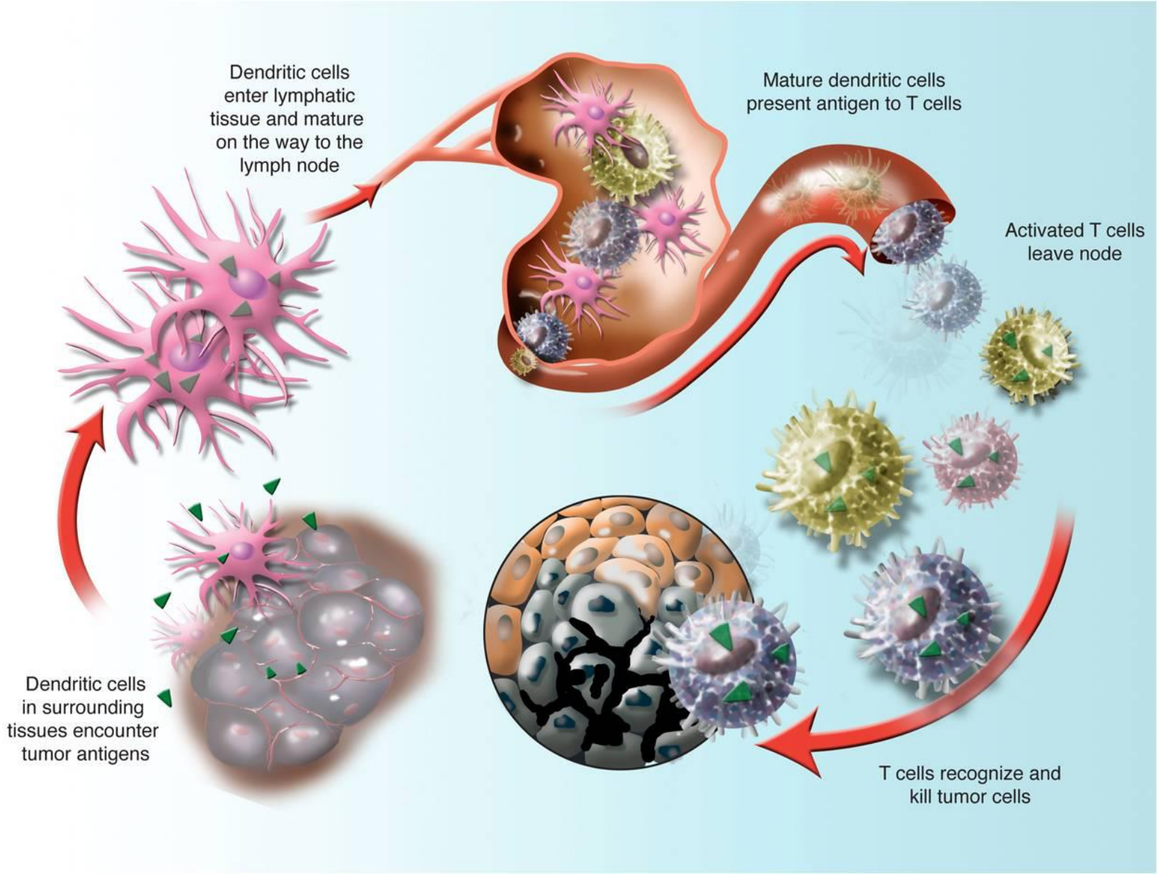


Hanahan and Weinberg, Cell 2000

Schreiber et al, Science 2011

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– Interacties immuunsysteem en kanker

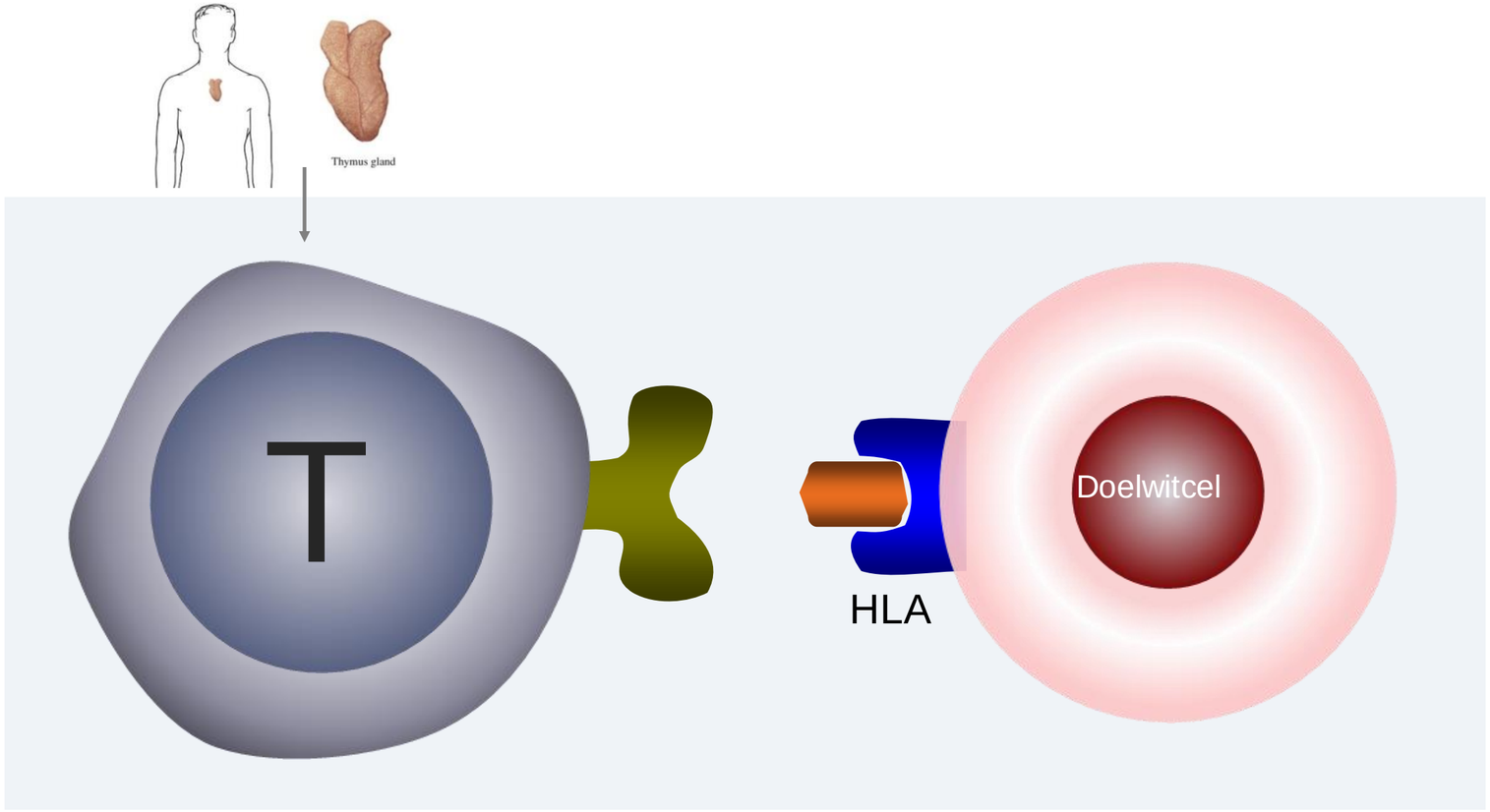


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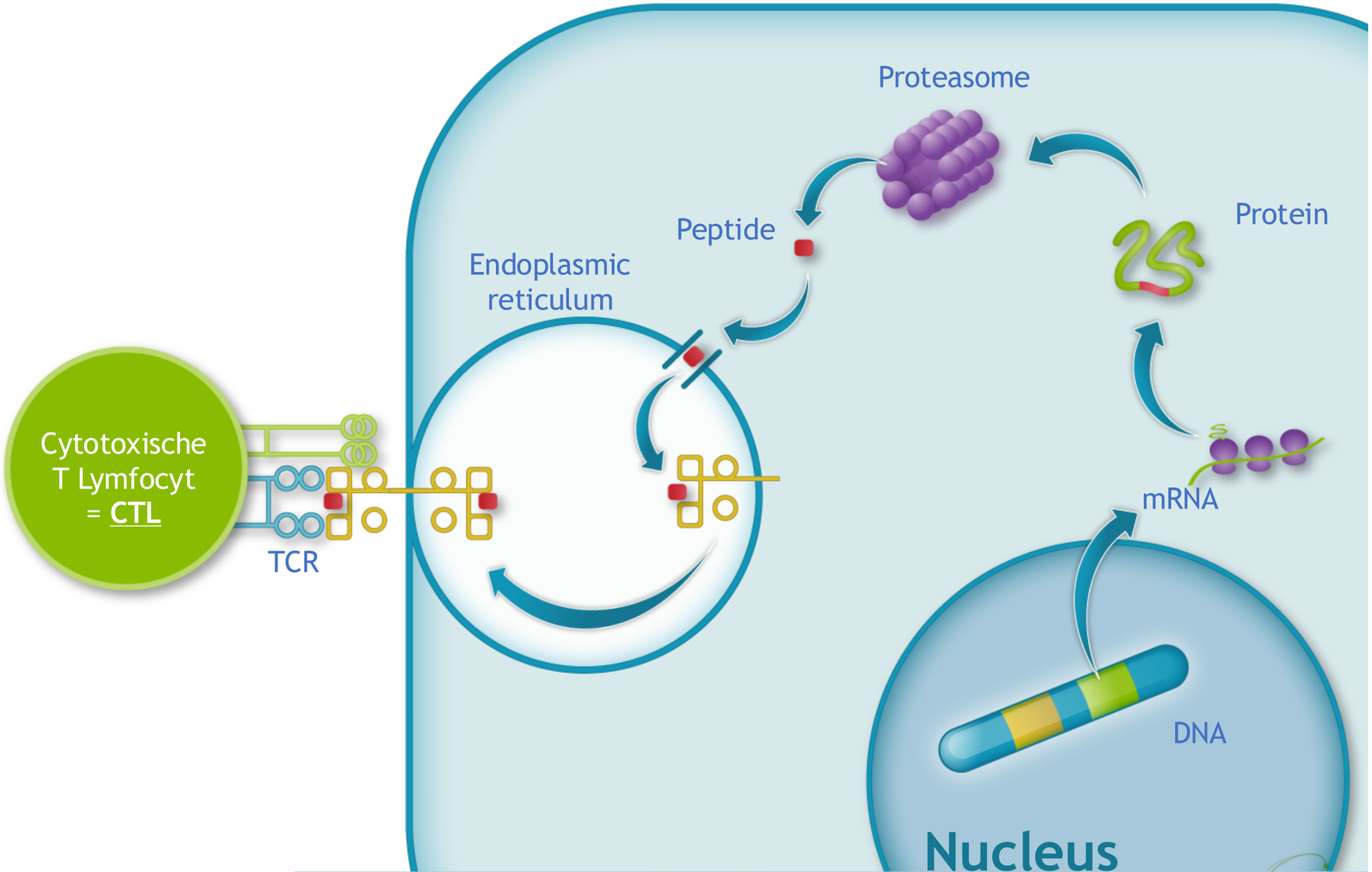
Penn University

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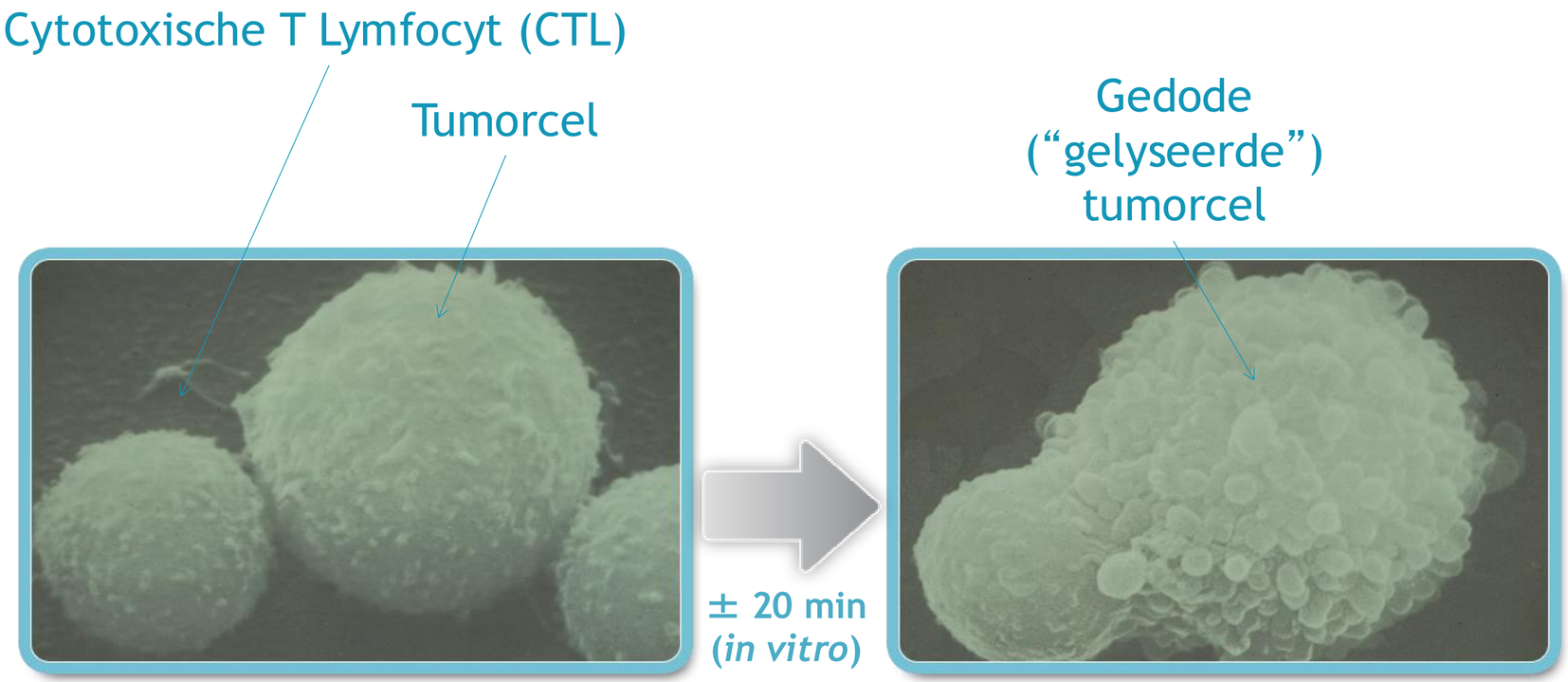


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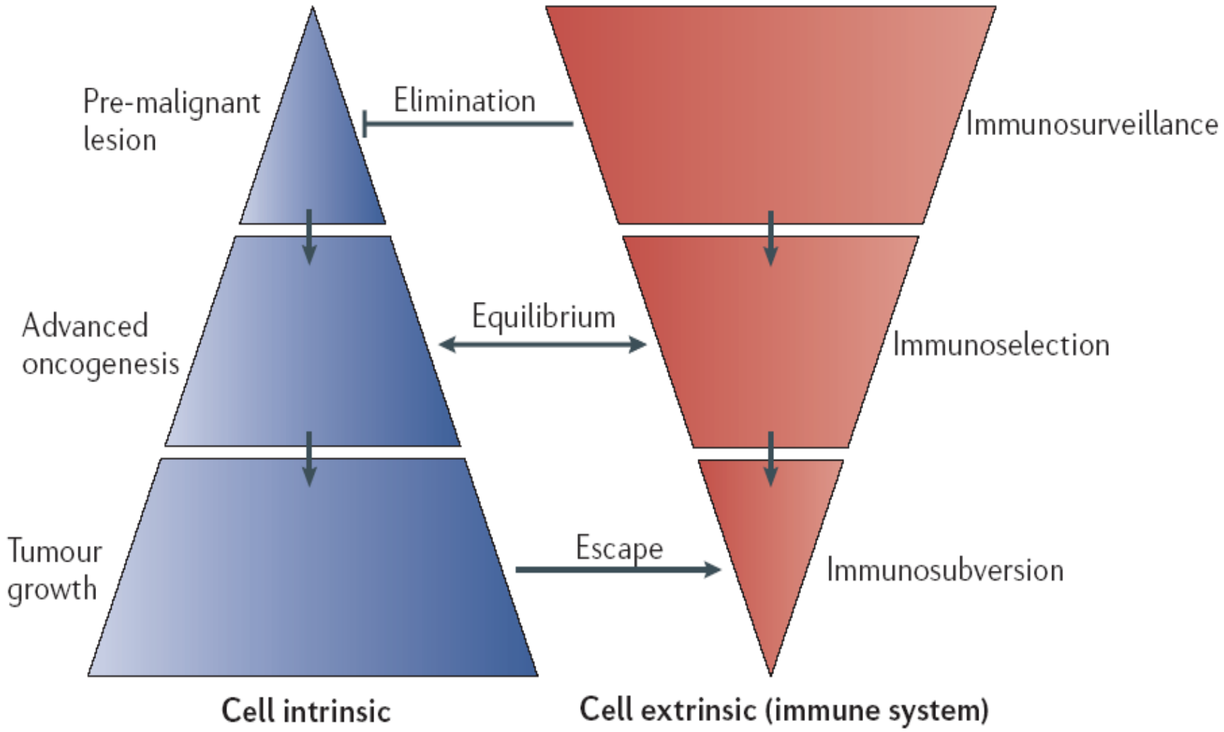
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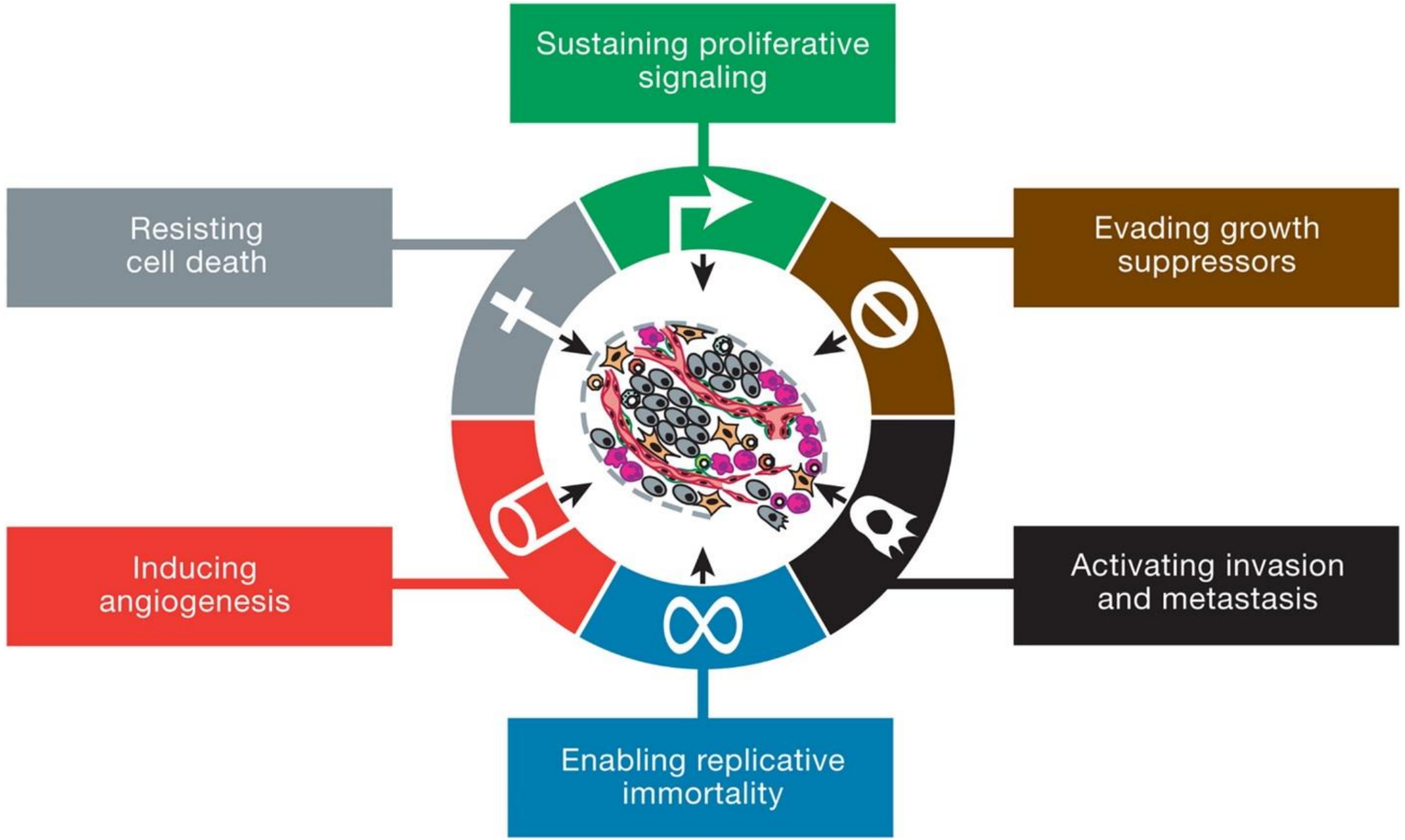
– Equilibrium



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Zitvogel L. et al., Nature Reviews Immunology, 2006

HALLMARKS OF CANCER

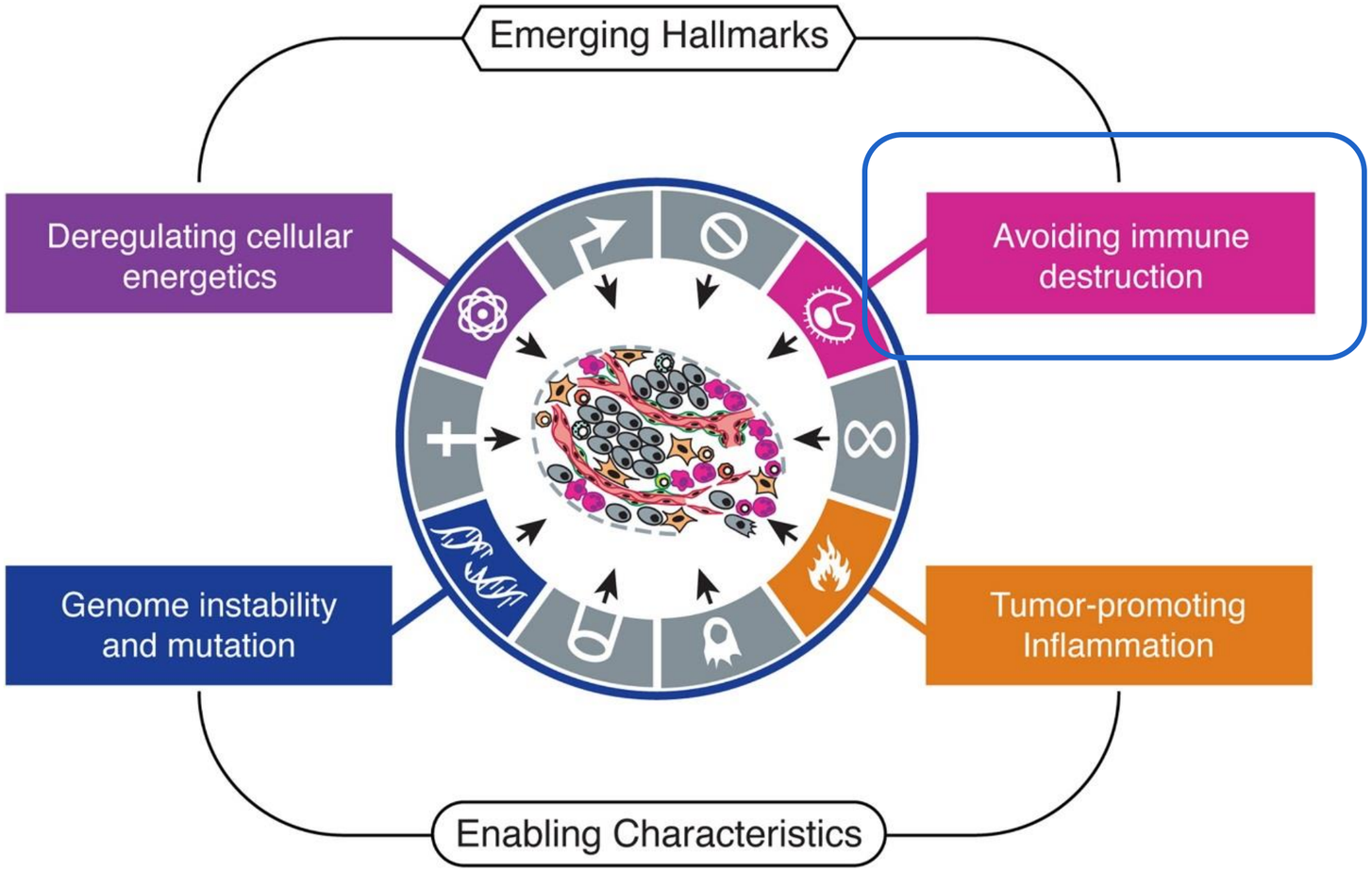


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D Hanahan and R Weinberg, Cell, 2011

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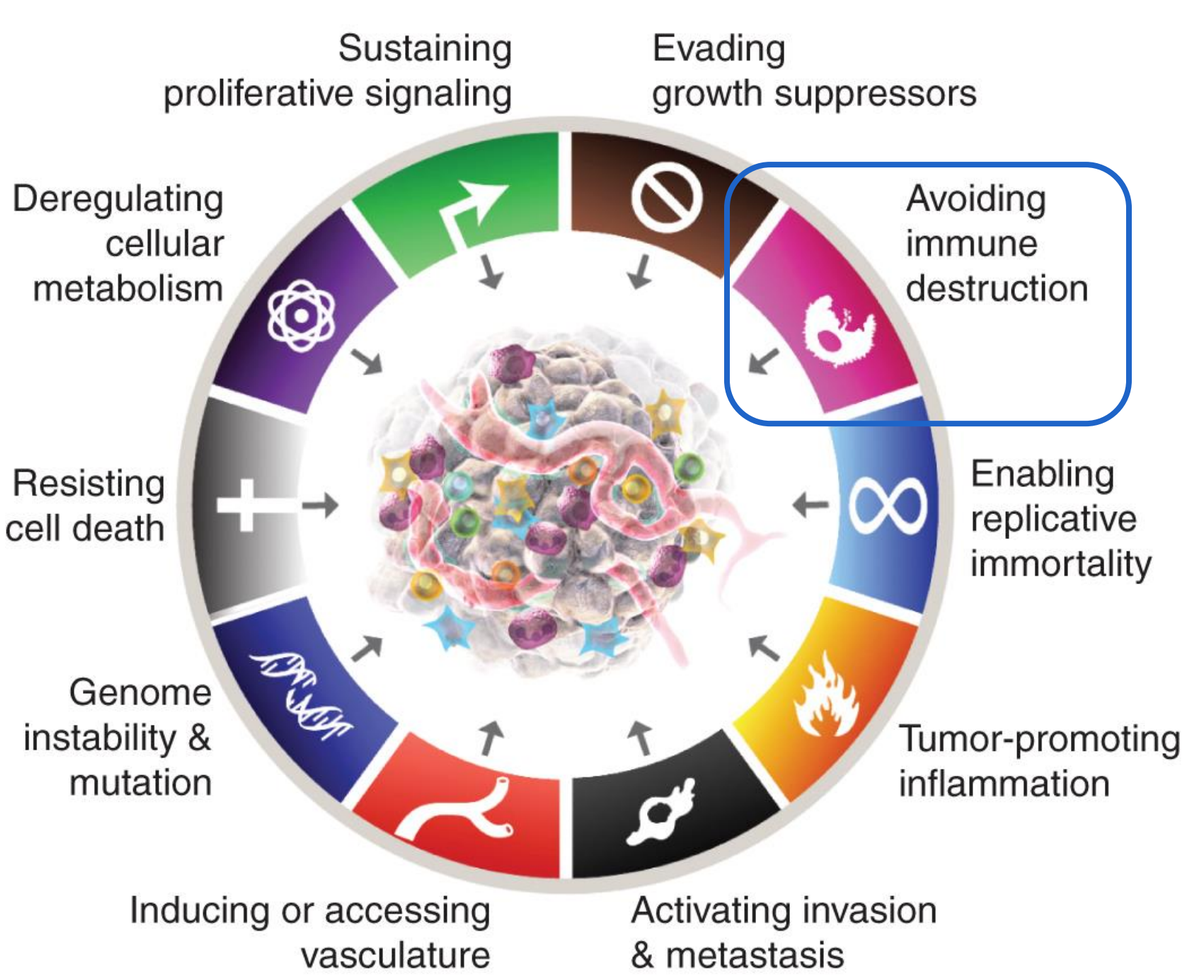


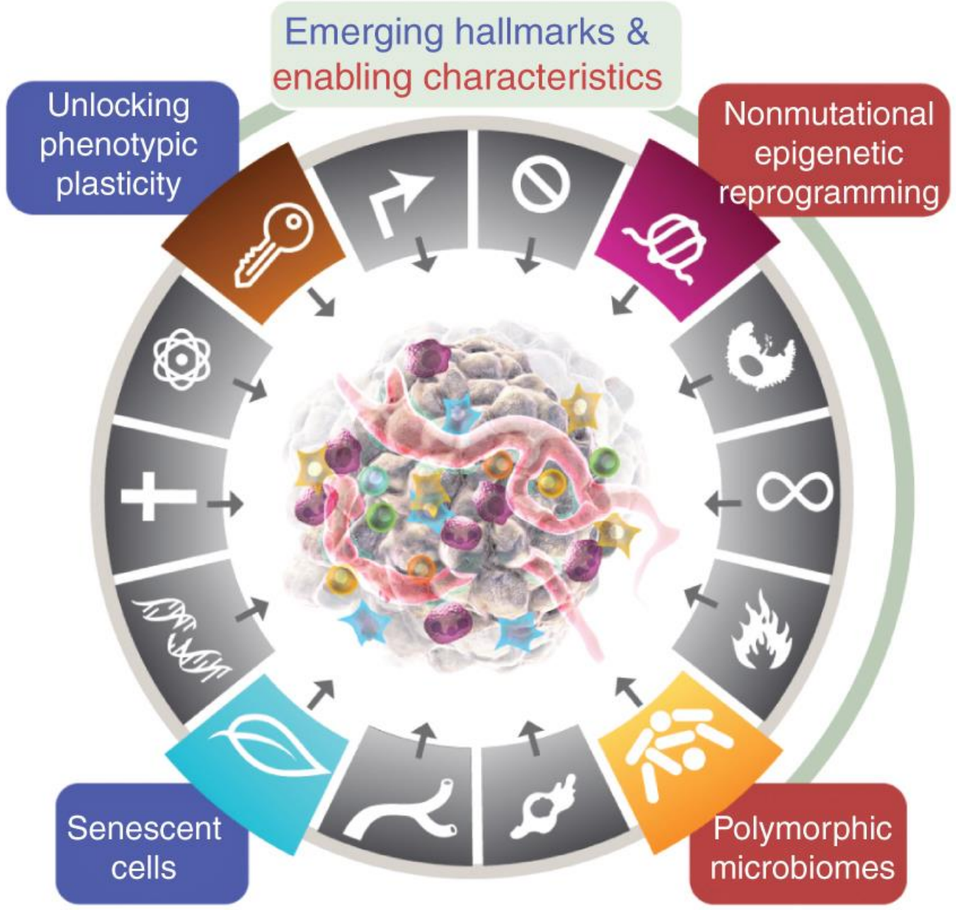
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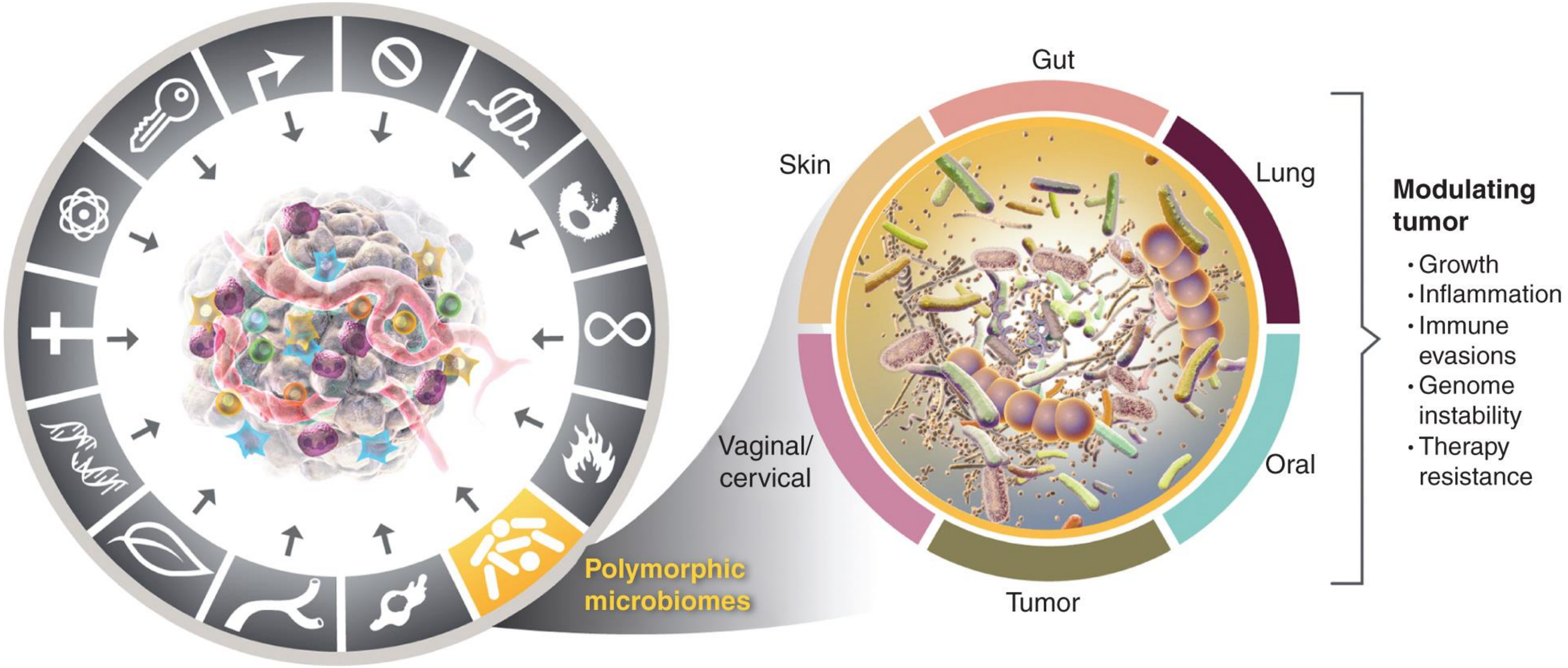




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D Hanahan, Cancer Discovery, 2022

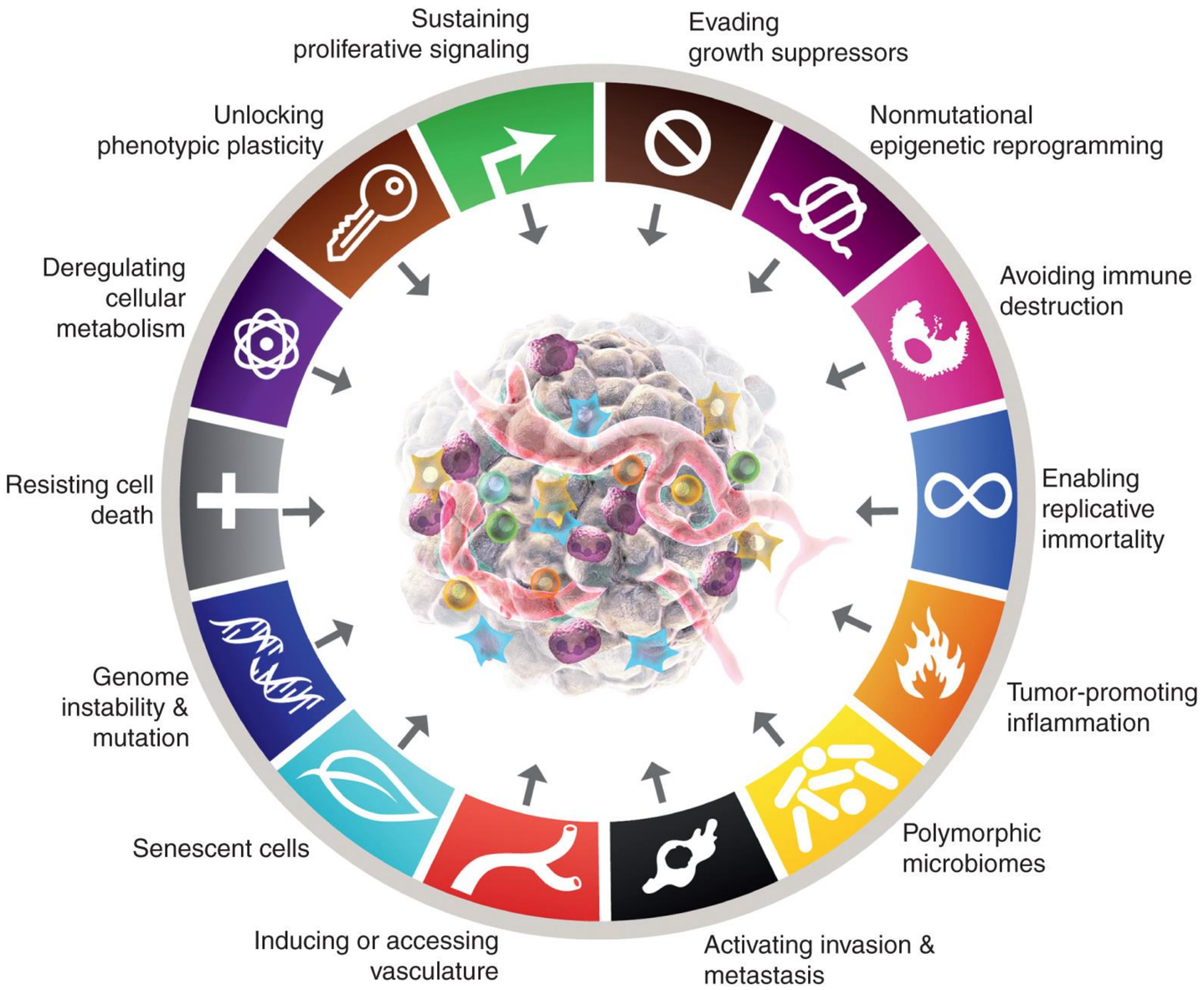
HALLMARKS OF CANCER



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D Hanahan, Cancer Discovery, 2022

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D Hanahan, Cancer Discovery, 2022

WAAROM ONTSNAPT KANKER AAN HET MMUUNSYSTEEM?

- **Falend immuunsysteem**
  - T cellen die tumor herkennen zijn afwezig
  - Het immuunsysteem faalt: patiënten die immuunsuppressiva nemen, AIDS, chemotherapie/radiotherapie, …

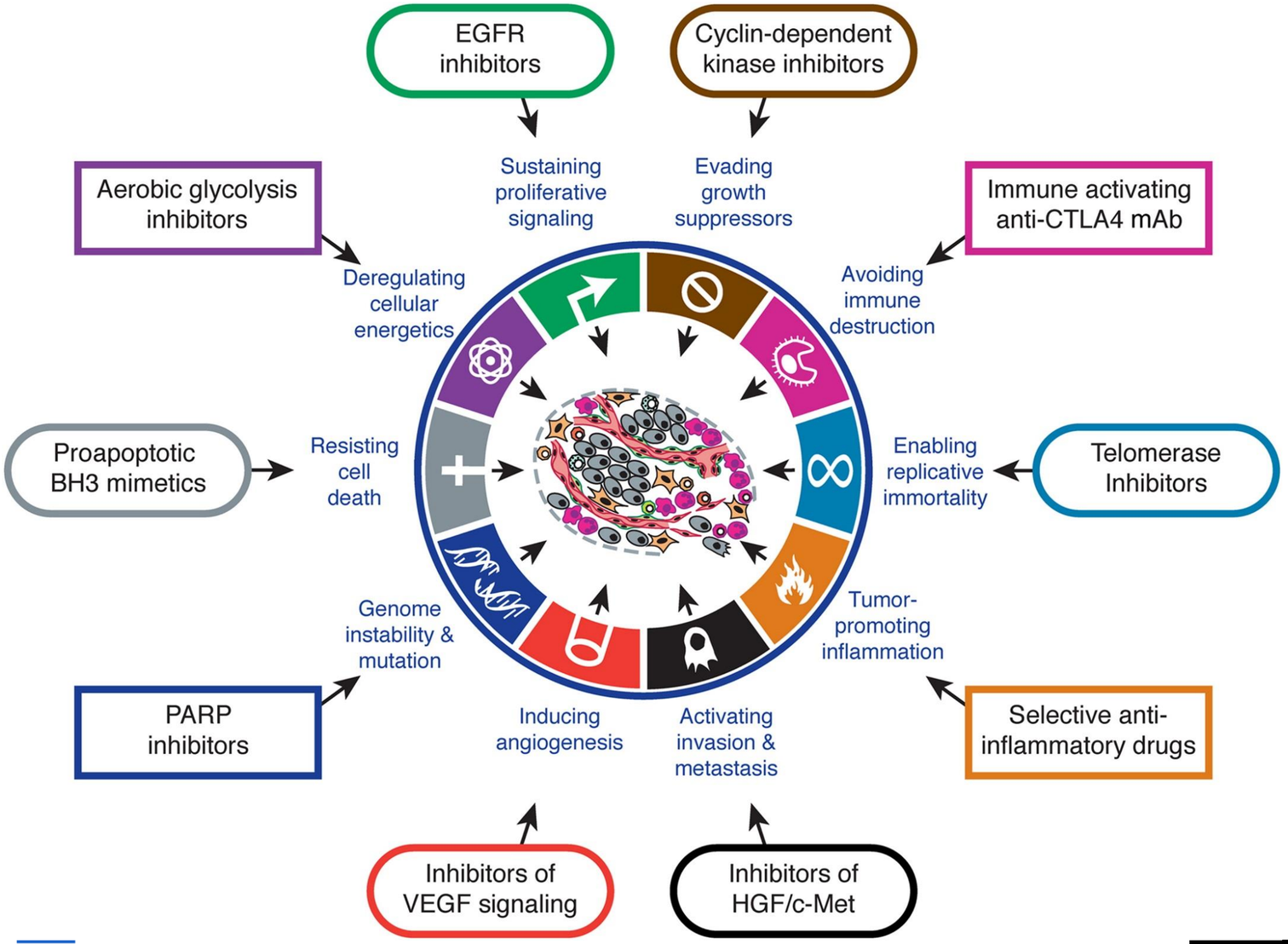
- **Tumor onderdrukt het immuunsysteem**
  - Verdwijnen van tumorantigenen en/of HLA molekules op het celoppervlak van de tumorcellen
  - Aantrekken van cellen en oplosbare factoren die immuunreacties onderdrukken
  - Expressie van eiwitten die binden op T-cellen, en daardoor de T-cellen onderdrukken

HOE KUNNEN WE HET IMMUUNSYSTEEM STERKER MAKEN IN DE STRIJD TEGEN KANKER?

→ IMMUNOTHERAPIE

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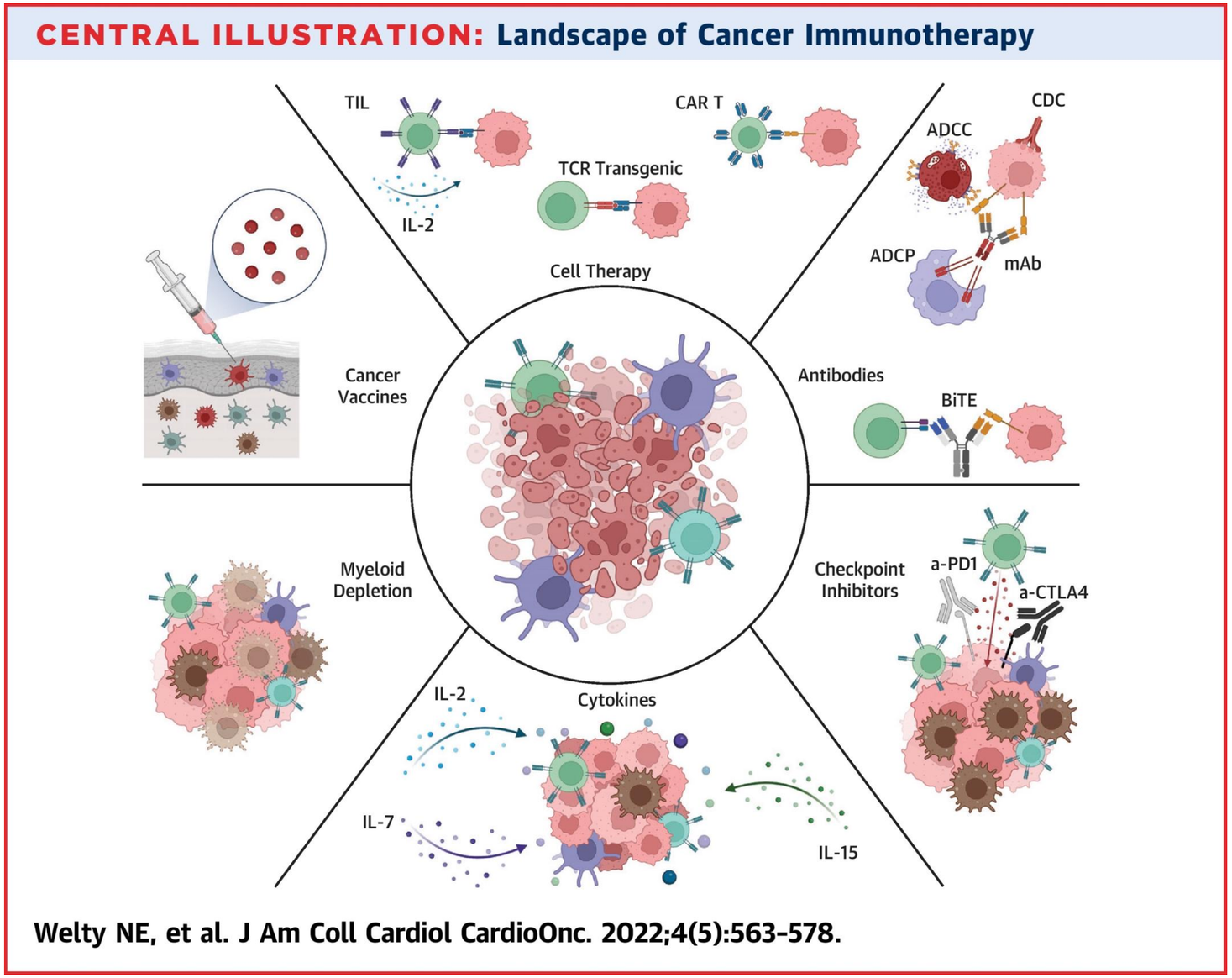
‘NIEUWE’ BEHANDELINGEN VAN KANKER



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D Hanahan and R Weinberg, Cell, 2011

IMMUNOTHERAPIE



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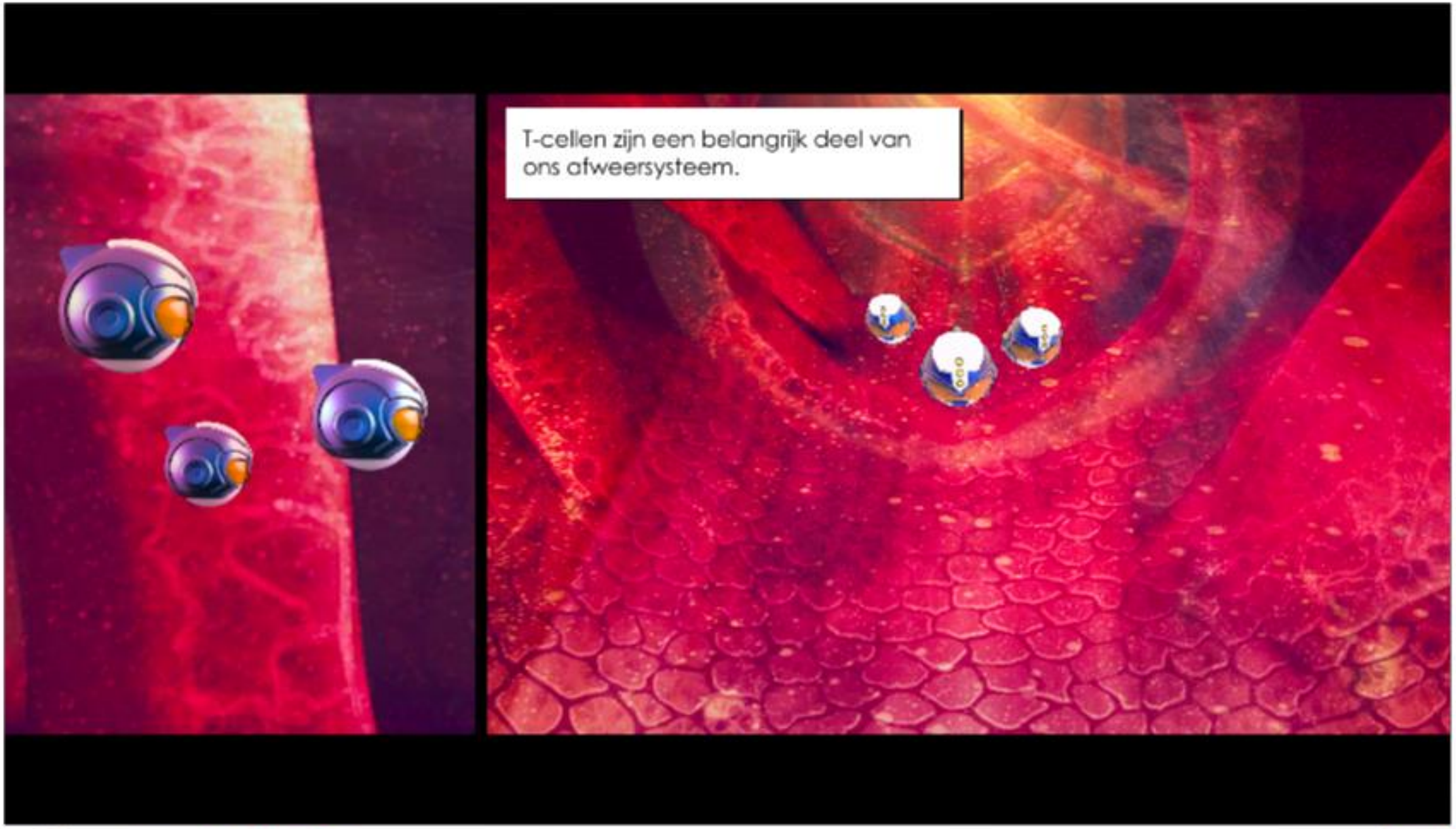
Nathan E. Welty et al. J Am Coll Cardiol CardioOnc 2022

HET VERHAAL VAN IMMUNO-T



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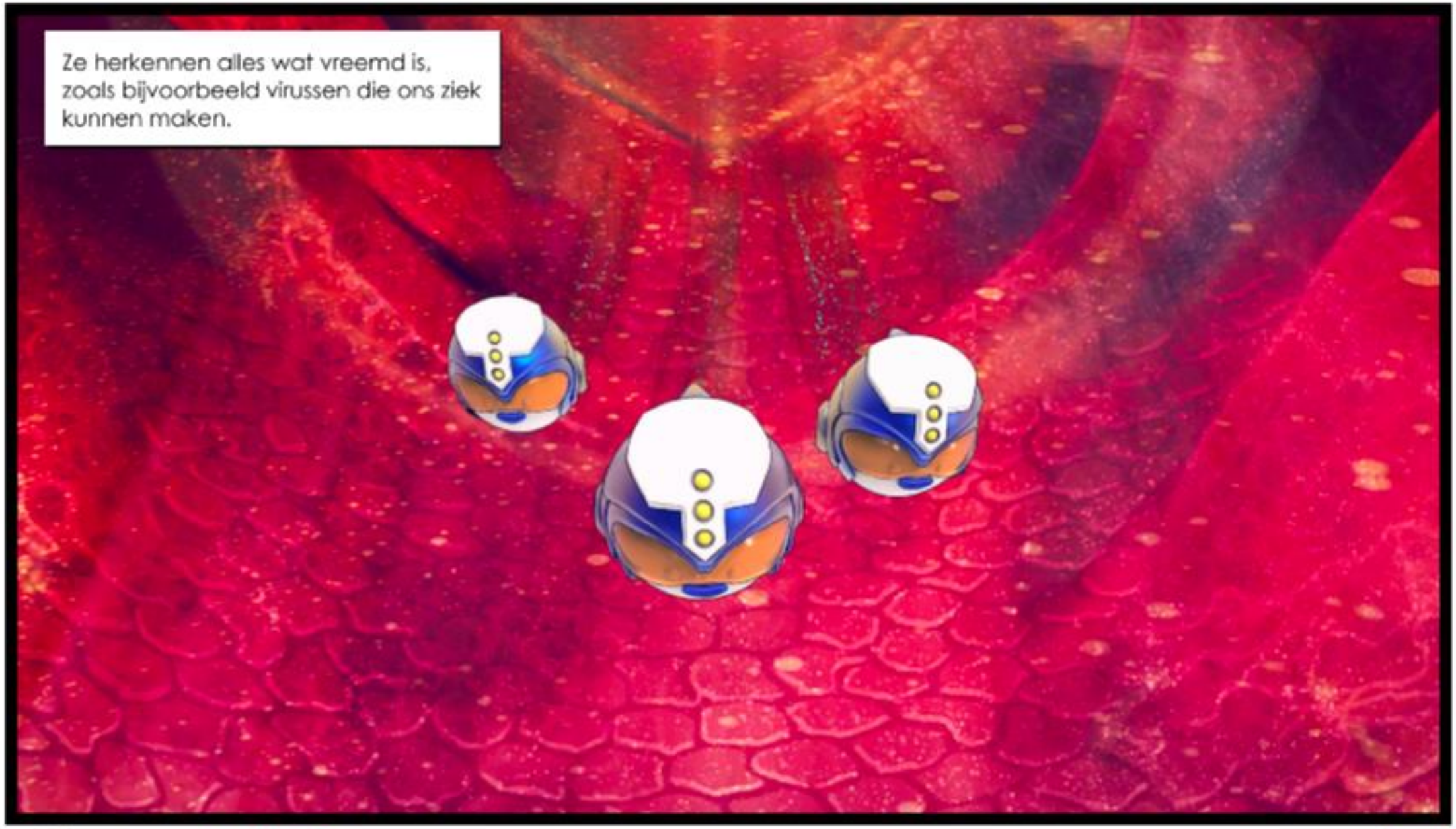
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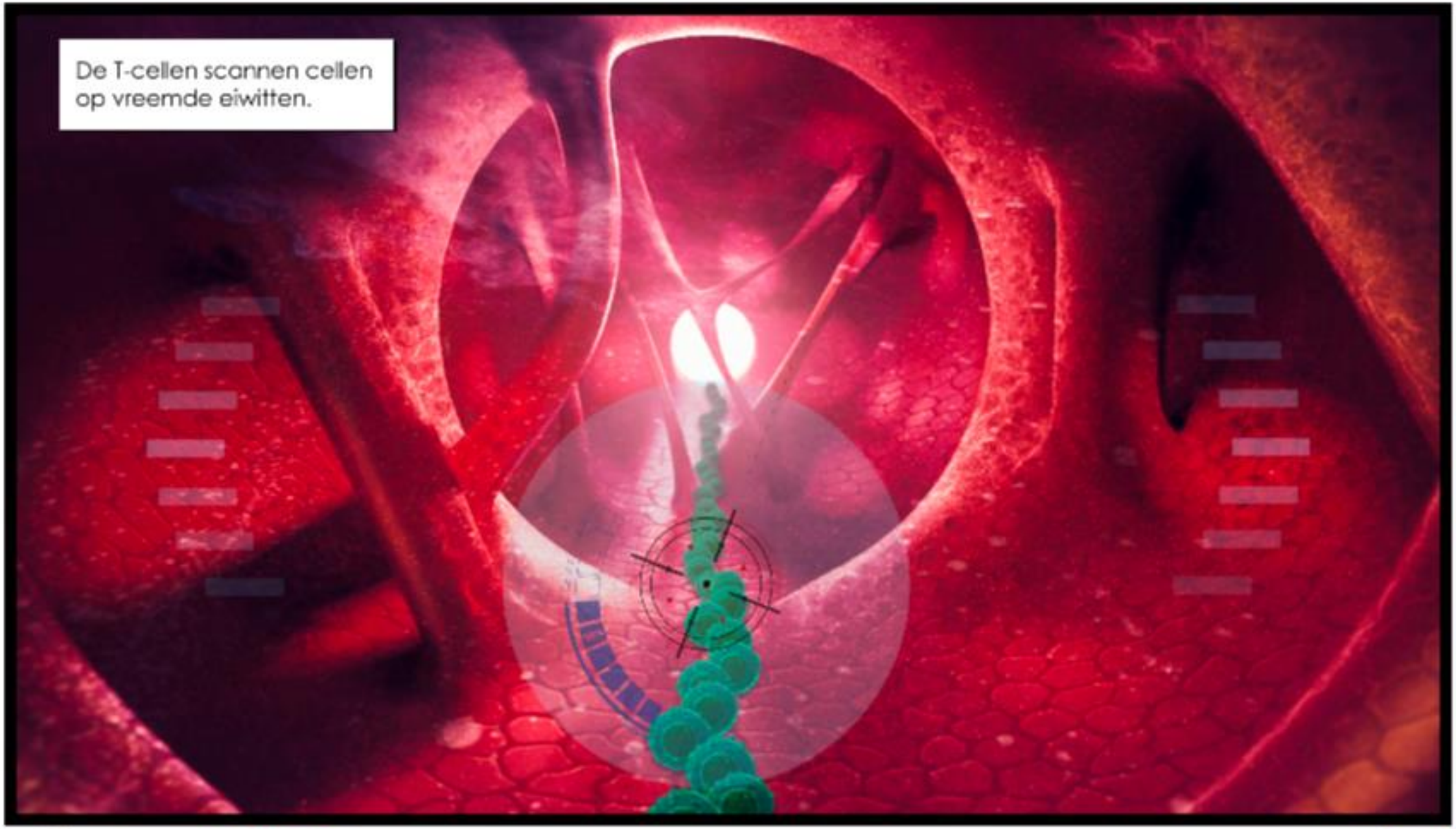
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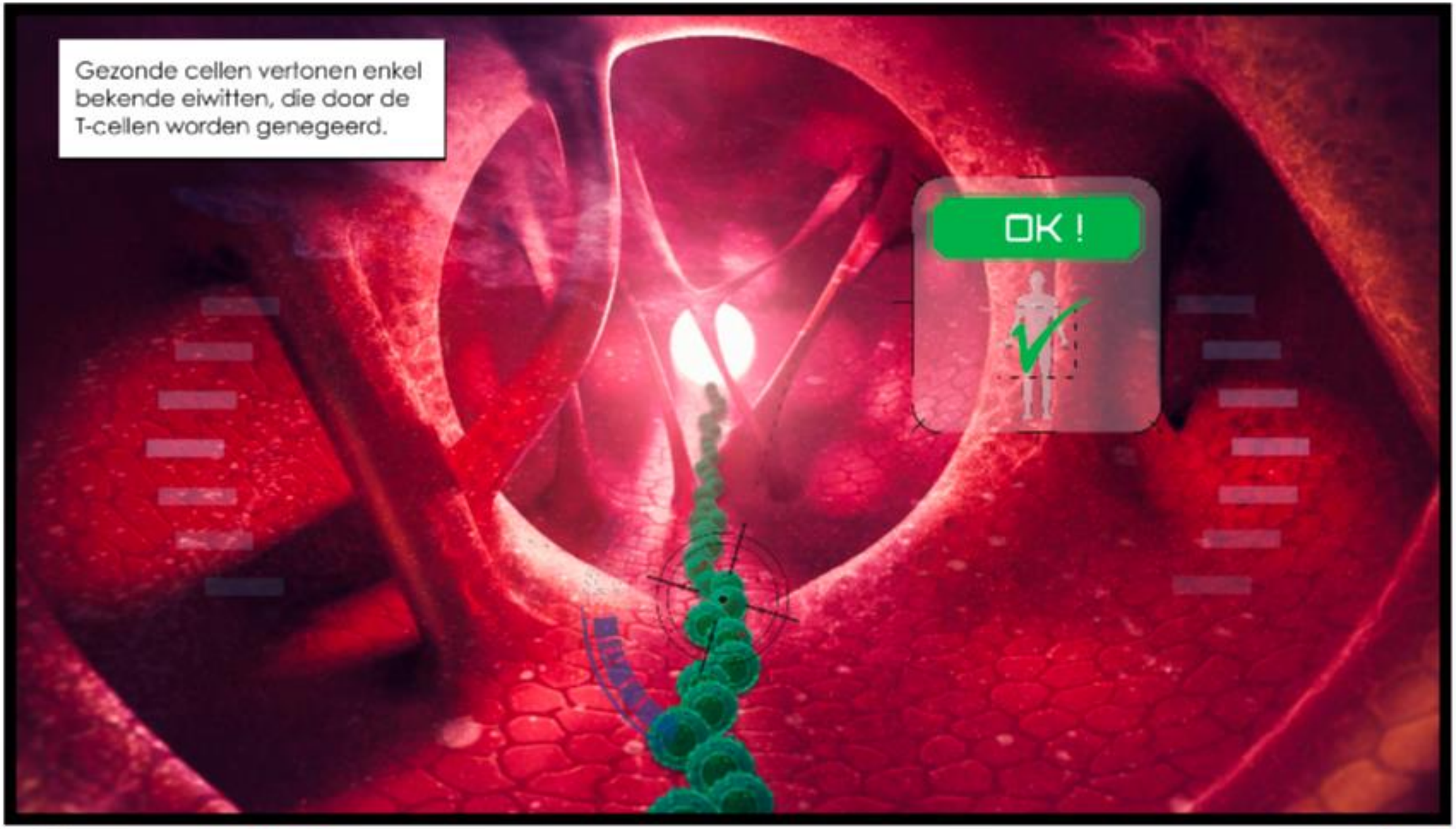
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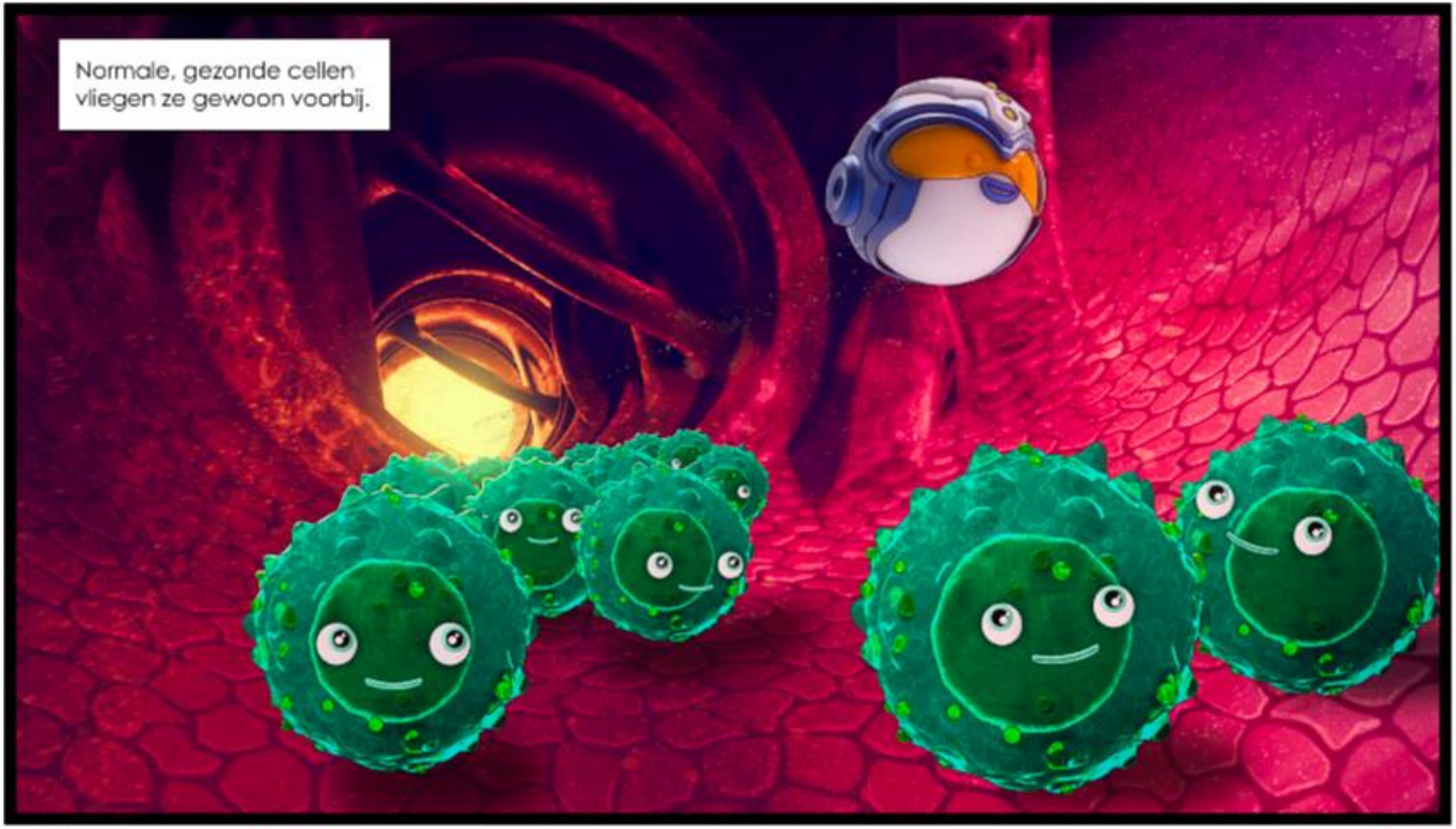
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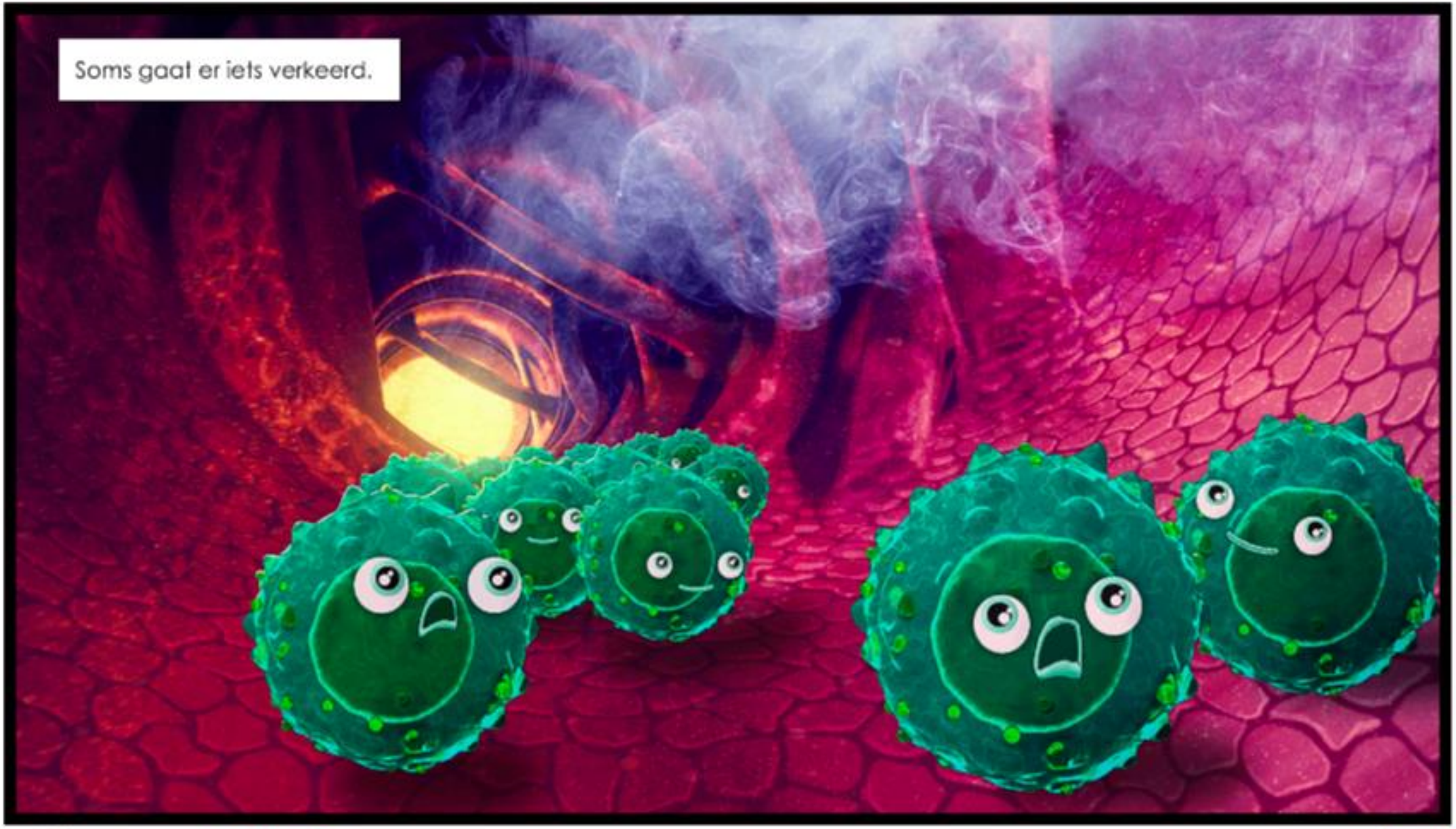
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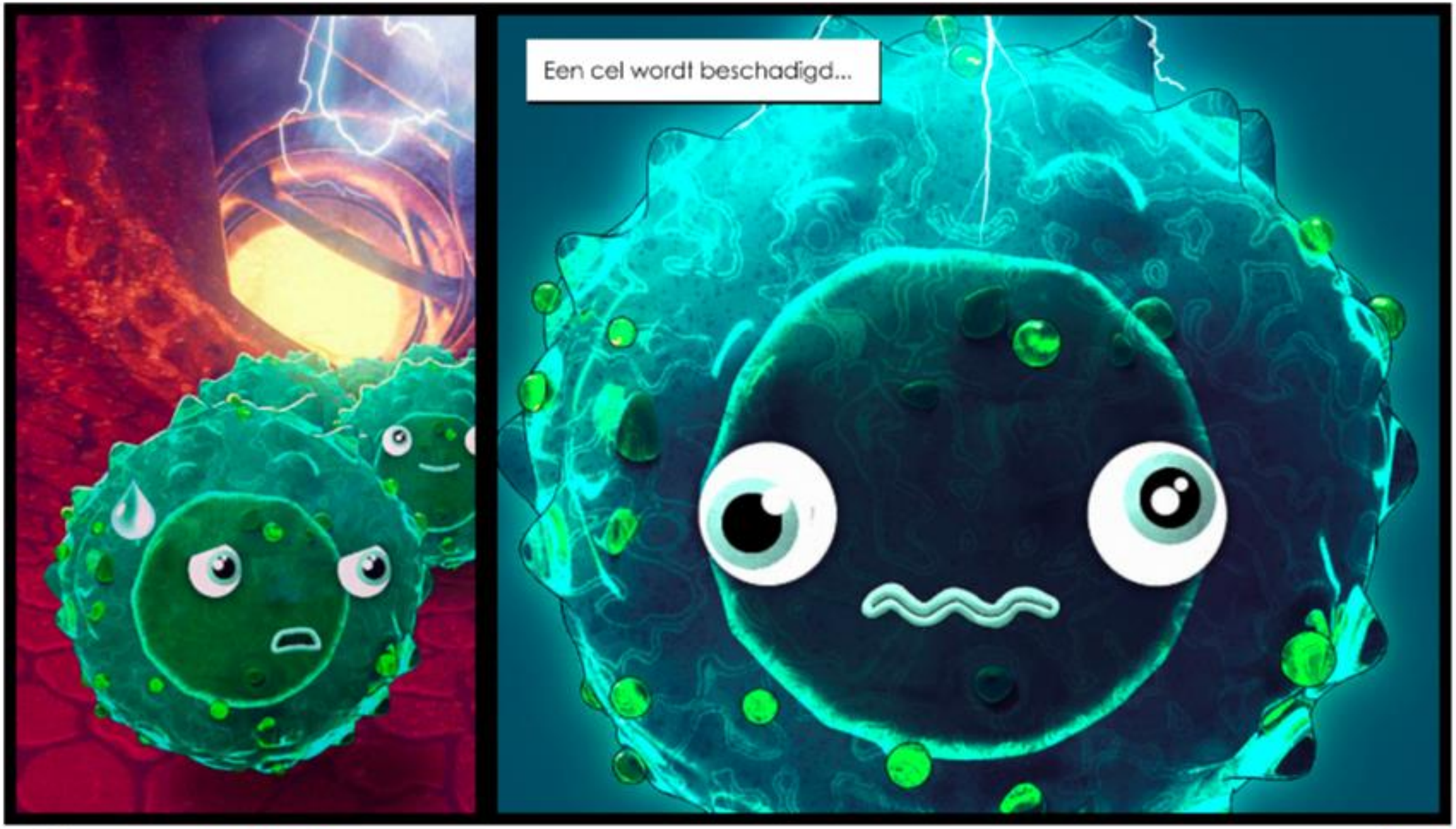
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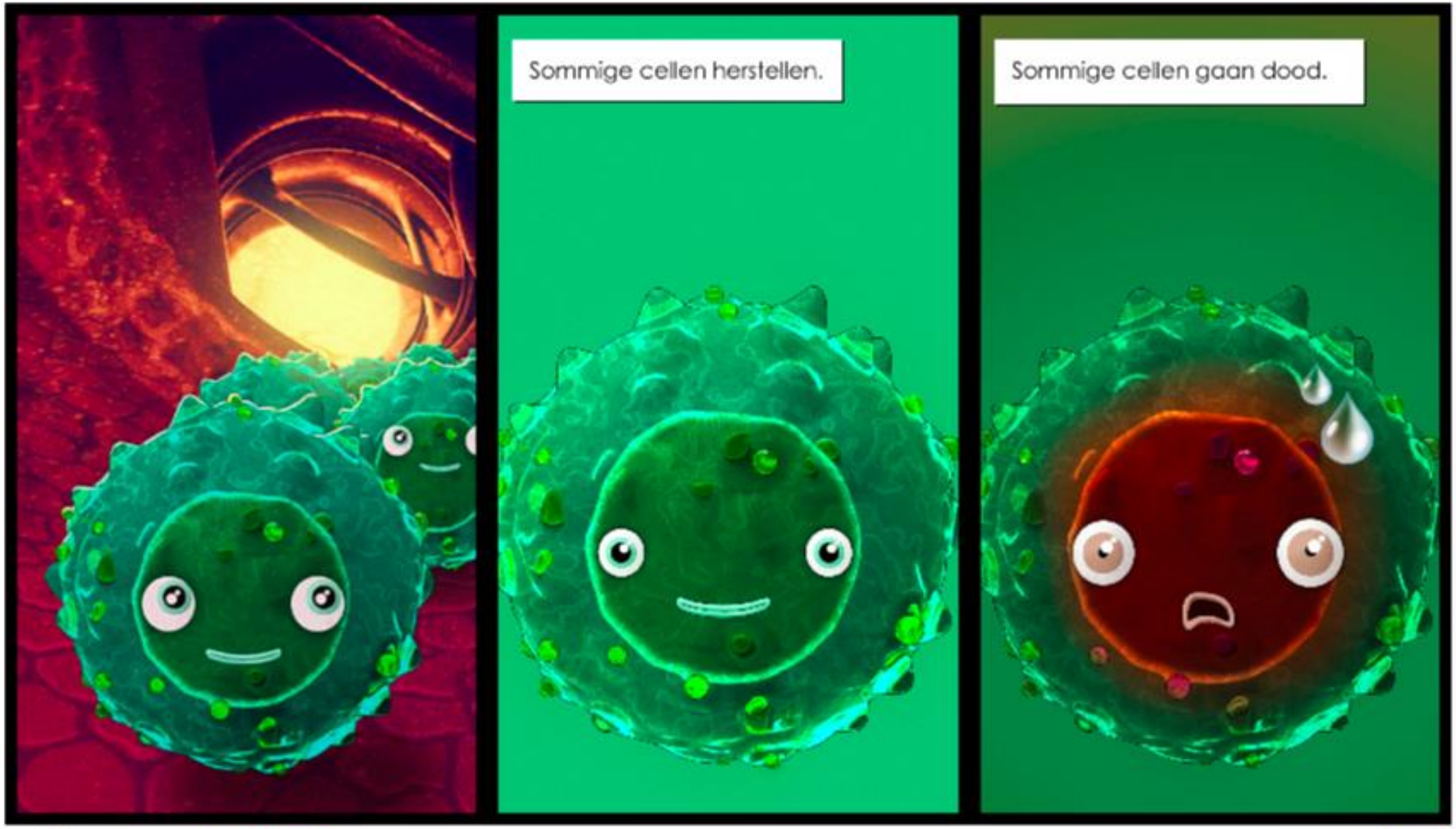
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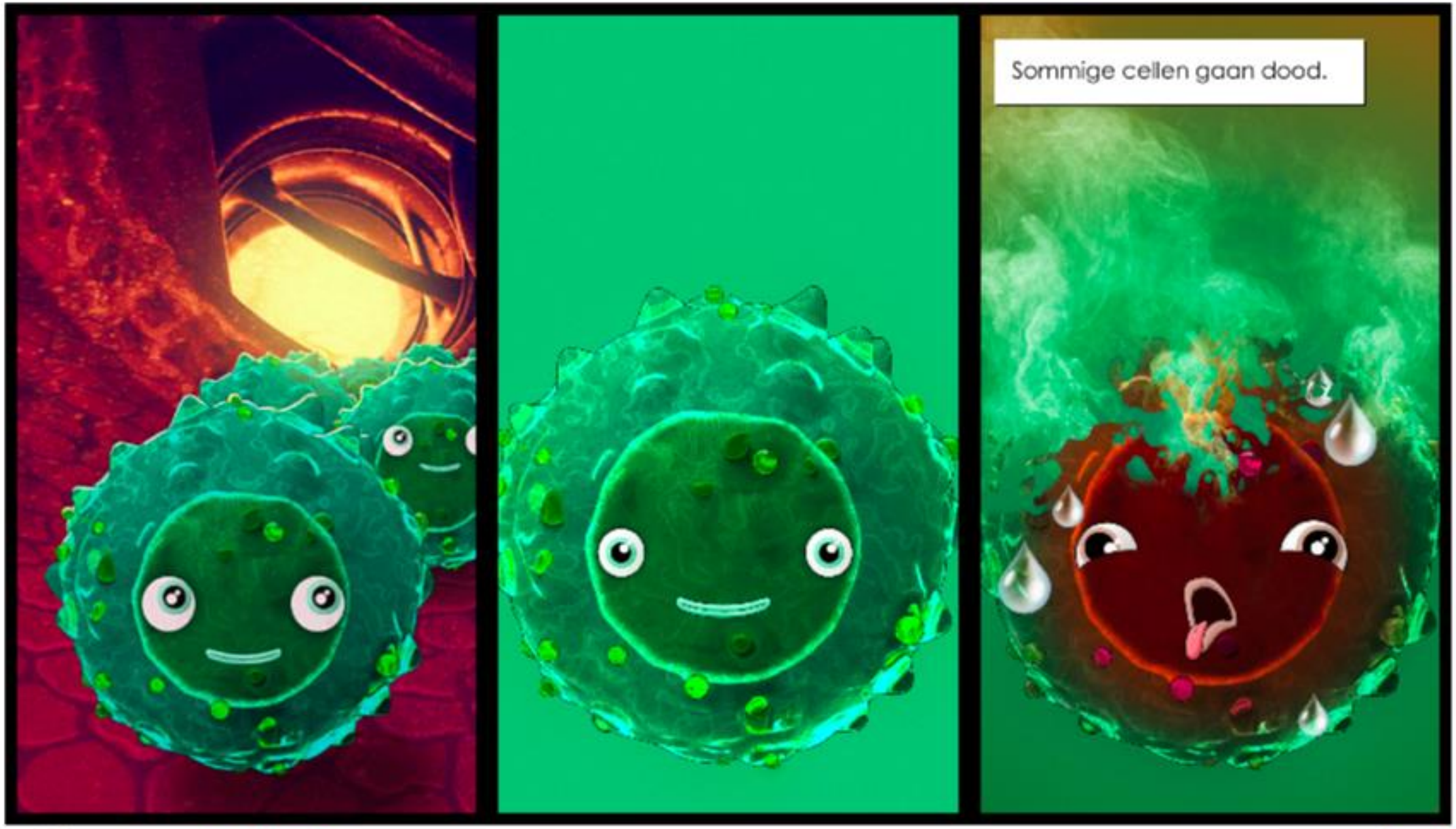
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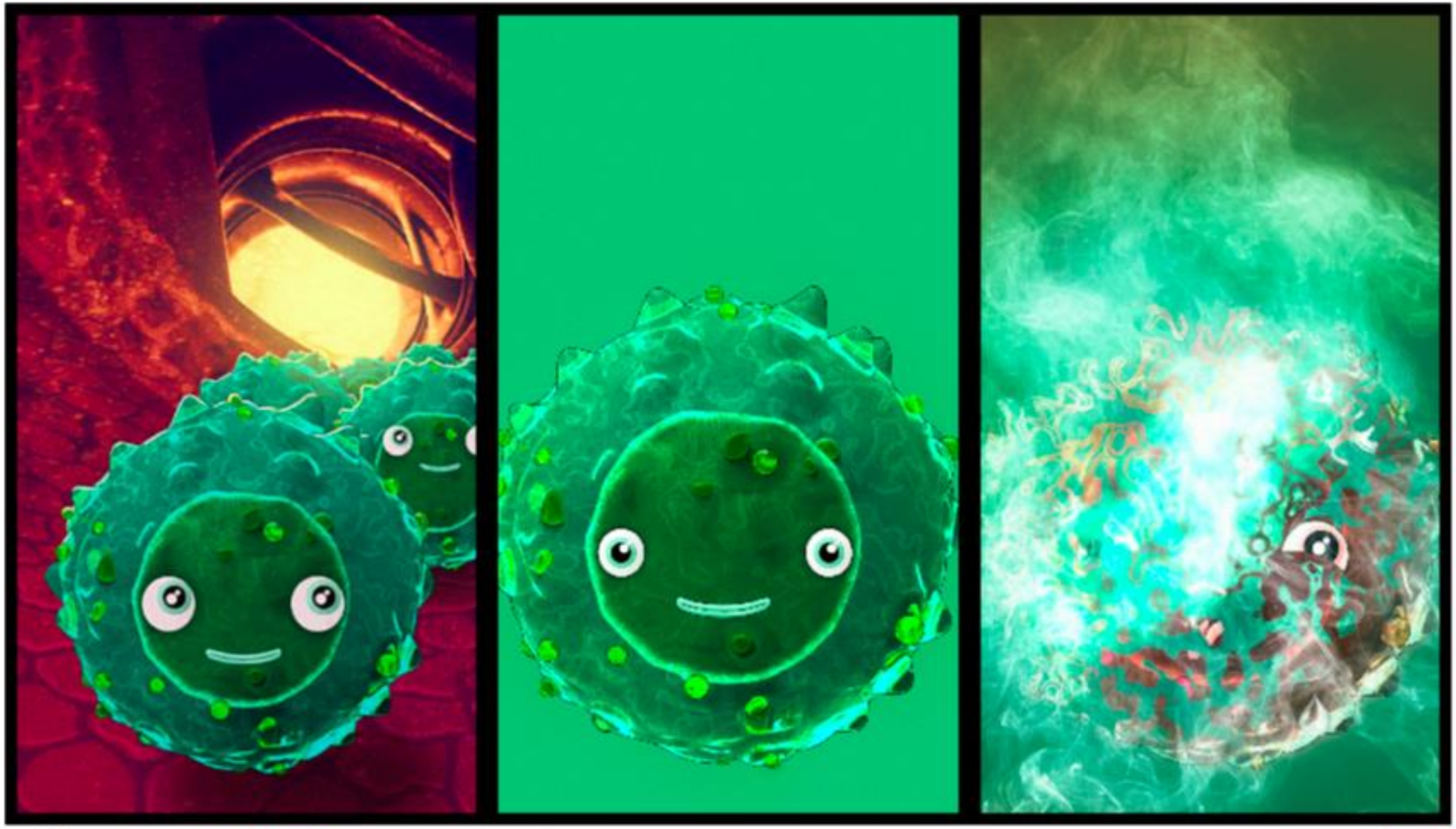


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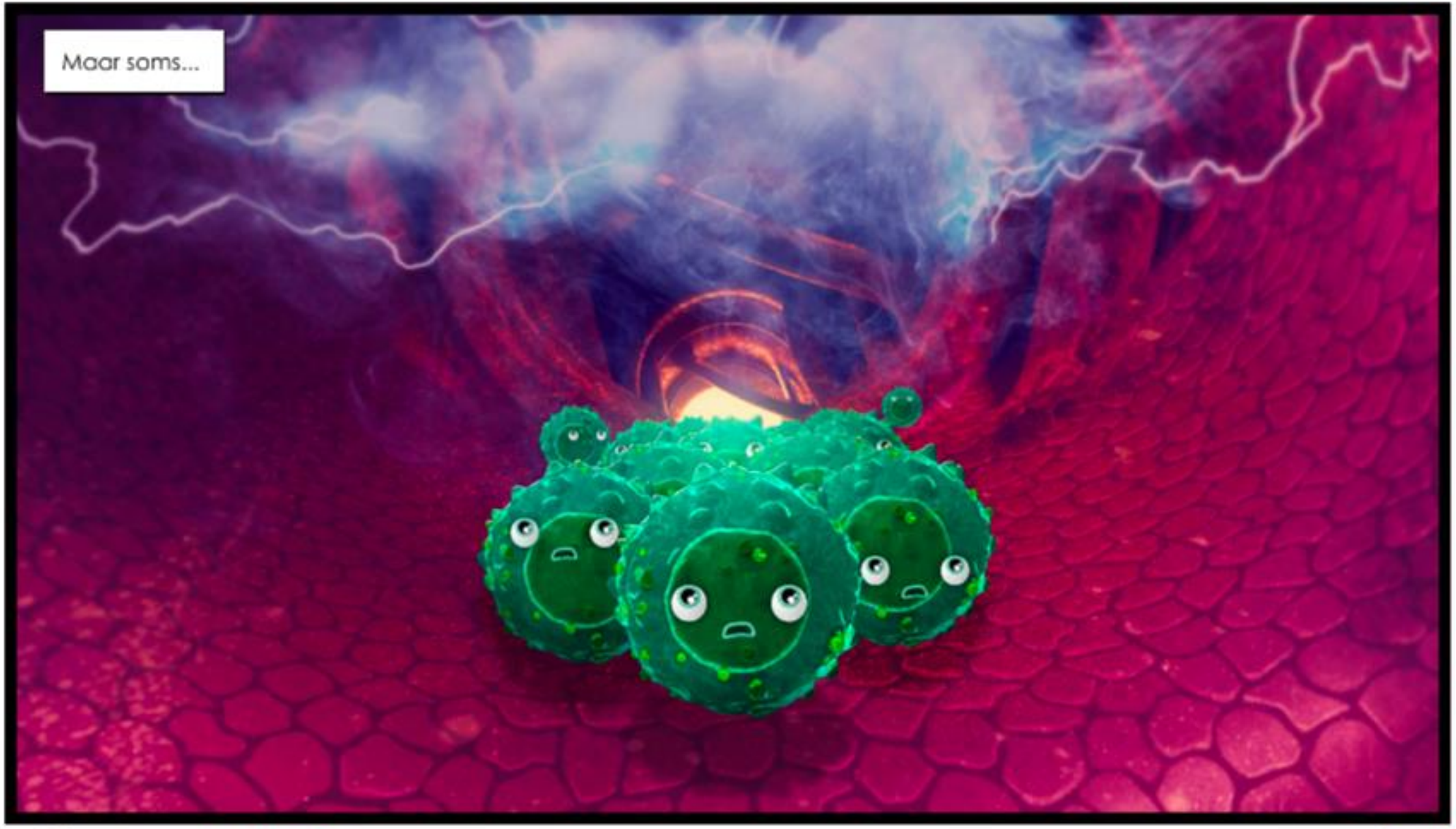

Sommige cellen gaan dood.



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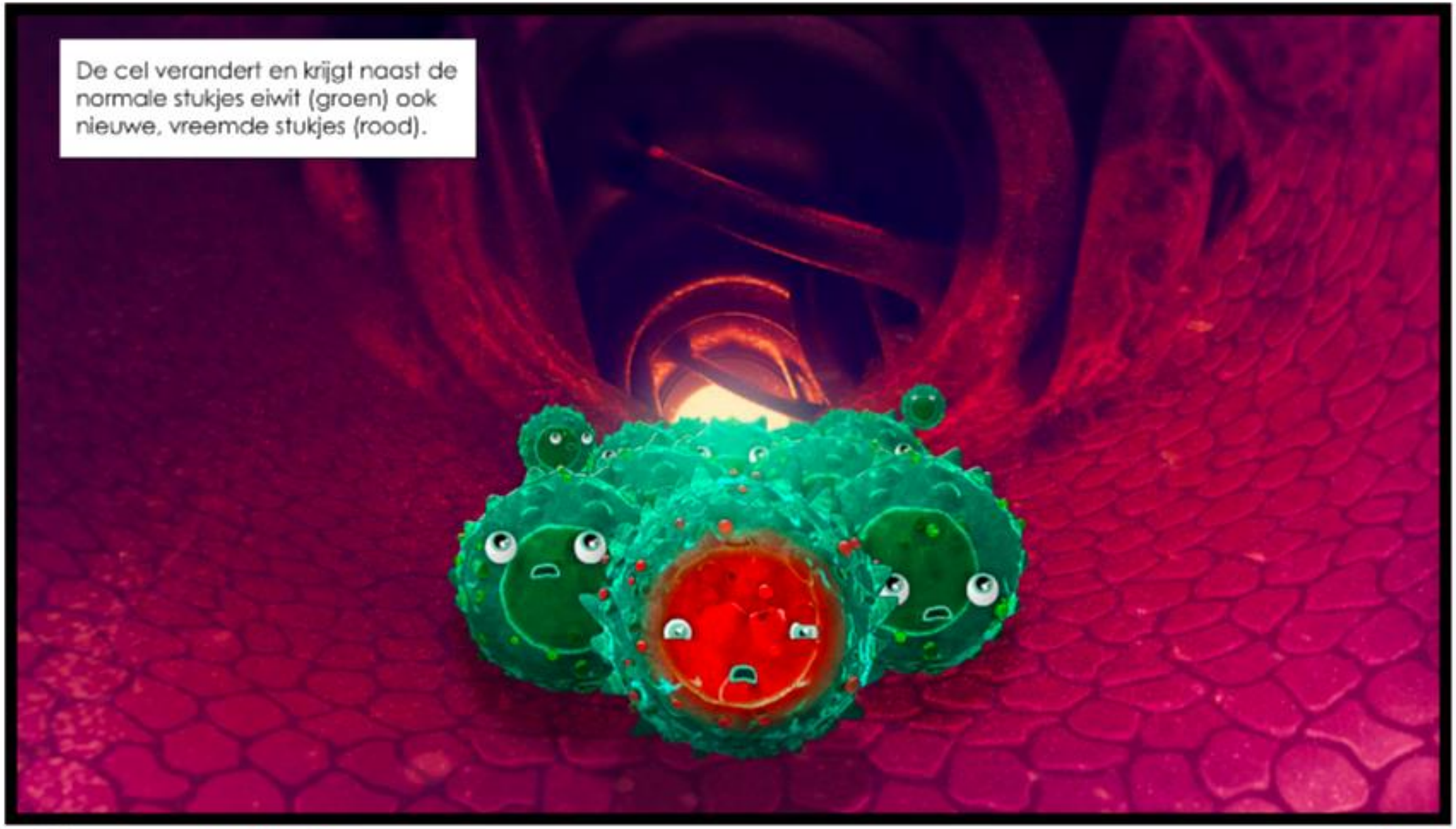
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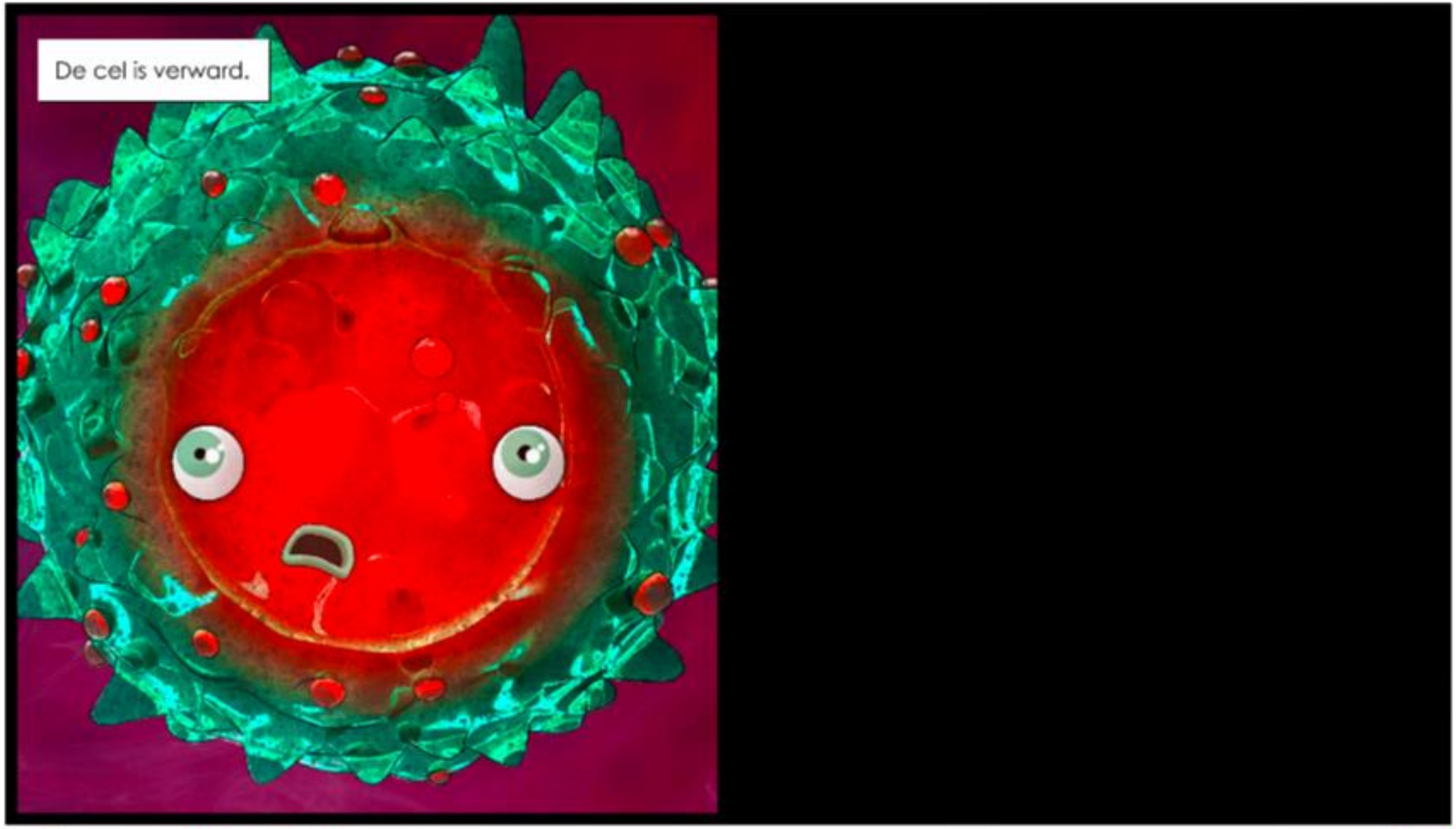
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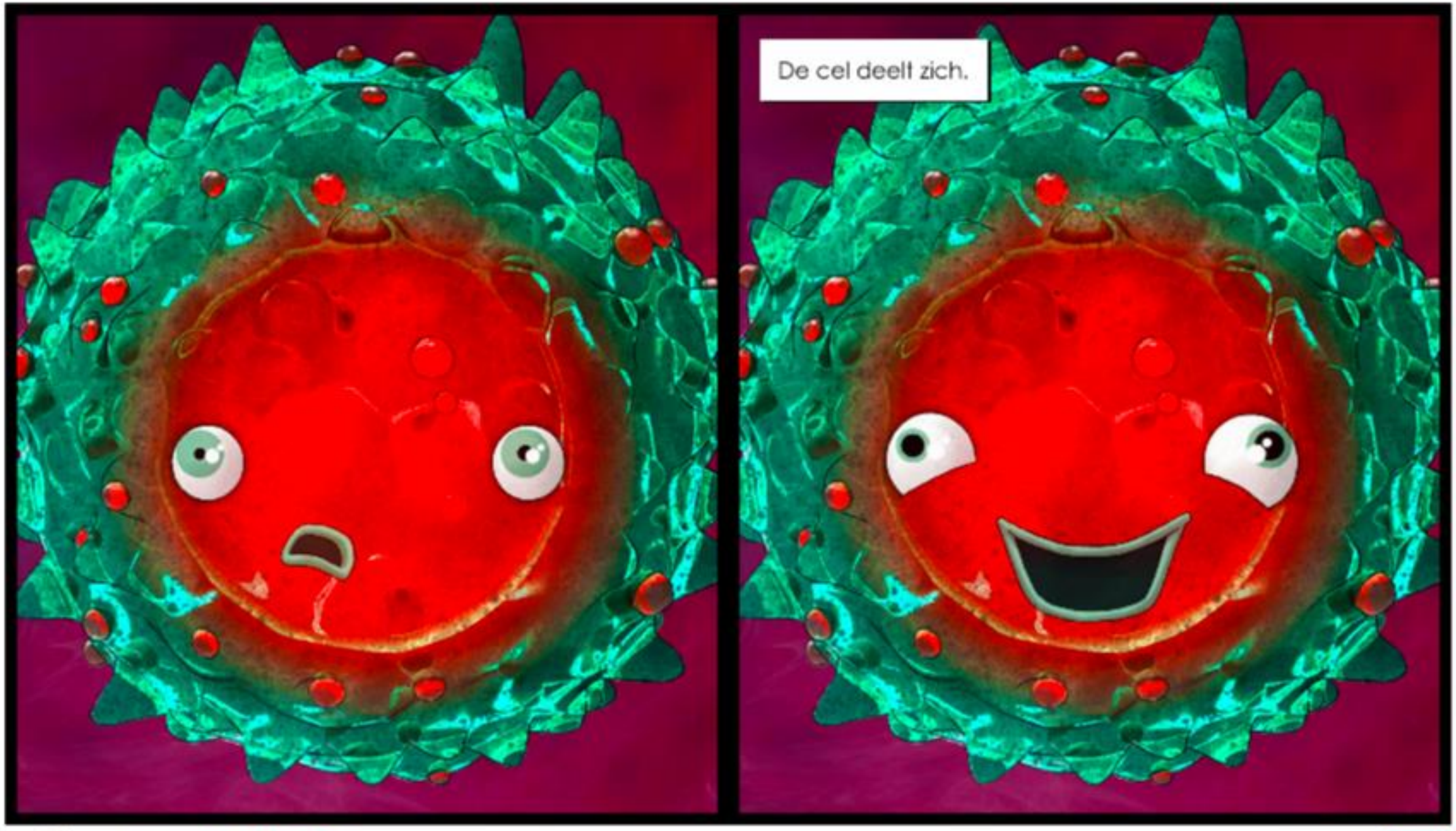
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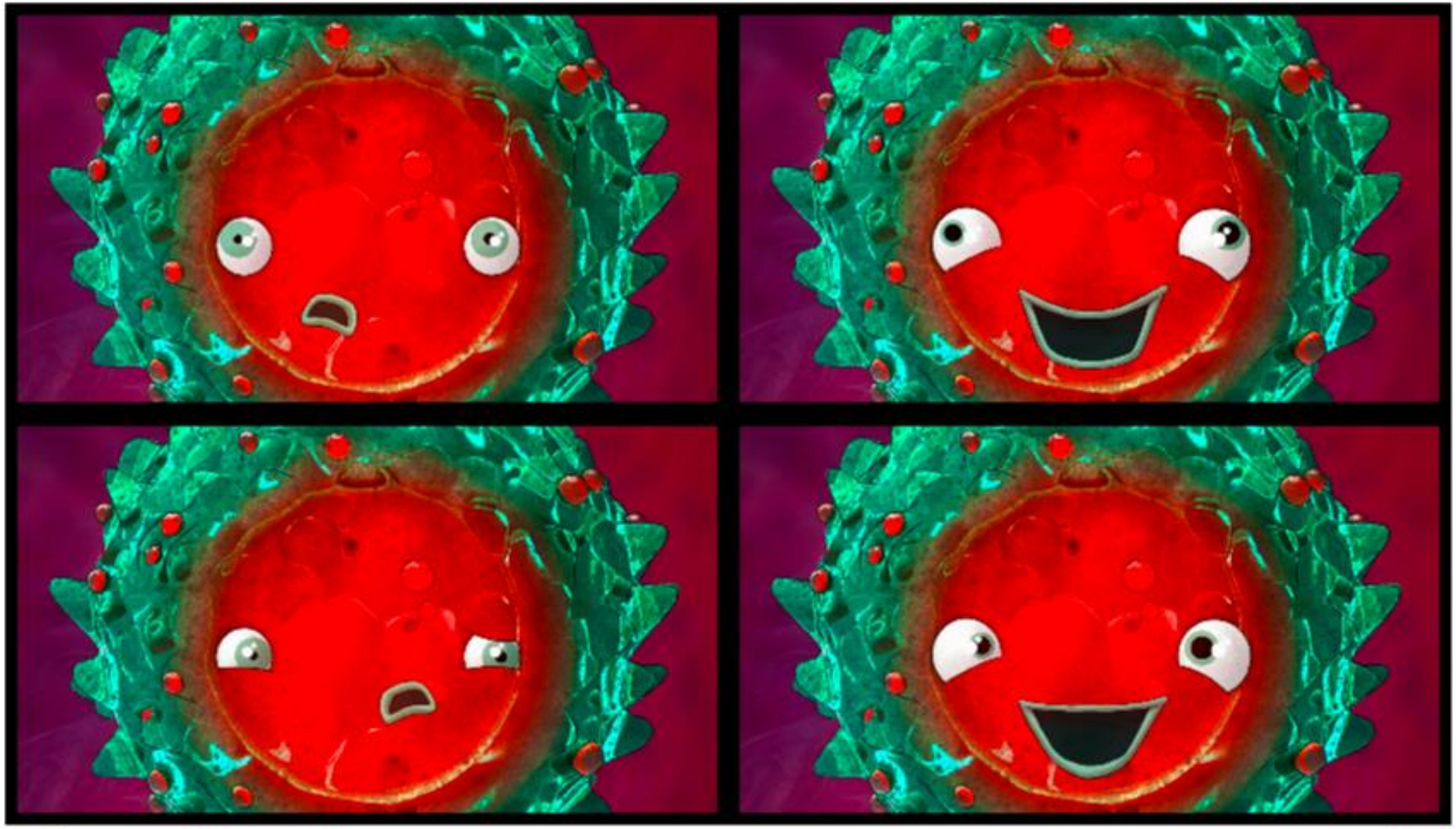
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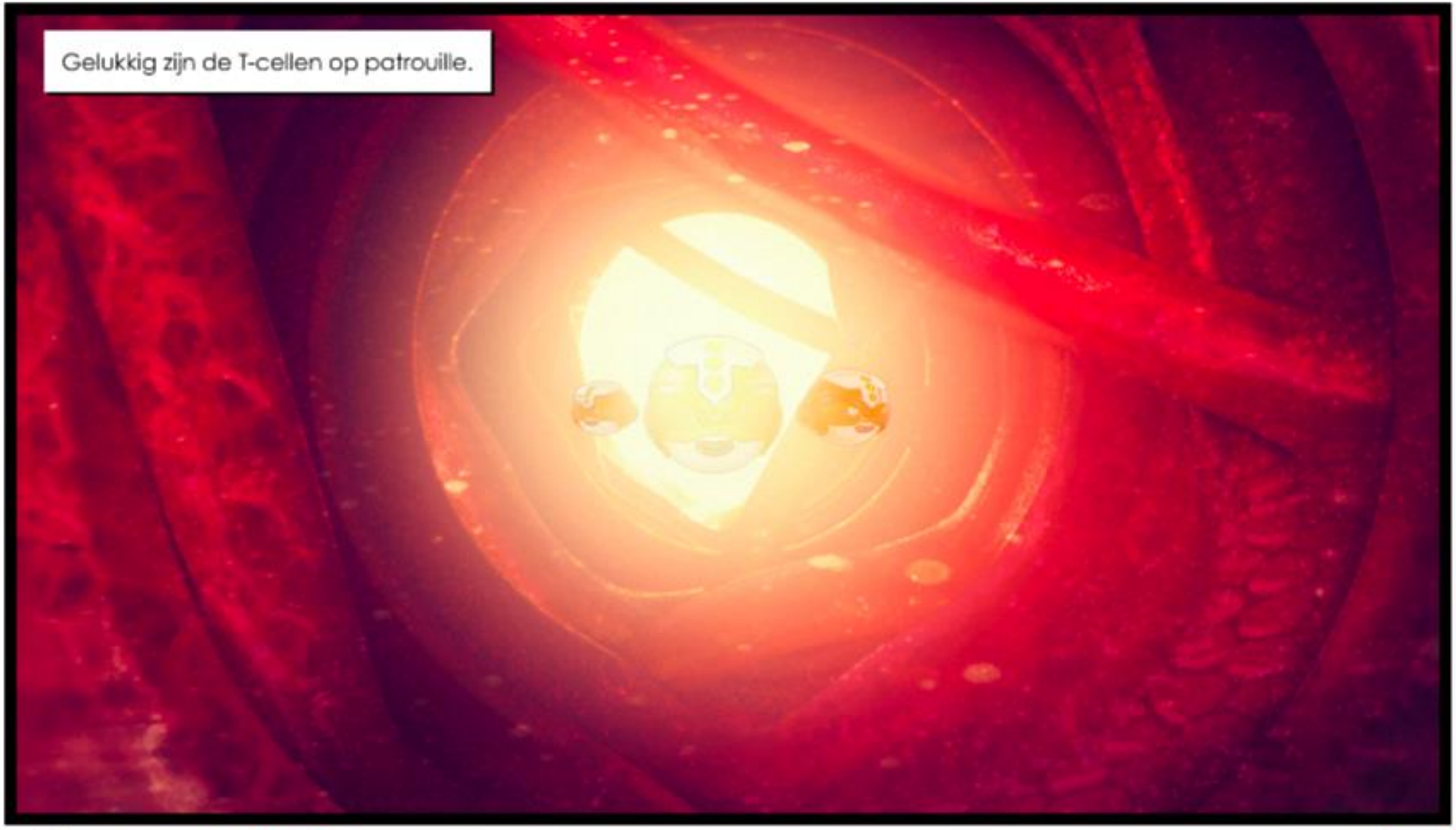
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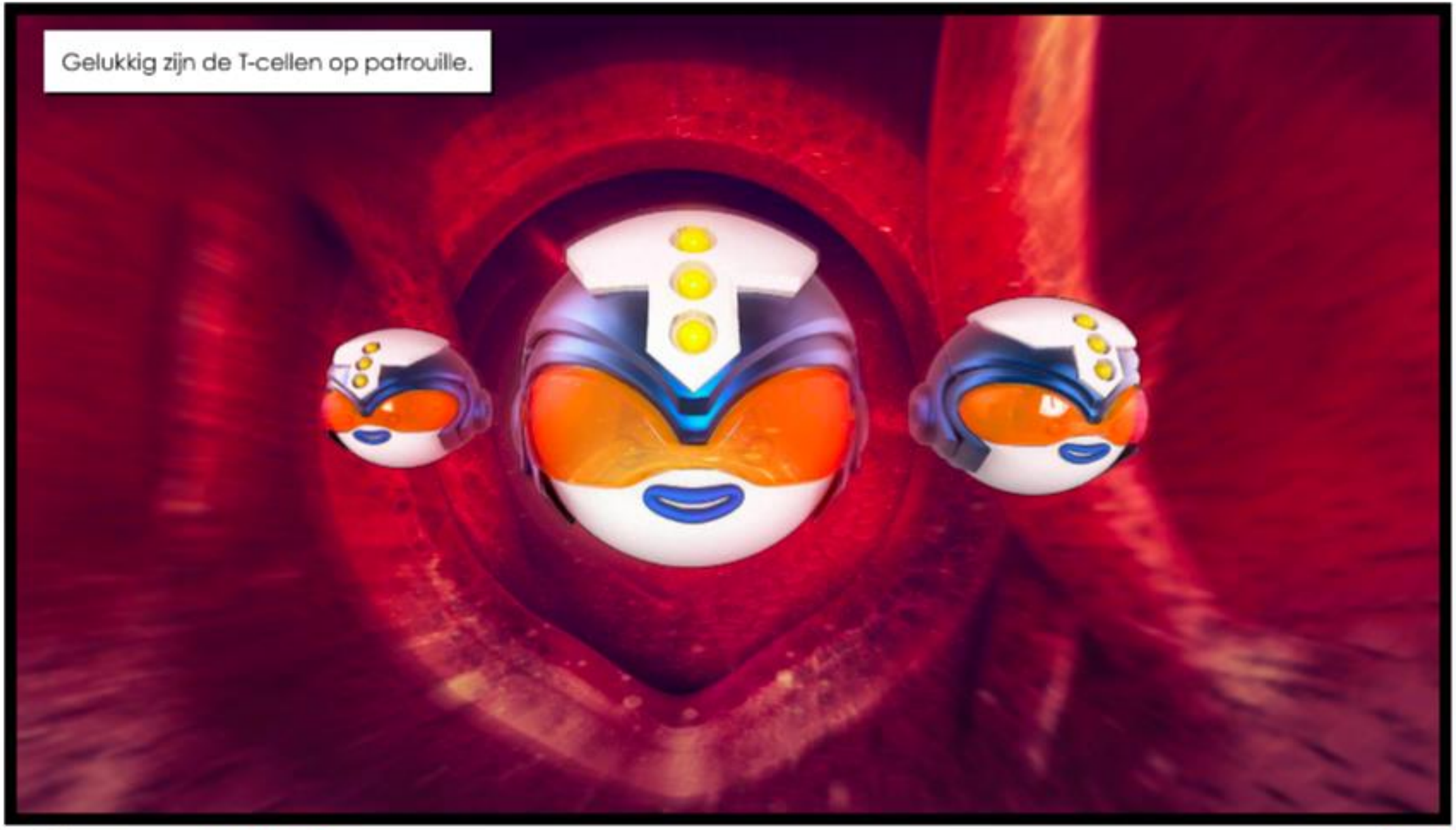
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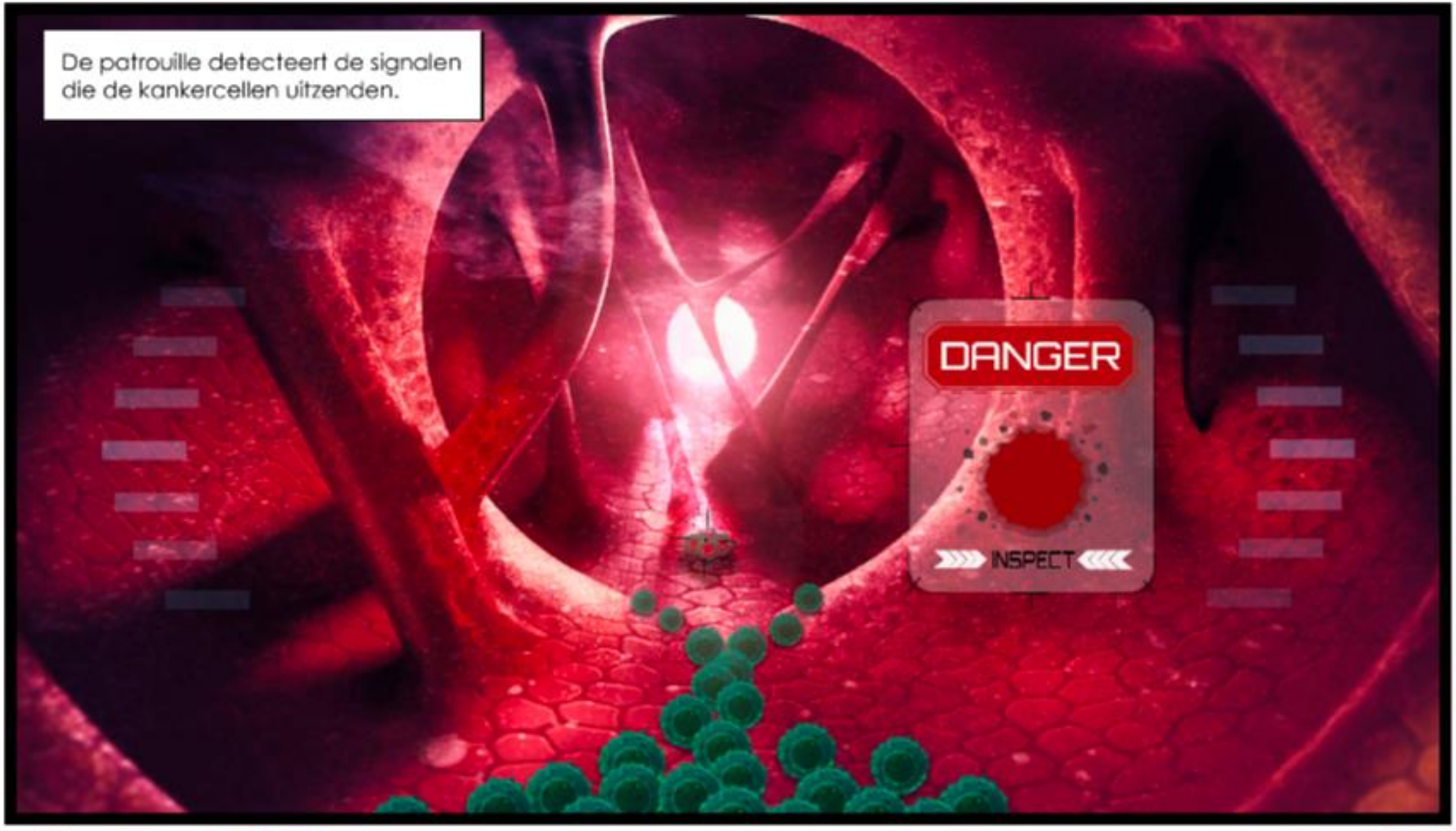
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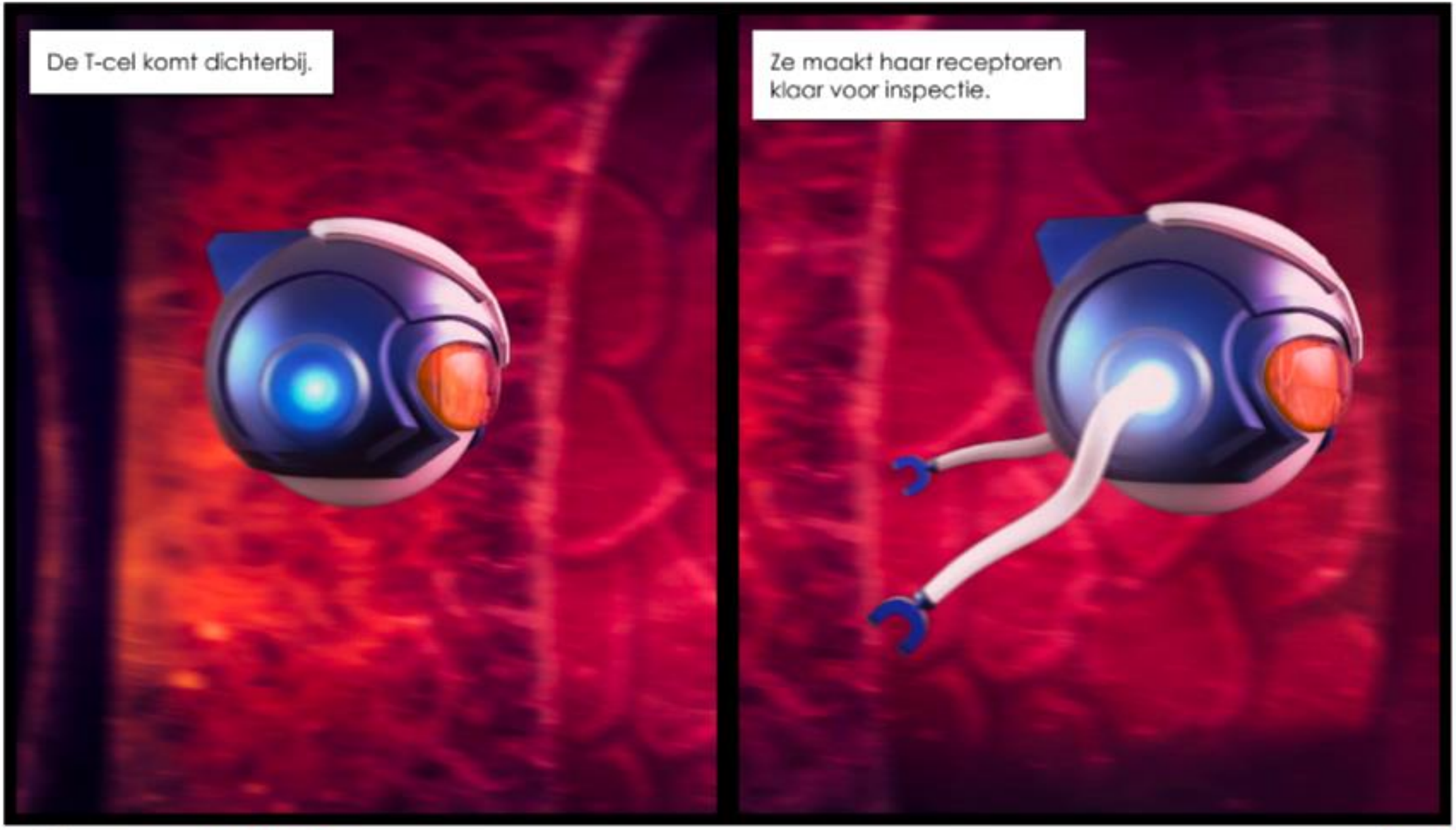
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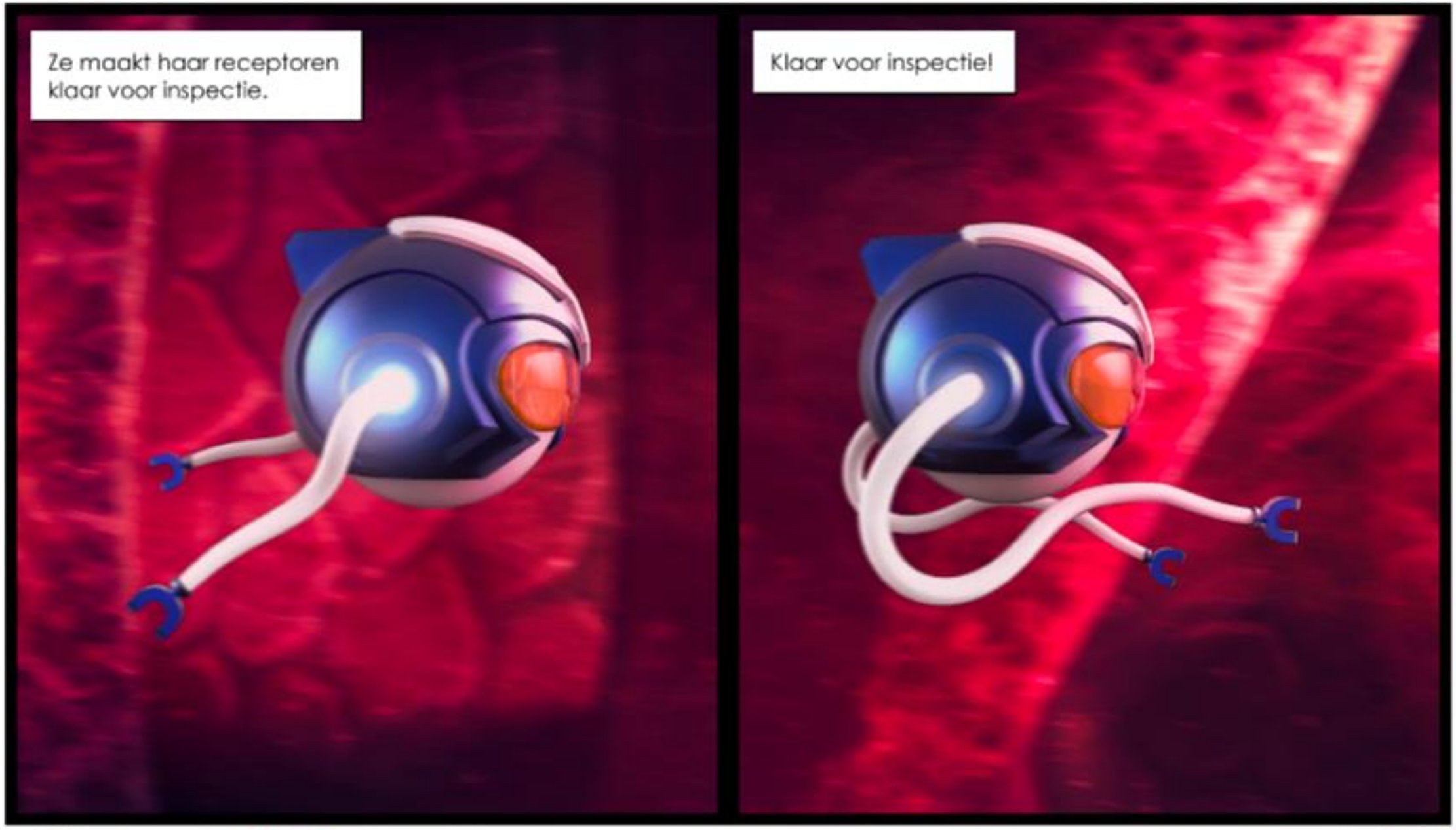
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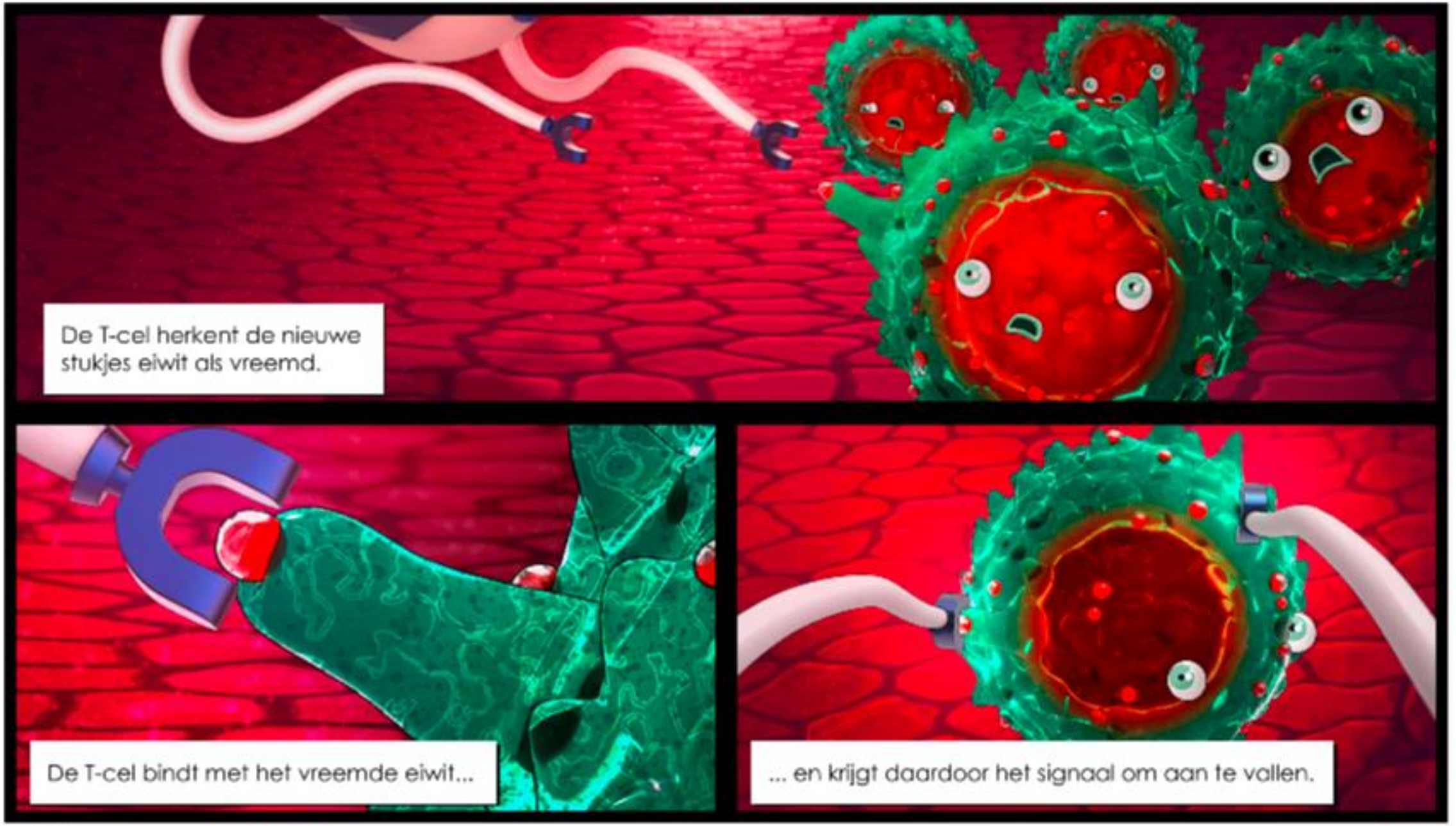
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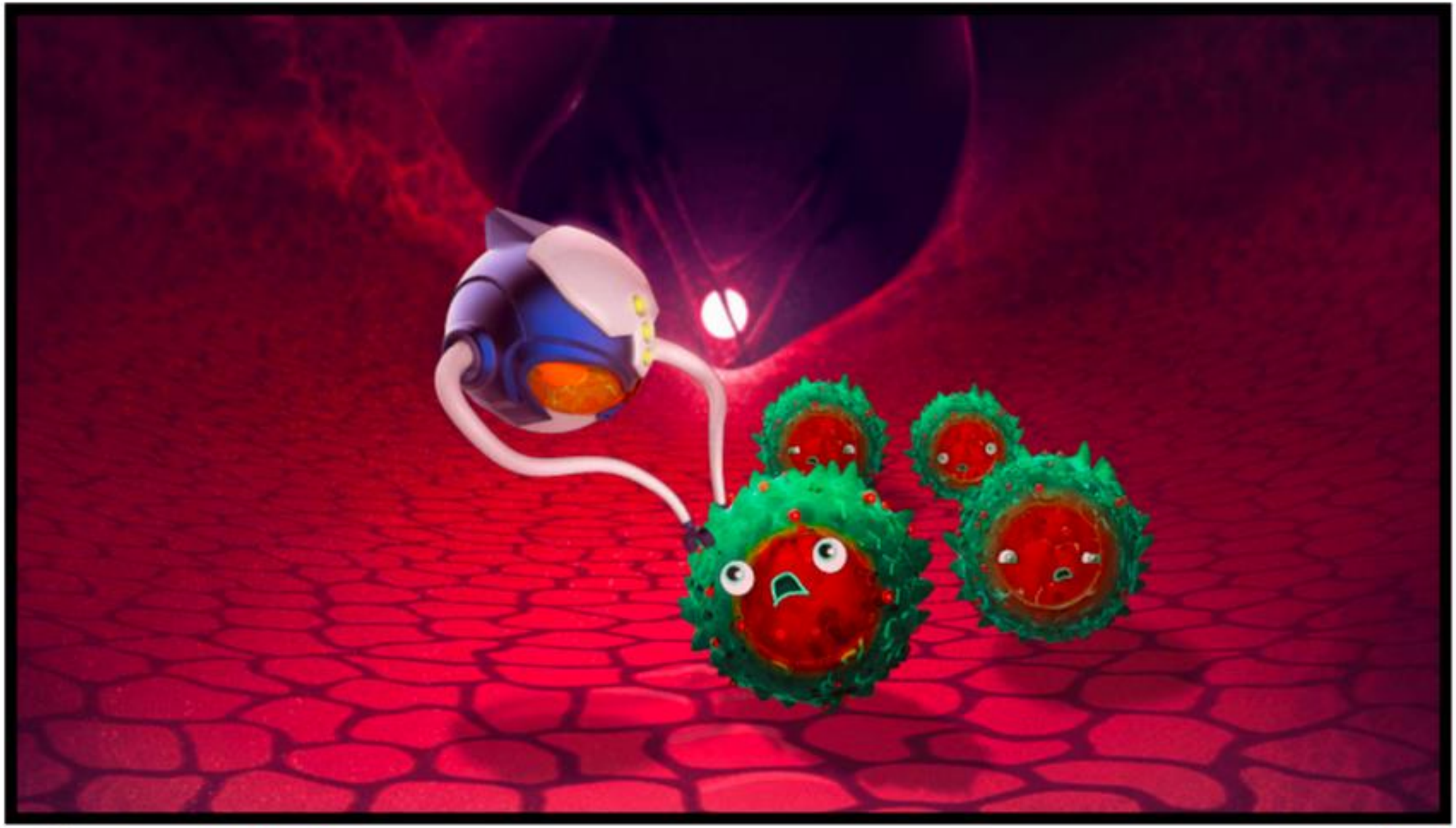
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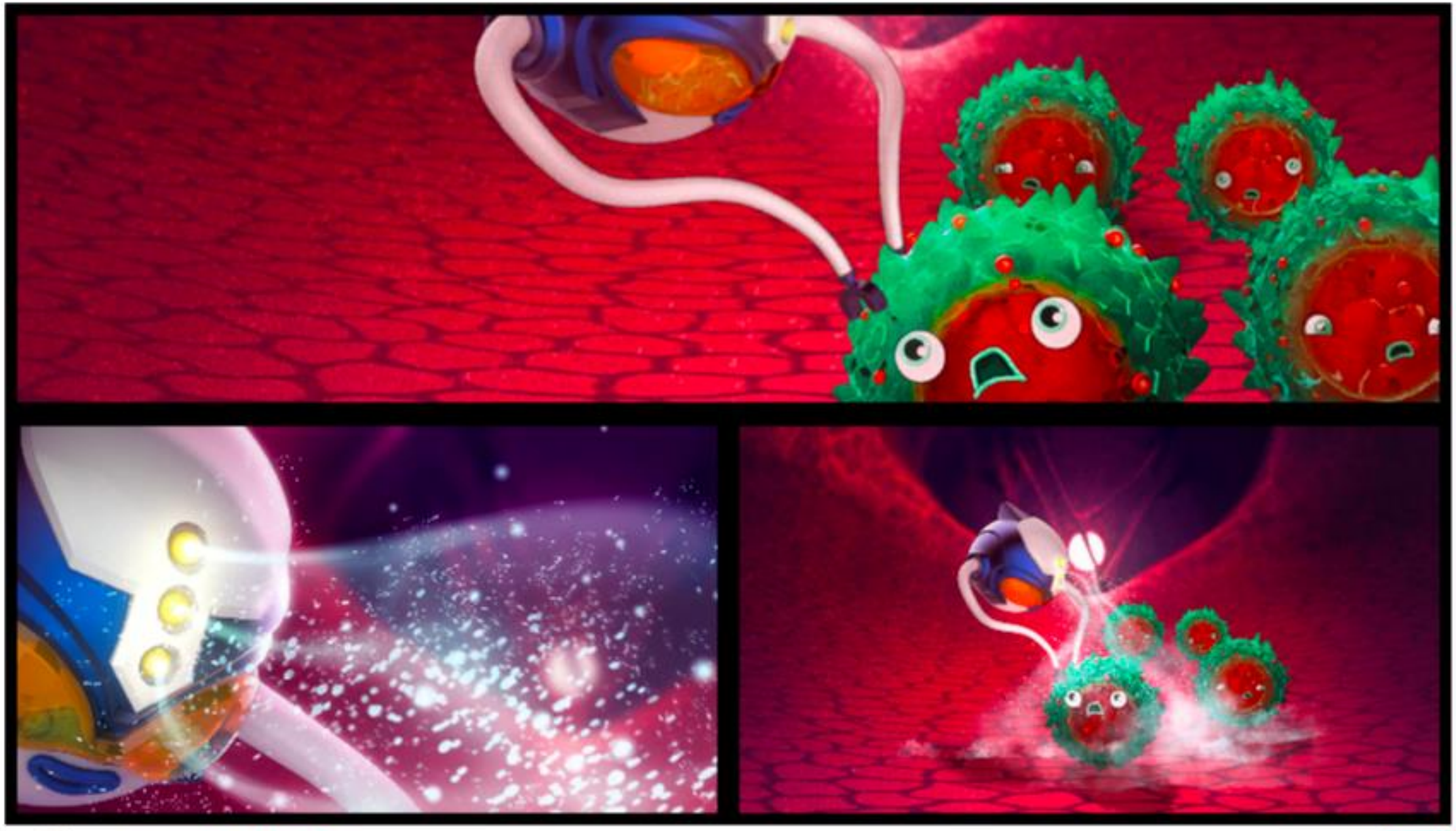
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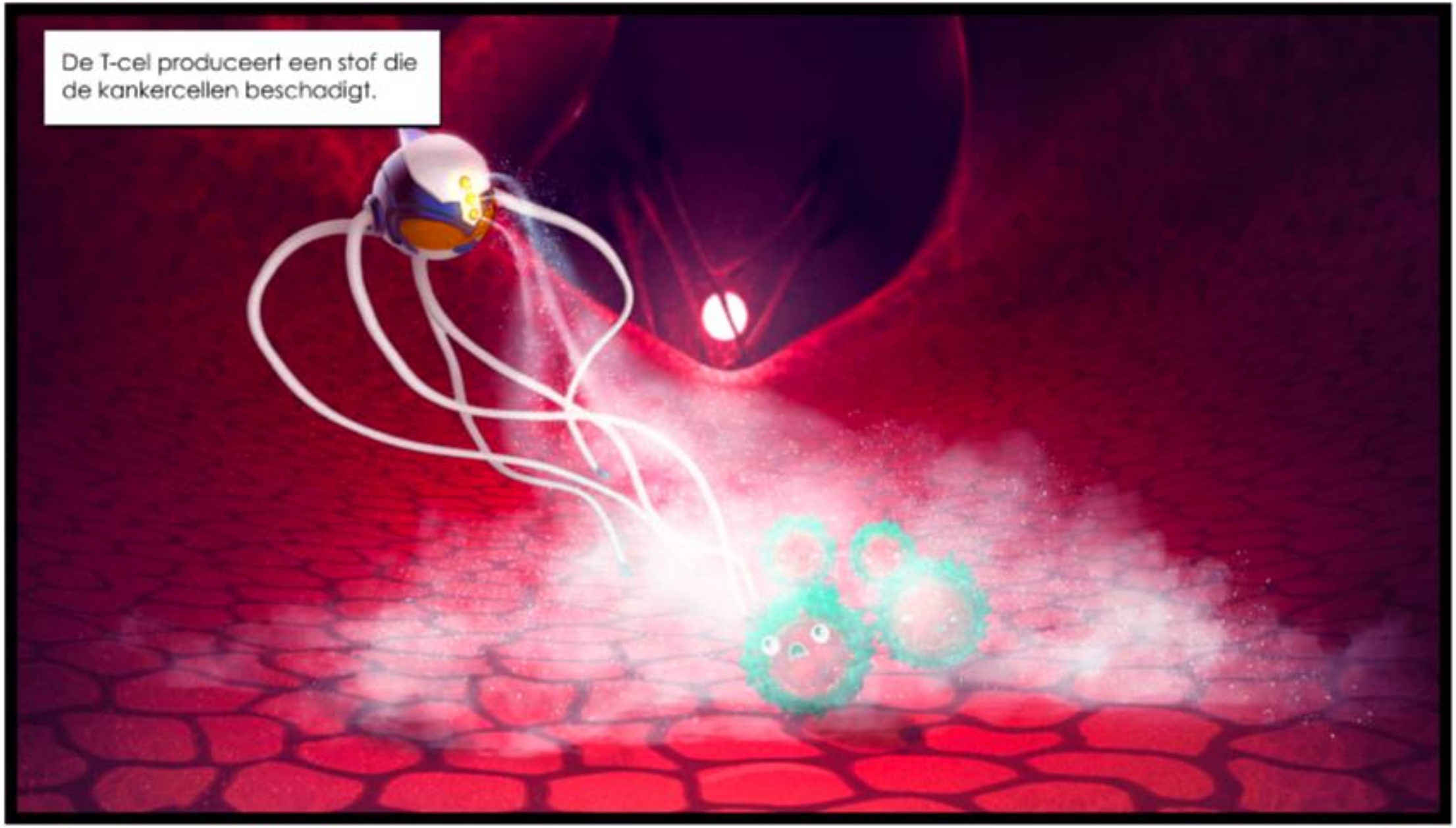
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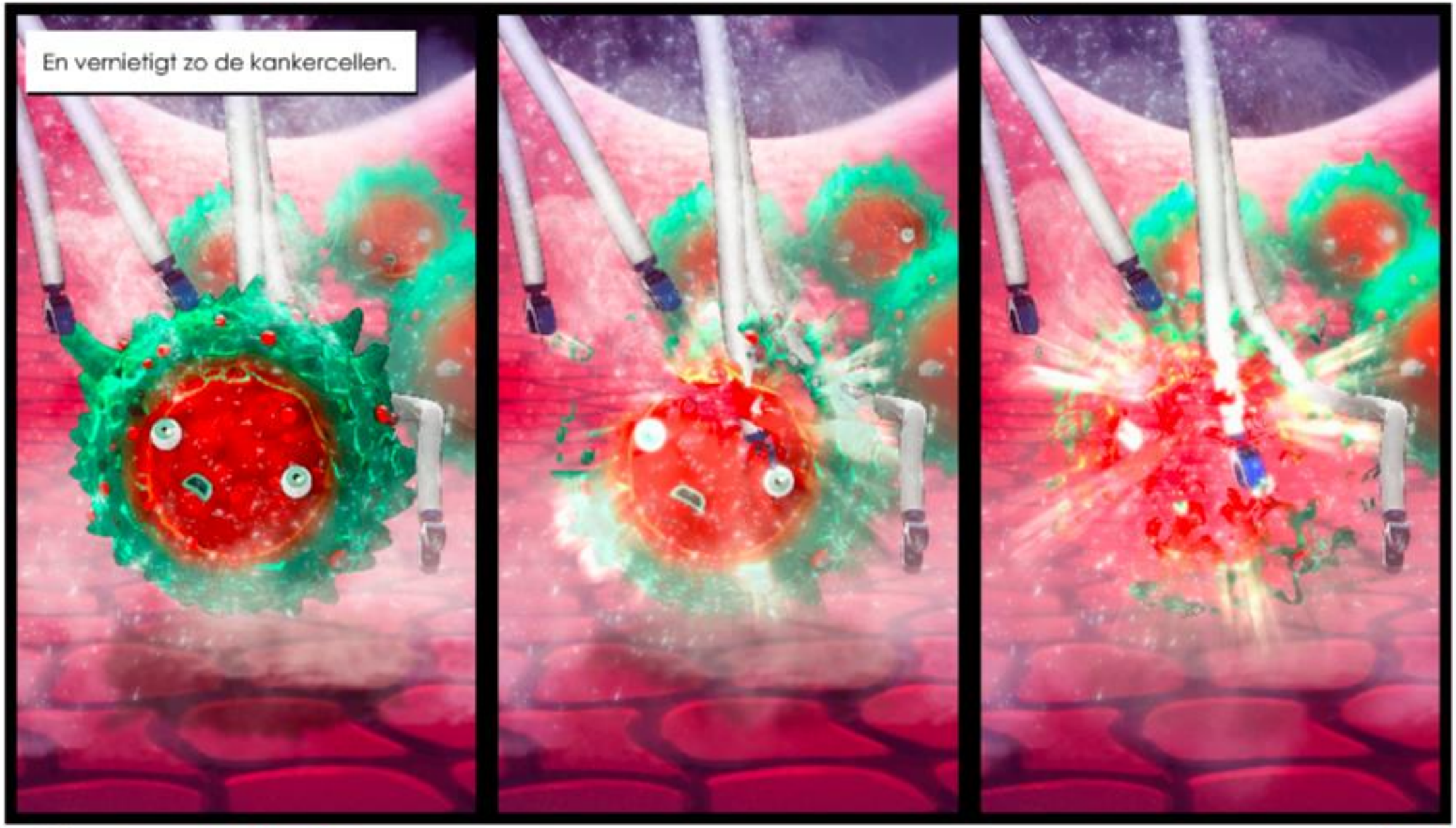
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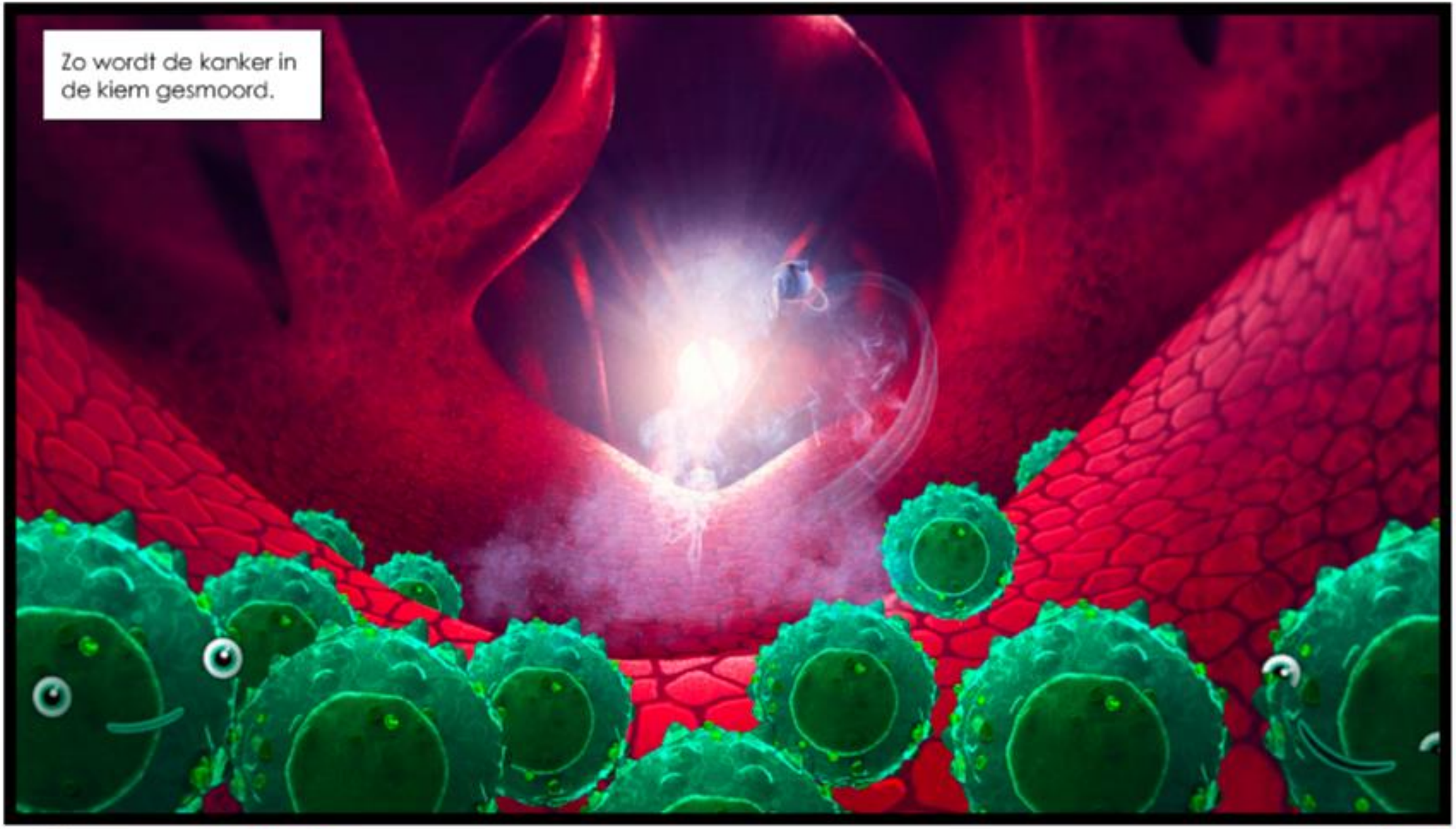
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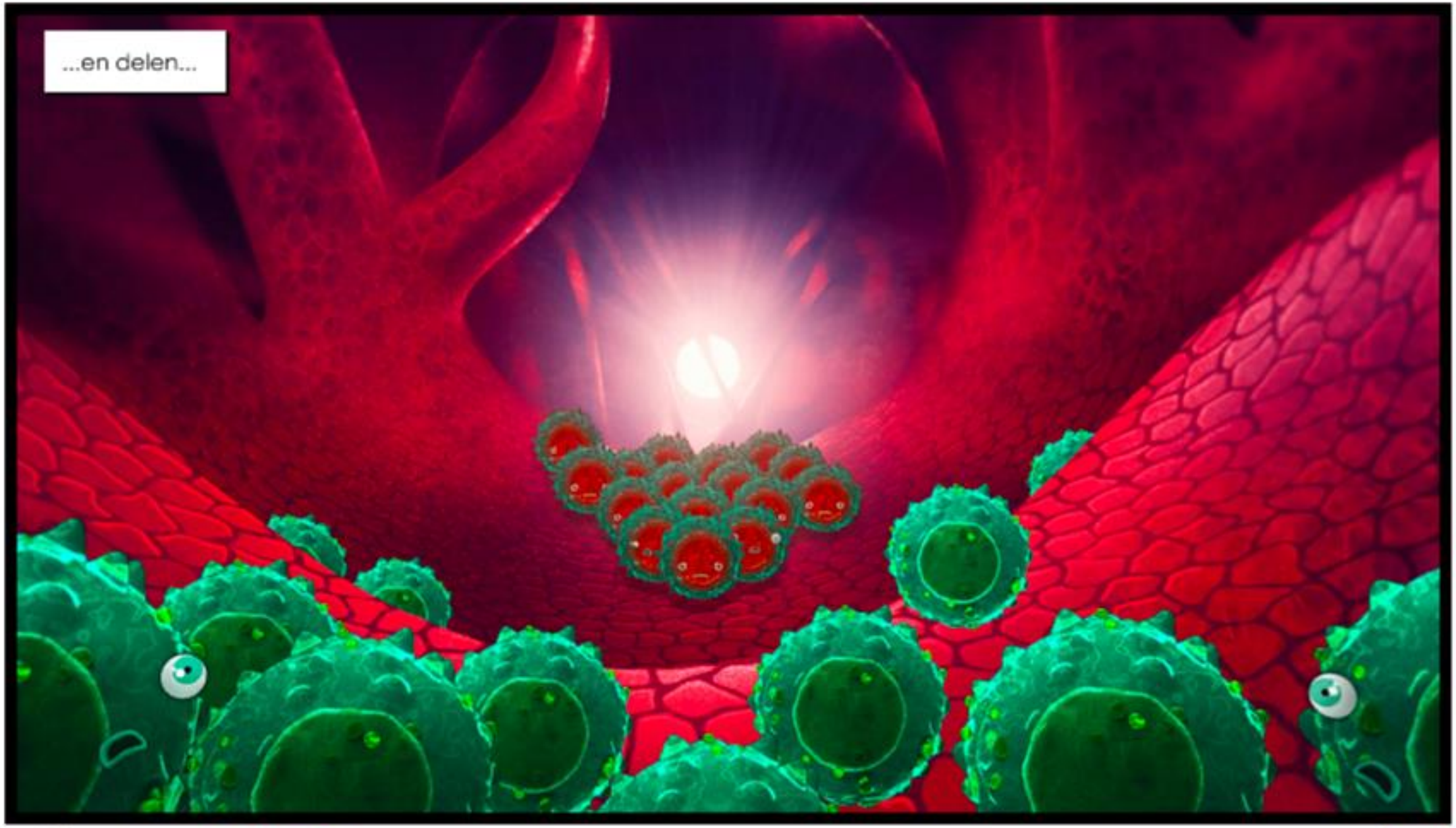
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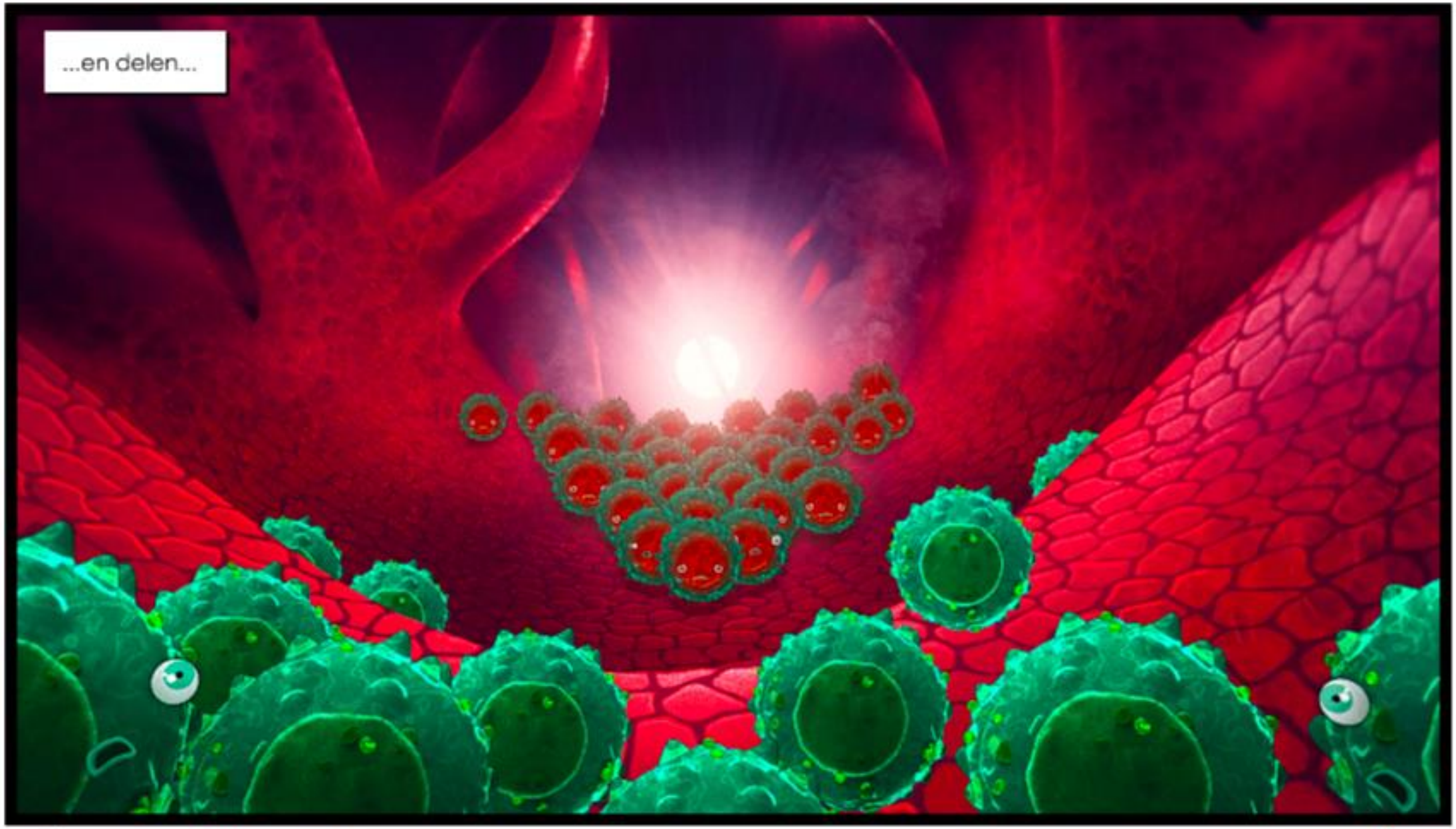
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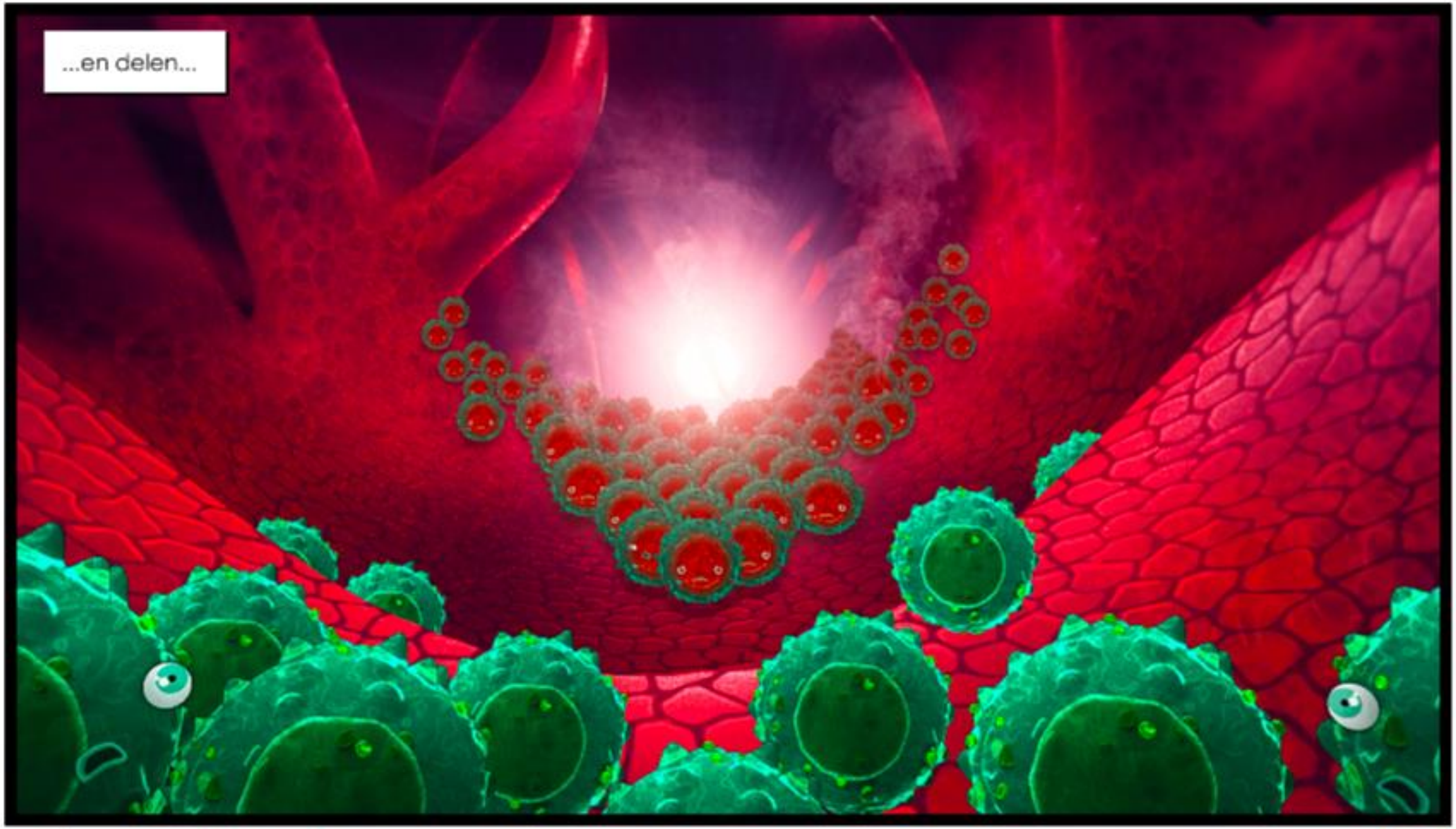
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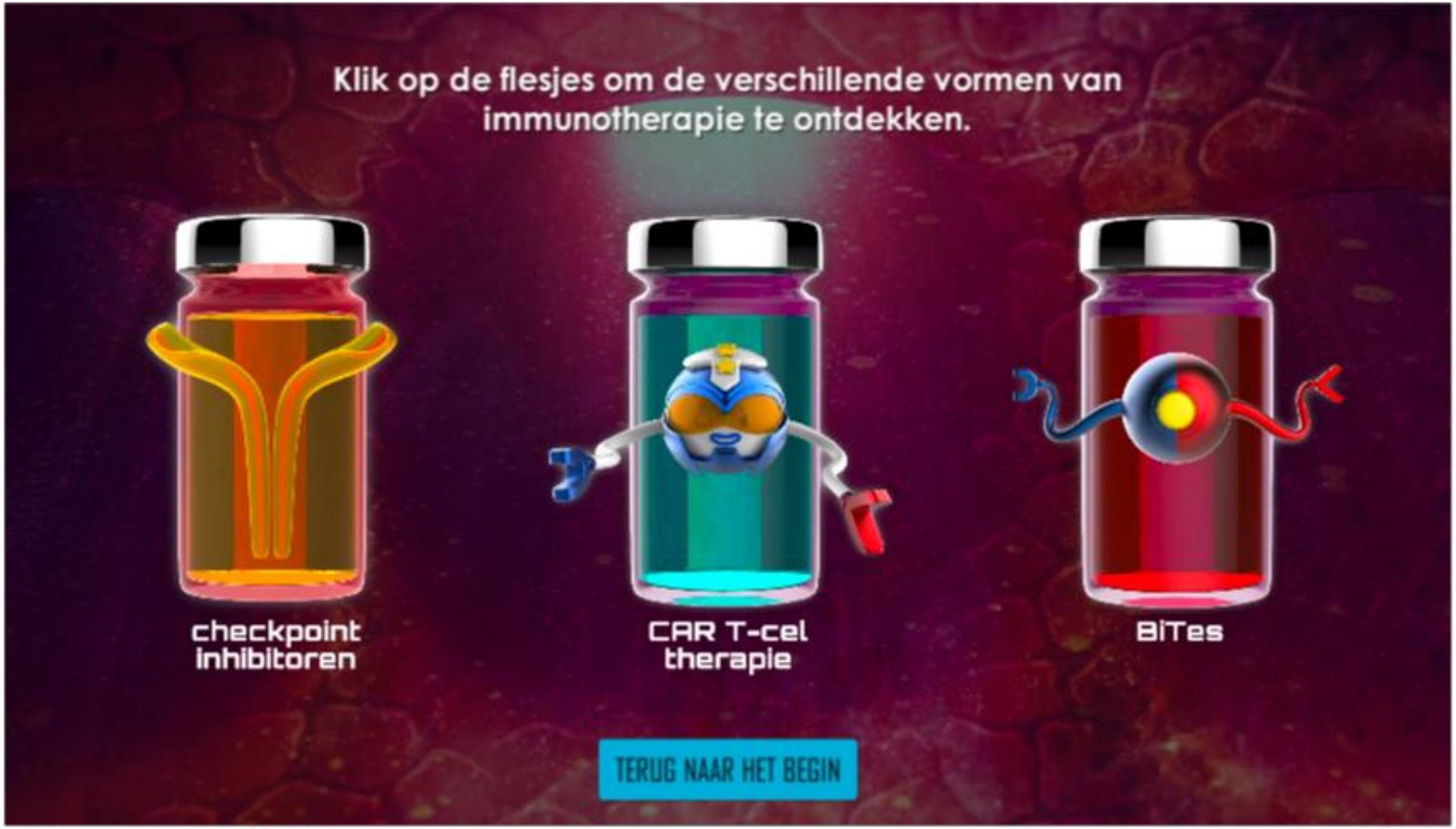


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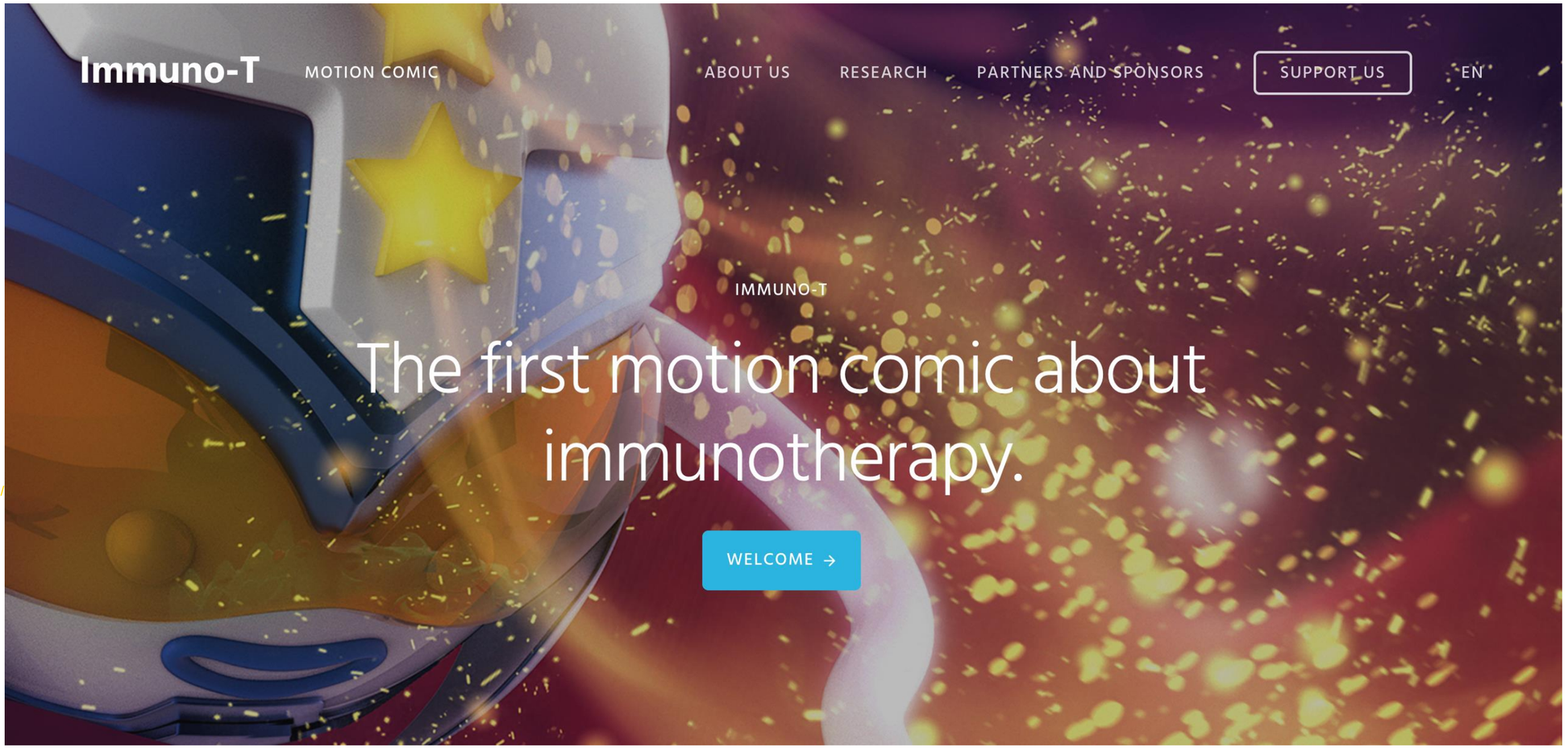
immuno_web

HET VERHAAL VAN IMMUNO-T



IMMUNOTHERAPIE

- Patiënt educatie: immuno-T.inmotion.care



OVERZICHT: IMMUNOTHERAPIE

- **Monoklonale antistoffen**
- **Vaccinatie**
  - Tumorextract
  - Peptide of mengsels van peptiden
  - Peptide gebonden op dendritische cellen
- **Oncolytische virussen**
- **Checkpoint inhibitoren**
- **Allogene stamceltransplantatie**
- **T cel therapie**
  - TCR/CAR transductie van circulerende T cellen
  - Antigen specifieke T cellen maken uit stamcellen

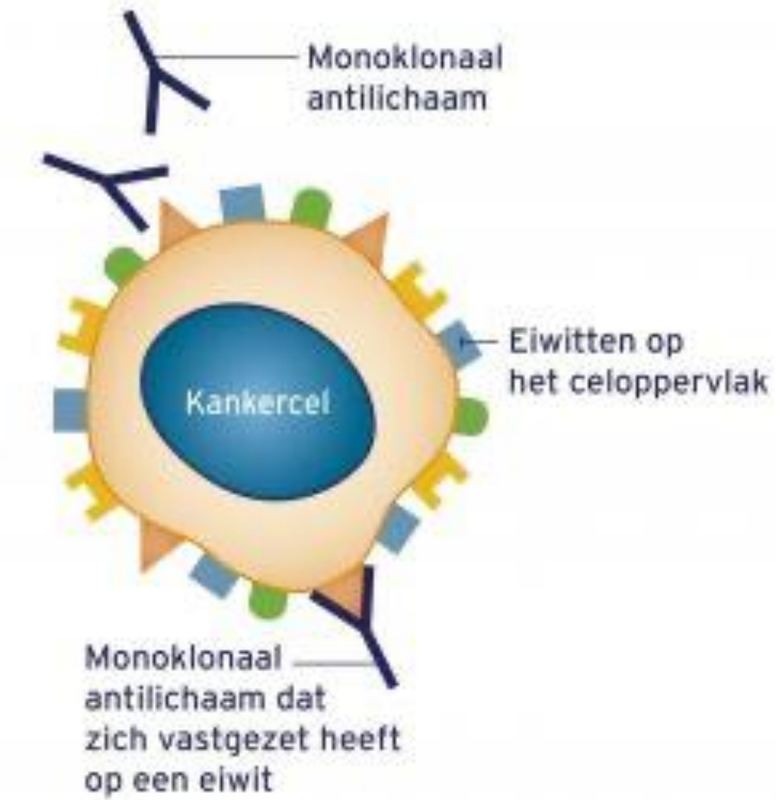
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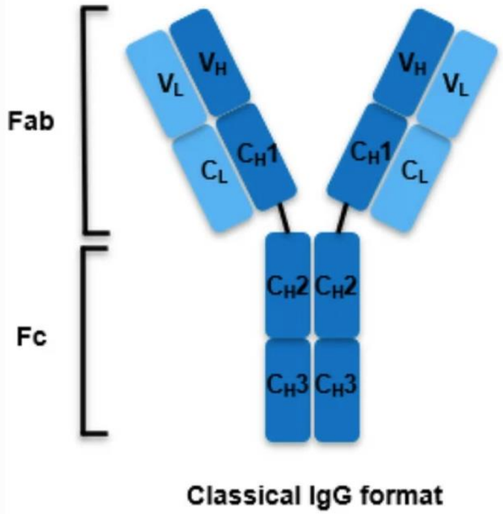
MONOKLONALE ANTISTOFFEN

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MONOKLONALE ANTISTOFFEN

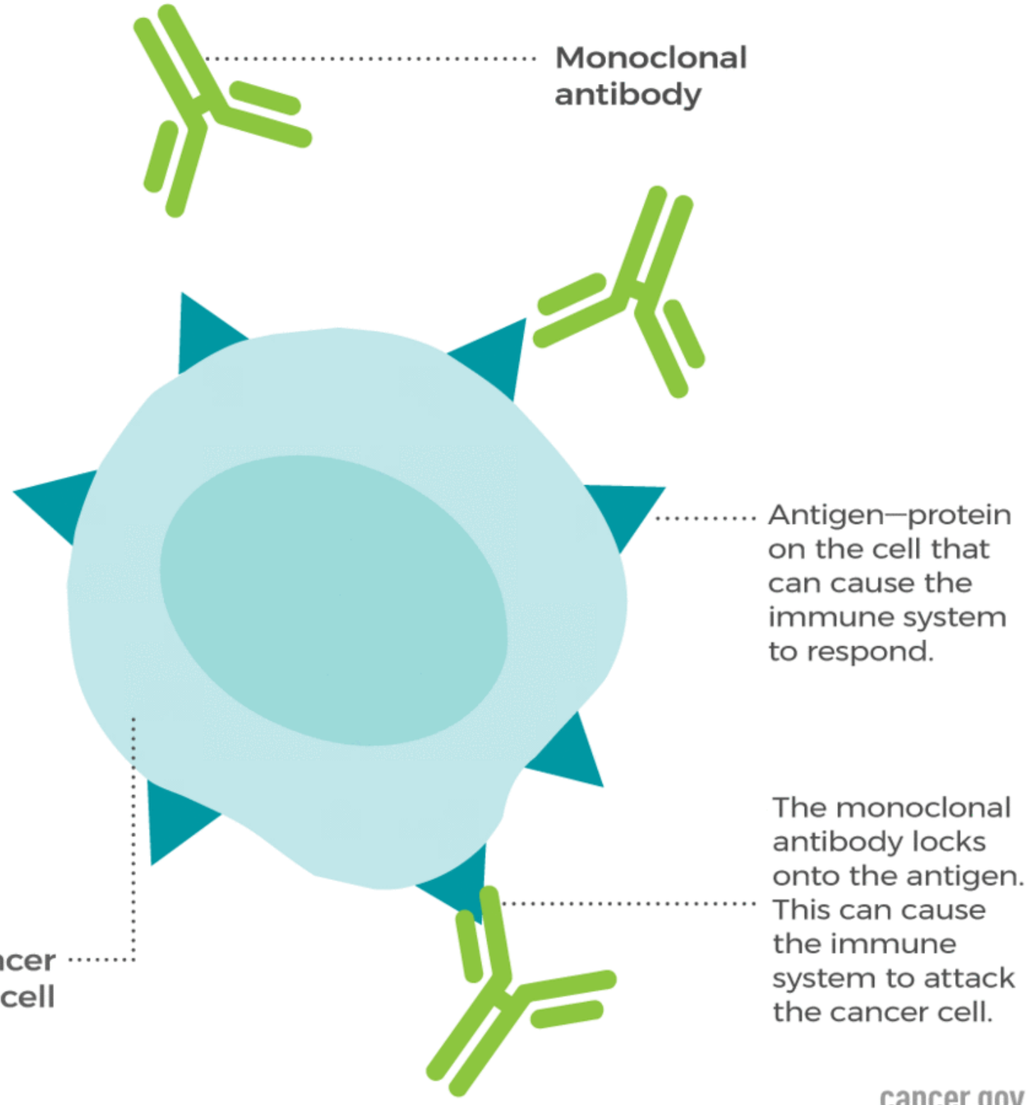
– Principe





Classical IgG format

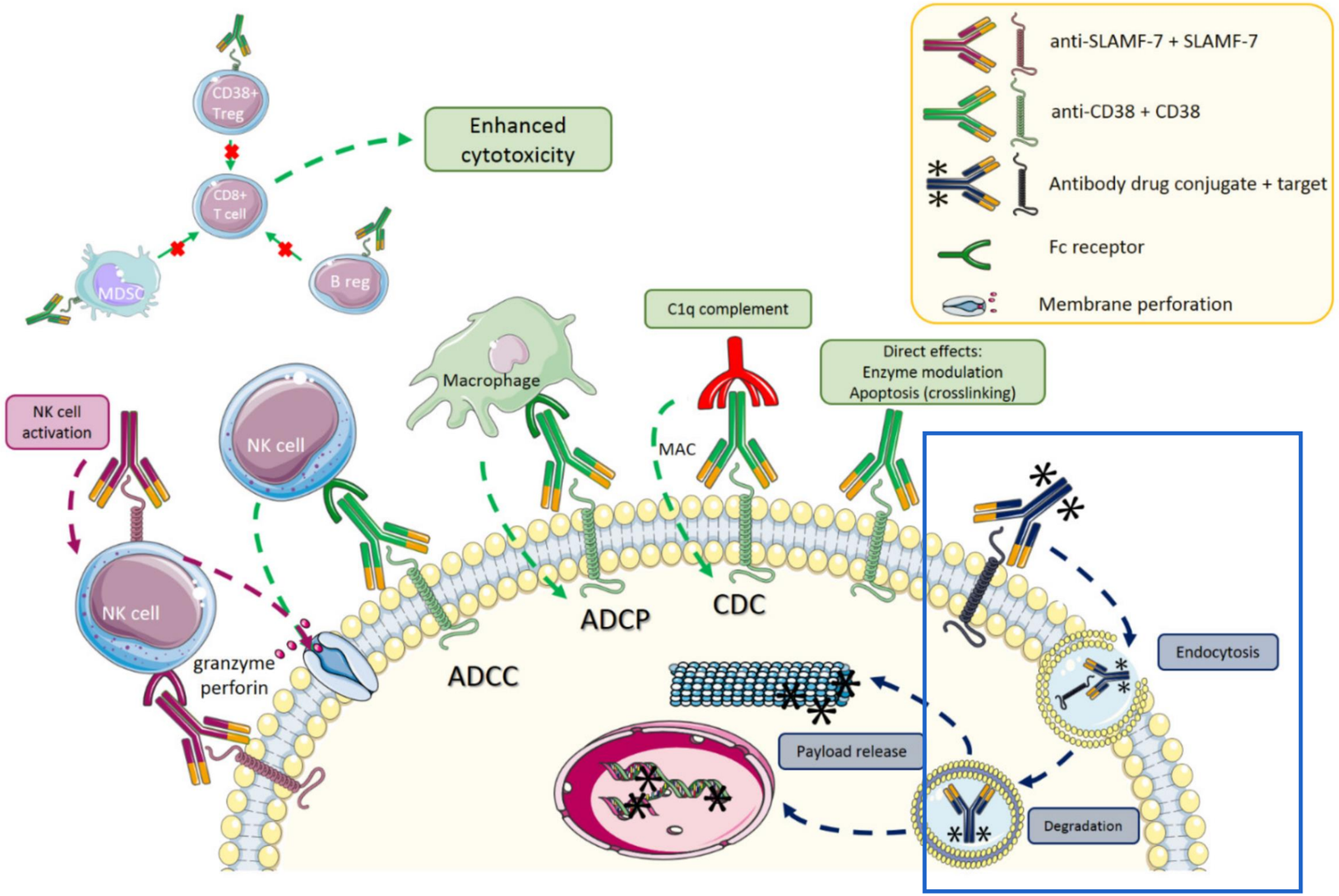
S Huang et al, J Cancer Res and Clin Oncol, 2020



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MONOKLONALE ANTISTOFFEN

– Werking

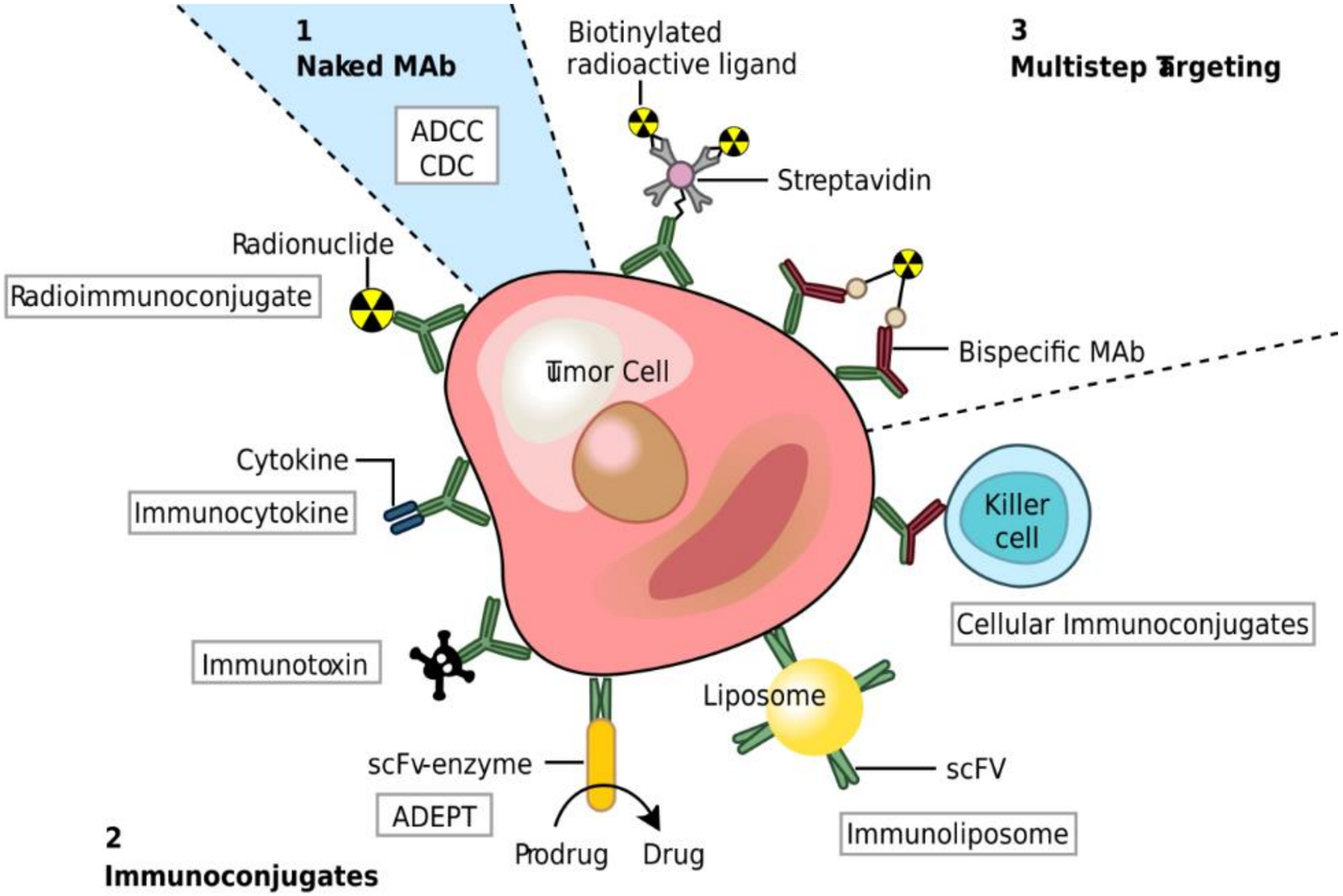


UNIVERSITEIT GENT

J Radocha, Cancers, 2021

MONOKLONALE ANTISTOFFEN

– Naakt of gekoppeld

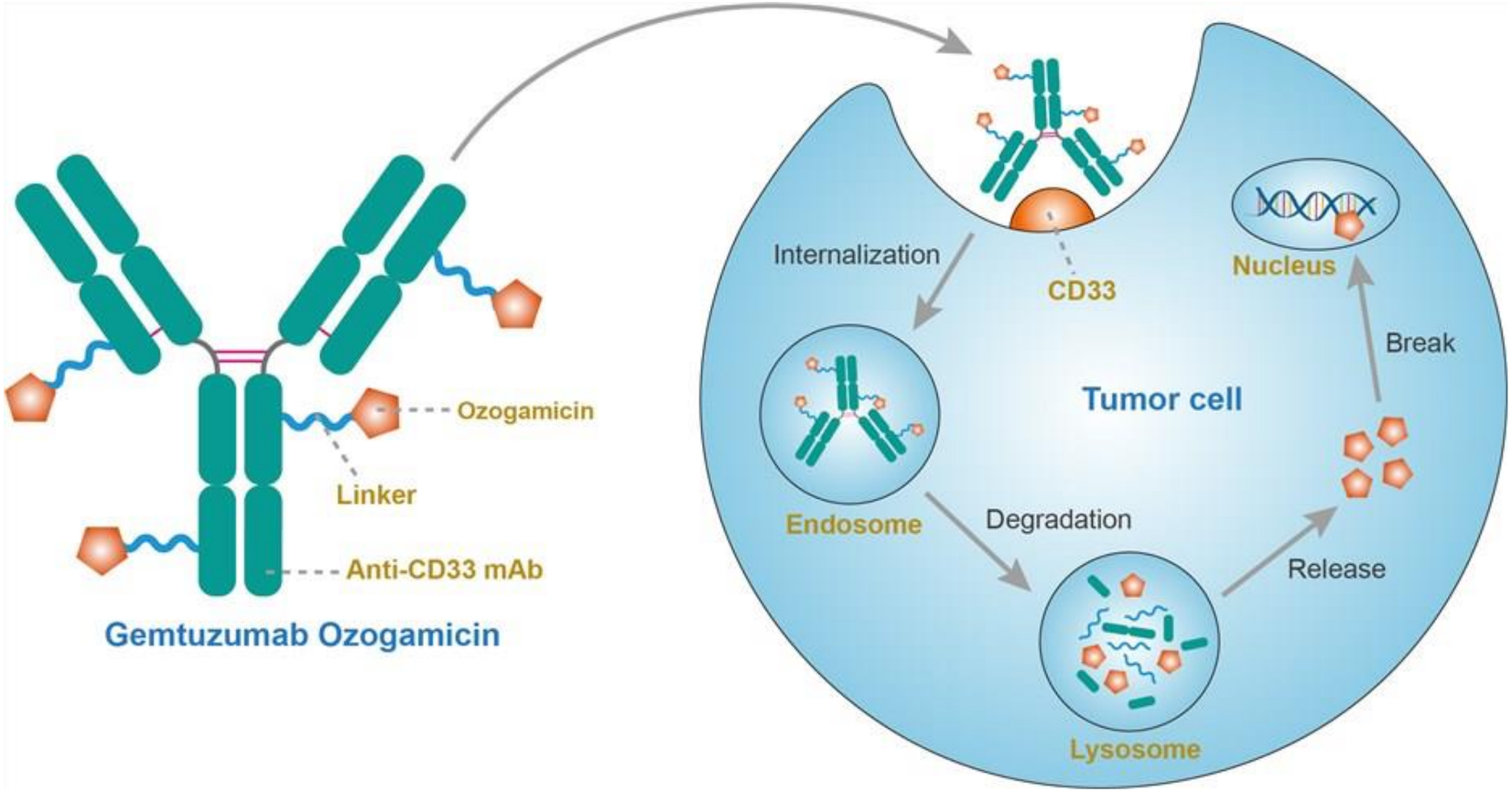


UNIVERSITEIT GENT

Carter P, Nature Reviews in cancer

MONOKLONALE ANTISTOFFEN: GEKOPPELD

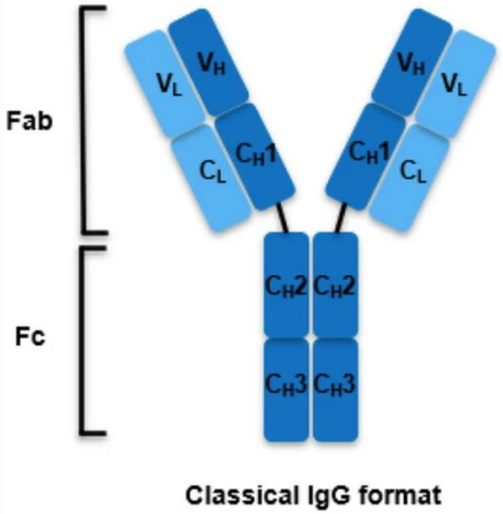
- mAb - drug conjugate, eg Mylotarg (gemtuzumab (anti-CD33 mAB) – ozogamcyn



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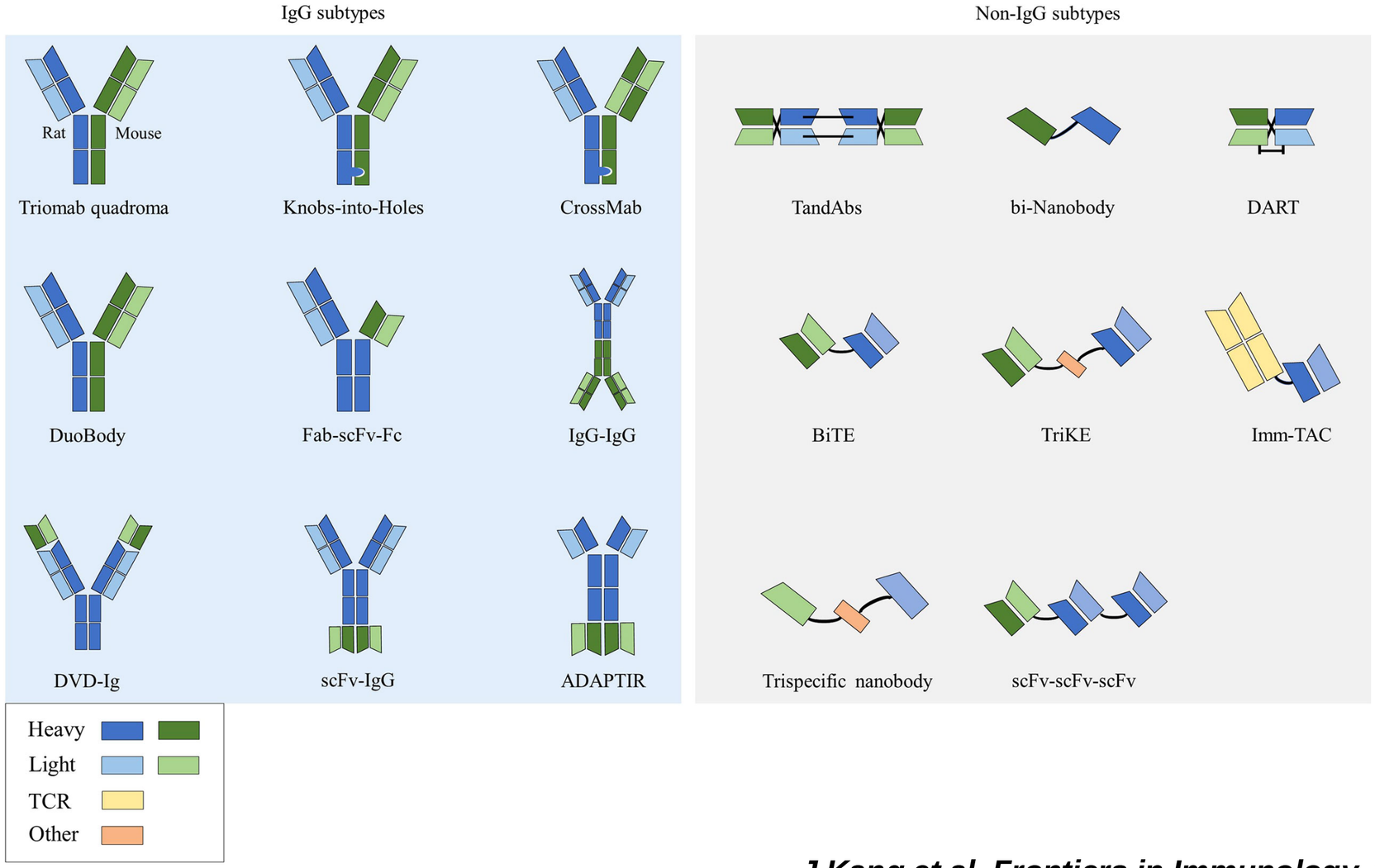
MULTISPECIFIEKE ANTISTOFFEN

Structuur



Classical IgG format

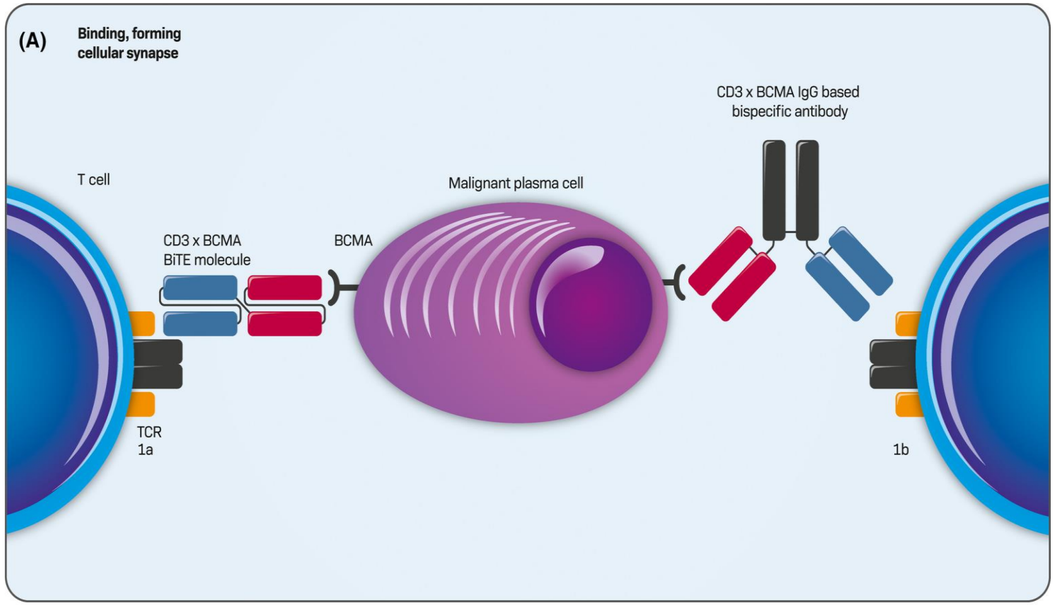
S Huang et al, J Cancer Res and Clin Oncol, 2020

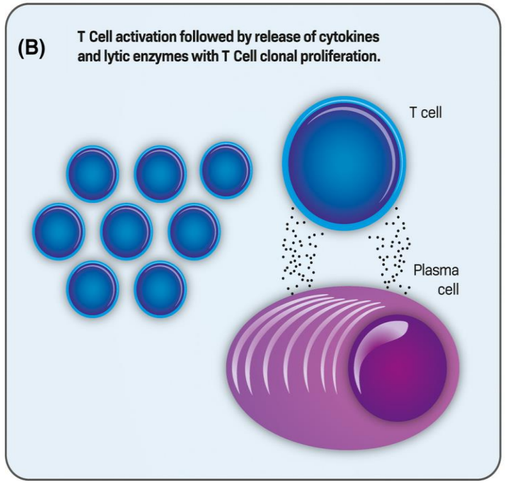


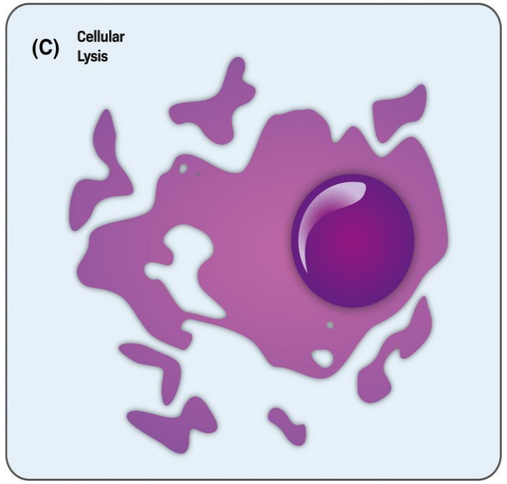
J Kang et al, Frontiers in Immunology, 2022

BISPECIFIEKE ANTISTOFFEN EN BITES

– Bispecific T-cell engager (BiTes) vs Bispecific antibody







UNIVERSITEIT GENT

E Demel et al, BJH, 2021

Klik op de flesjes om de verschillende vormen van immunotherapie te ontdekken.



checkpoint inhibitoren



CAR T-cel therapie

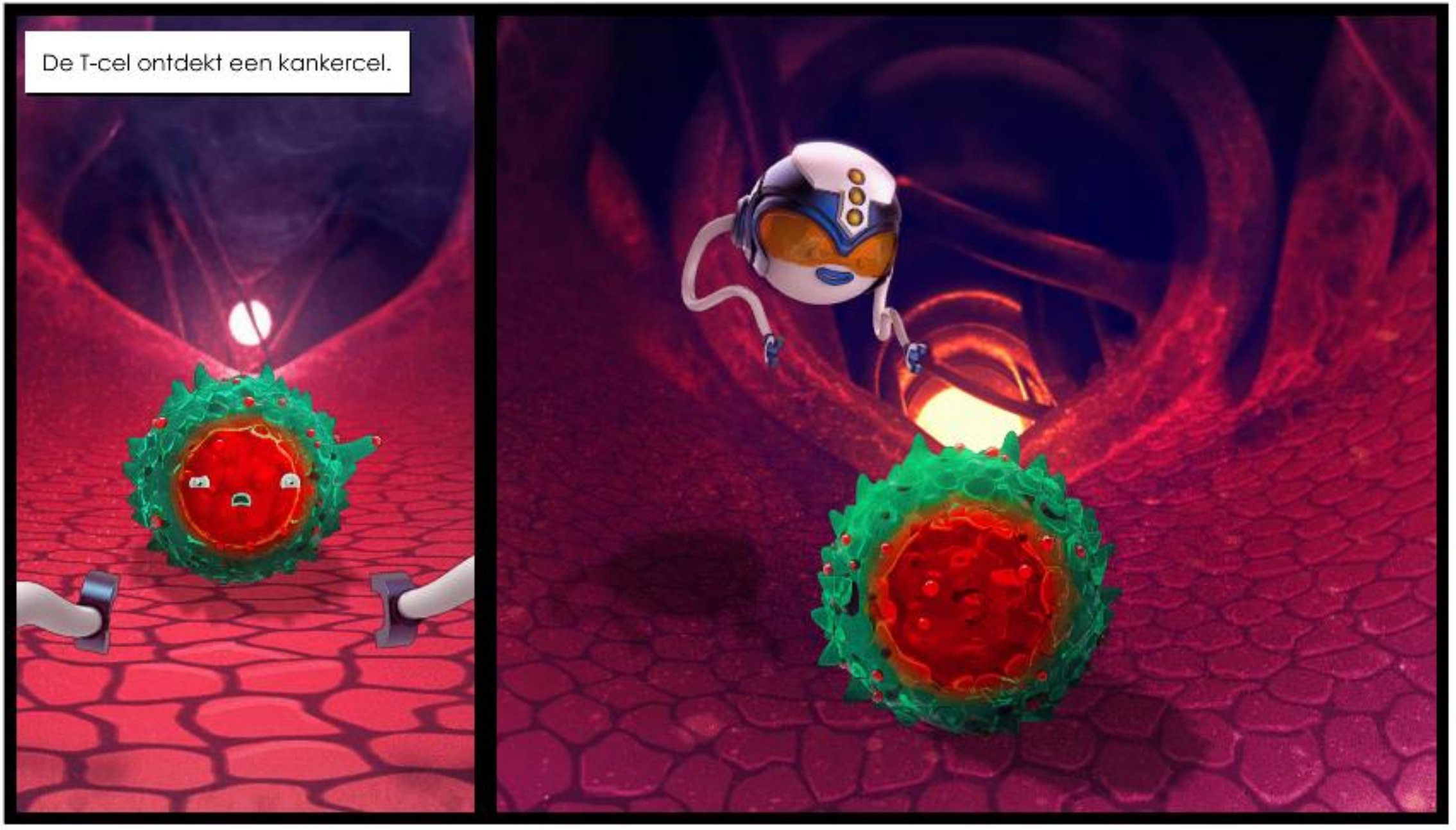


BiTes

TERUG NAAR HET BEGIN

unity WebGL

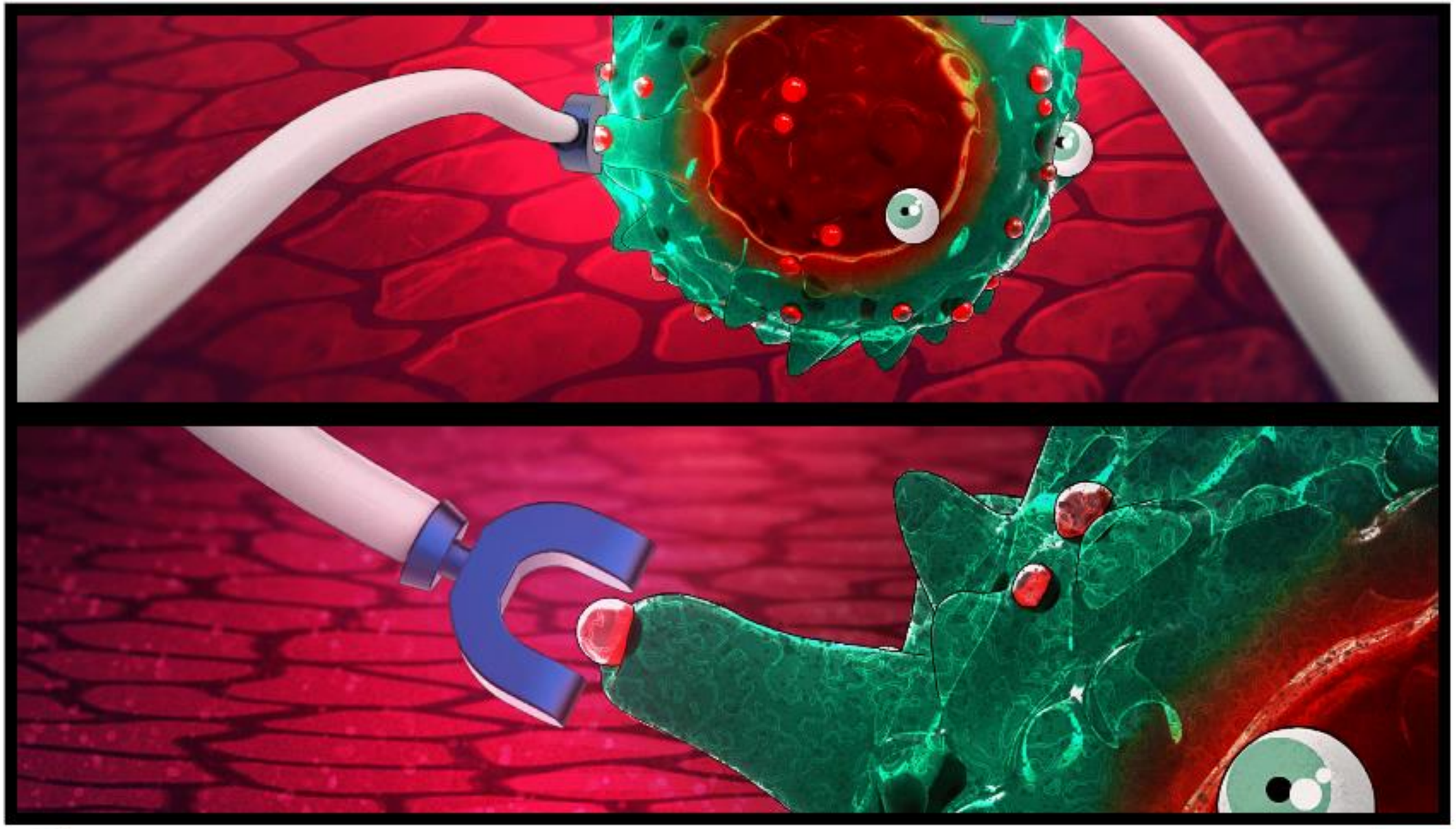
immuno_web



unity WebGL

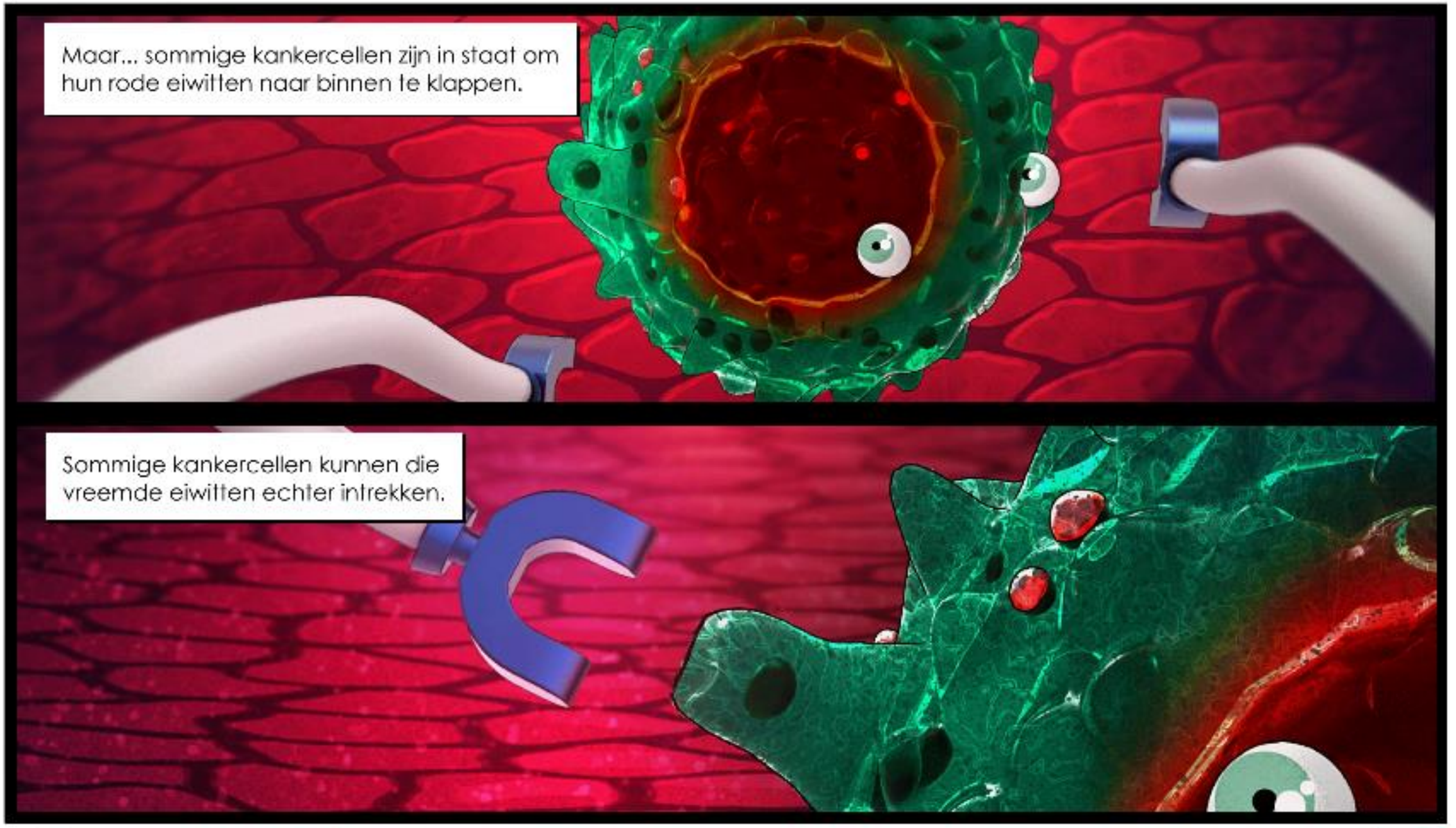
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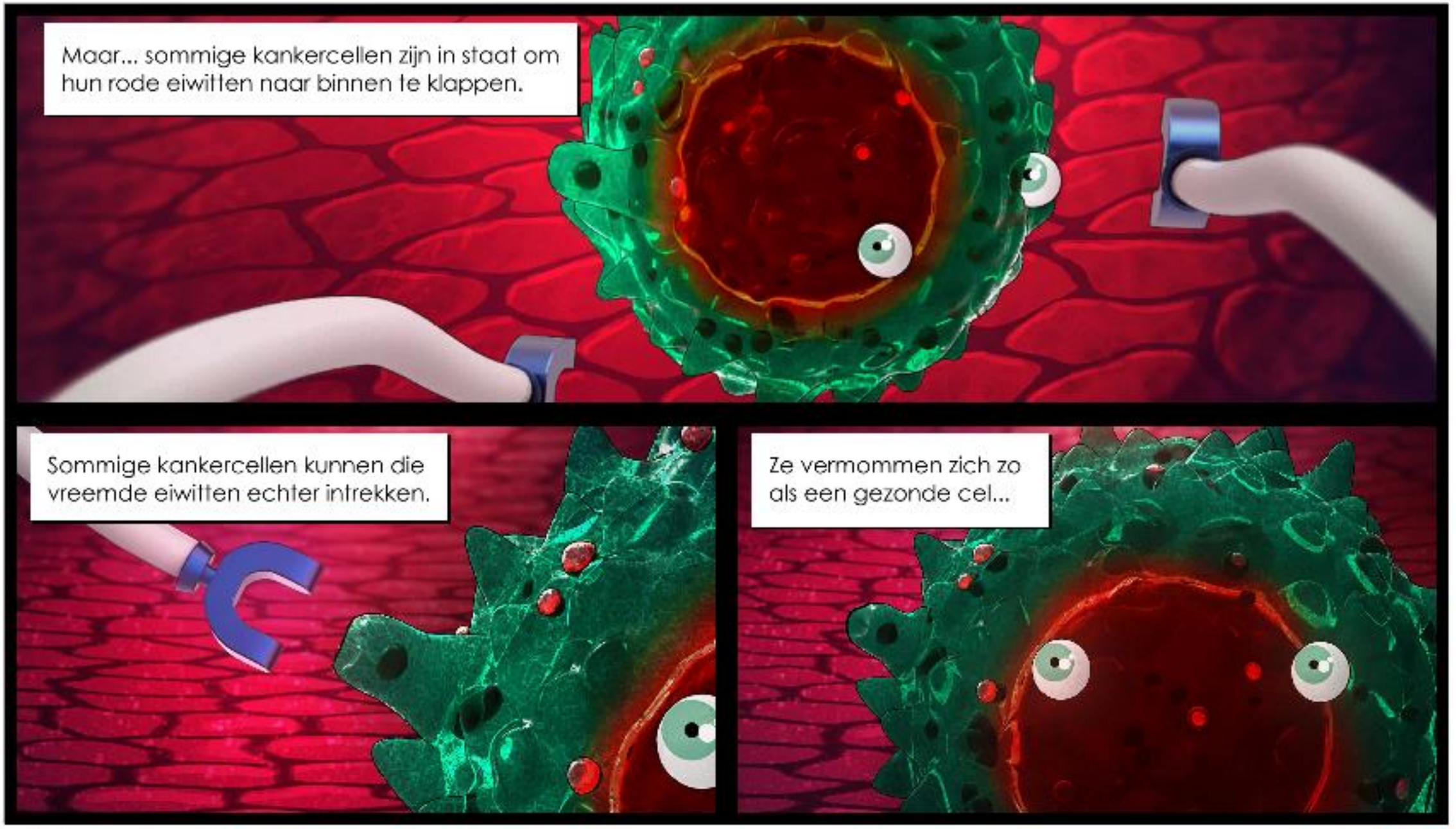

Ze herkent de kankercel aan de vreemde eiwitten die erop voorkomen.

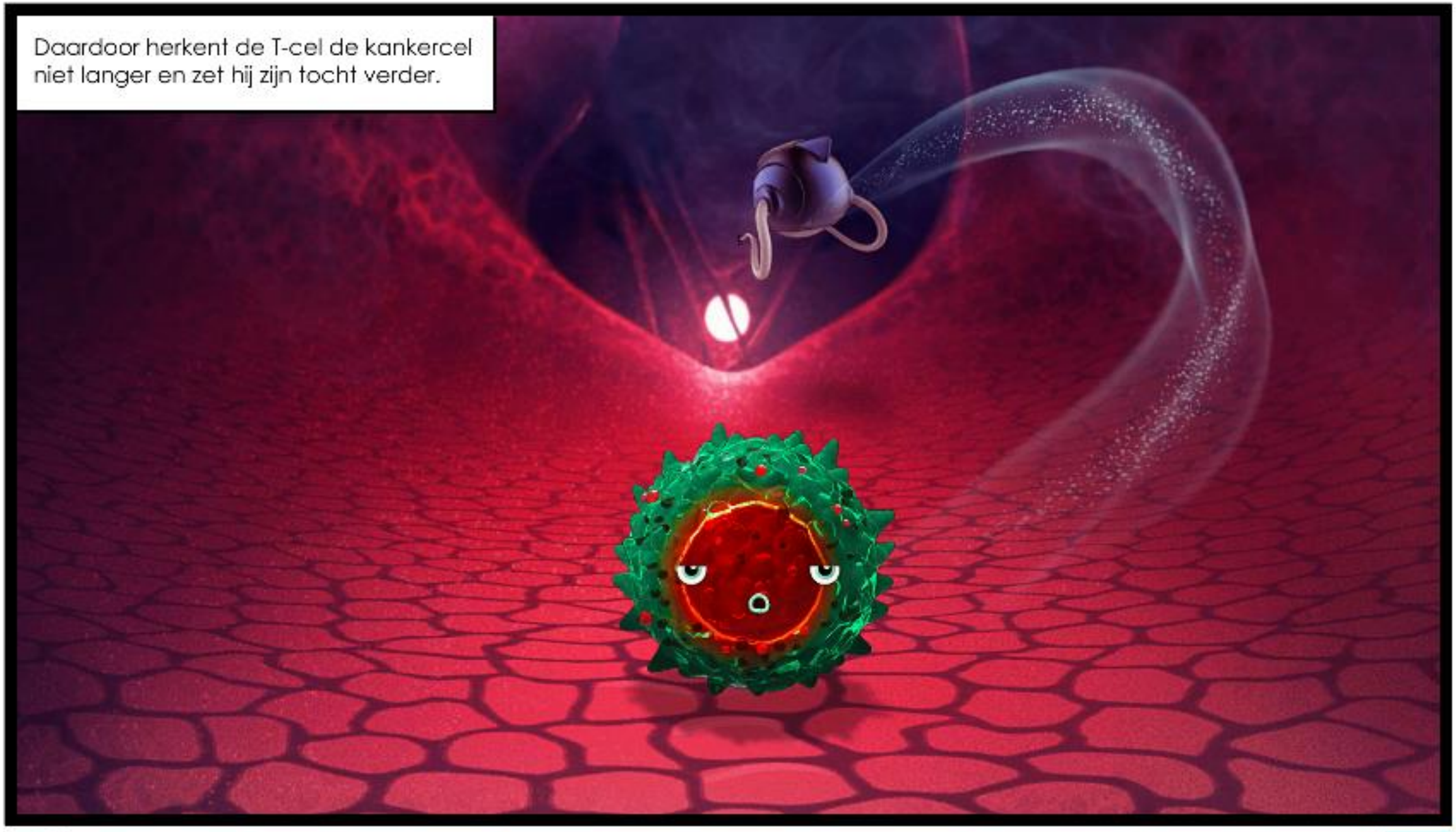


unity WebGL

immuno_web

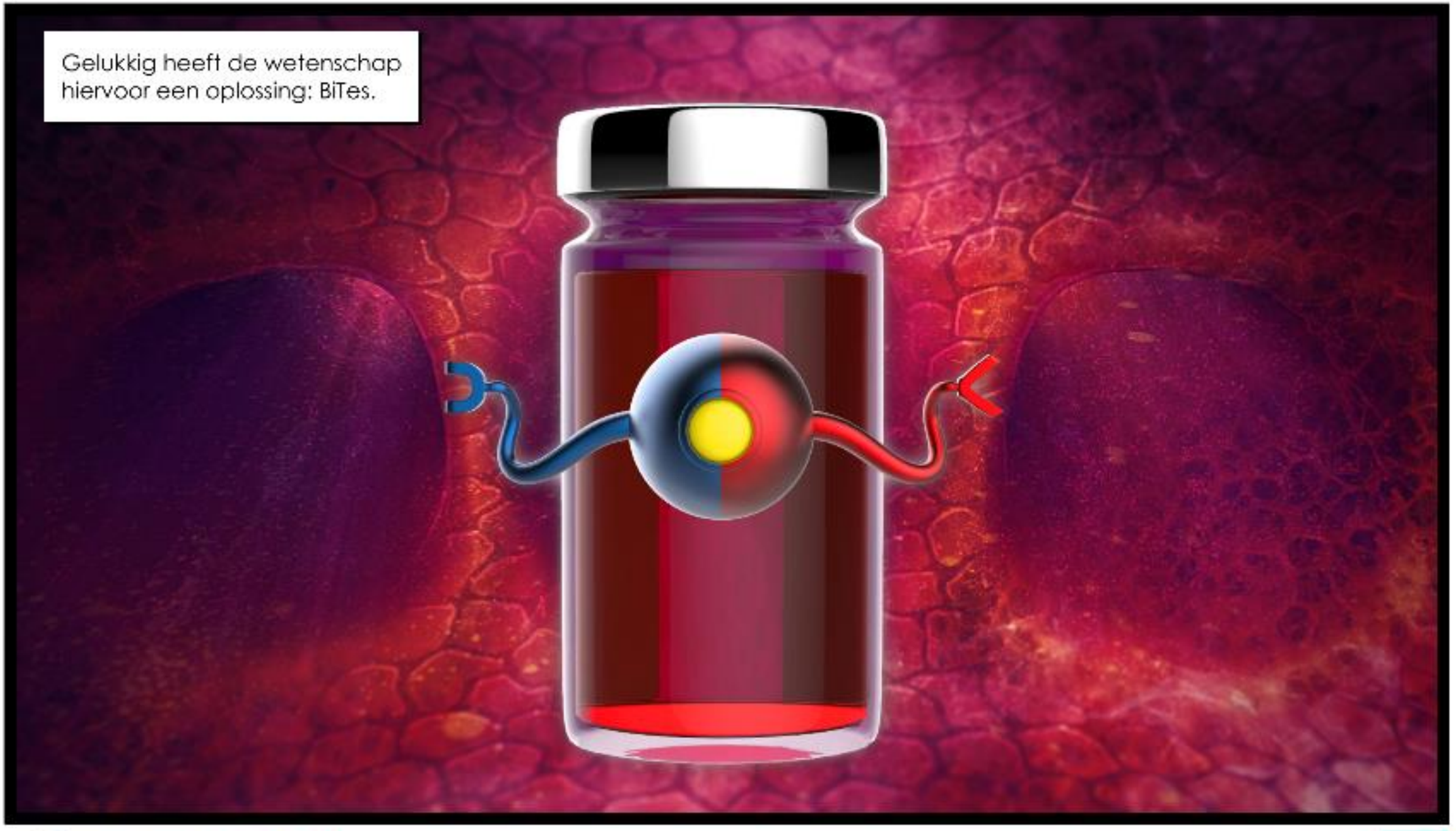

Maar... sommige kankercellen zijn in staat om hun rode eiwitten naar binnen te klappen.
Sommige kankercellen kunnen die vreemde eiwitten echter intrekken.


Maar... sommige kankercellen zijn in staat om hun rode eiwitten naar binnen te klappen.
Sommige kankercellen kunnen die vreemde eiwitten echter intrekken.
Ze vermommen zich zo als een gezonde cel...



unity WebGL

immuno_web



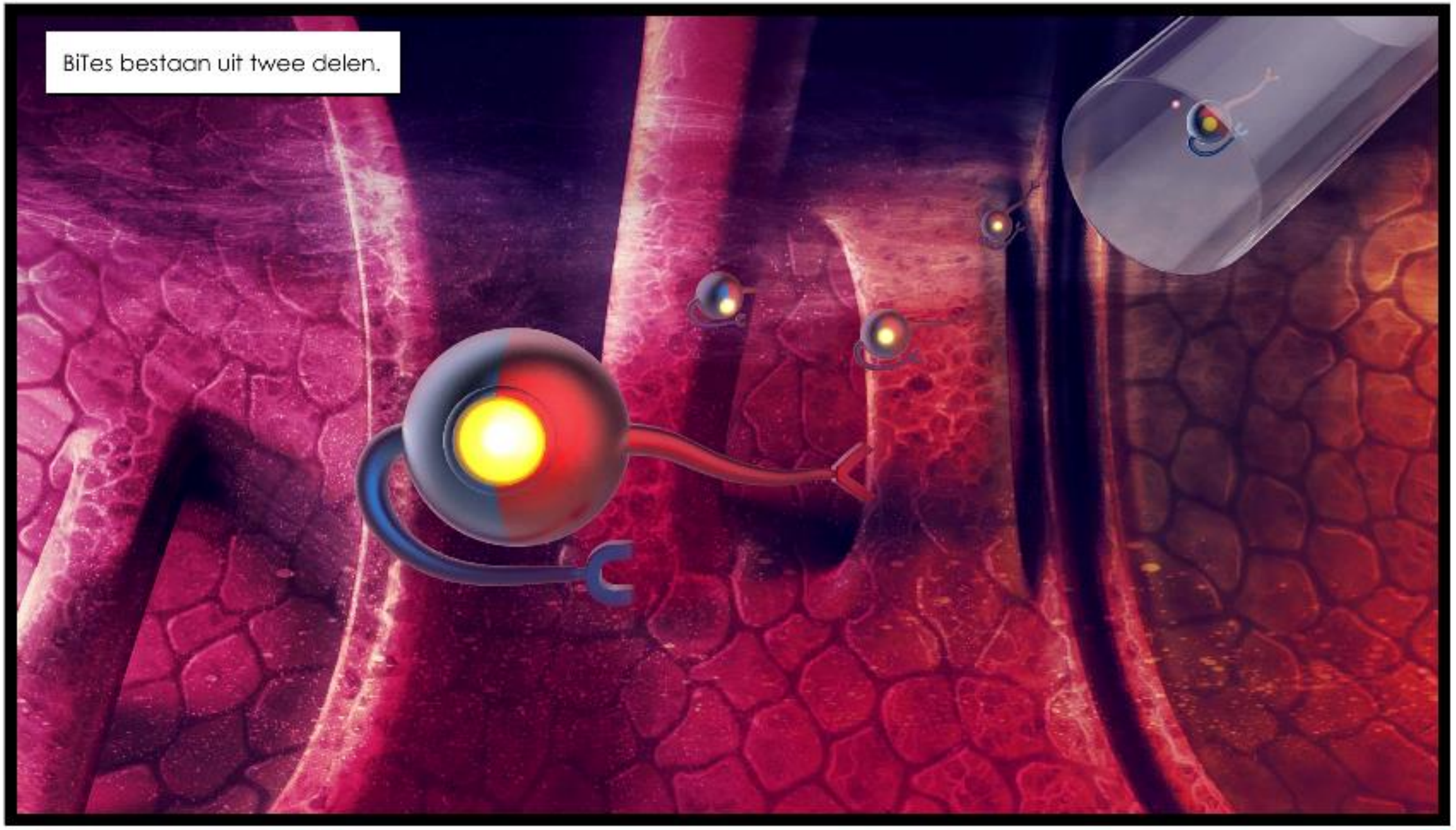
unity WebGL

immuno_web



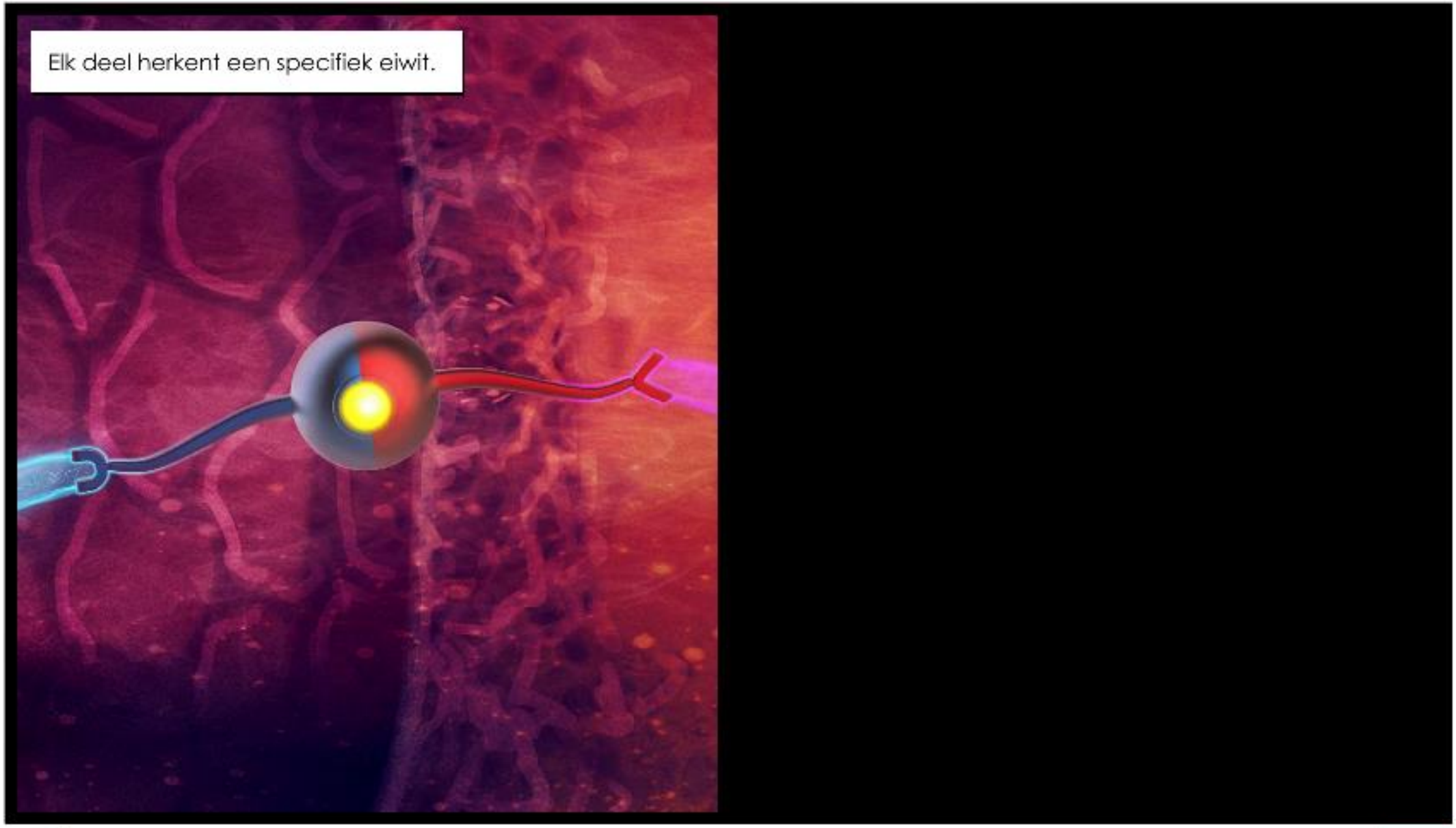
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immuno_web



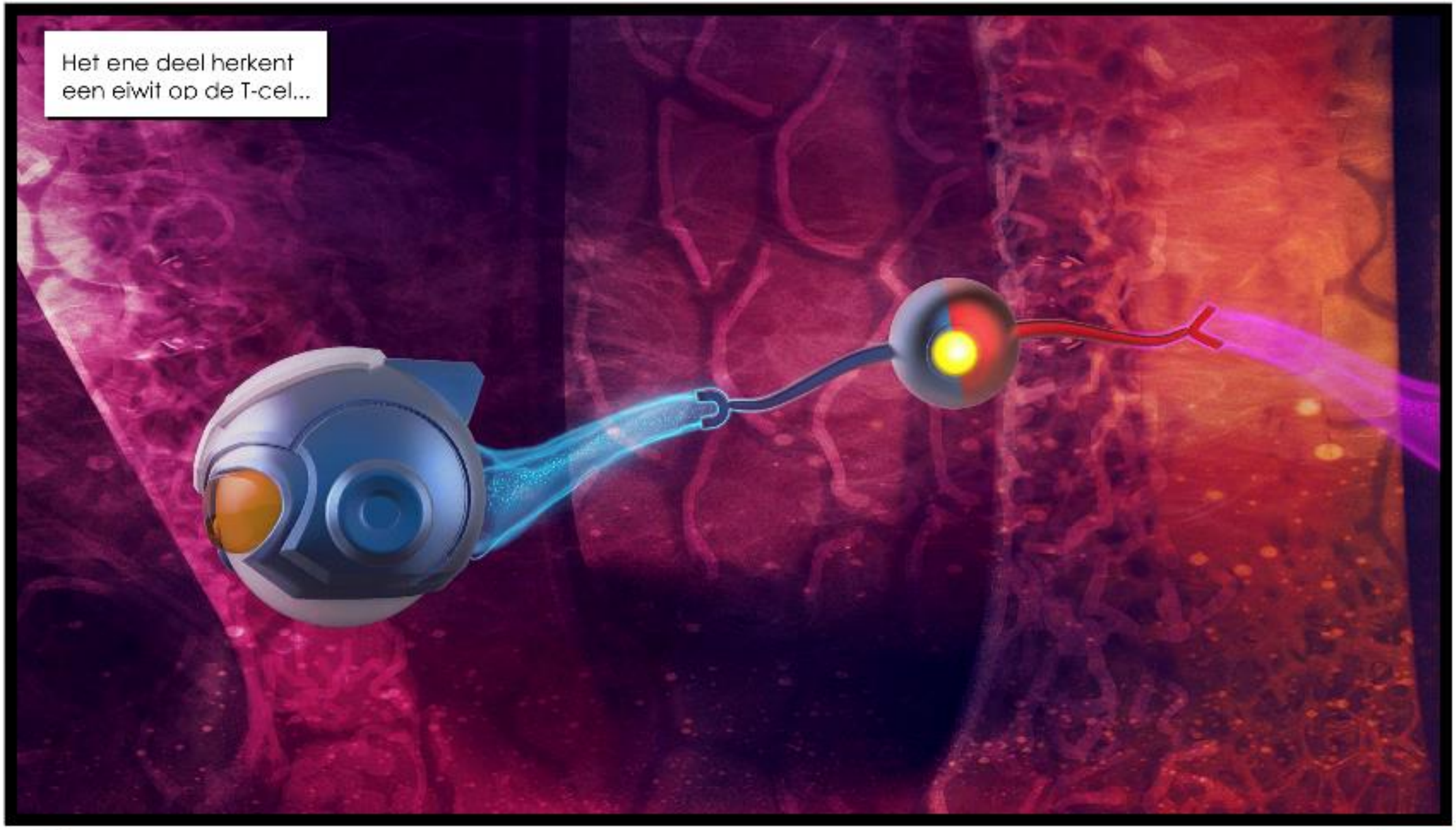
unity WebGL

immuno_web



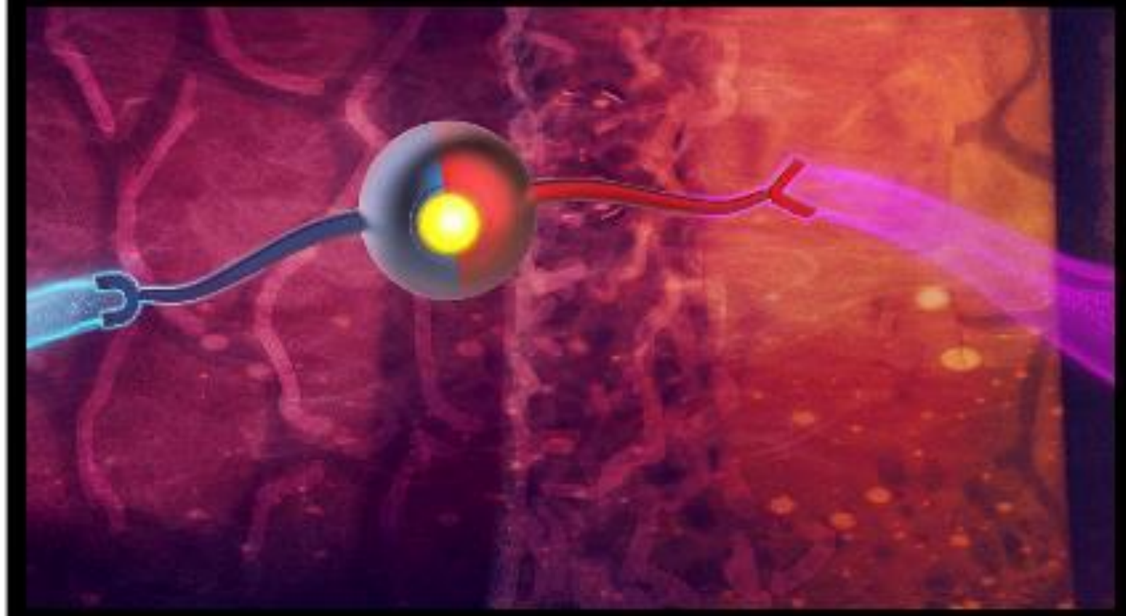
unity WebGL

immuno_web



unity WebGL

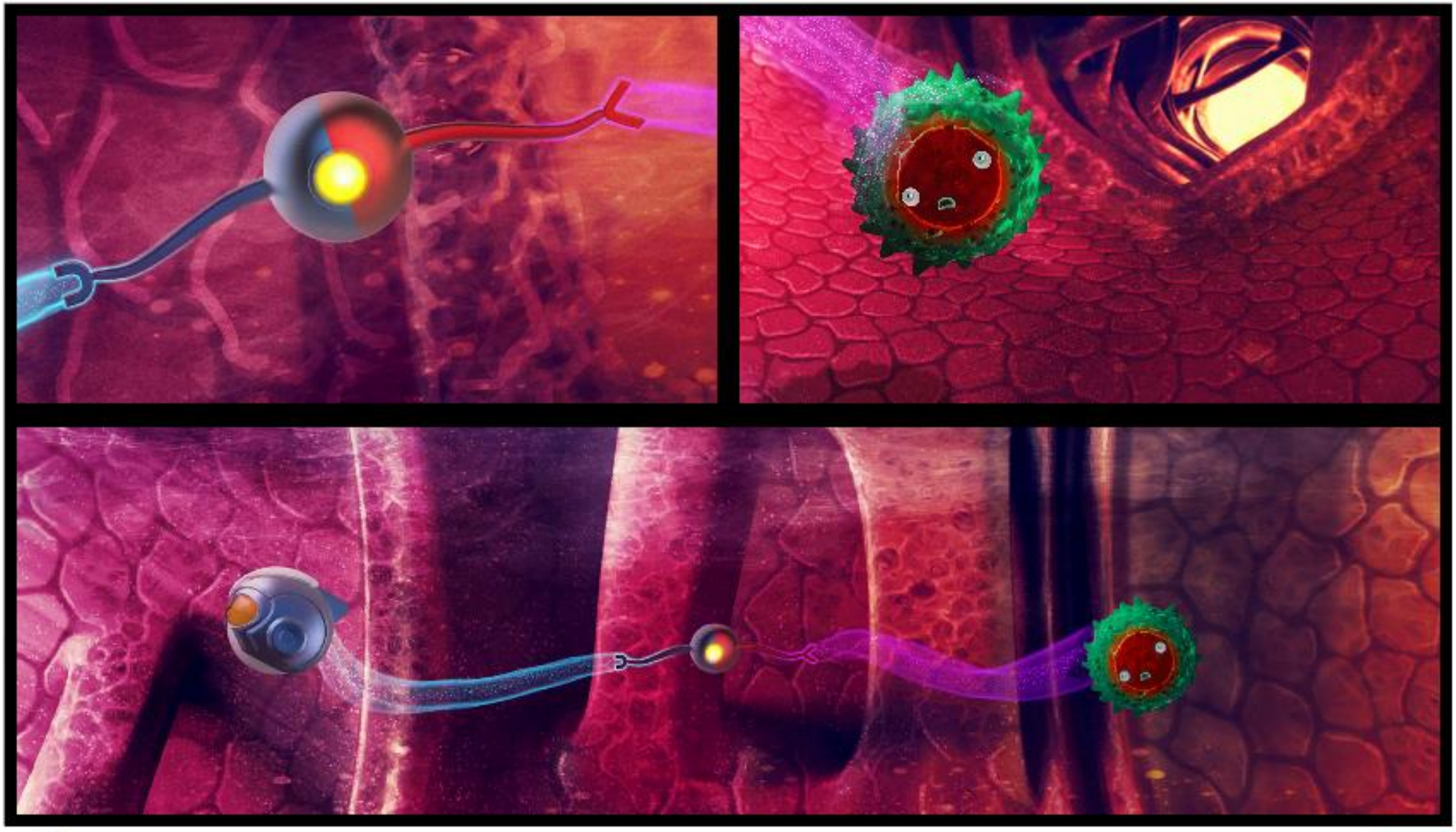
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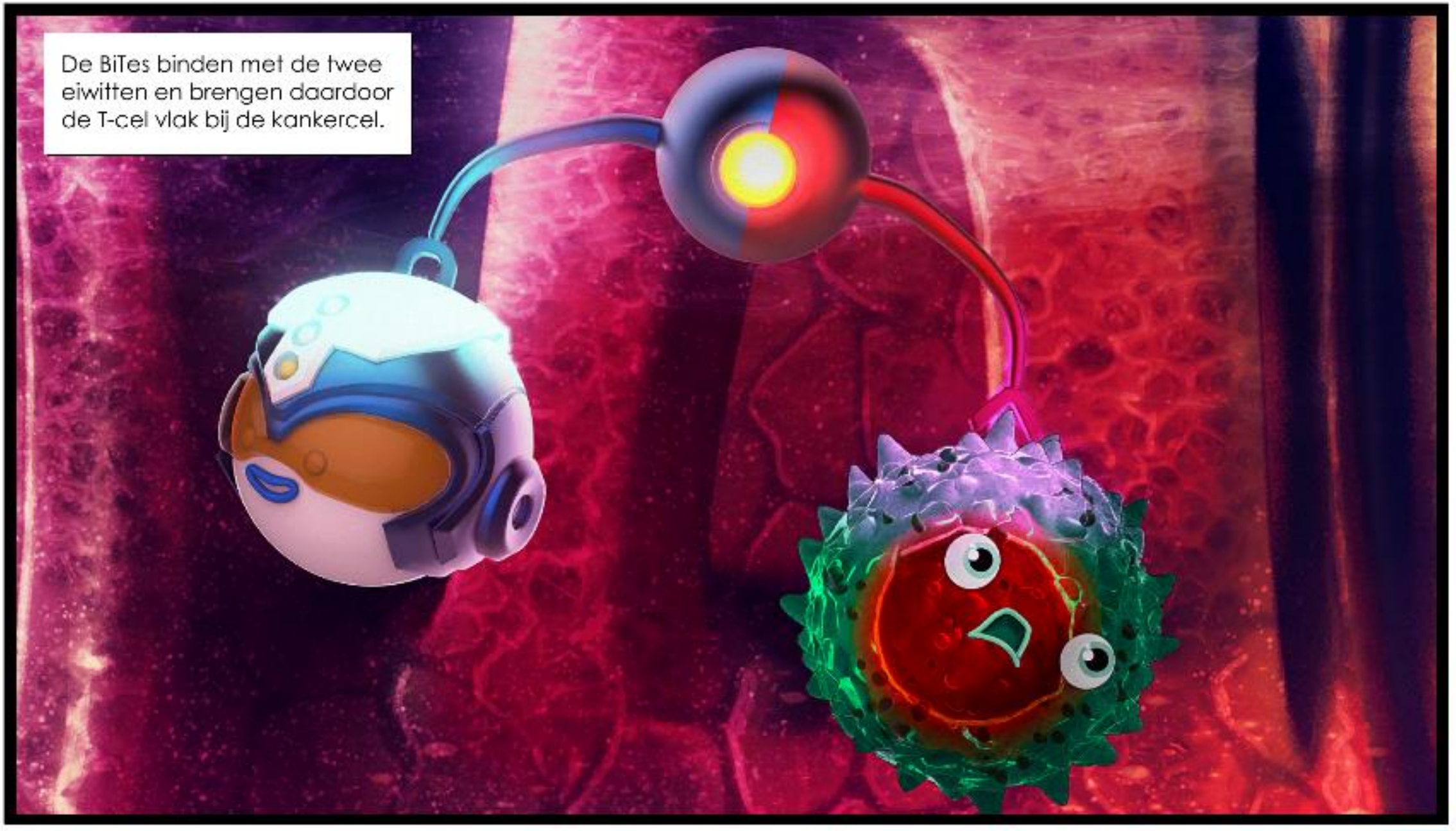
unity WebGL

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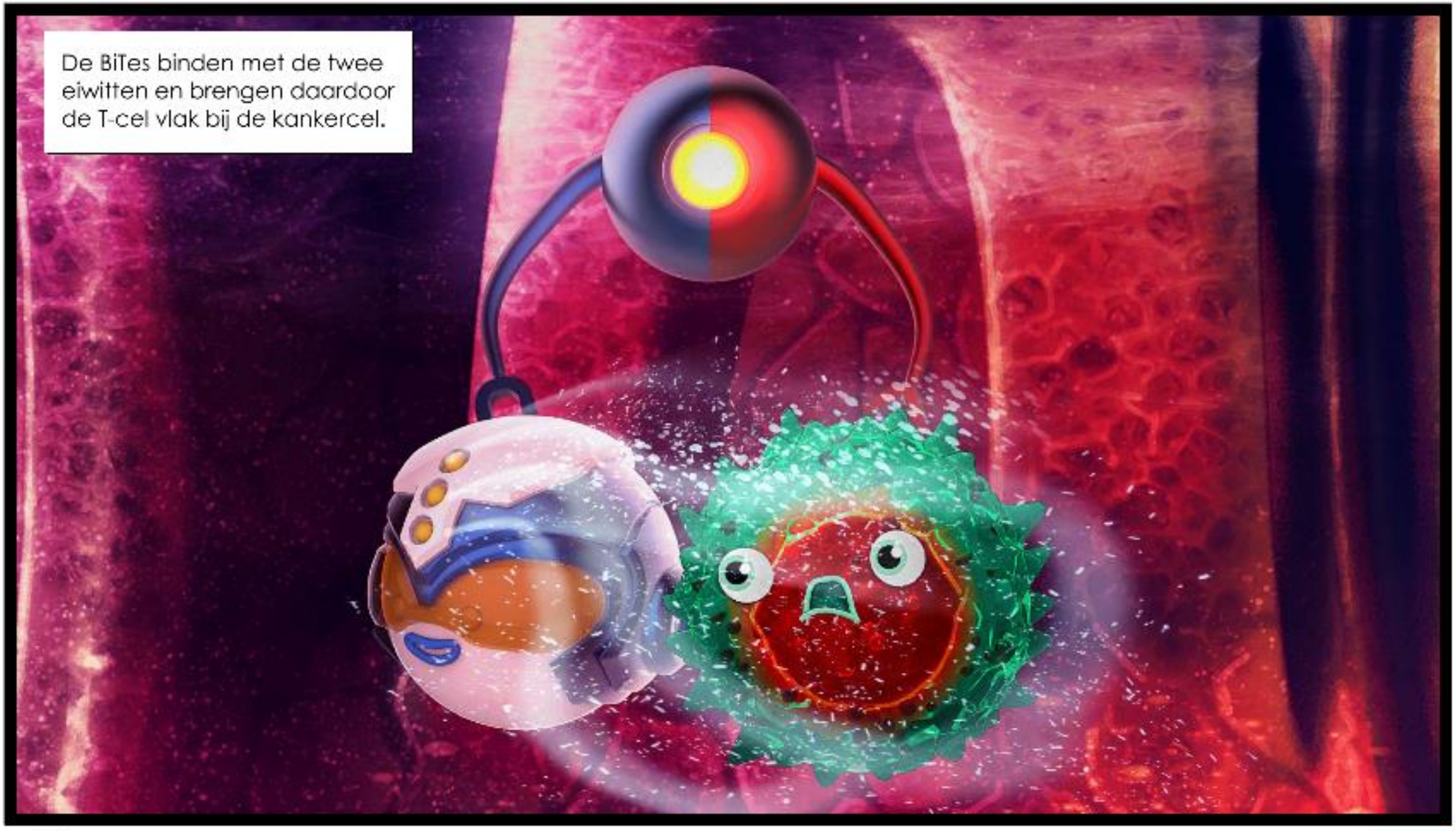
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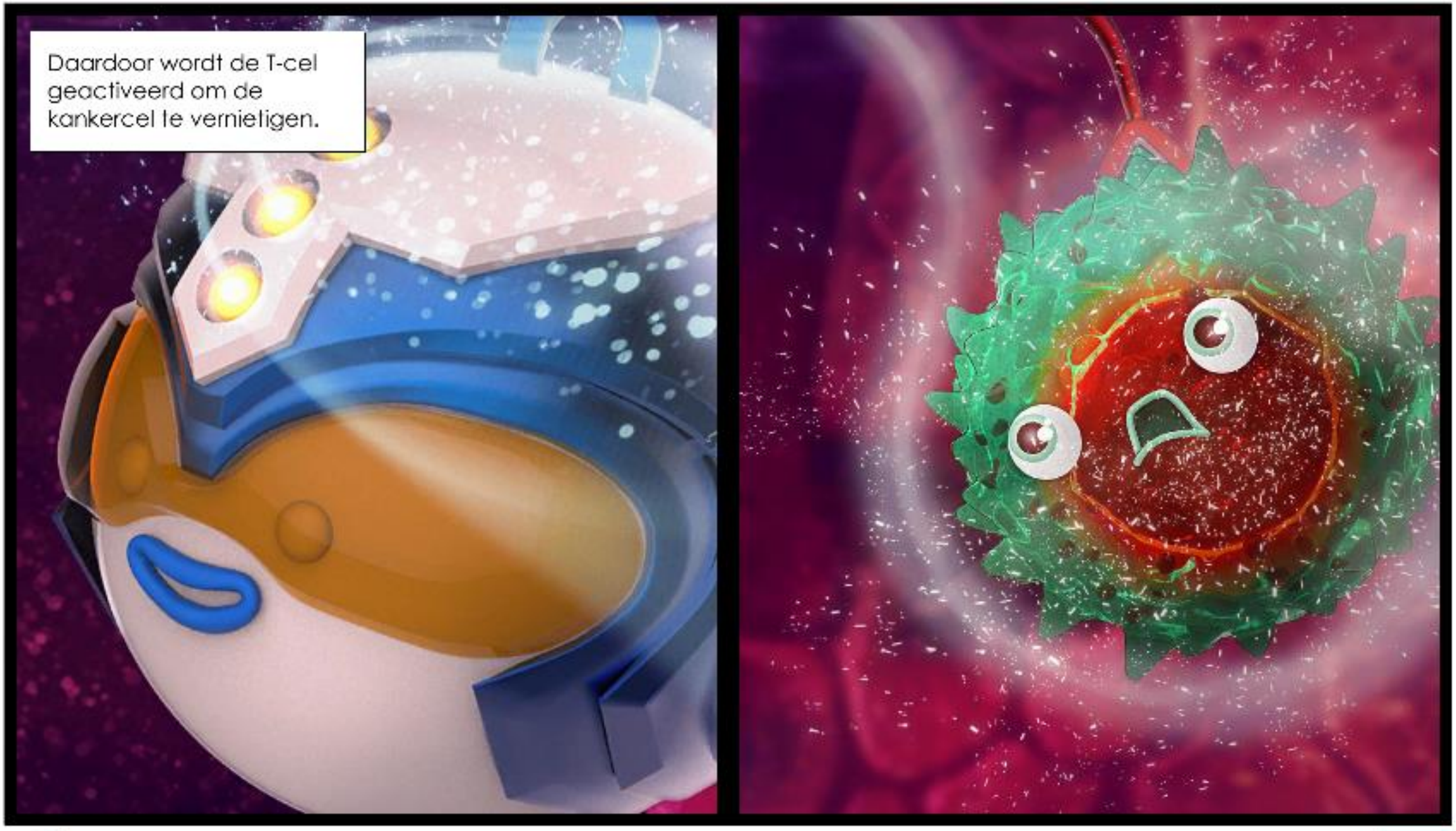
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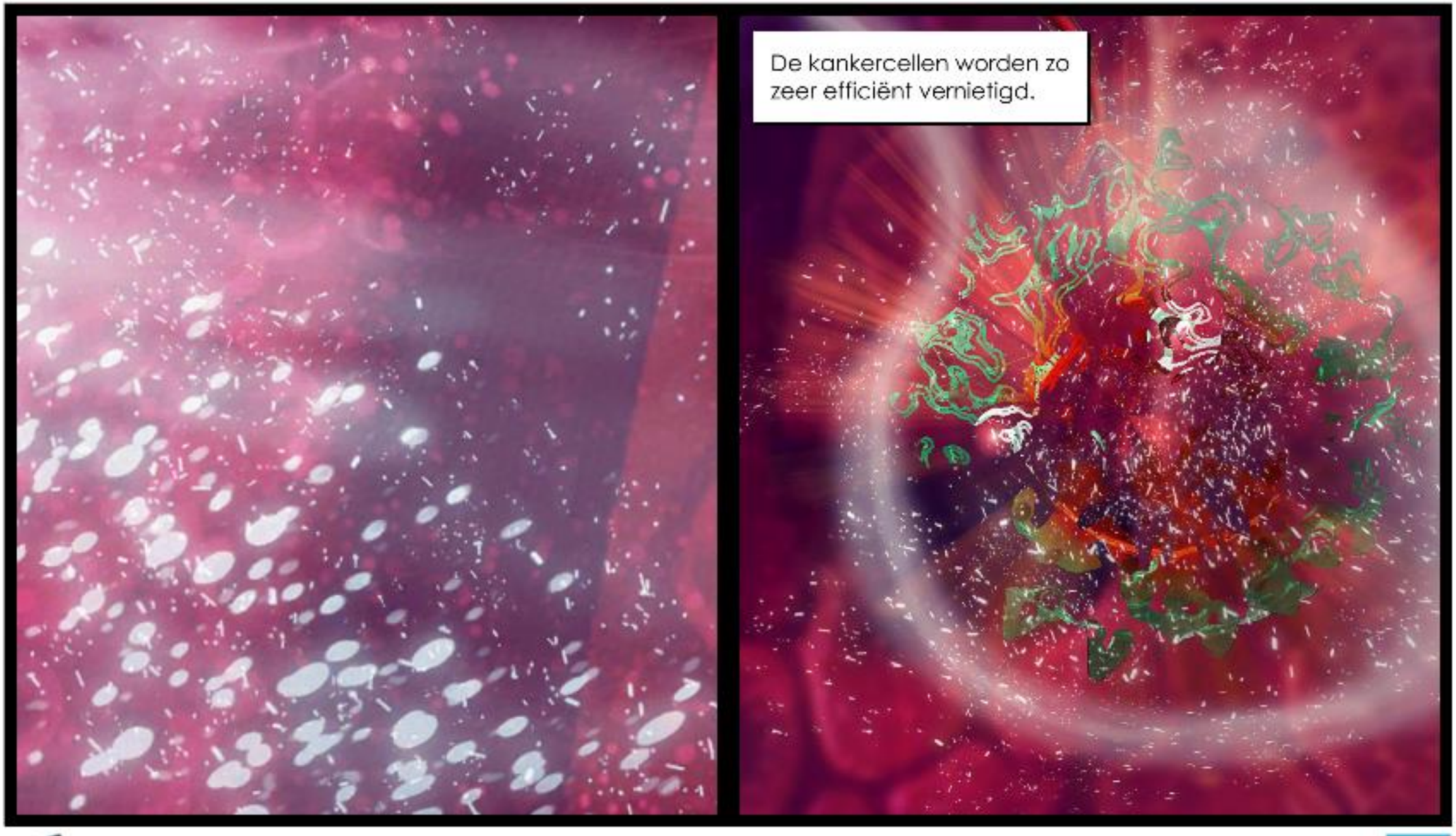


unity WebGL

immuno_web

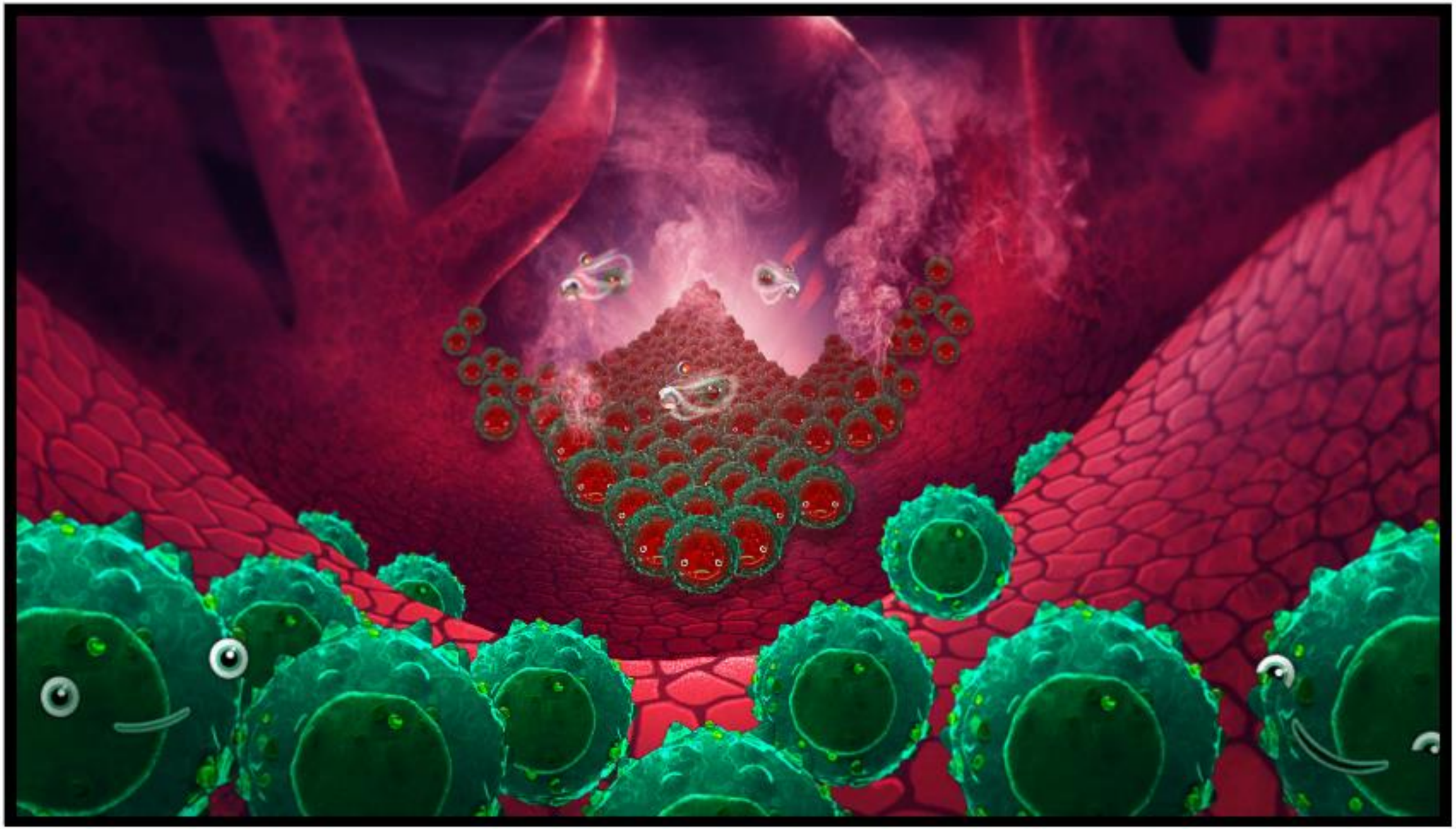

Daardoor wordt de T-cel geactiveerd om de kankercel te vernietigen.


De kankercellen worden zo zeer efficiënt vernietigd.



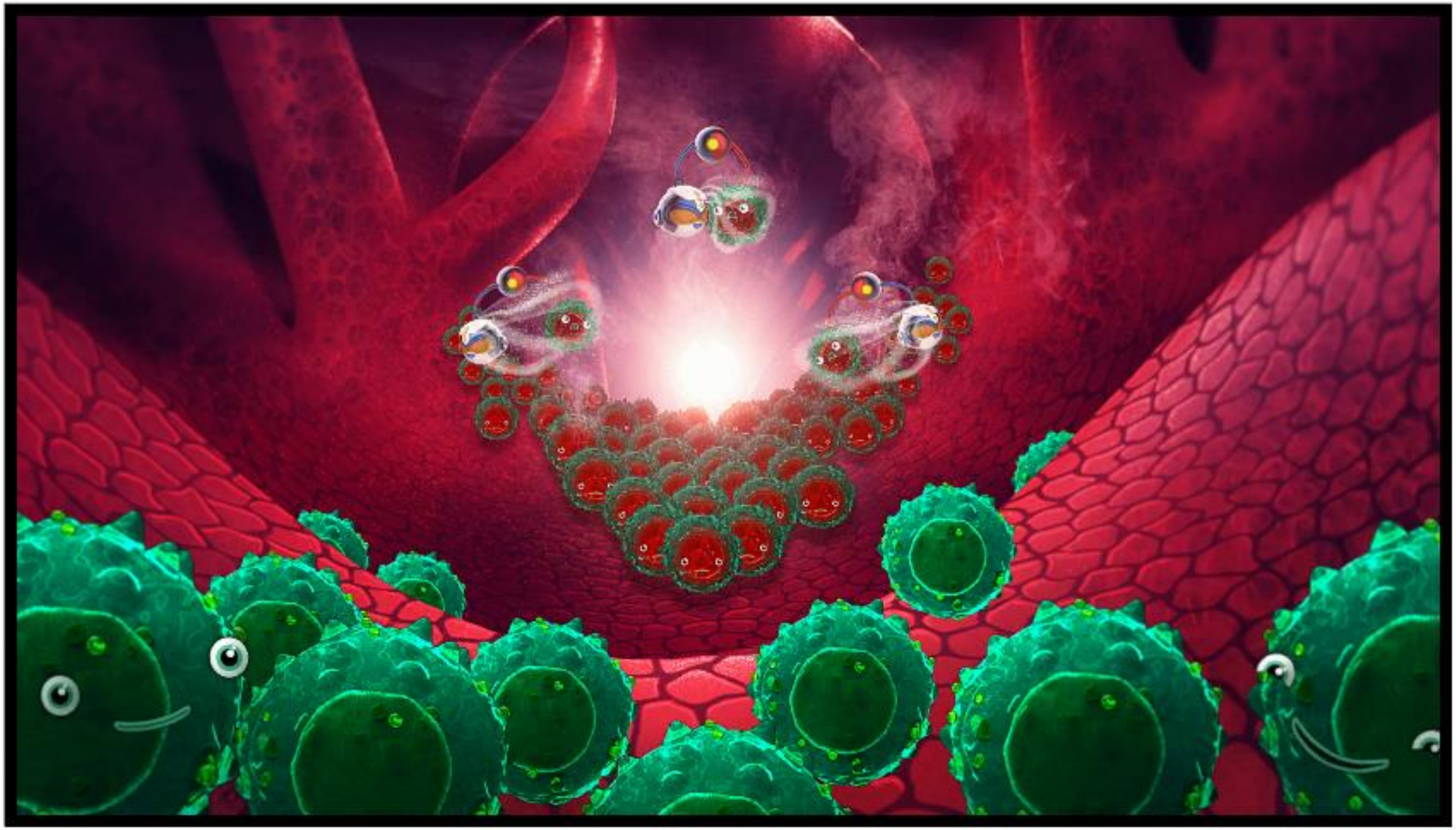
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immuno_web



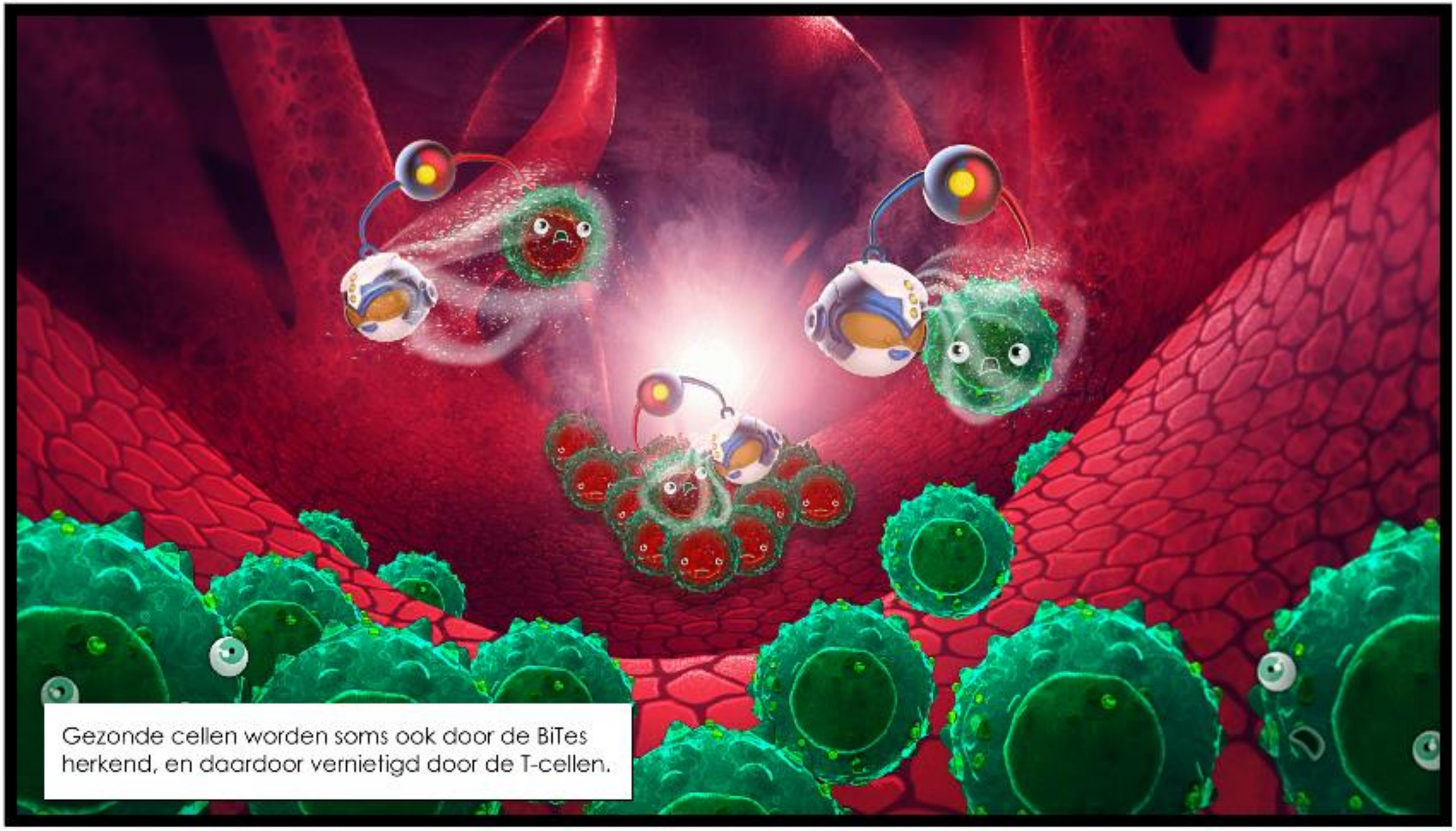
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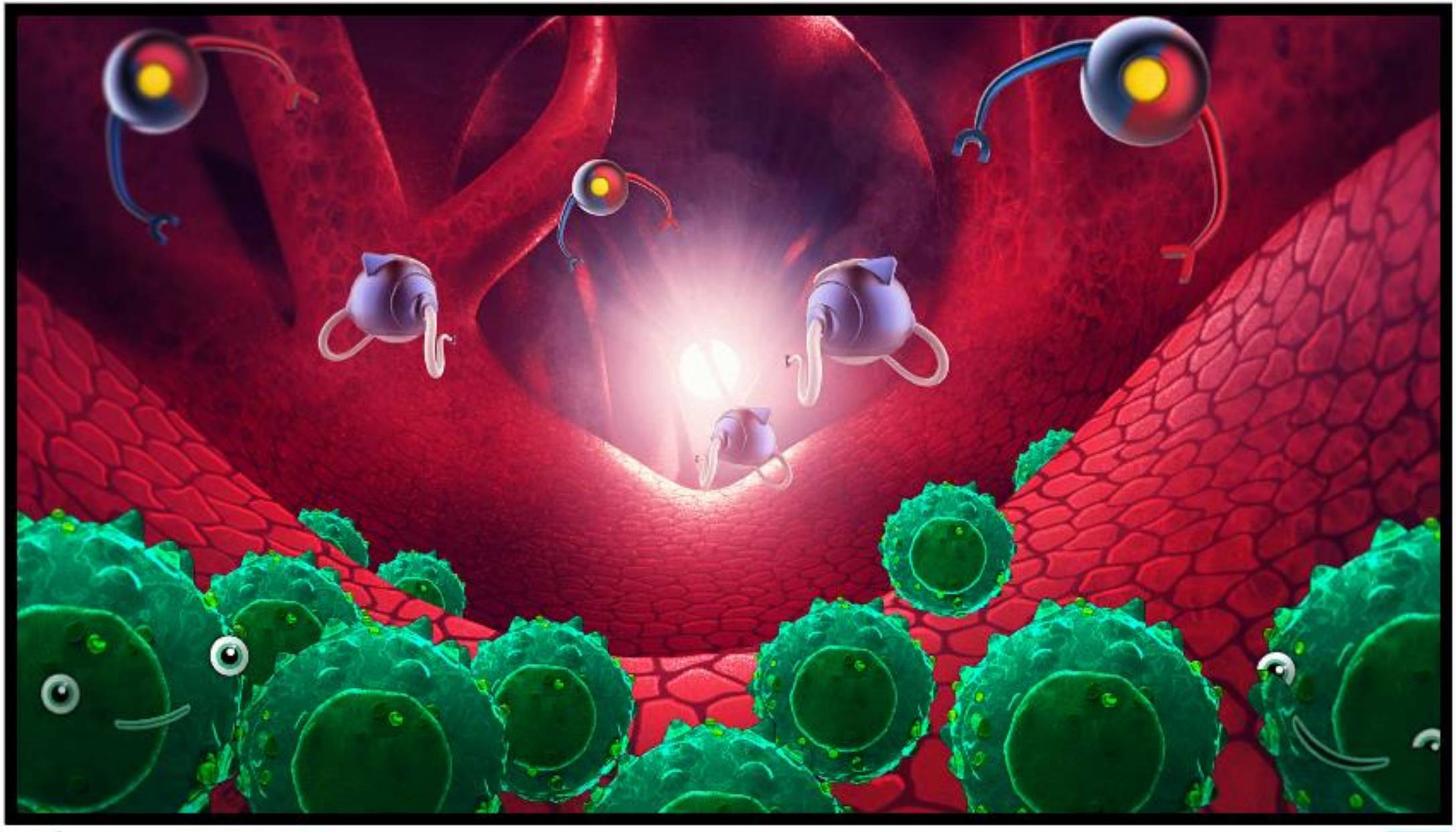
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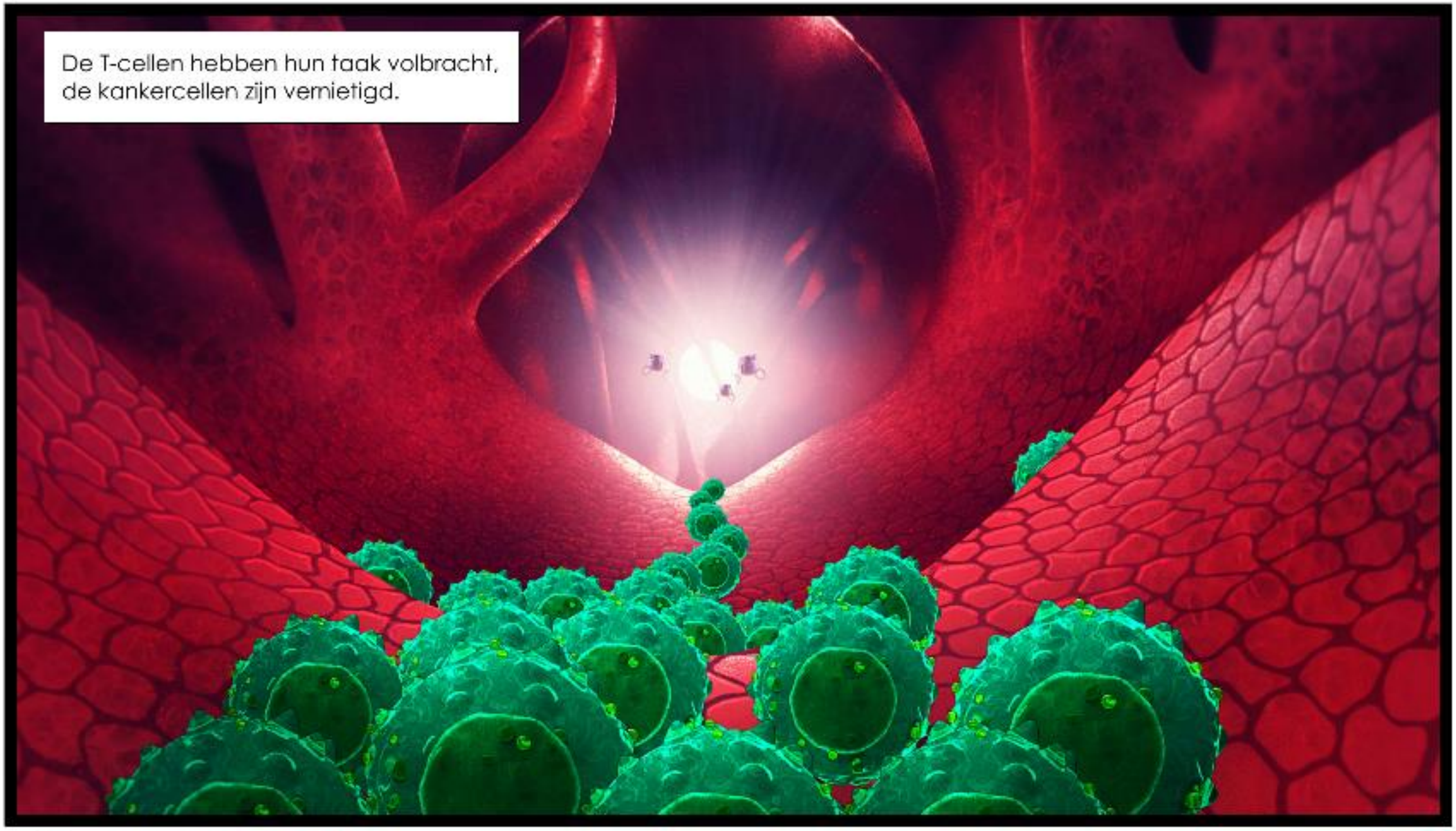
immuno_web


Gezonde cellen worden soms ook door de BiTes herkend, en daardoor vernietigd door de T-cellen.



unity WebGL

immuno_web

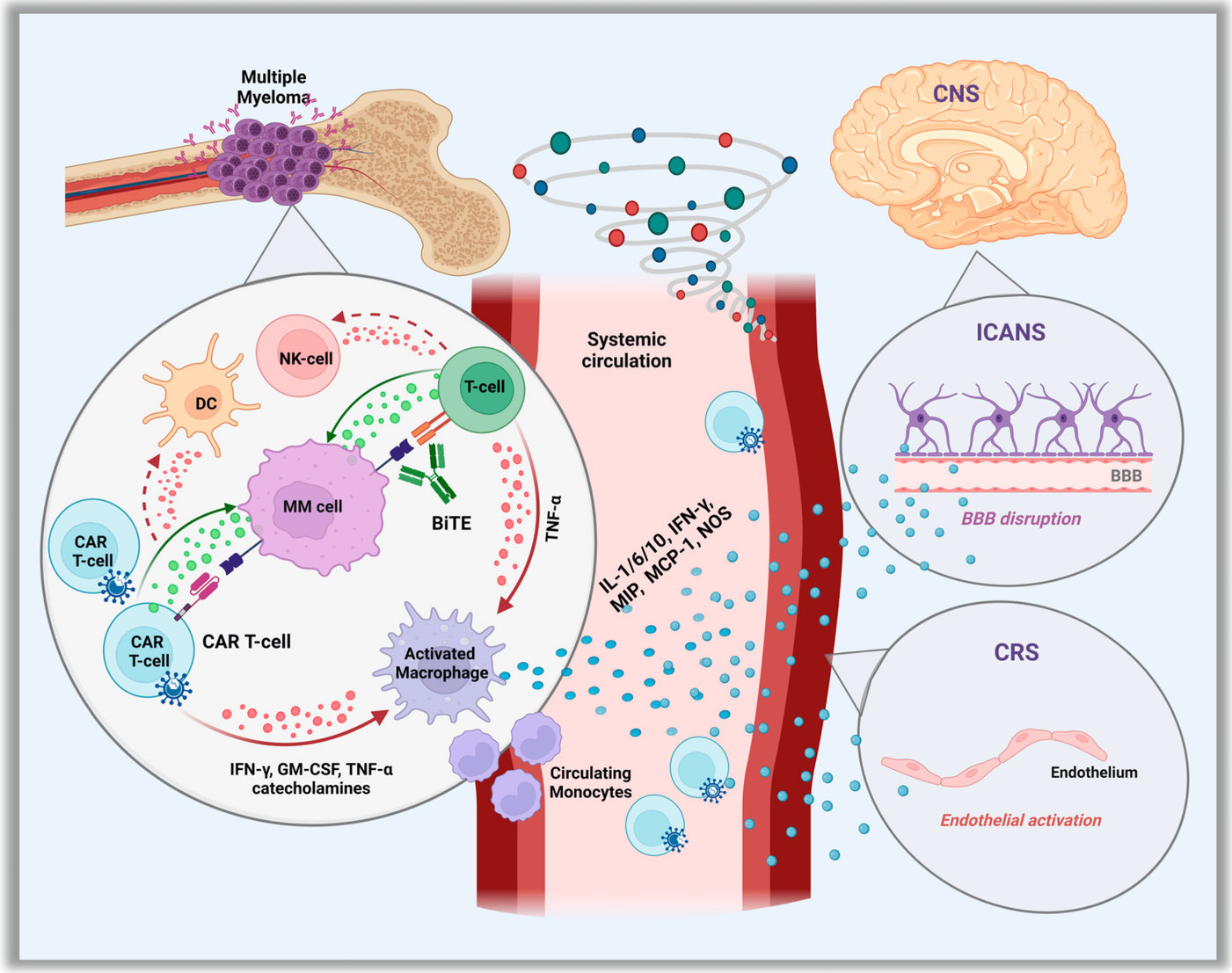


unity WebGL

immuno_web

MULTISPECIFIEKE ANTISTOFFEN

Multispecifieke antistoffen: bijwerkingen



- CRS
- ICANS
- On-target, off-tumour (afhankelijk van het doelwit)

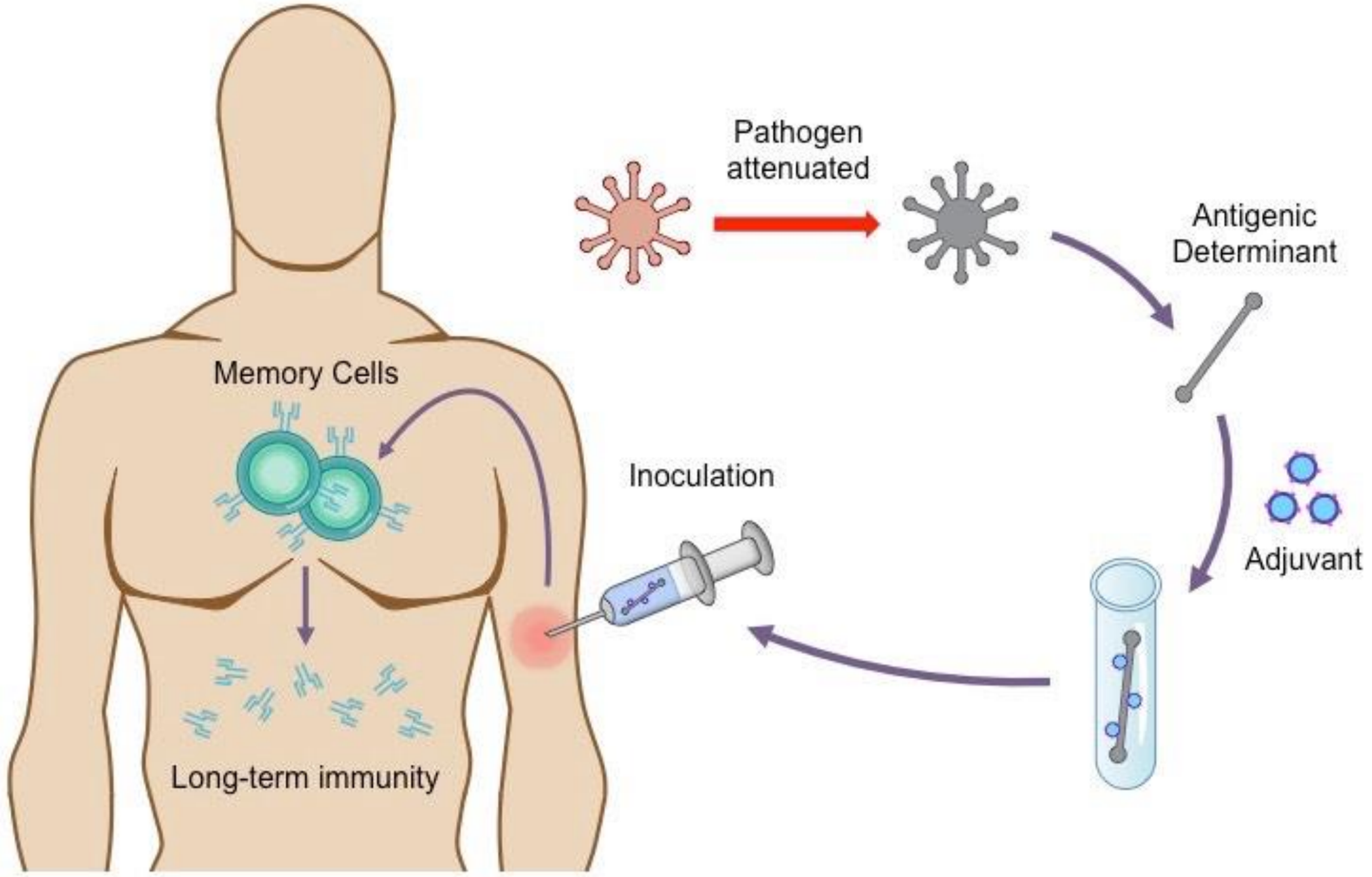
M Markouli et al, Curr Oncol, 2023

VACCINATIE

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VACCINATIE

– Principe



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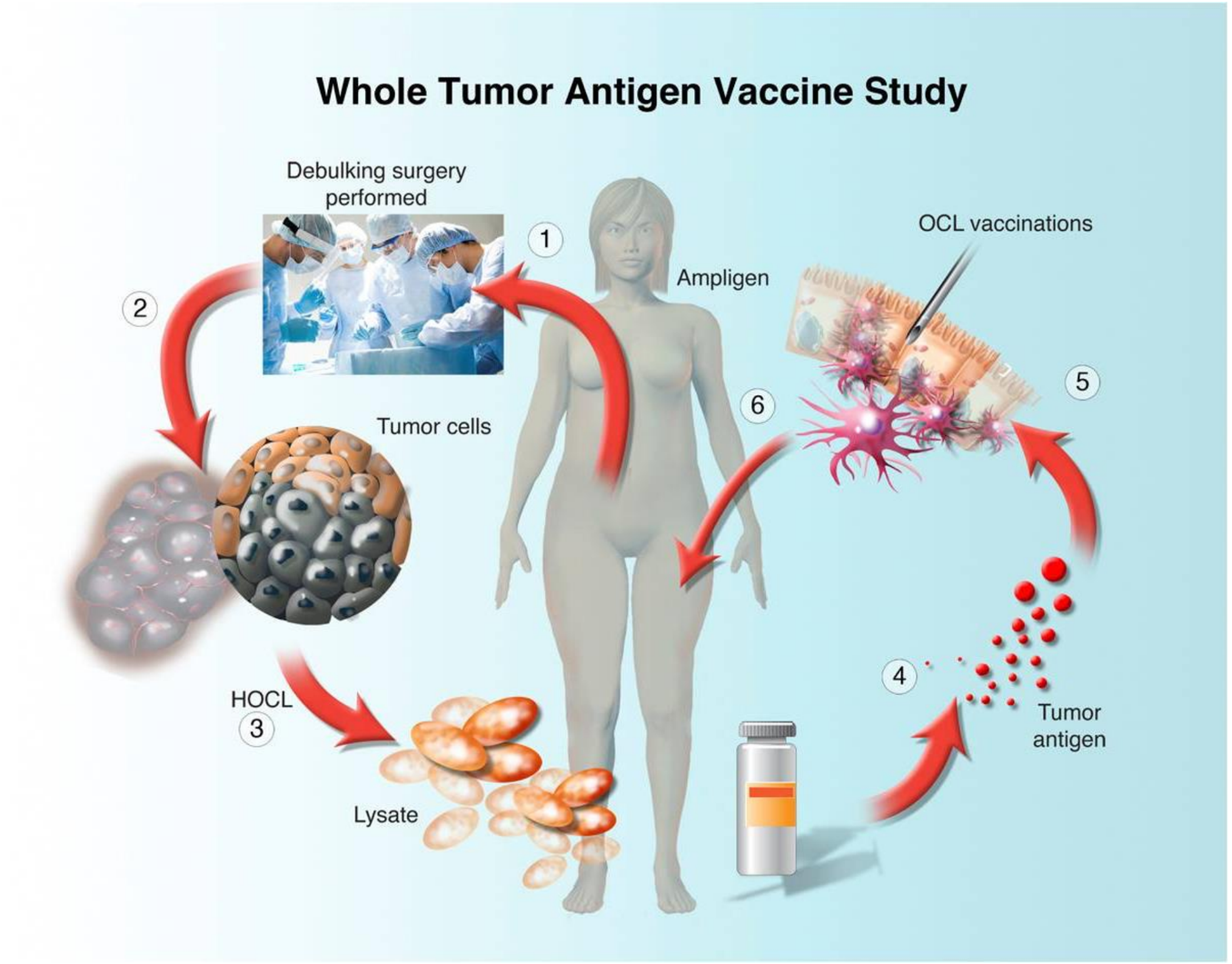
VACCINATIE

- Tumor extract
- Peptide of peptide mixes
- Peptide geladen op dendritische cellen
- mRNA gebaseerd
- DNA gebaseerd

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VACCINATIE

– Tumor vaccinatie

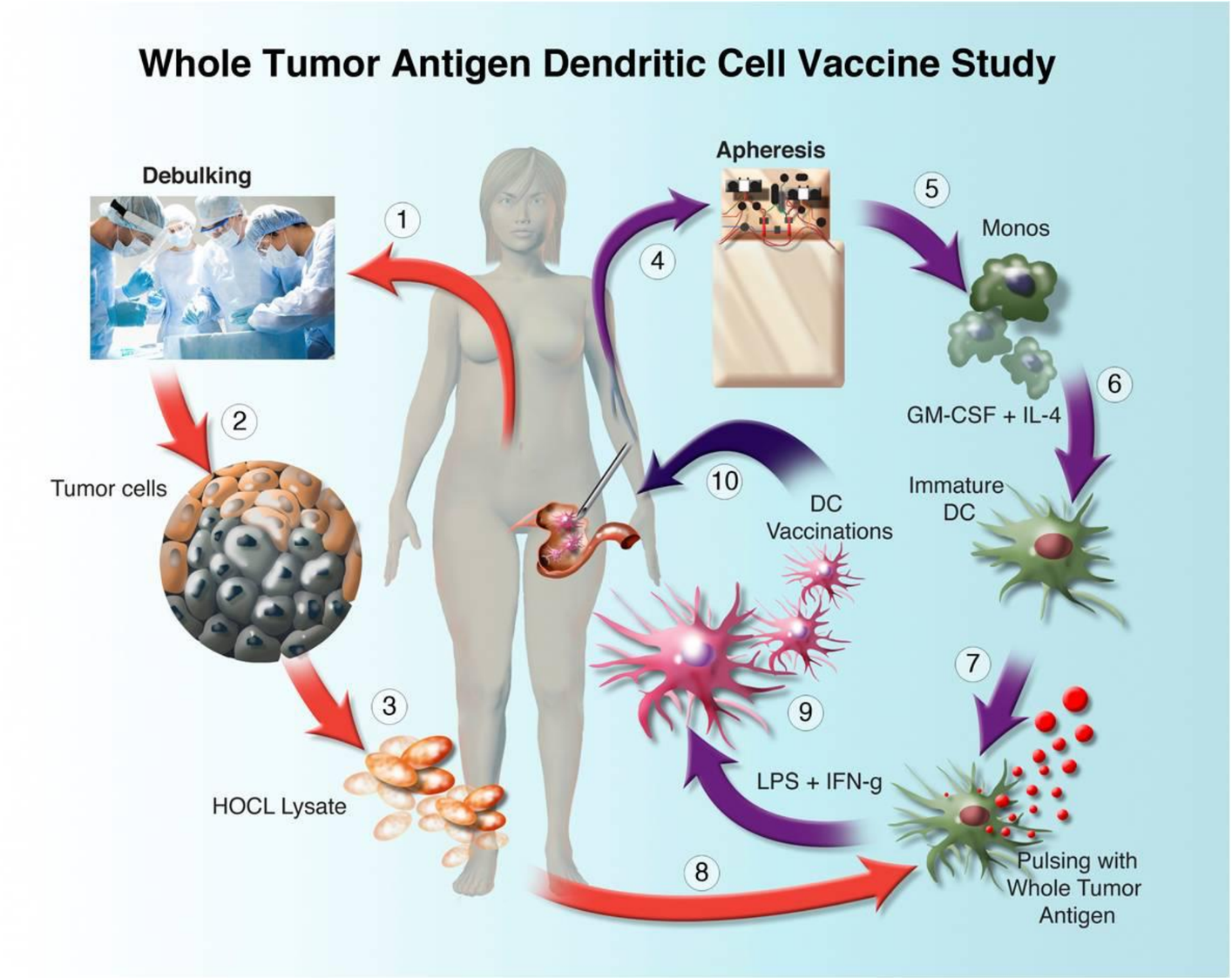


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Penn University

VACCINATIE

– Tumor / DC vaccinatie



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Penn University

VACCINATIE

- Preventief vs therapeutisch
  - Preventief: bvb vaccin gericht tov HPV, bvb **Gardasil** (preventie van baarmoederhalskanker)
  - Therapeutisch (behandeling van of actieve ziekte of preventie van herval): bvb
    - **Bacillus Calmette-Guérin (BCG):** verzwakte bacteriën om het immuunsysteem te stimuleren (early-stage blaascarcinoom)
    - **Sipuleucel-T (Provenge®):** DC gebaseerd (prostaatkanker)
    - vaccin gericht tegen WT-1 voor AML (preventie herval)
- Globaal: kleine successen, gewoonlijk in klein percentage van patiënten
- Reden: T cellen werken onvoldoende of zijn onderdrukt door immunosuppressieve micro-omgeving
- Toekomst: gepersonaliseerde kankervaccins

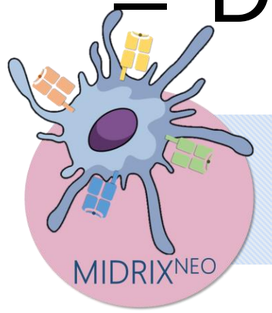
VACCINATIE

- DC vaccins voor **longkanker** (Prof Karim Vermaelen – prof Bart Vandekerckhove – Joline Ingels – Laurenz De Cock (UG/UZG))

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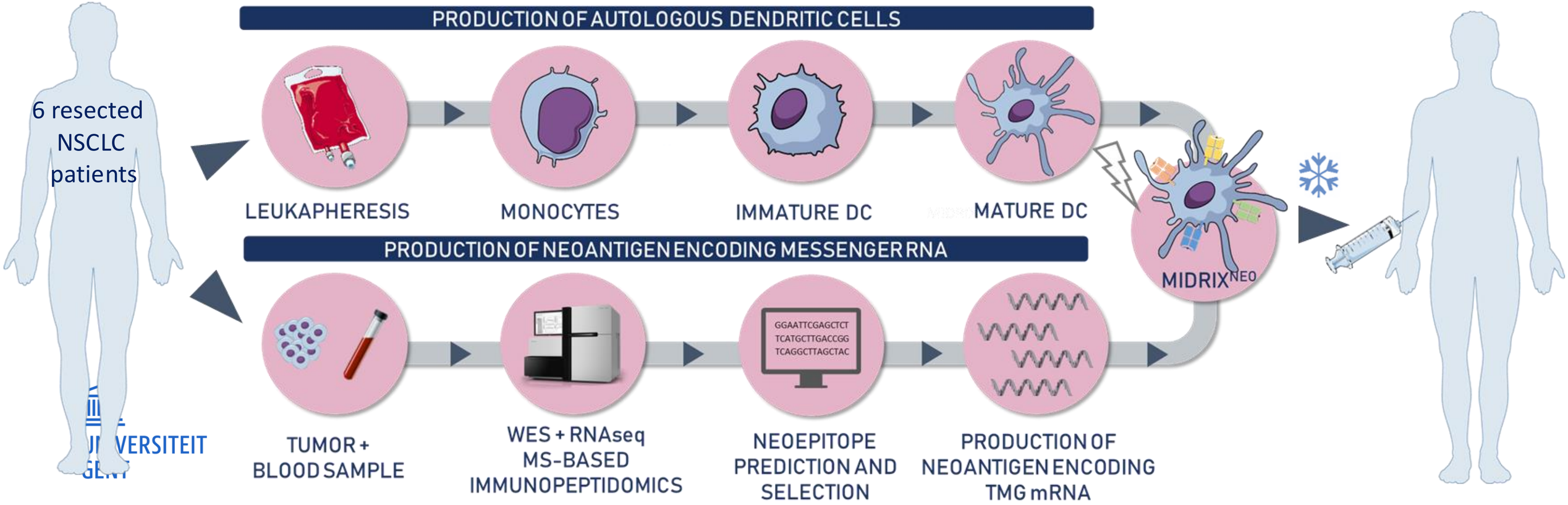
VACCINATIE

– DC vaccins voor **longkanker**



| MIDRIX^{NEO} phase I trial @ UZ Gent

J. Ingels - K. Vermaelen – B. Vandekerckhove

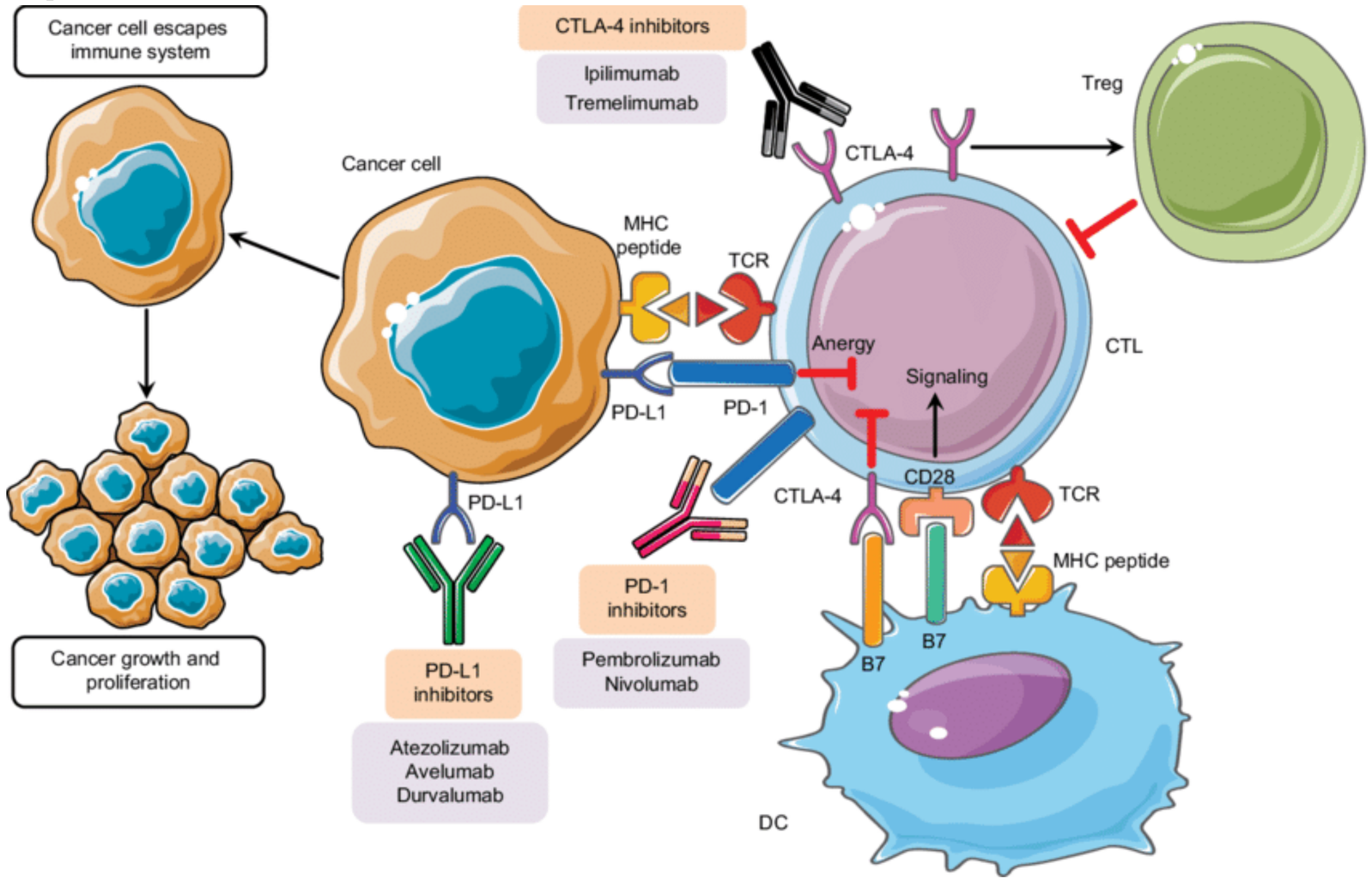


CHECKPOINT INHIBITOREN

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CHECKPOINT INHIBITOREN

– Principe

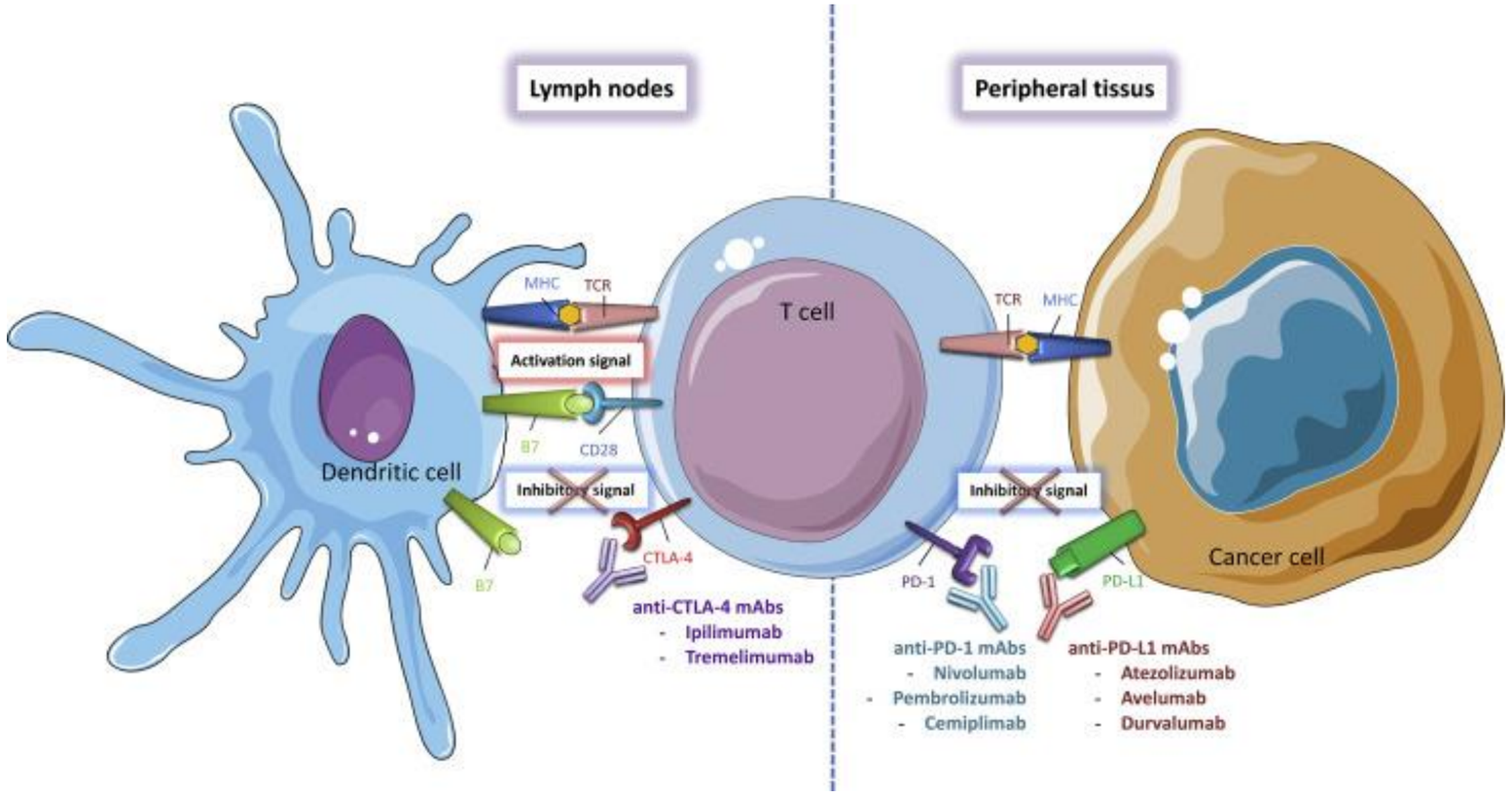


UNIVERSITEIT GENT

N Ayoub et al, Breast cancer: targets and therapy, 2019

CHECKPOINT INHIBITOREN

– Principe



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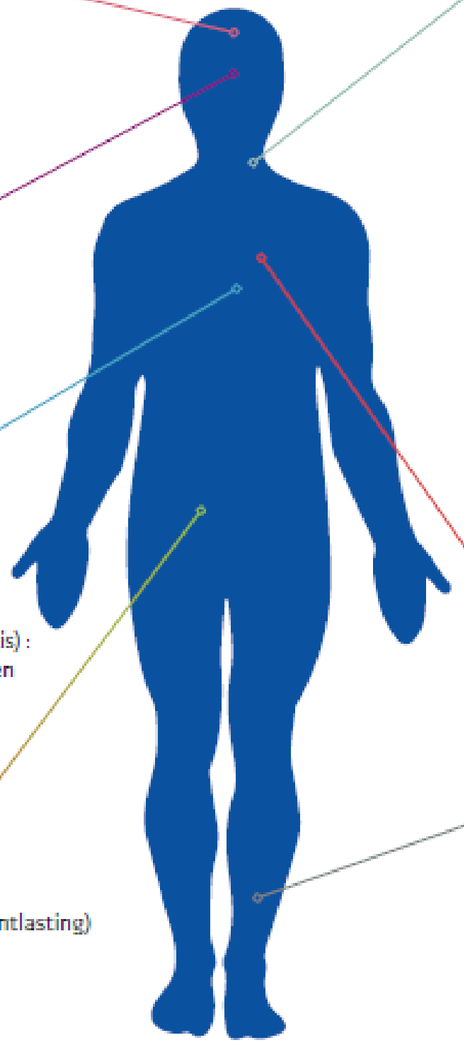
A Desnoyer et al, Eur J Cancer, 2020

CHECKPOINT INHIBITOREN

- **Indicaties Keytruda (Pembrolizumab) = PD-1 inhibitor**
- Melanoom
- Borstcarcinoom
- Niercelcarcinoom
- Hoofd-halsplaveiselcelcarcinoom Slokdarmcarcinoom
- (klassiek) Hodgkin lymfoom

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CHECKPOINT INHIBITOREN: BIJWERKINGEN



Zenuwstelsel

- Hoofdpijn
- Ontsteking van de zenuwen :
  - Gevoelloosheid
  - Zwakte
  - Tinteling of brandende pijn in de armen en benen
- Duizeligheid

Ogen

- Ontsteking van het oog :
  - Pijn en roodheid
  - Zichtproblemen of troebel zicht

Longen

- Infecties van de bovenste luchtwegen
- Enstige longinfectie (pneumonie)
- Ontsteking van de longen (pneumonitis) :
  - Hoesten en moeite met ademhalen
  - Bloedpropjes
  - Kortademigheid (dyspnoe)
  - Hoesten

Darmen Lever

- Diarree (waterige, losse of zachte ontlasting)
- Braken, misselijkheid
- Buikpijn
- Ontsteking van de darmen (colitis)
- Ontsteking van de maag (gastritis)
- Constipatie
- Ontsteking van de lever

Hormoonklieren

- Te weinig werkende schildklier :
  - Vermoeidheid
  - Toename in lichaamsgewicht
- Afname in de uitscheiding van hormonen die geproduceerd worden door de bijnieren
- Verminderde functie (hypopituïtarisme) of ontsteking (hypofysitis) van de hypofyse die zich aan de basis van de hersenen bevindt;
- Overactieve schildklier :
  - Versnelde hartslag
  - Zweten
  - Gewichtsverlies
- Ontsteking van de schildklier
- Zwelling van de schildklier
- Hoge bloedsuikerspiegels

Cardiovasculair

- Snelle hartslag
- Hoge bloeddruk (hypertensie)

Huid

- Huiduitslag
- Jeuk
- Plekken met veranderde huidskleur (vitiligo)
- Droge huid
- Roodheid van de huid
- Ongewoon haarverlies of dunner wordend haar
- Netelroos (jeukende huiduitslag)
- Zweren en koortsblaasjes in de

Anderen

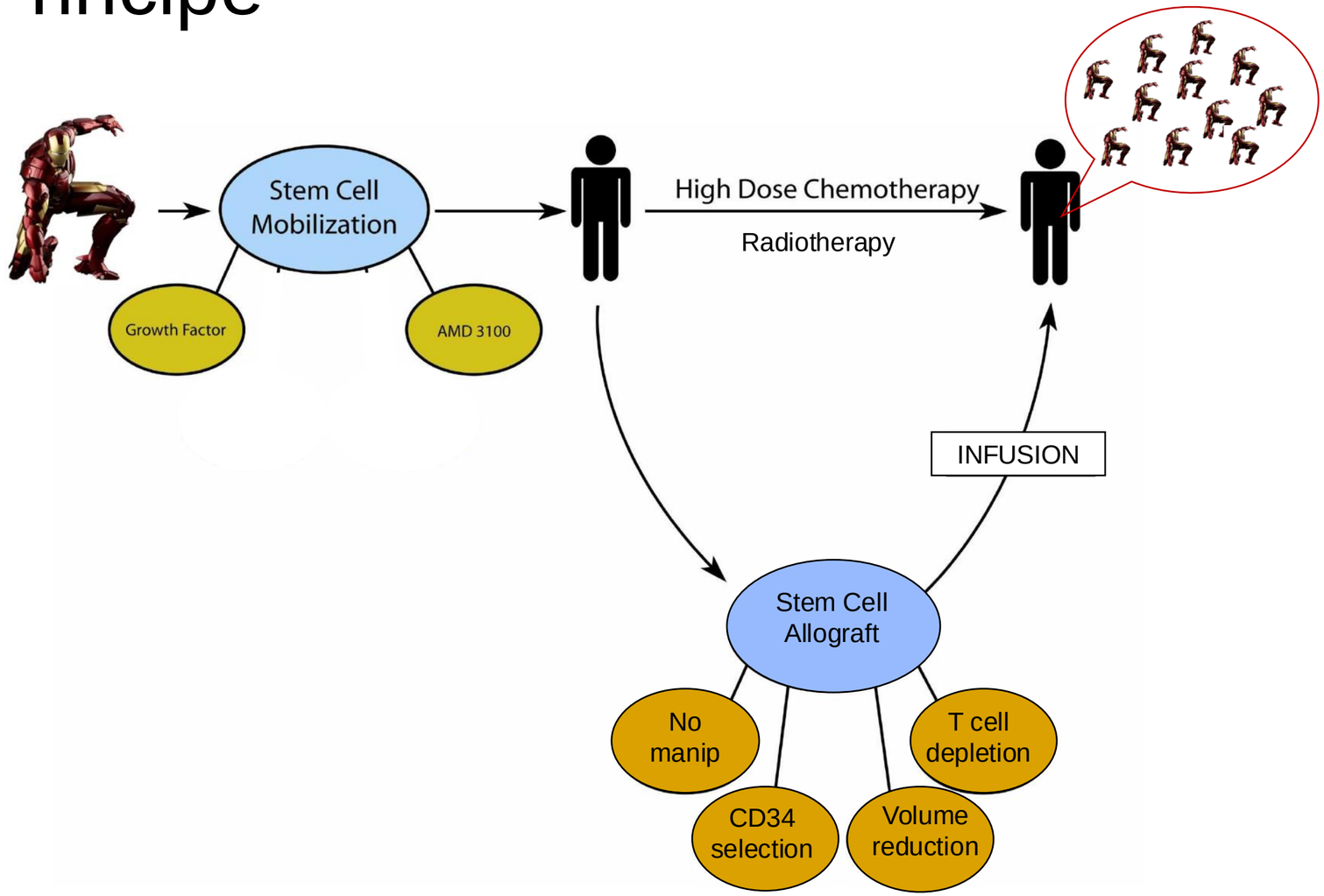
- Veranderingen in het gezichts vermogen
- Verminderde eetlust
- Pijn in de gewrichten
- Zich moe of zwak voelen
- Koorts
- Allergische reactie, reacties gerelateerd aan de infusie van het geneesmiddel
- Pijn in de spieren en botten
- Oedeem (zwelling), pijn
- Deshydratatie
- Toename in sommige witte bloedcellen
- Droge mond
- Nierfalen

ALLOGENE STAMCELTRANSPLANTATIE

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ALLOGENE STAMCELTRANSPLANTATIE

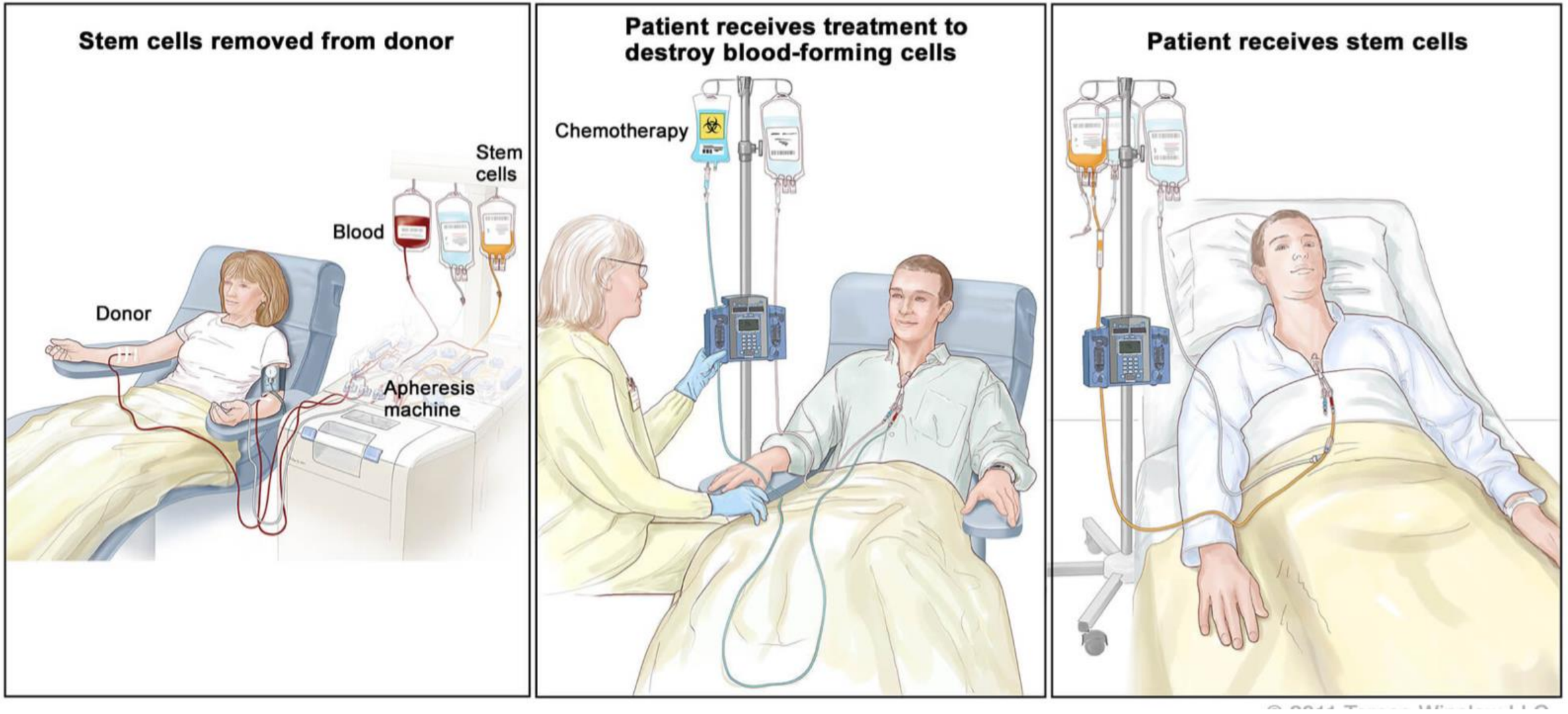
– Principe



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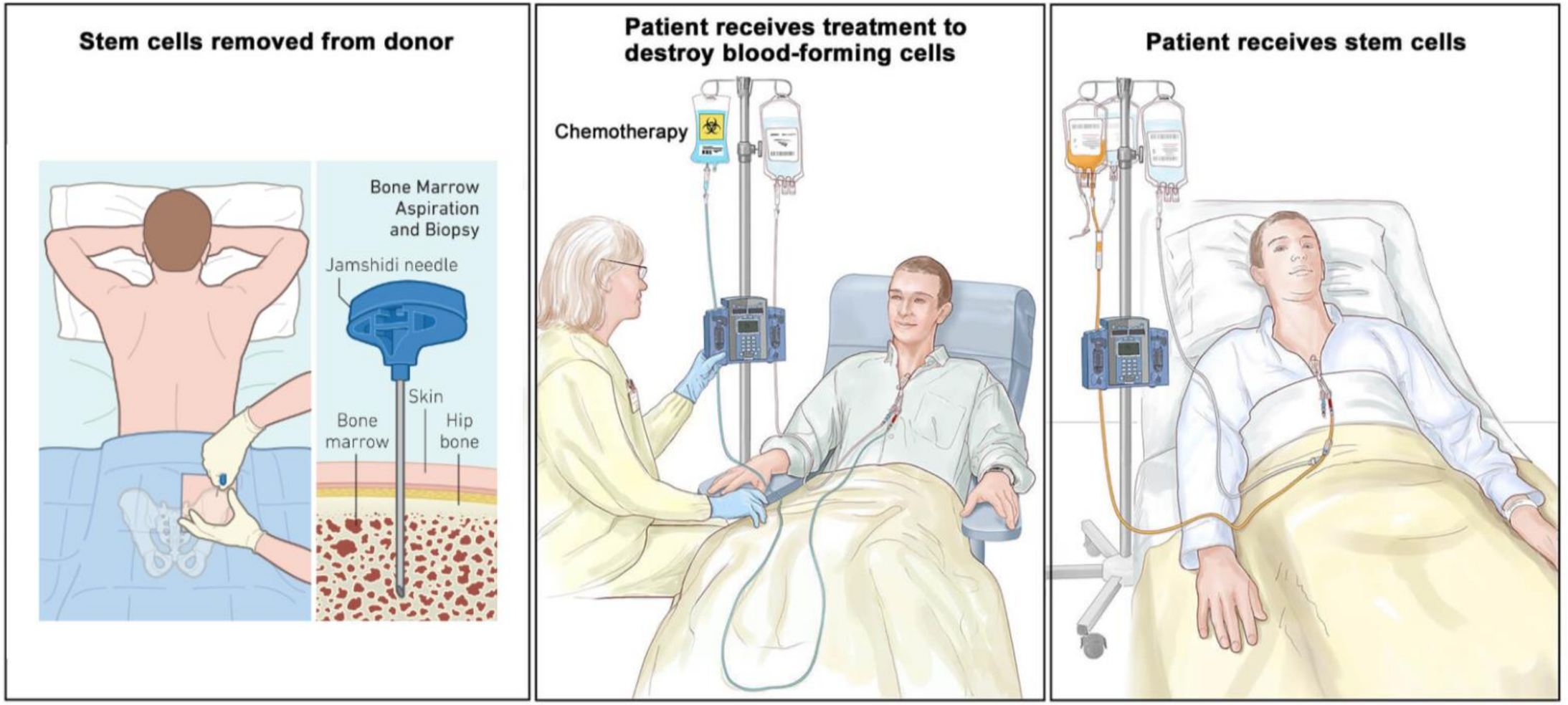
ALLOGENE STAMCELTRANSPLANTATIE

– Stamceloogst



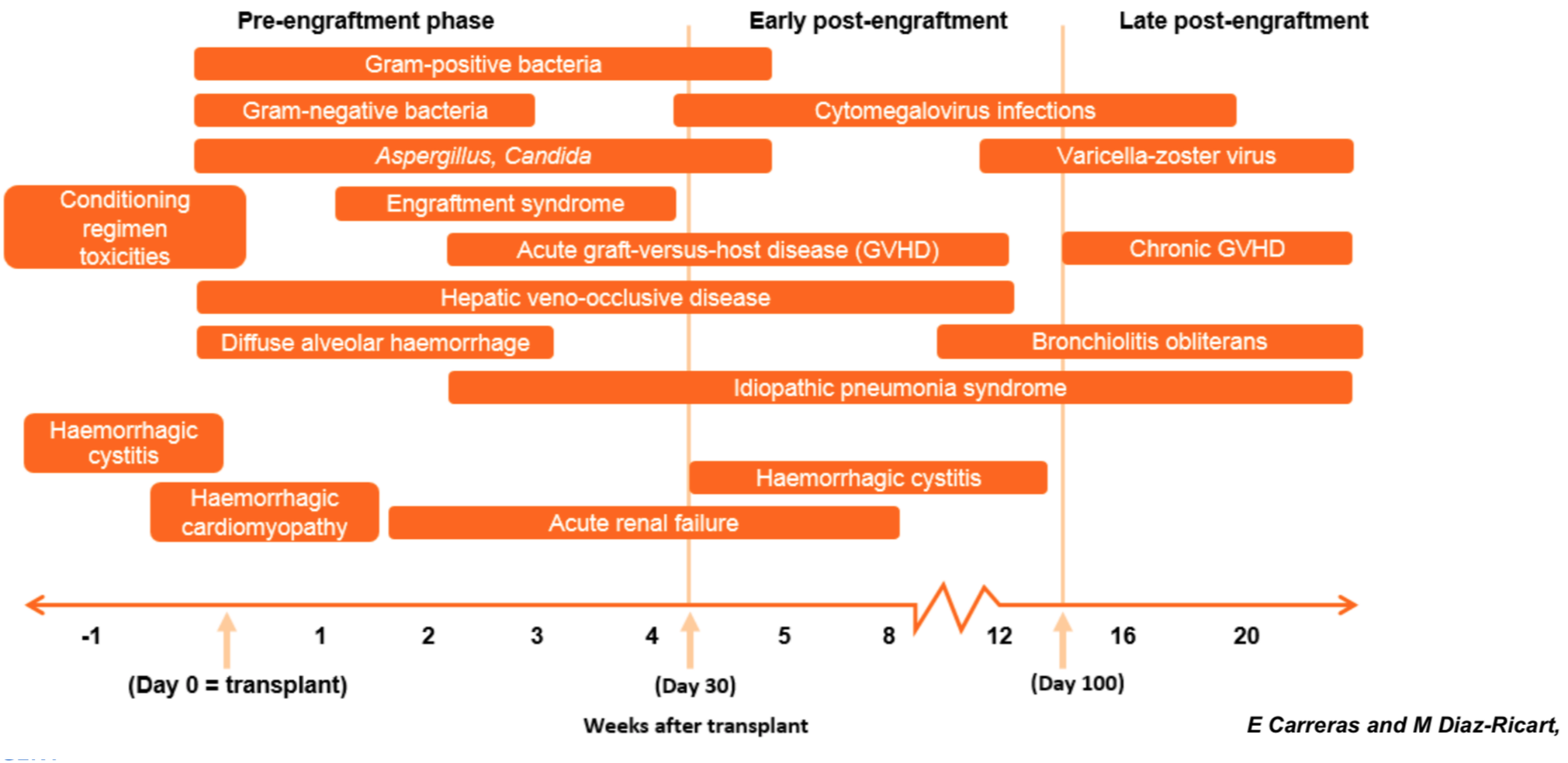
ALLOGENE STAMCELTRANSPLANTATIE

– Beenmergoogst



ALLOGENE STAMCELTRANSPLANTATIE

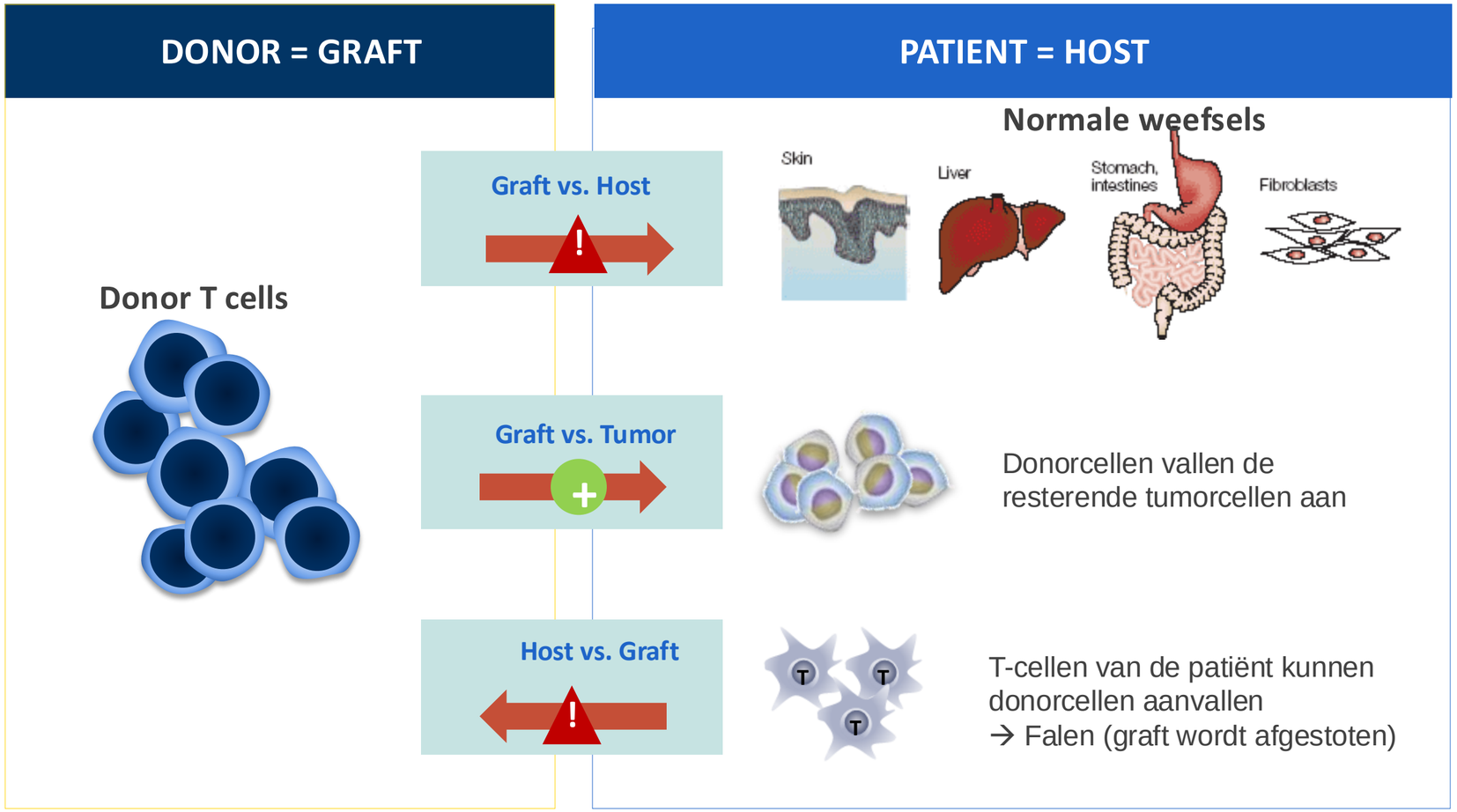
- Complicaties

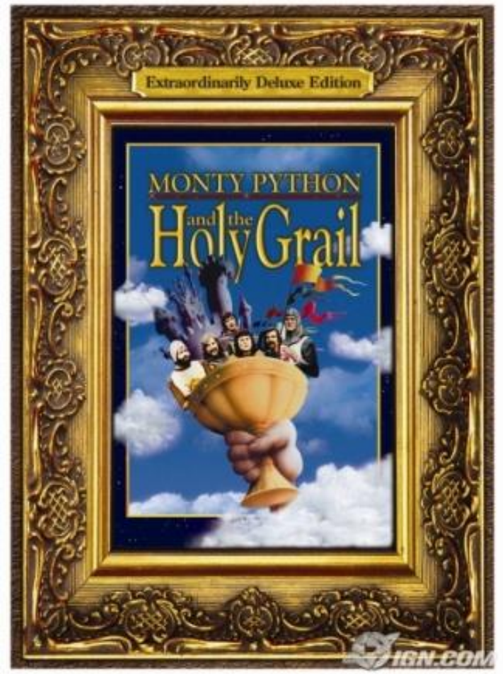


E Carreras and M Diaz-Ricart,

ALLOGENE STAMCELTRANSPLANTATIE

– Graft vs Host en Host vs Graft reacties





ALLOGENE STAMCELTRANSPLANTATIE

– Graft vs Host en Host vs Graft reacties



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ALLOGENE STAMCELTRANSPLANTATIE









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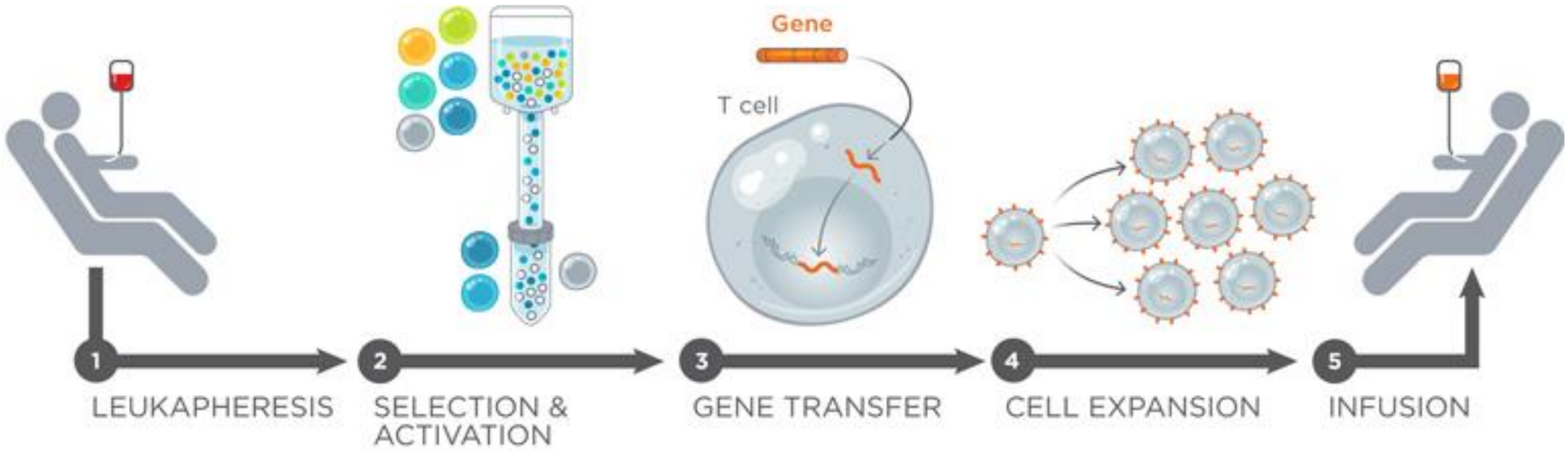
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T-CEL THERAPIE

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T-CEL THERAPIE

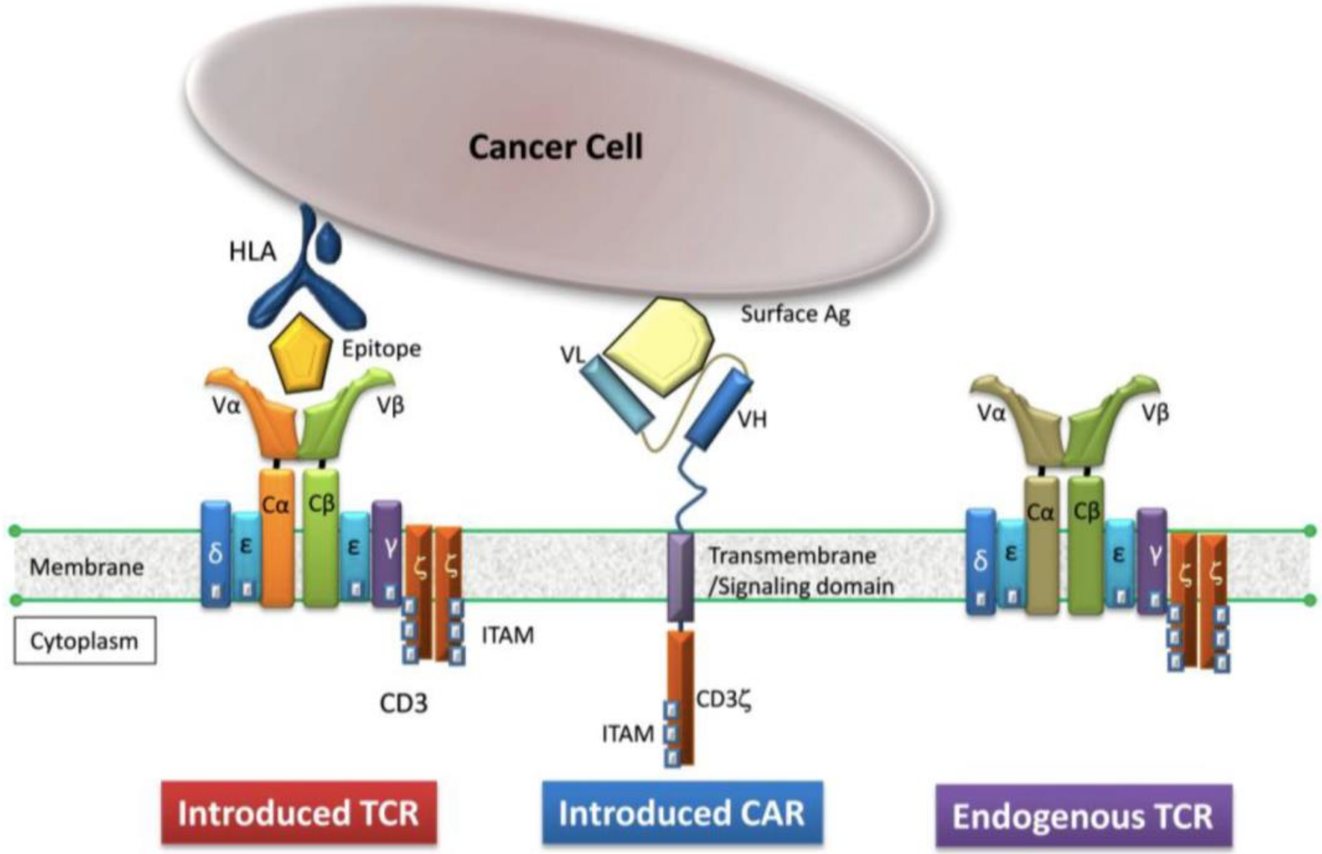
– Genetisch gemodificeerde T-cellen



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T-CEL THERAPIE

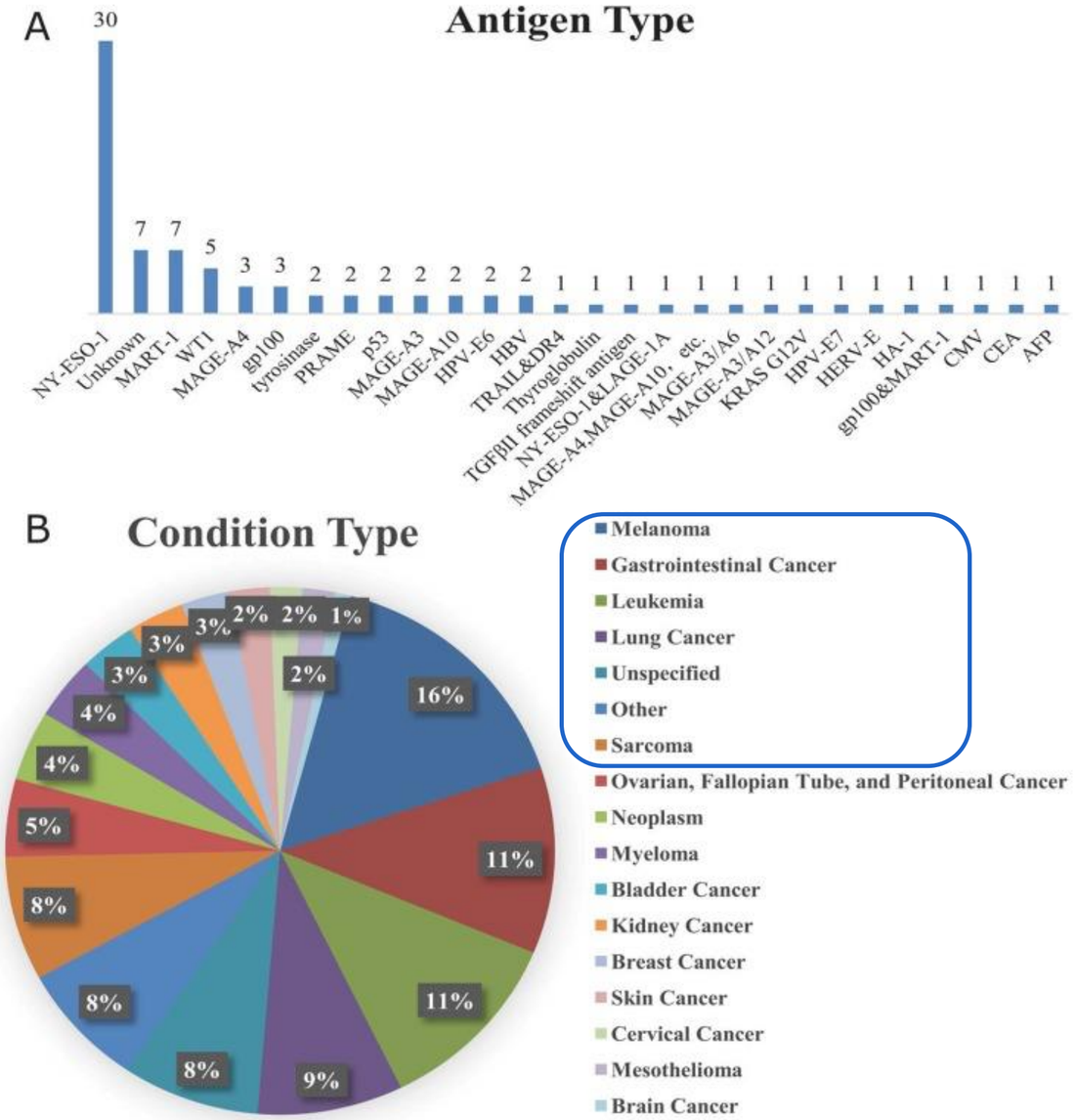
– CAR/TCR



Hiroshi Fujiwara, Pharmaceuticals, 2014

T CEL THERAPIE

– TCR

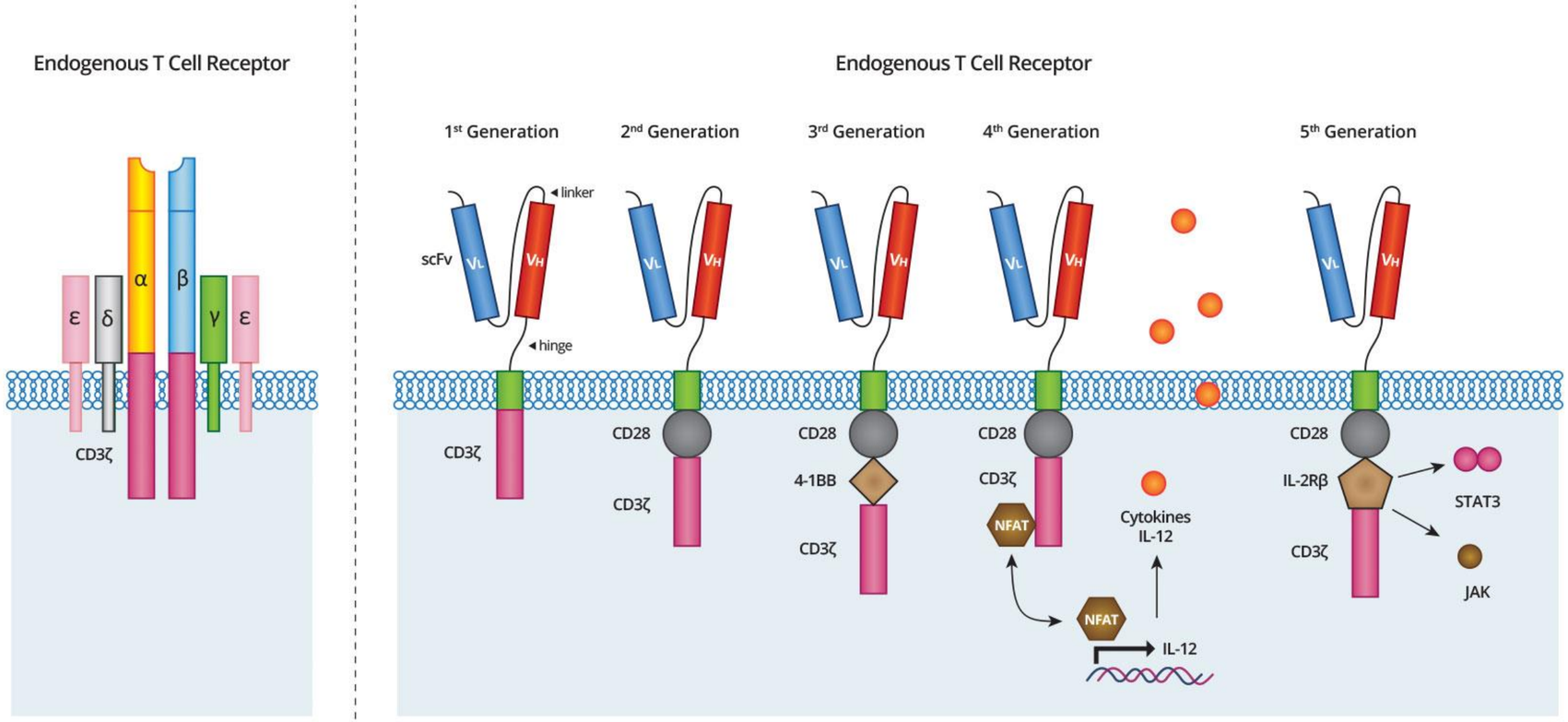


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J. Zhang & L. WangTechnol Cancer Res Treat, 2019

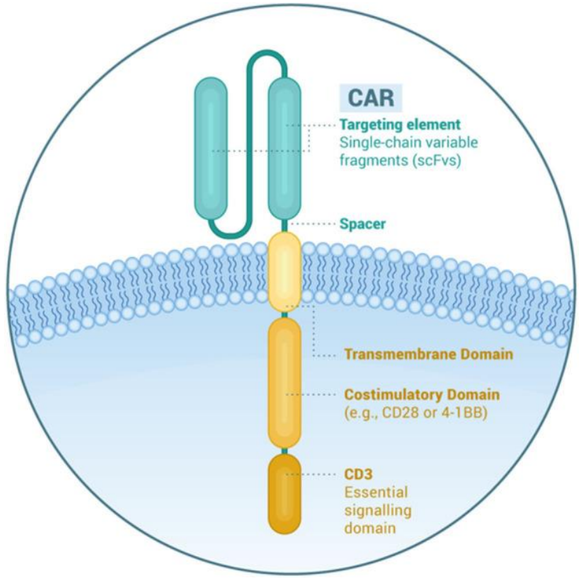
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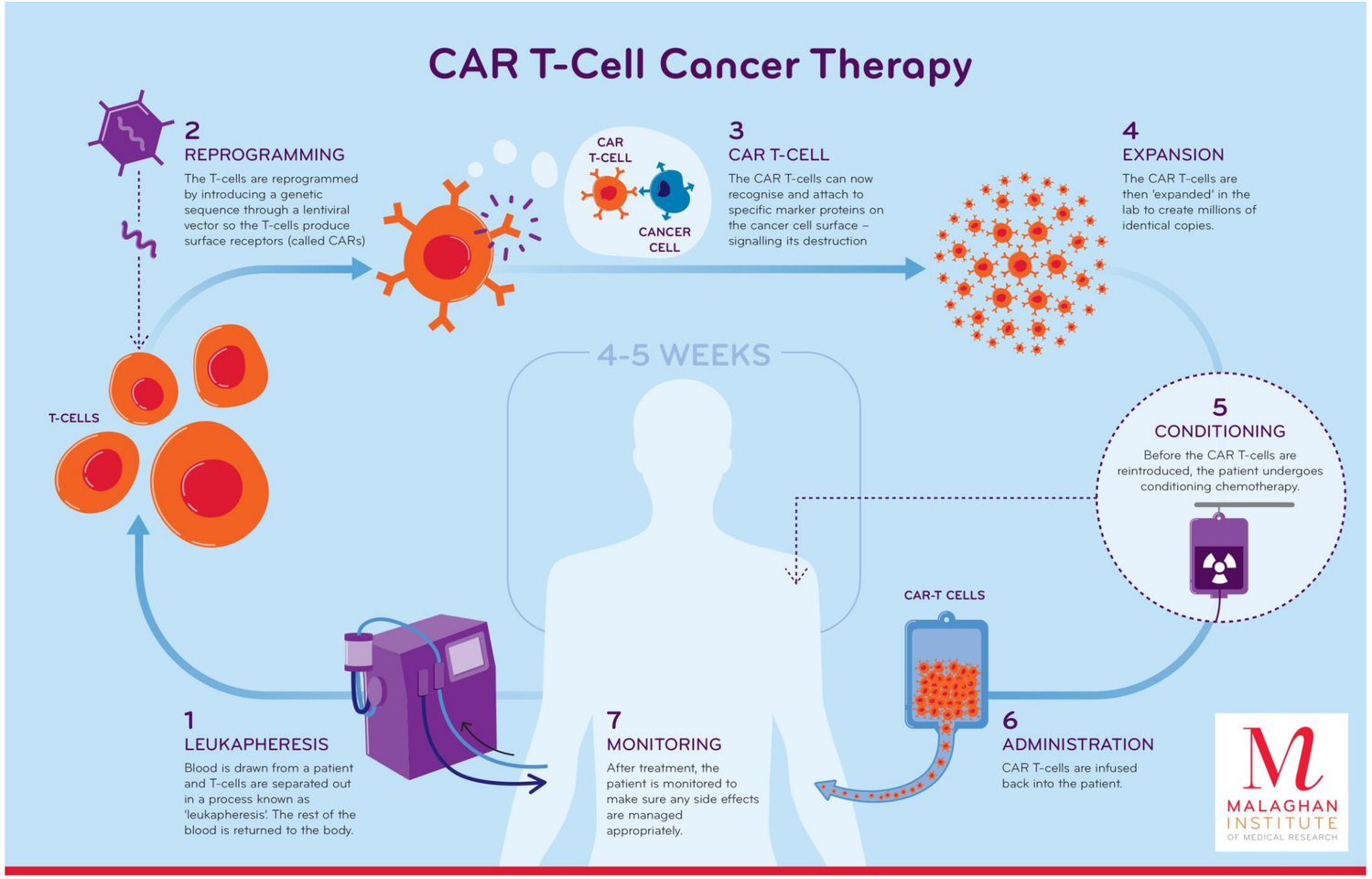
– CAR



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CAR T-CEL THERAPIE

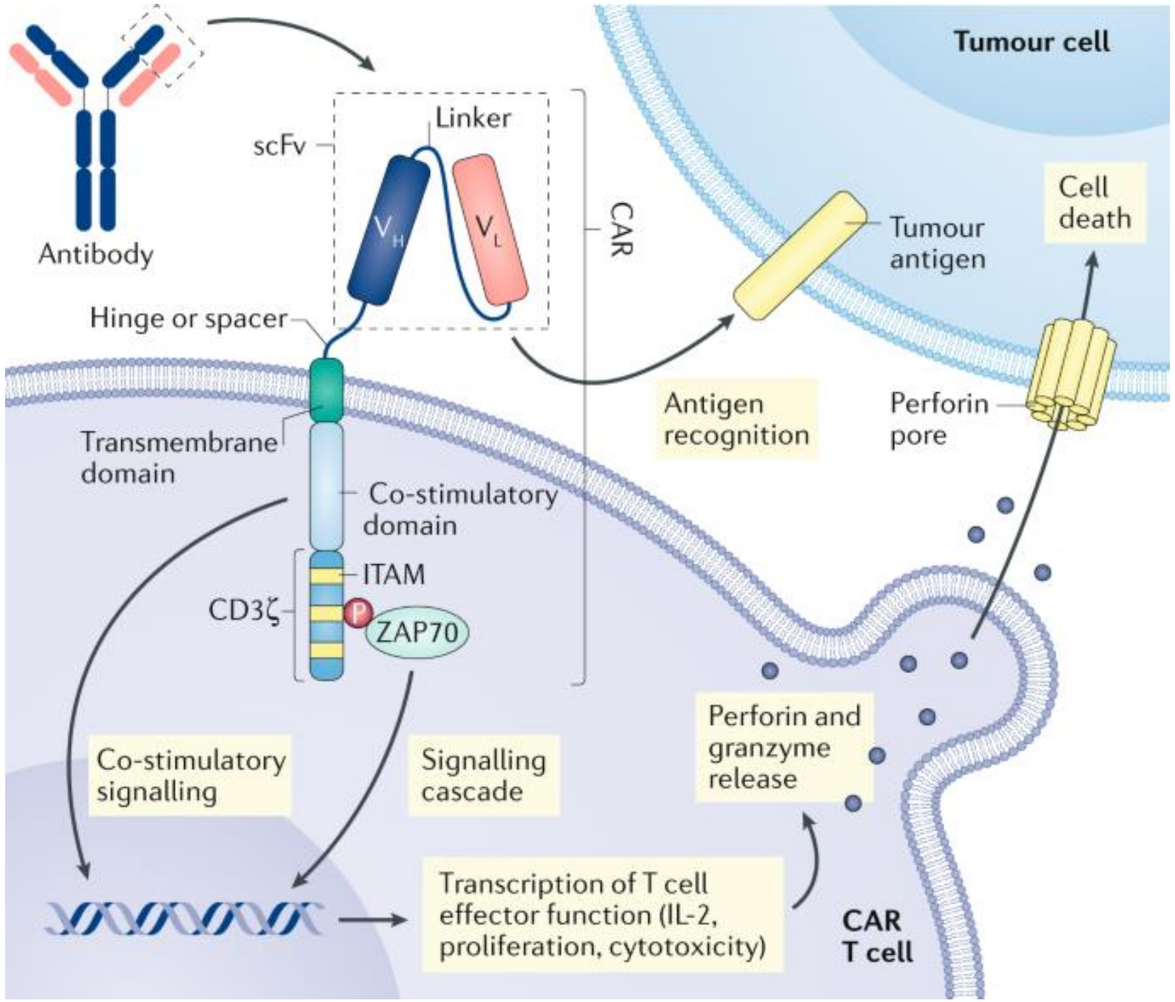


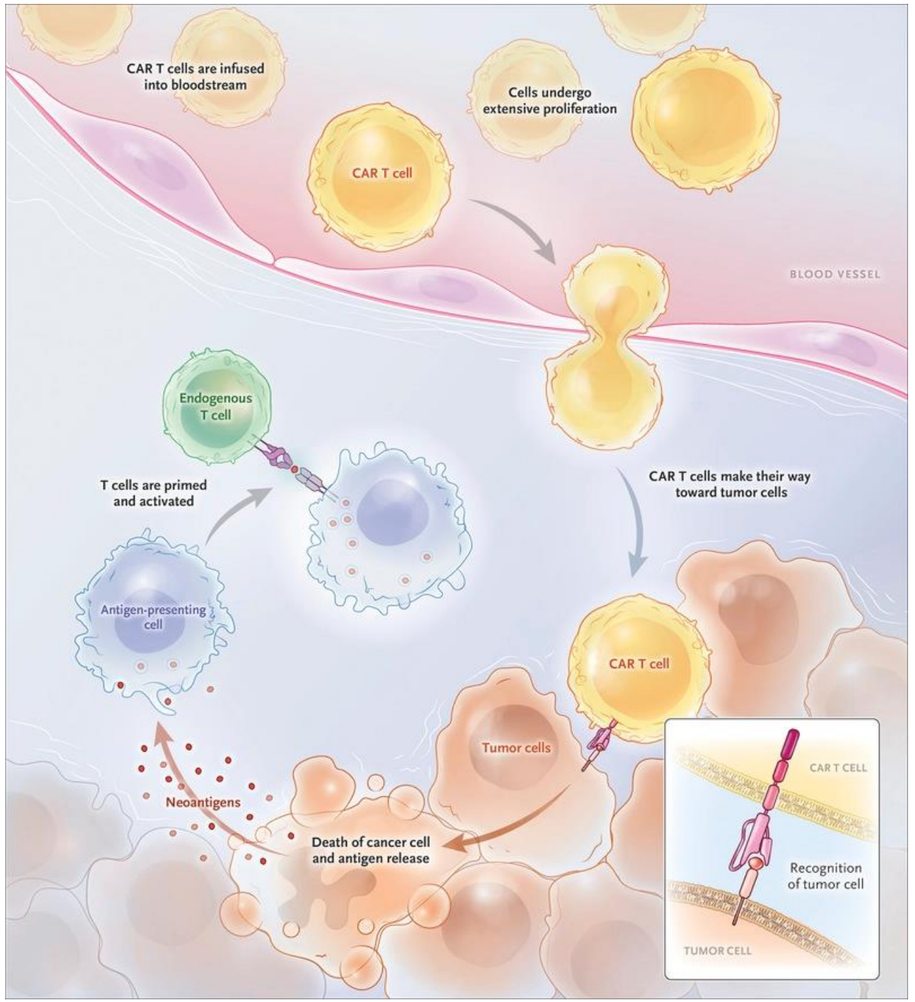


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LG Rodríguez-Lobato, Front Oncol, 2020

CAR T-CEL THERAPIE





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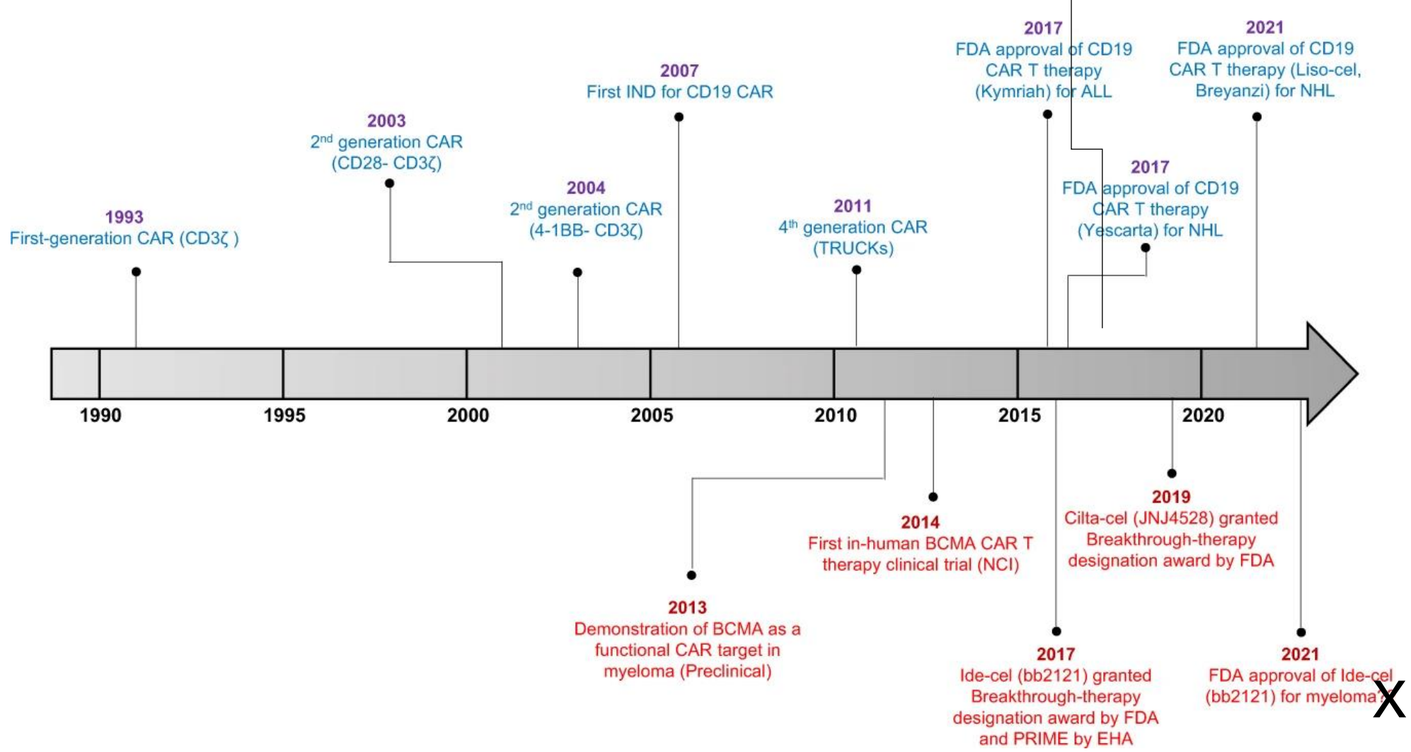
RC Larson and MV Maus, Nature Rev Cancer, 2021 131

CAR T-CEL THERAPIE

6/2019
RIZIV/INAMI (B)
Kymriah

4/2021
RIZIV/INAMI (B)
Yescarta

12/2022
RIZIV/INAMI (B)
Tecartus



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PJ Teoh and WJ Chng, Blood Cancer Journal, 2021

CAR T-CEL THERAPIE

Emily









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CAR T-CEL THERAPIE

Emily





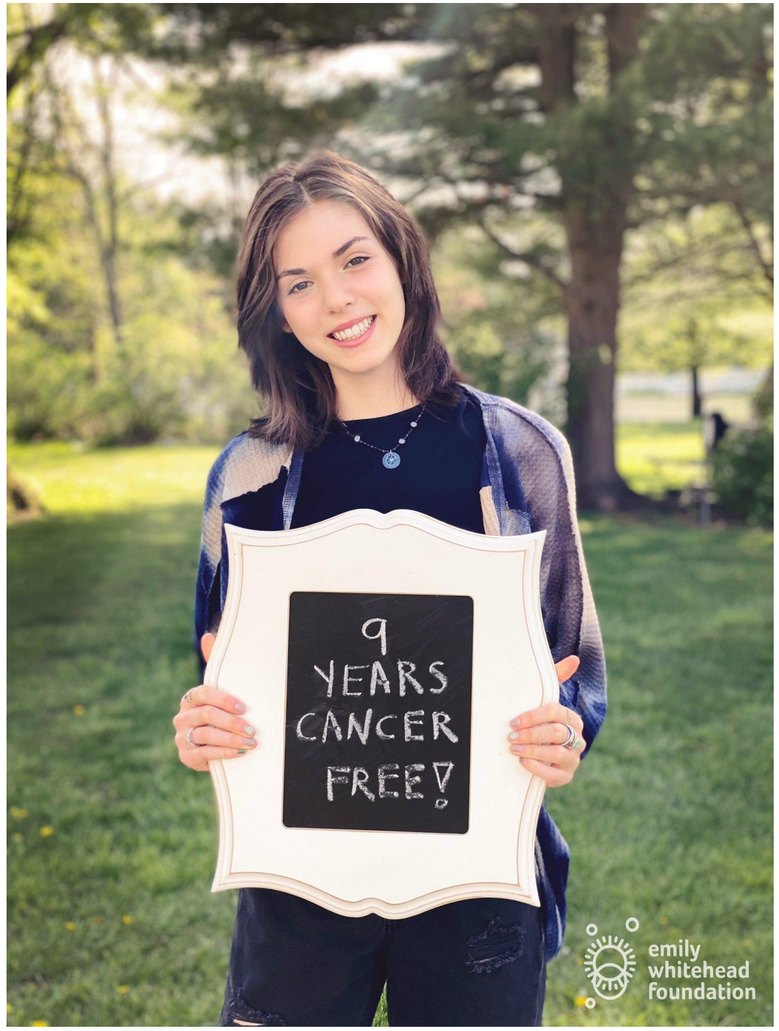




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CAR T-CEL THERAPIE

Emily







CAR T-CEL THERAPIE

- **Indicaties**
  - B cel maligniteiten (CD19, CD20, CD22)
  - Multipel myeloom (BCMA, CD138, CD38, CD56, LeY)
  - AML (CD33, 123, LeY, NKG2D liganden)
  - Hodgkin lymfoom, T cel lymfoom (CD30)
  - Vaste tumoren
    - Refractair neuroblastoma
    - Andere: sarcoma, glioblastoma, mesothelioma, carcinonomas (ovarium, colon, pancreas, nier), …

CAR T-CEL THERAPIE

– Complex proces



HCPs prescribe CAR-T therapy after all other treatments have failed	Patient has white blood cells collected at an Apheresis center	Patient's sample is cryogenically shipped to a manufacturing facility	T-Cells are separated, reengineered and grown to produce drug	HCP schedules patient for infusion once drug shipment is confirmed	CAR-T drug is cryogenically shipped to HCP	Patient is infused with CAR-T drug that was made with their own cells

Demand forecasting & Scheduling

Network Design & Capacity Planning
Process engineering & Manufacturing Technology

Service operations
Billing/Invoicing

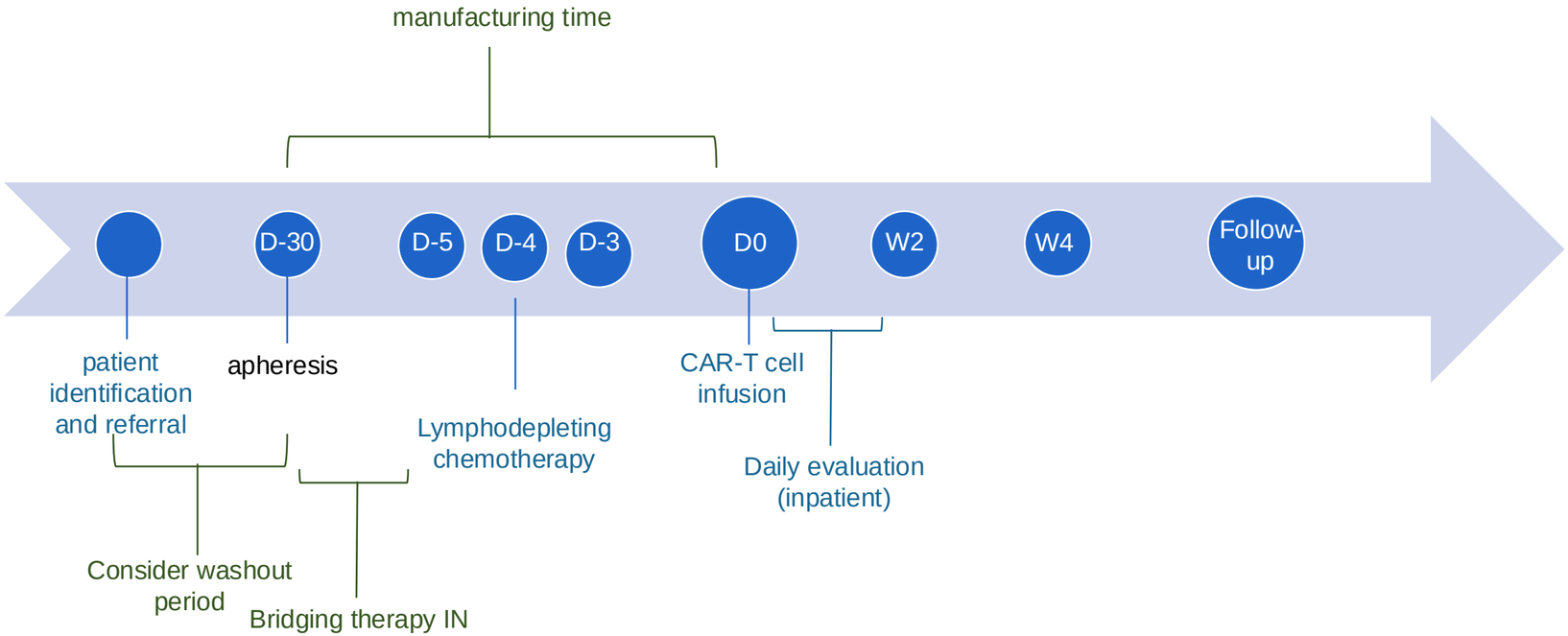
End-End Tracking, Visibility, and Coordination

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Shankar Suryanarayanan et al, Pharmexec.com

CAR T-CEL THERAPIE

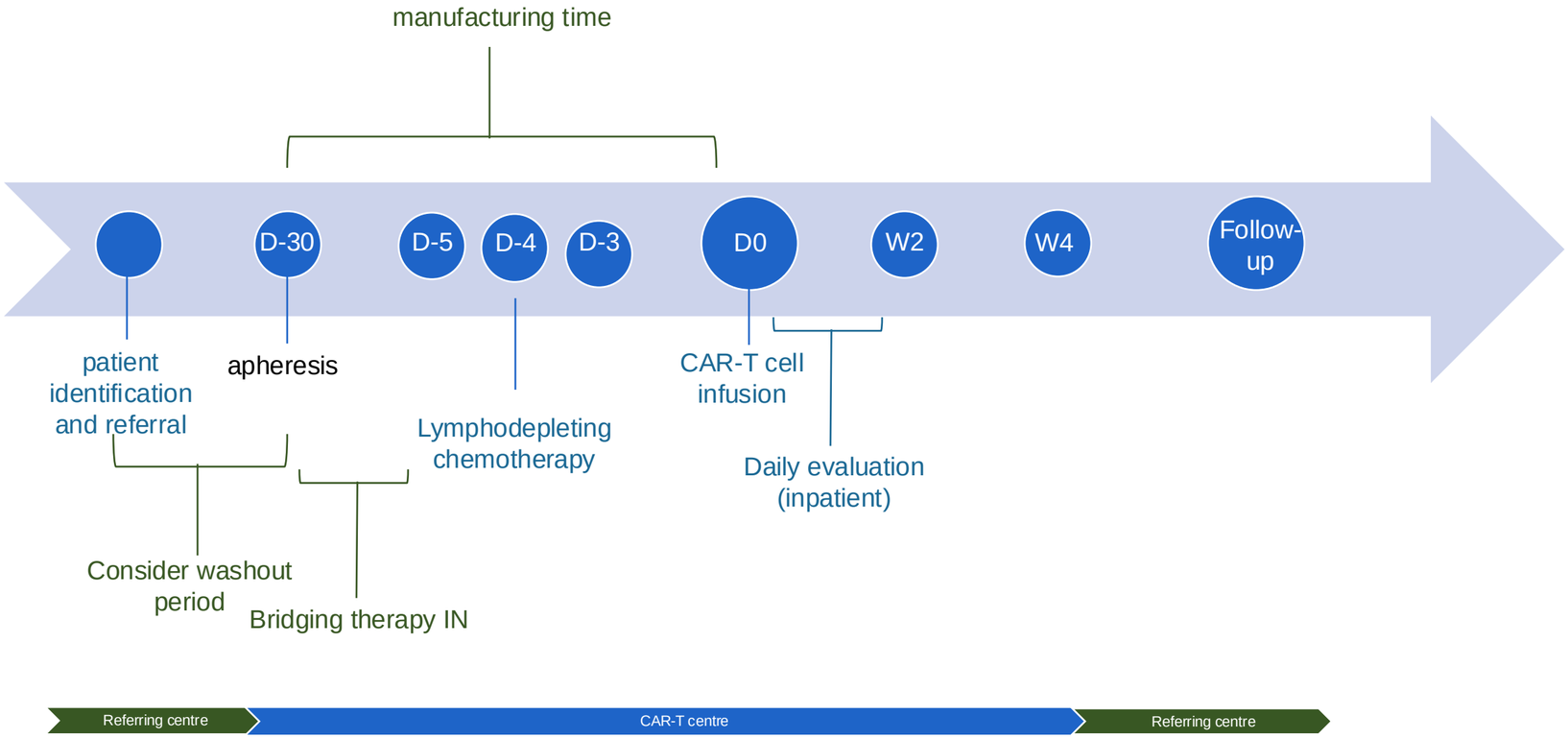
– Complex proces



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CAR T-CEL THERAPIE

– Complex proces



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CAR T-CEL THERAPIE

– Beschikbare produkten, EMA / FDA goedgekeurd

Name	abbreviation	commercial	target	costimulation	indication
Tisagenlecleucel	tisa-cel	Kymriah	CD19	4-1BB	B-ALL, DLBCL
Axicabtagene ciloleucel	axi-cel	Yescarta	CD19	CD28	DLBCL, PMBL
Lisocabtagene maraleucel	liso-cel	Breyanzi	CD19	4-1BB	DLBCL
Brexucabtagene autoleucel	brexu-cel	Tecartus	CD19	CD28	MCL
Idecabtagene vicleucel	ide-cel	Abecma	BCMA	4-1BB	Multiple myeloma
Ciltacabtagene autoleucel	cilta-cel	Carvykti	BCMA	4-1BB	Multiple myeloma

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Courtesy of K Polgarova, GUH Prague

EERSTE CAR-T THERAPIE TERUGBETAALD IN BELGIE

Hoop voor 140 kankerpatiënten: peperdure therapie wordt terugbetaald

23/05/2019 om 03:00 door Nina Bernaerts en Jonas Mayeur - Print - Corrigeer



(FOTO: TELEFACTS)

NIEUWS

Het Nieuwsblad, 23/05/2019

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CAR-T THERAPIE IN UZ GENT

- **Klinische studies**
  - CD19
  - NKG2D
  - BCMA

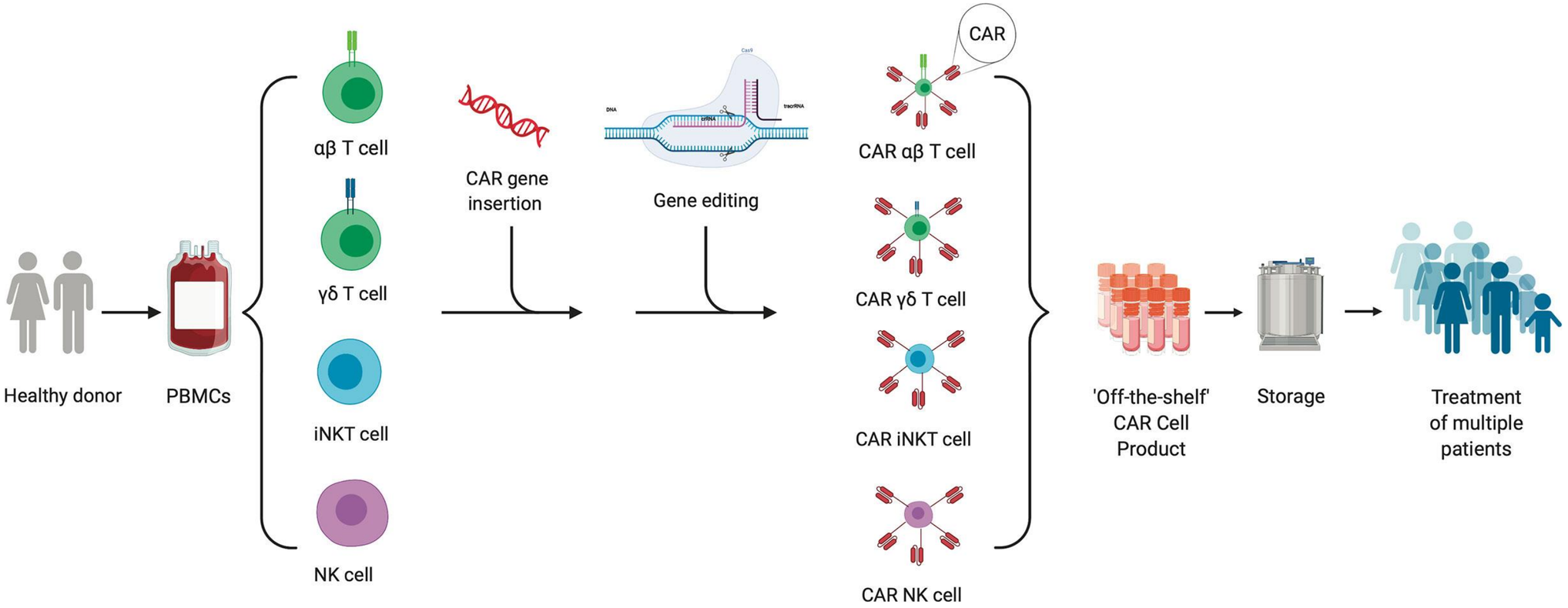
- **Commercieel**
  - Kymriah
  - Yescarta
  - Tecartus

  - Totaal februari 2025: >165 infusies

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CAR T: OPTIMALISATIE VAN PRODUKTIEPROCES

– Allo-CARs

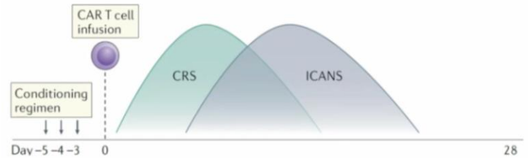


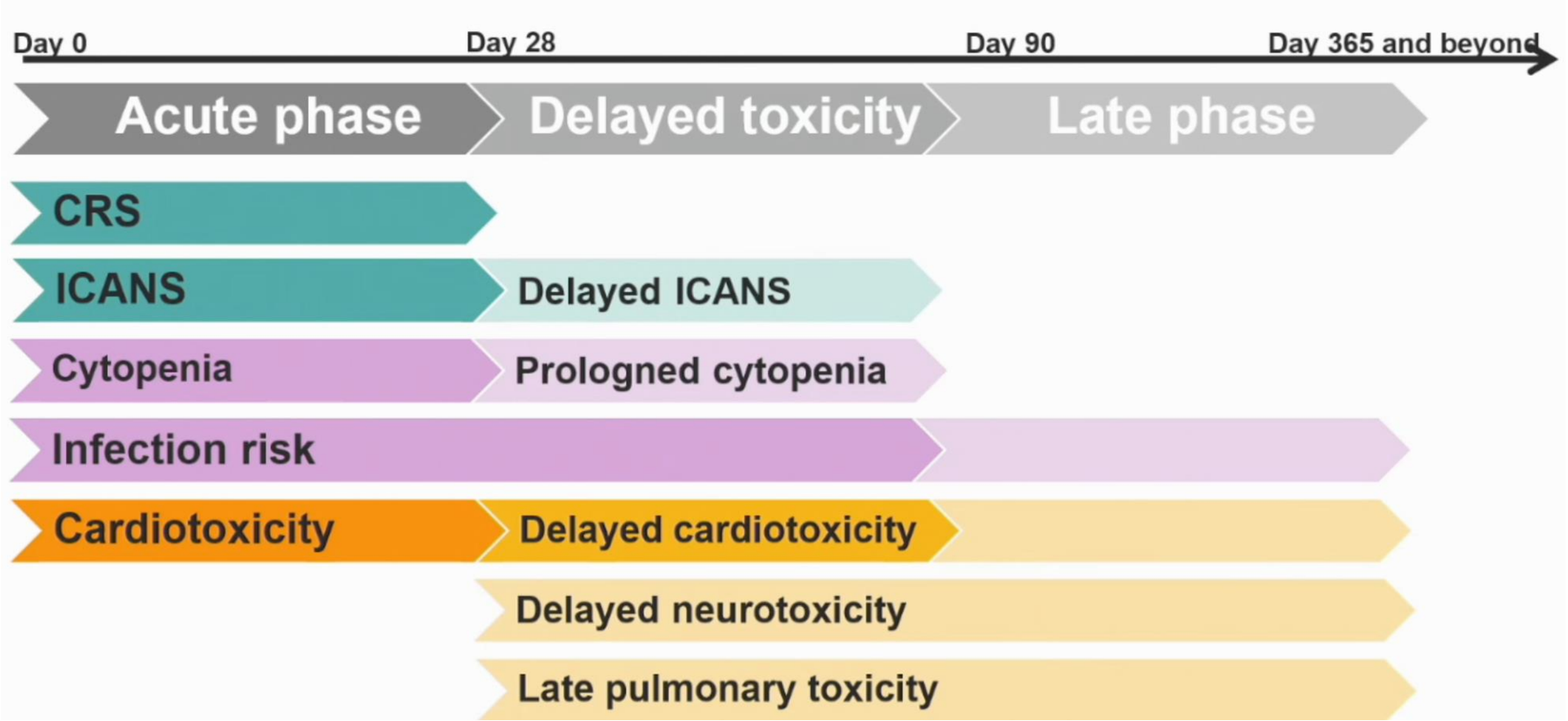
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K. Caldwell et al, Frontiers Immunol, 2021

CAR T: TOXICITEIT

– Complicaties





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Courtesy of K Polgarova, GUH Prague; P. Hayden et al, Ann Oncol, 2022

Klik op de flesjes om de verschillende vormen van immunotherapie te ontdekken.



checkpoint inhibitoren

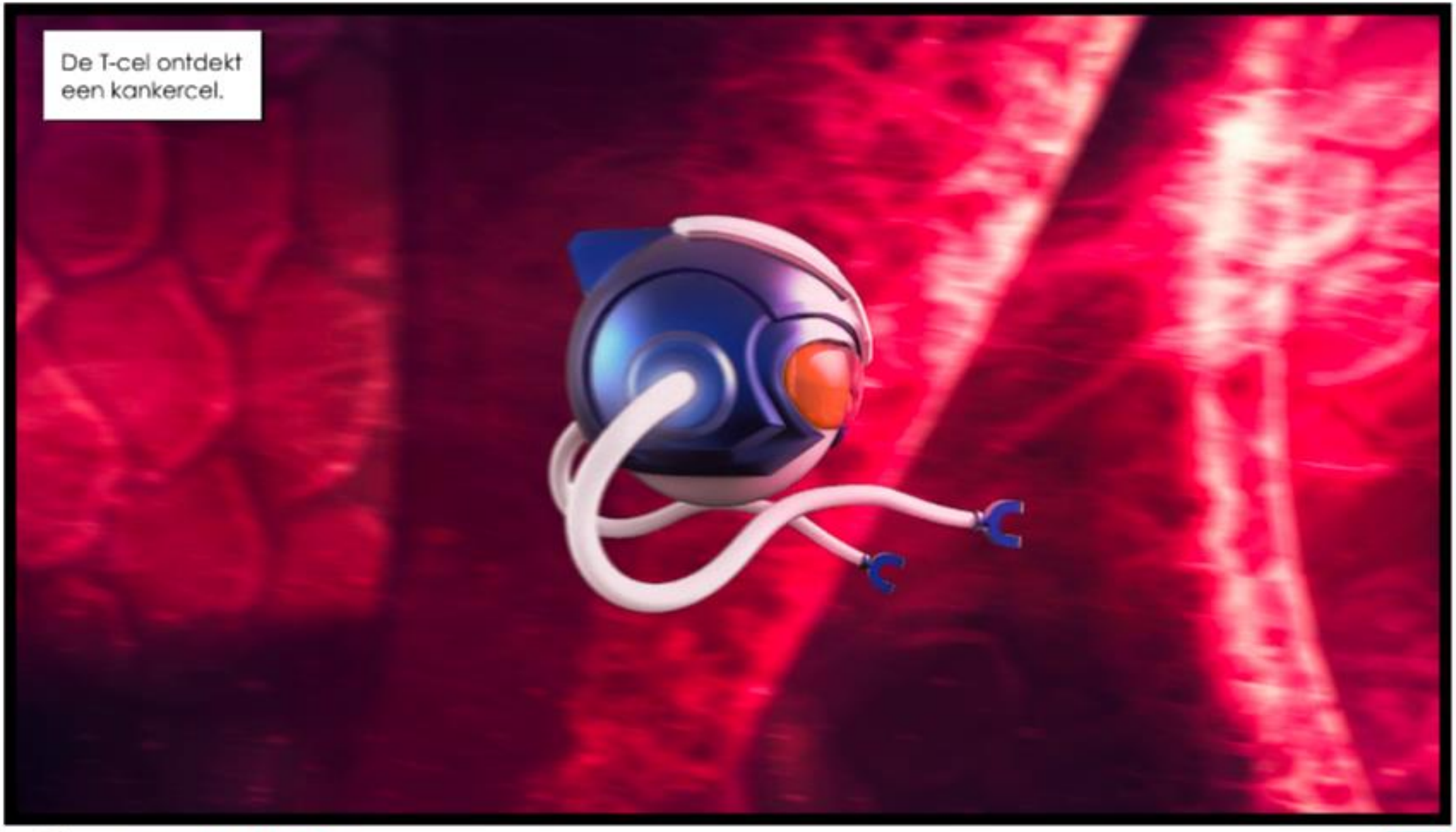


CAR T-cel therapie



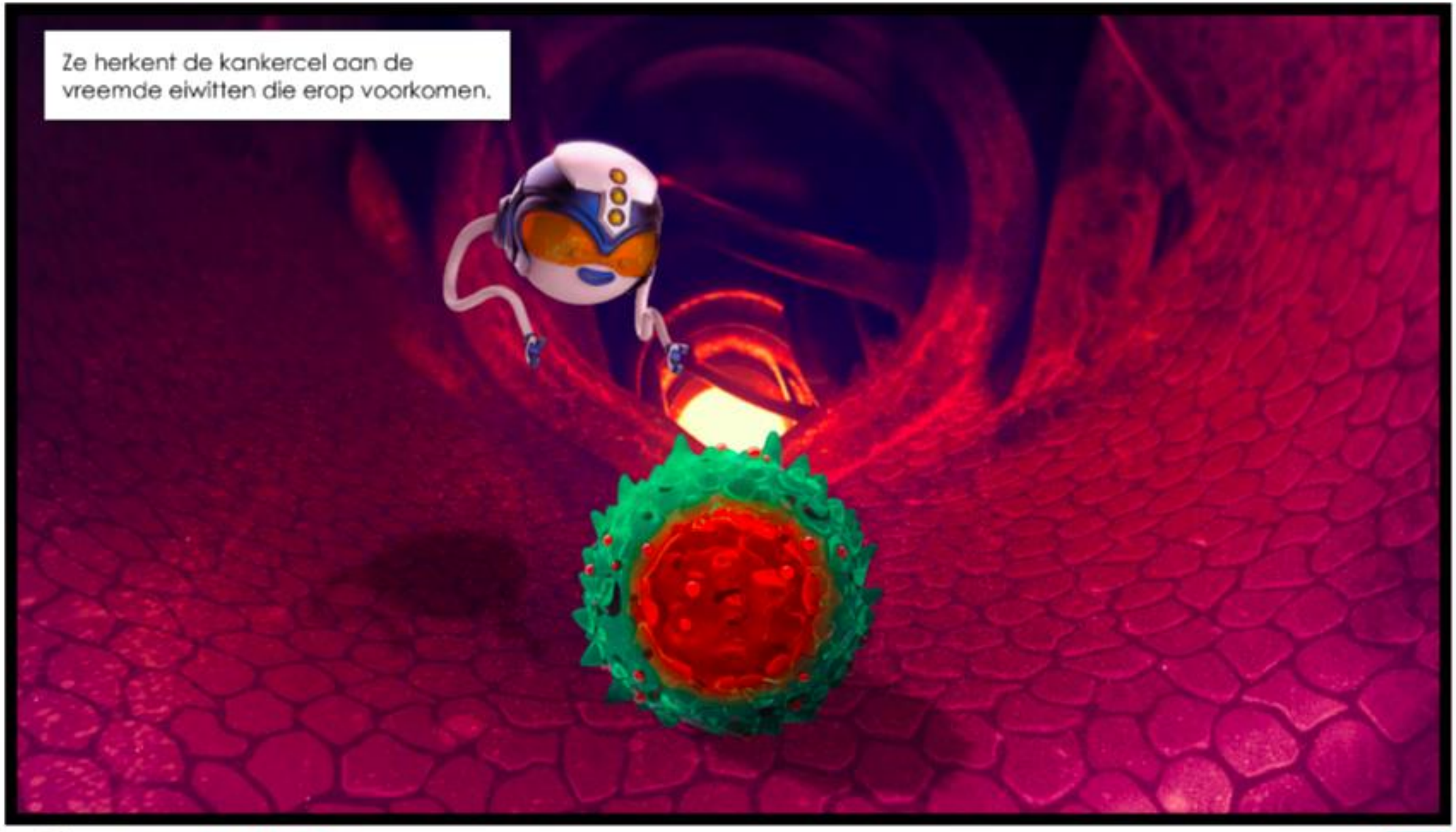
BiTes

TERUG NAAR HET BEGIN



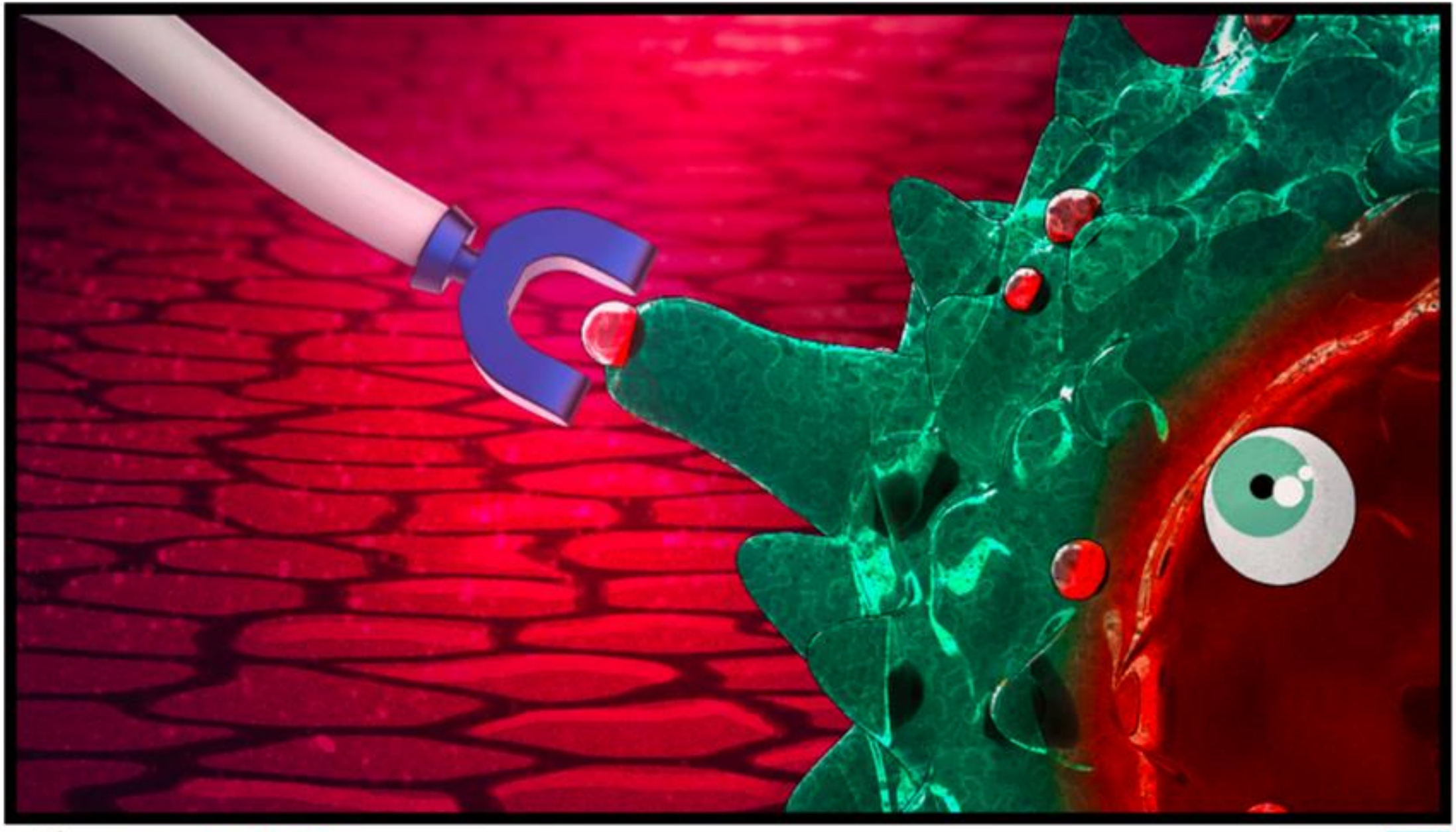
unity WebGL

immuno_web



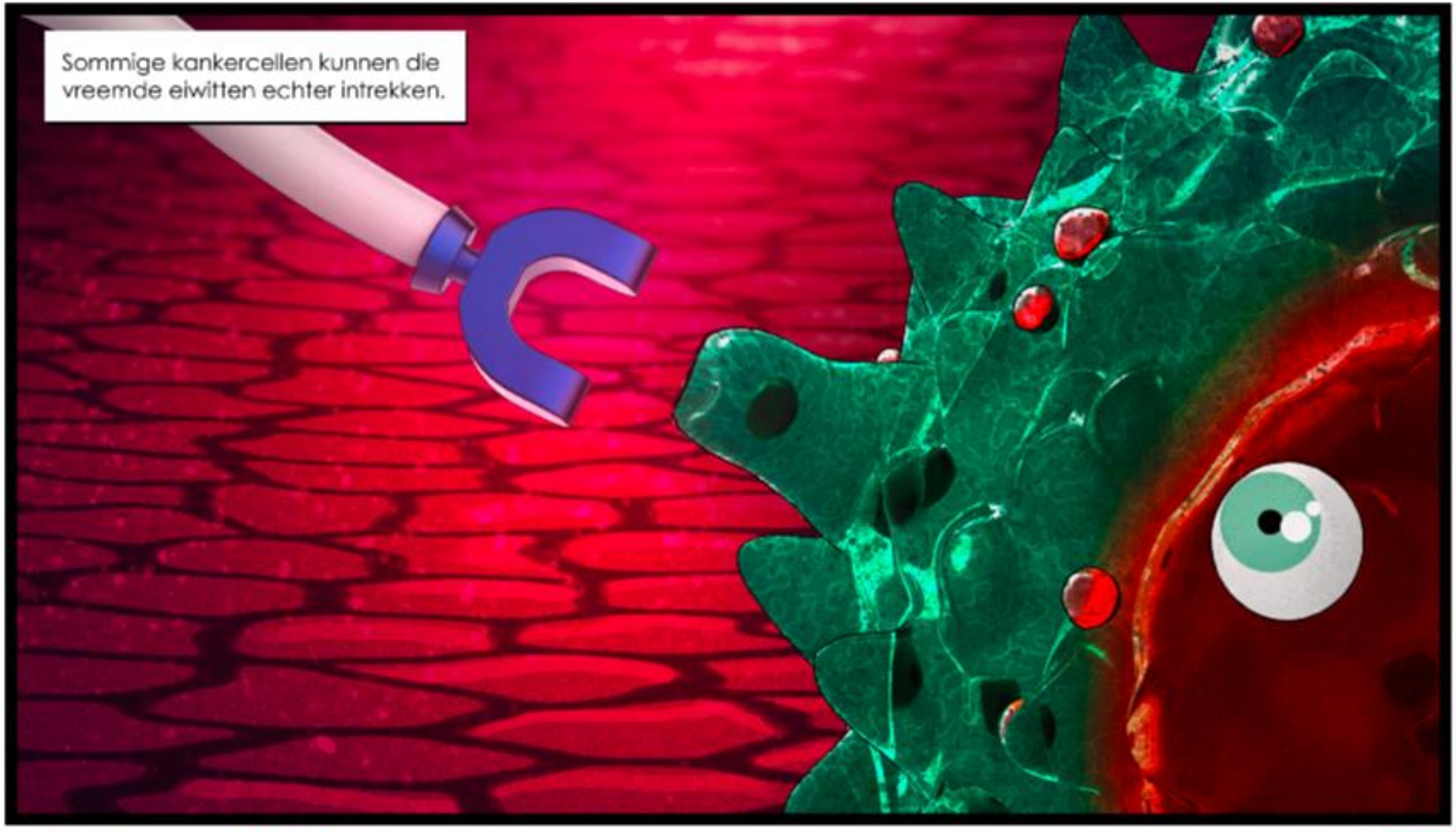
unity WebGL

immuno_web



unity WebGL

immuno_web



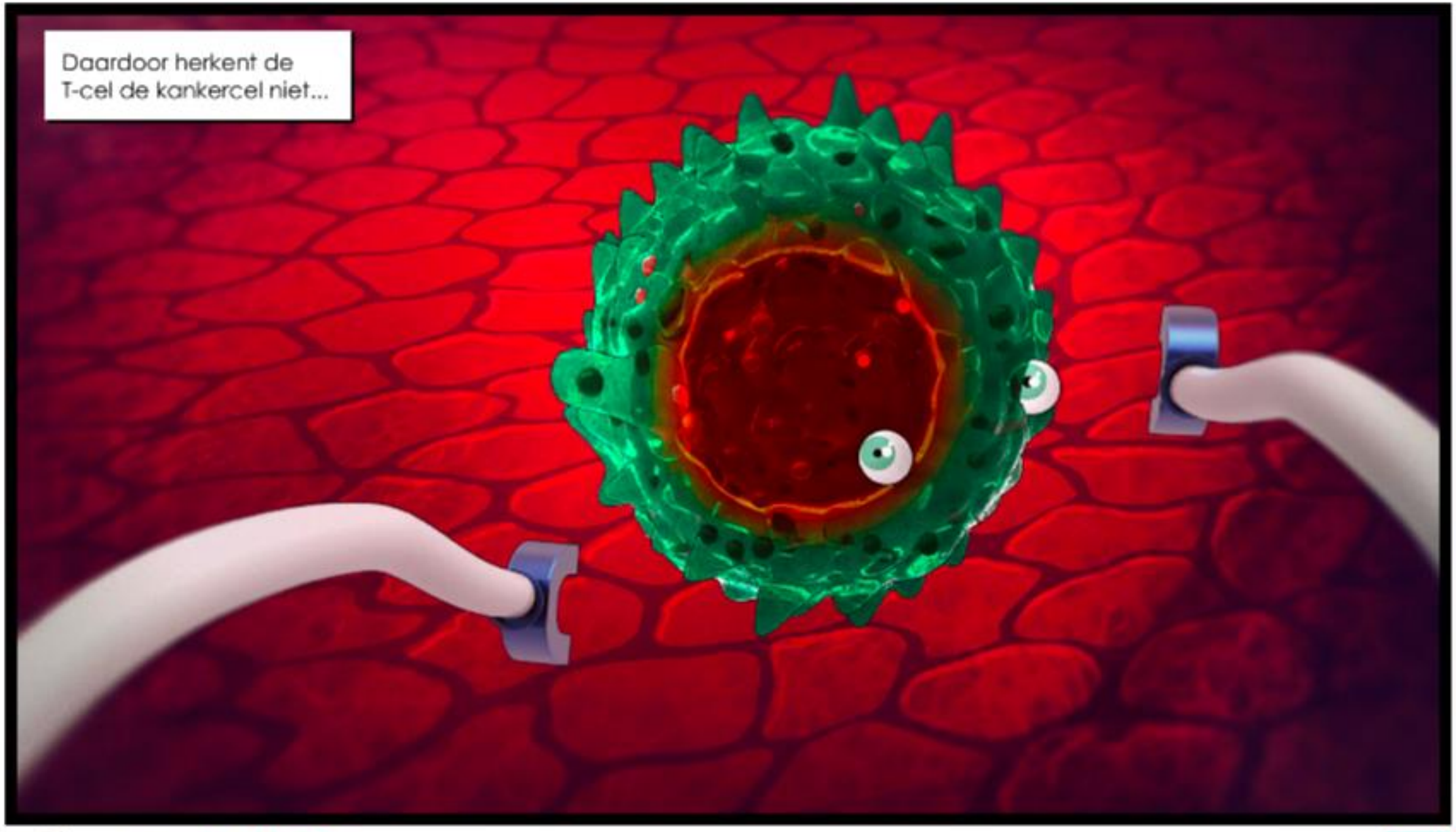
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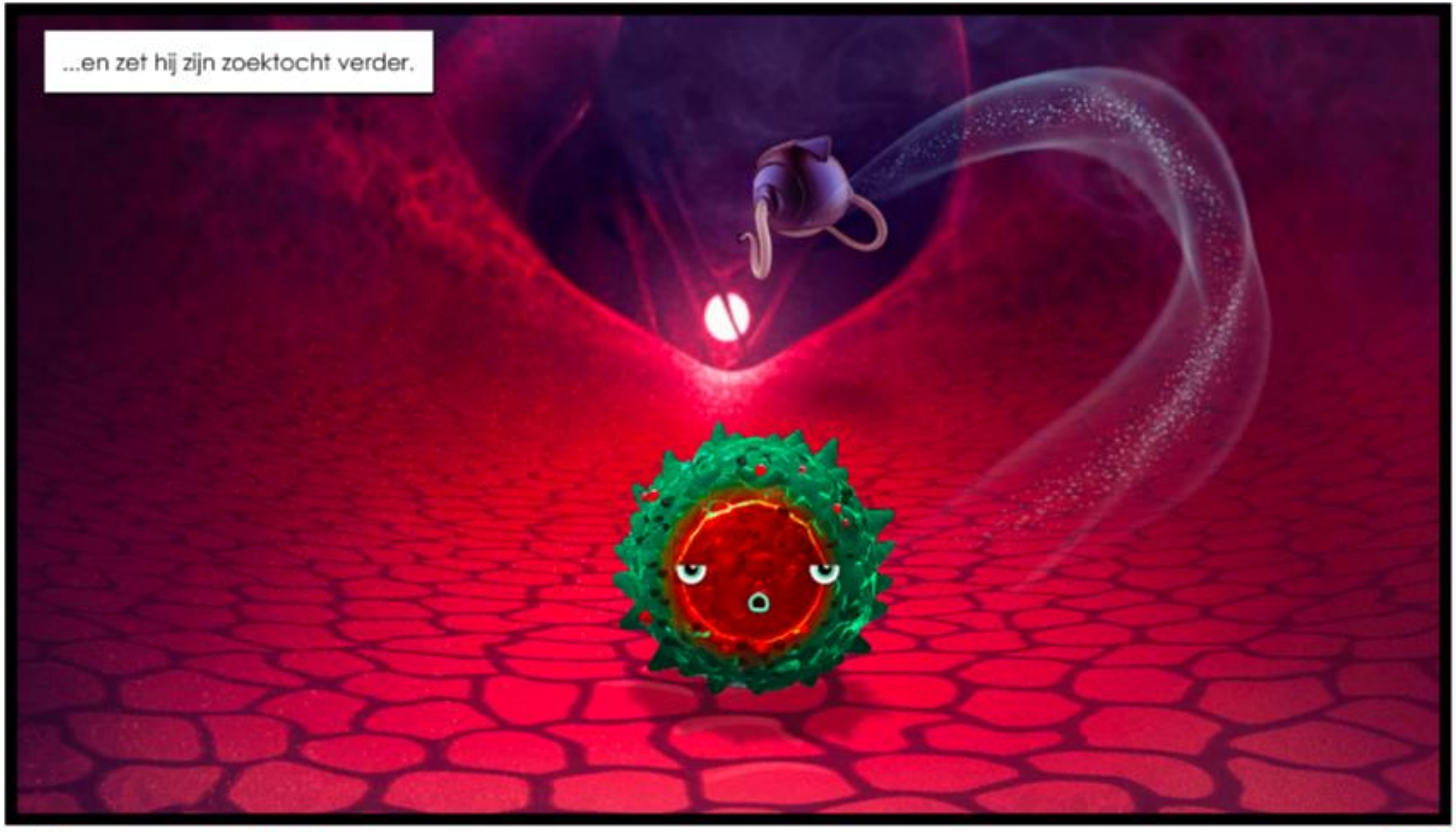
unity WebGL

immuno_web



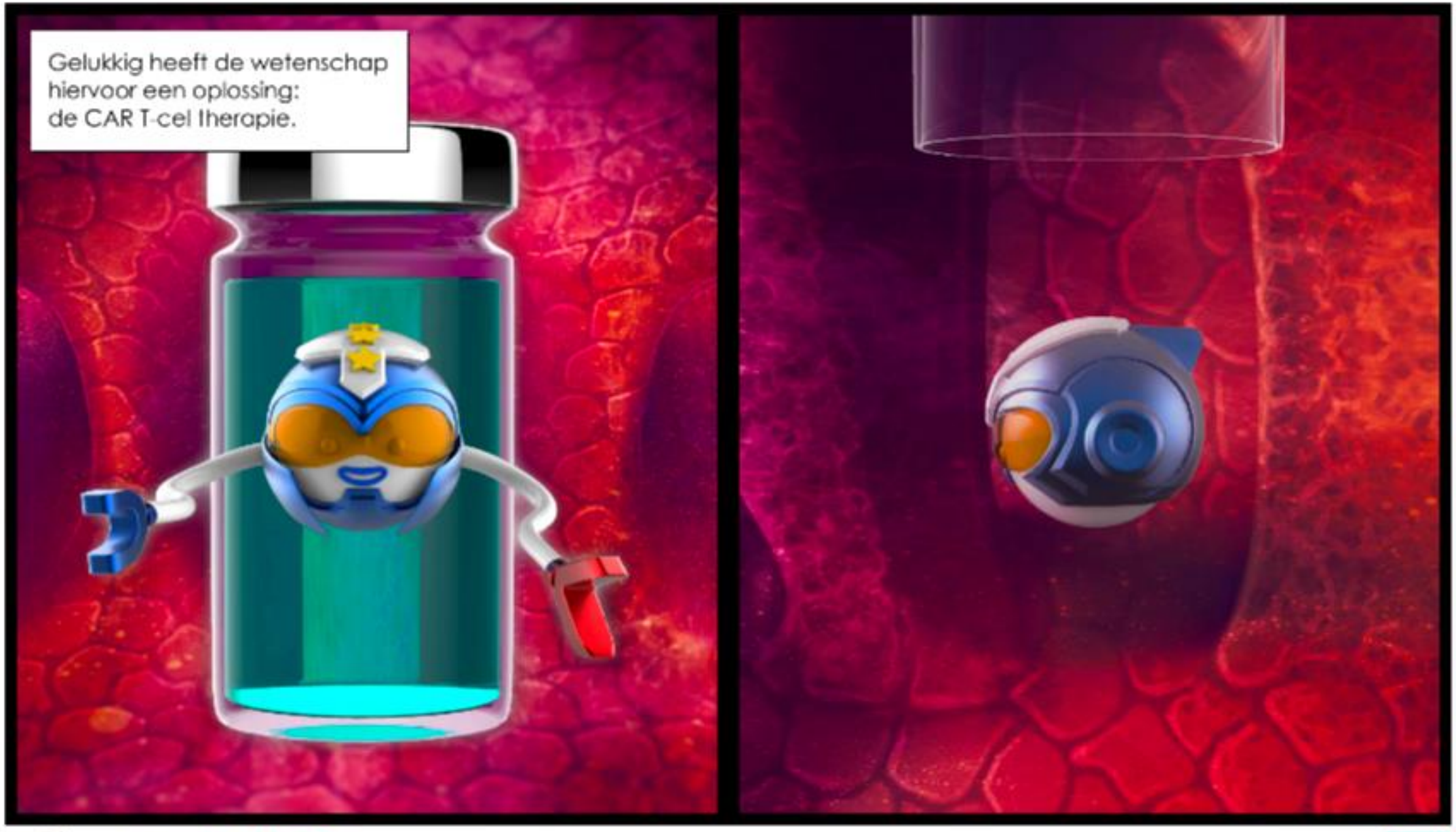
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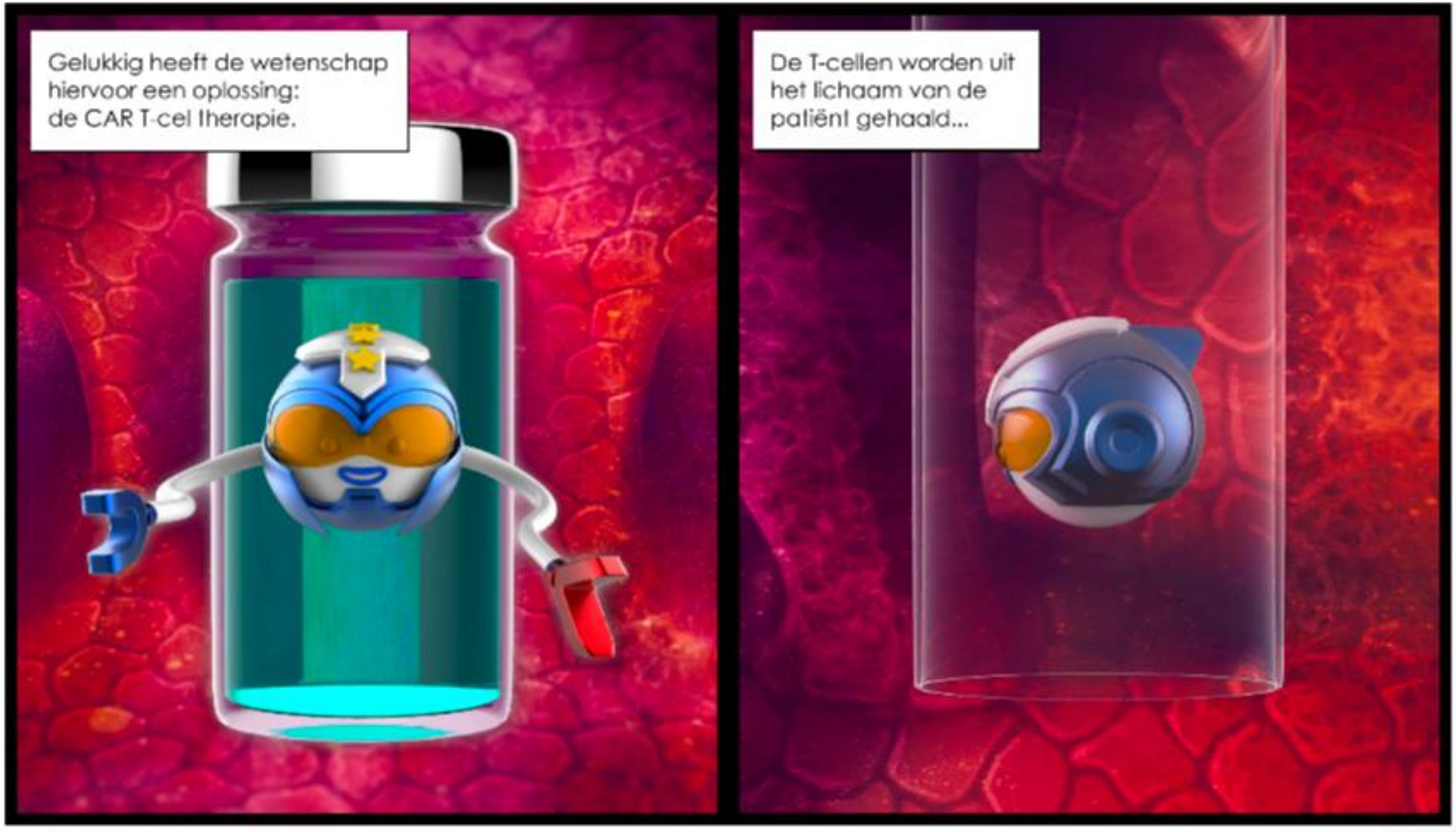
unity WebGL

immuno_web



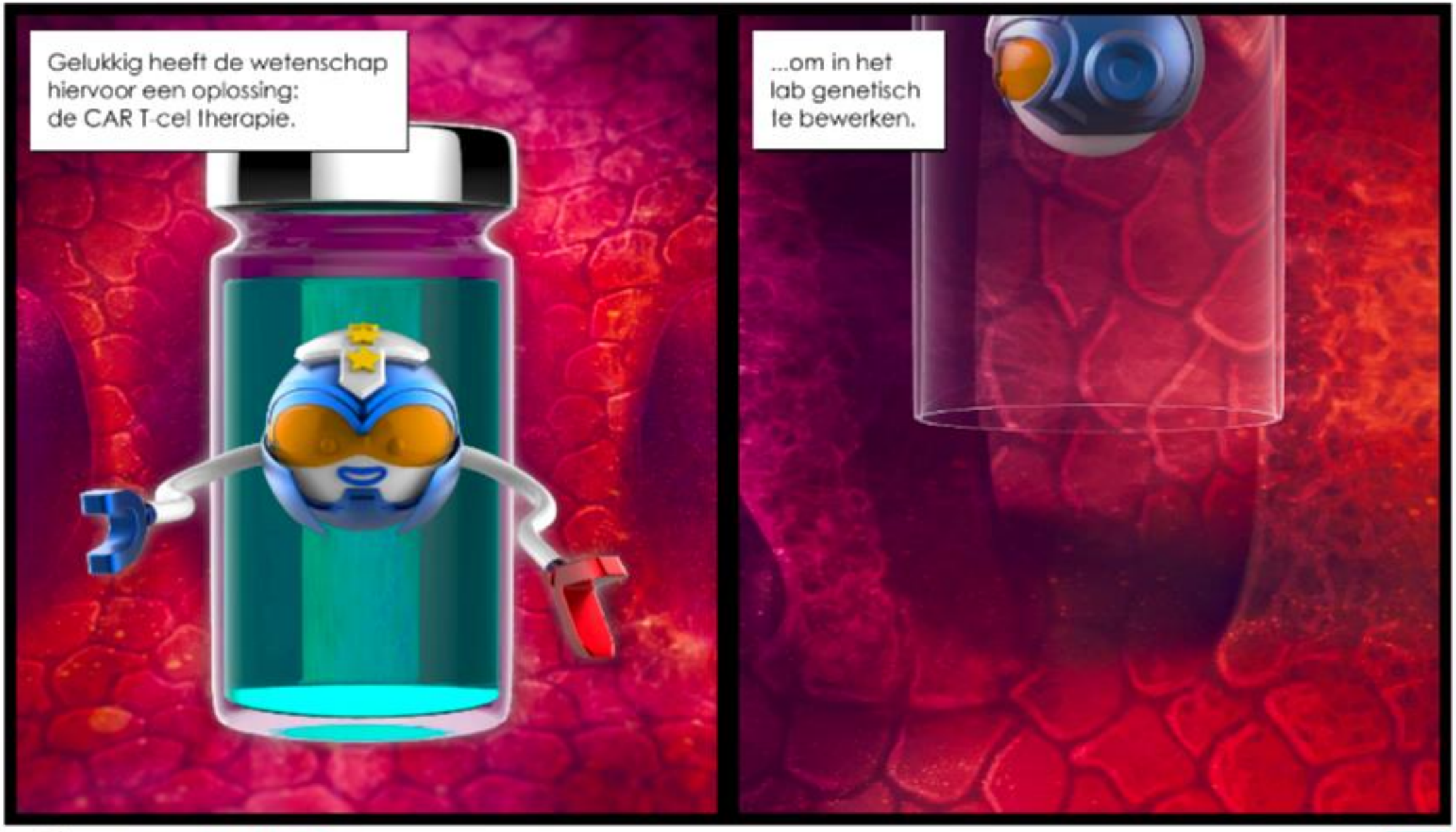
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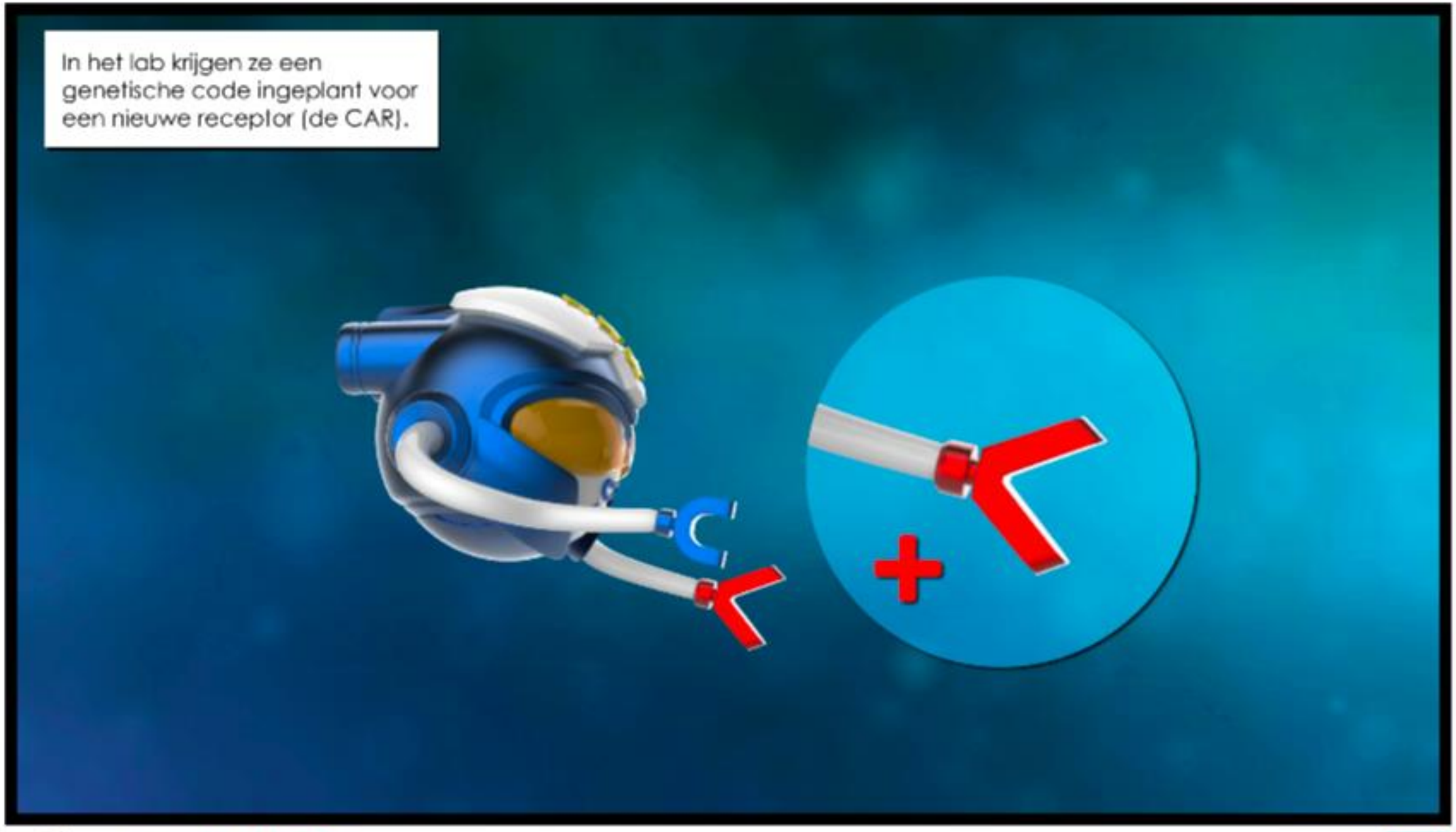
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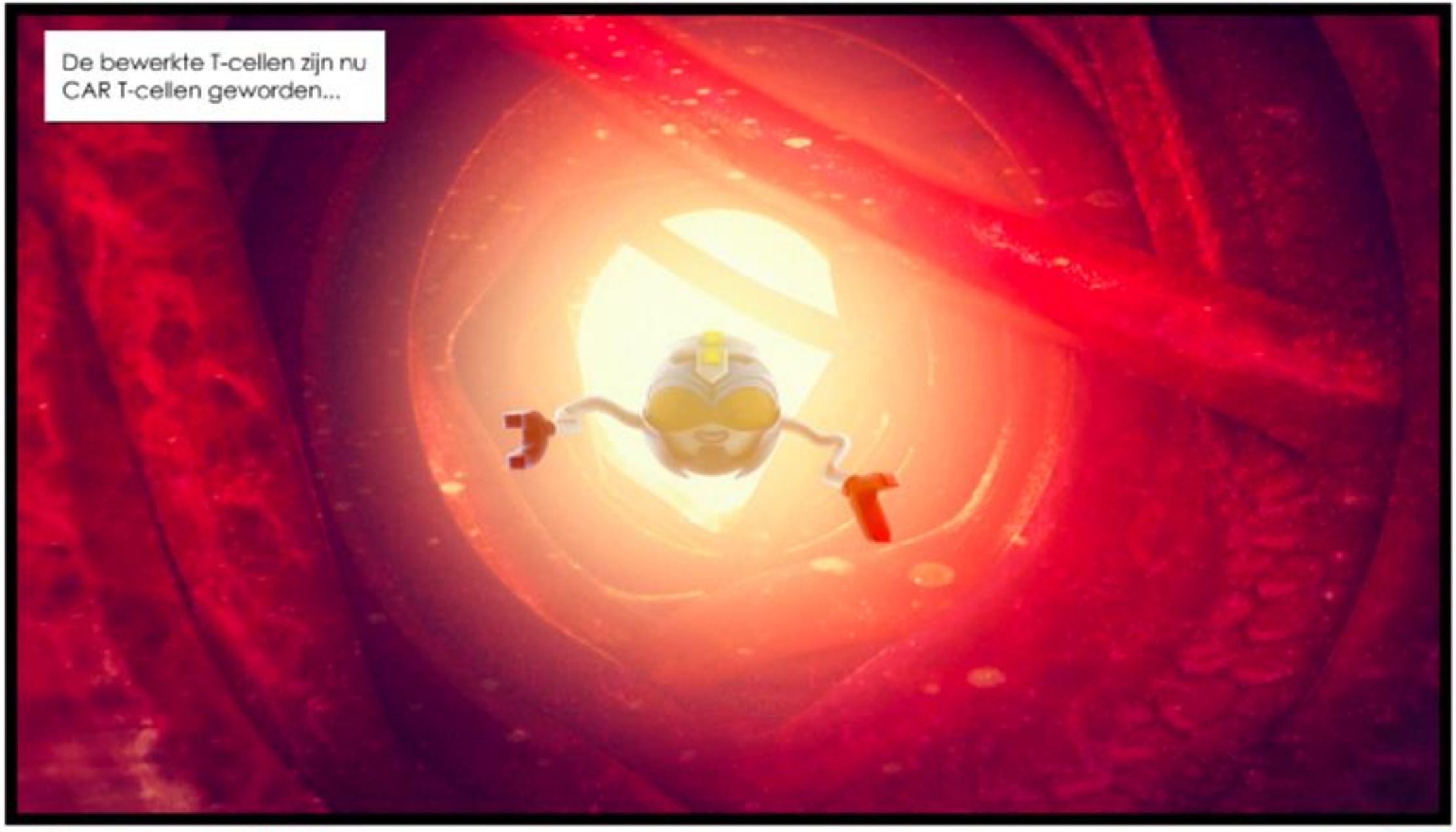
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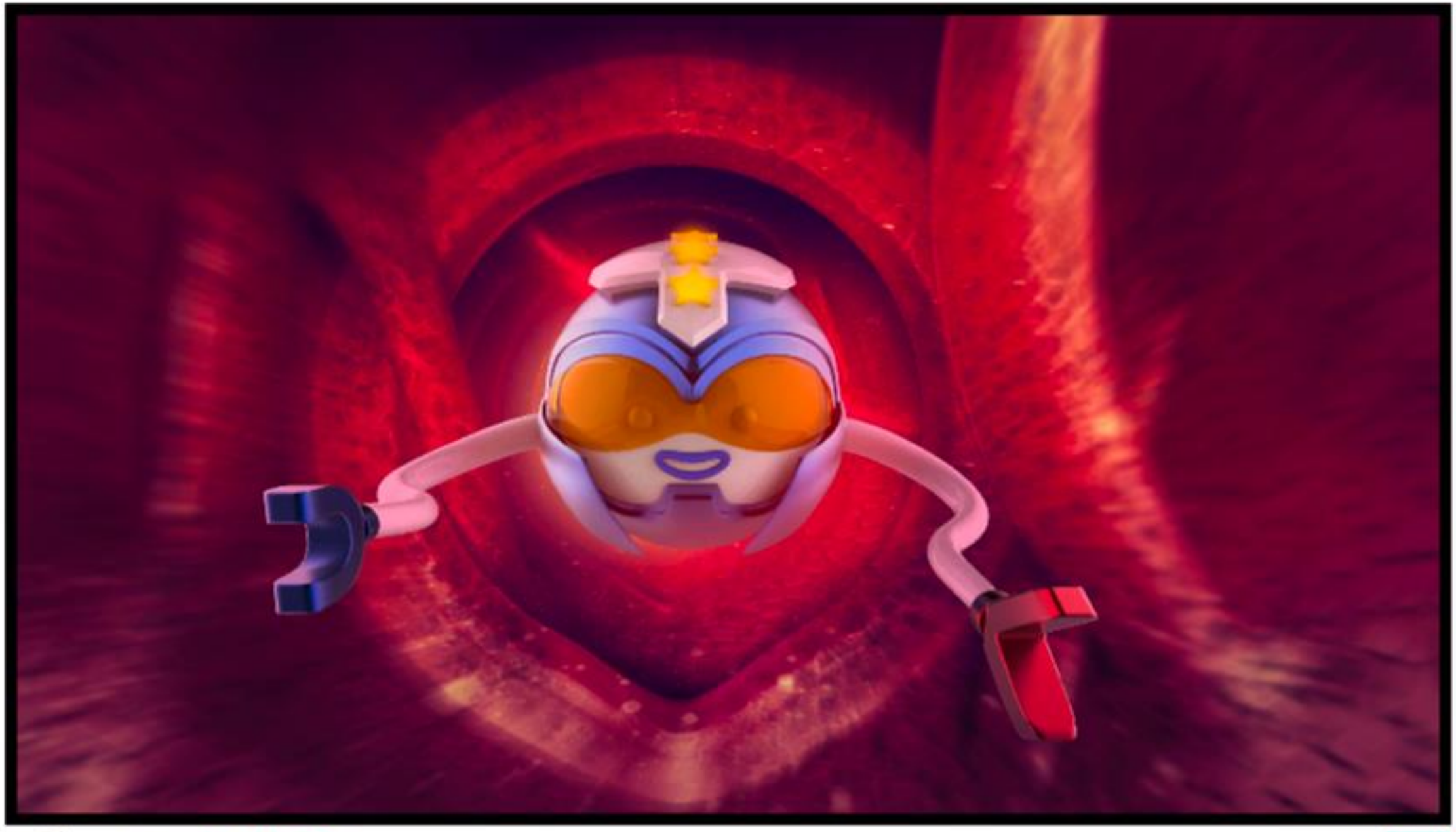
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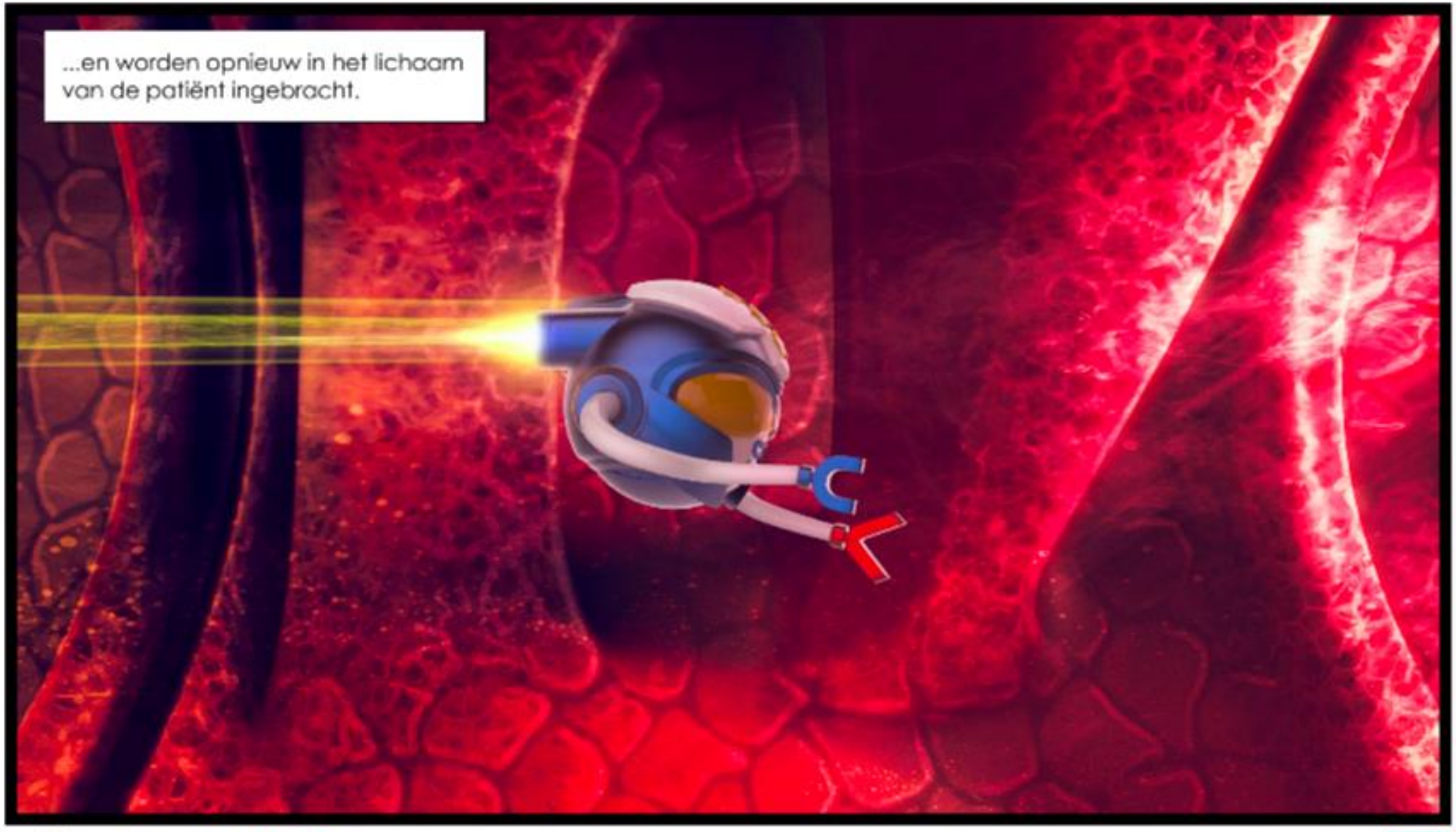
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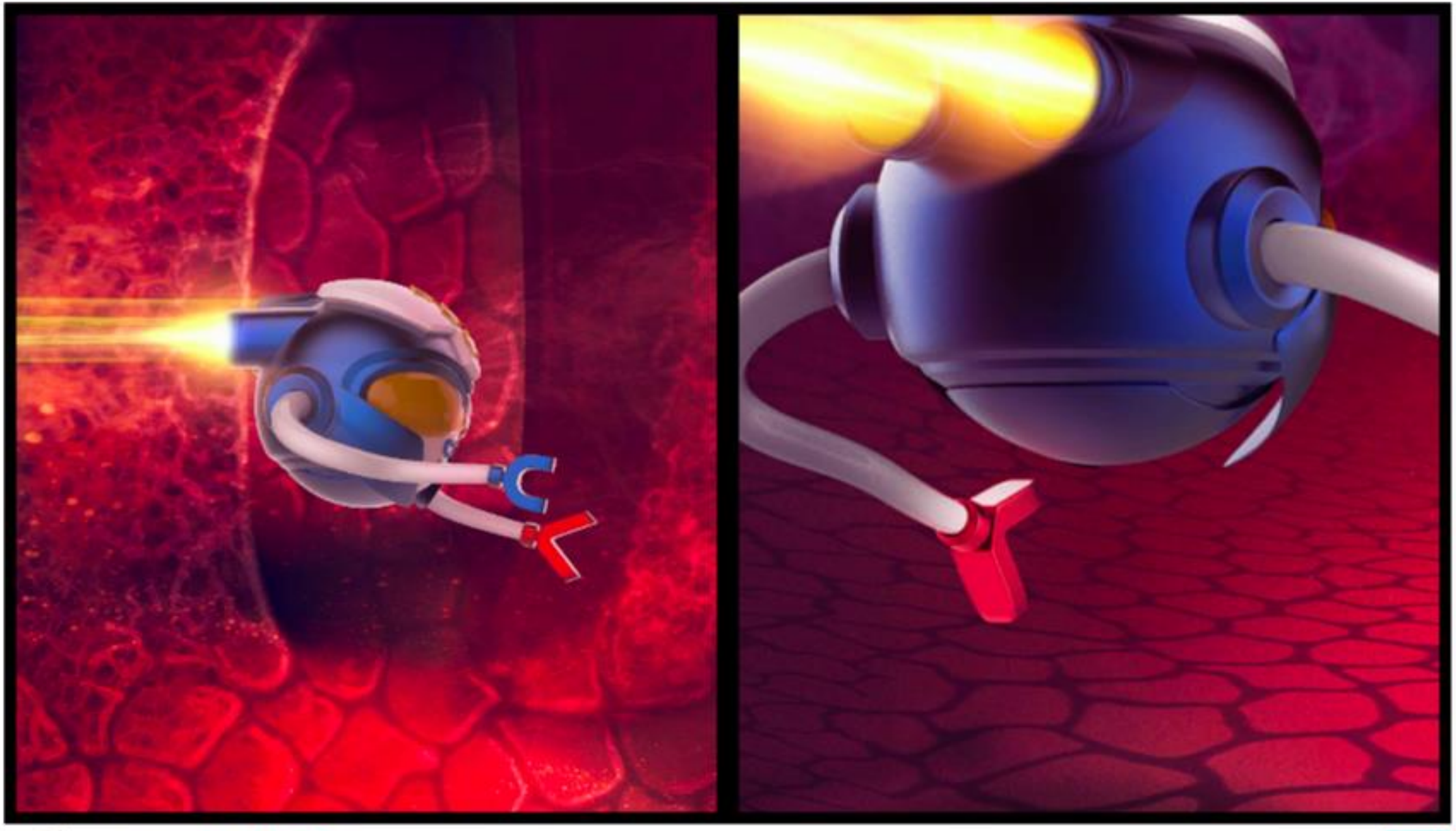
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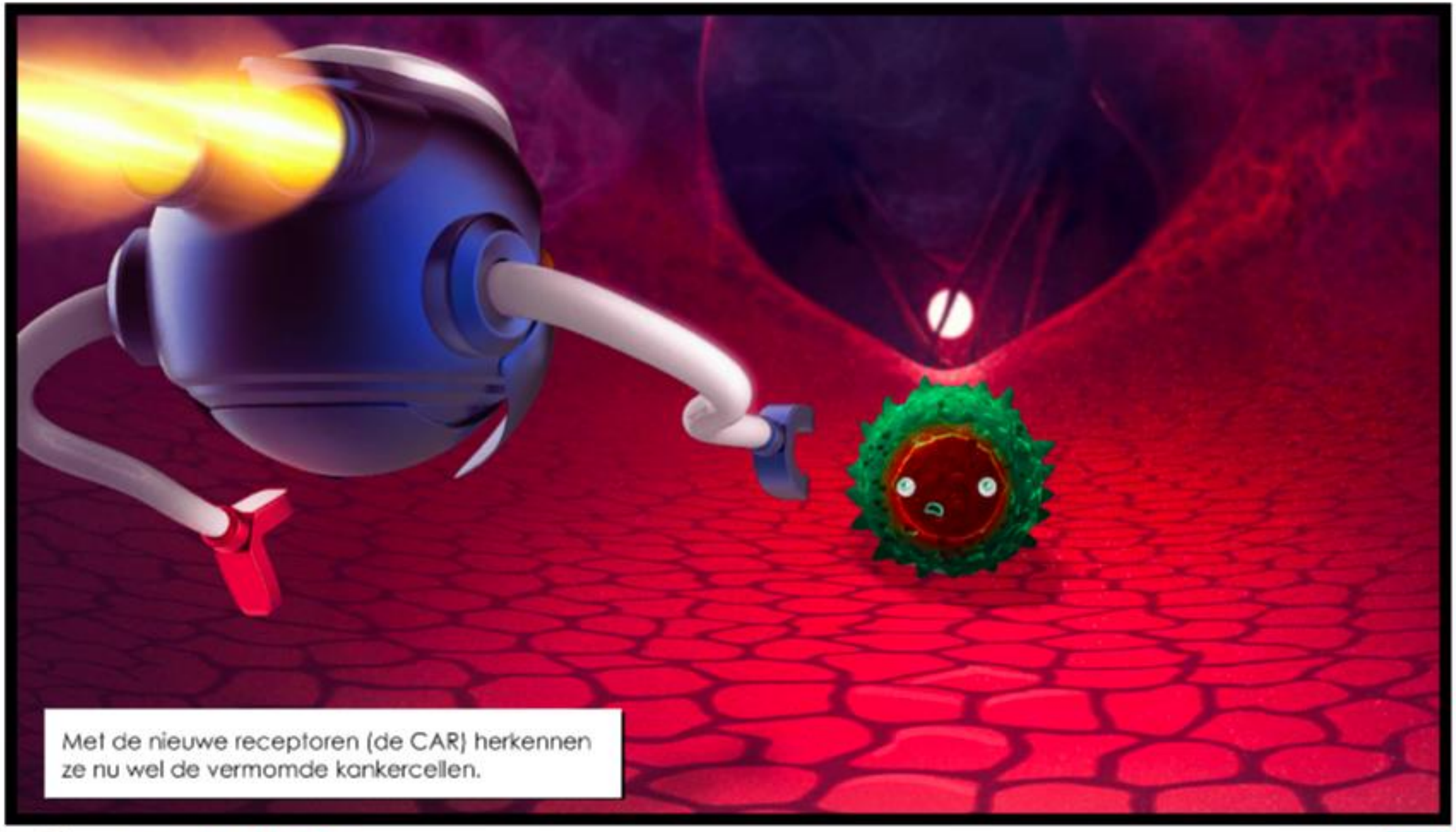
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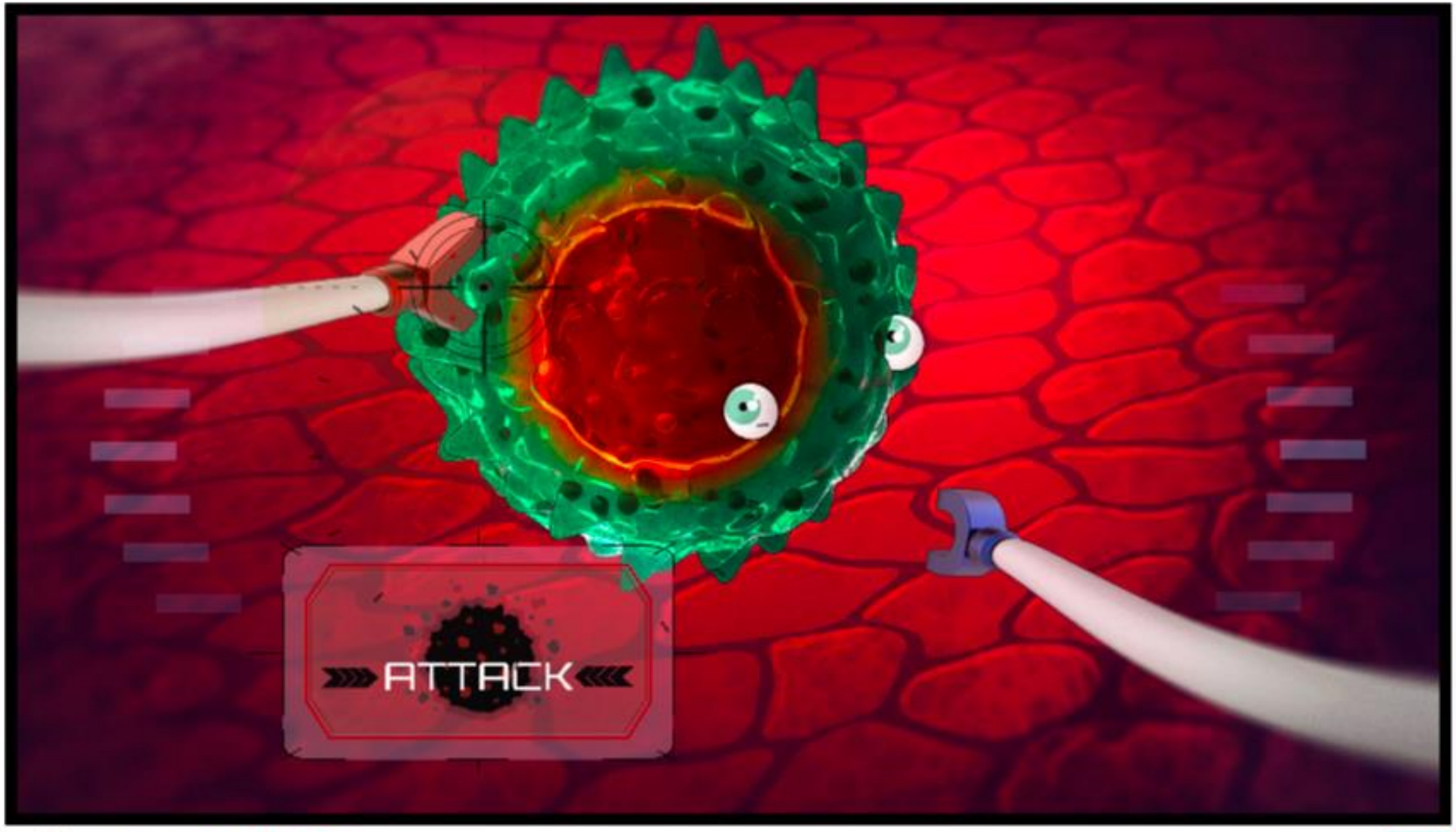
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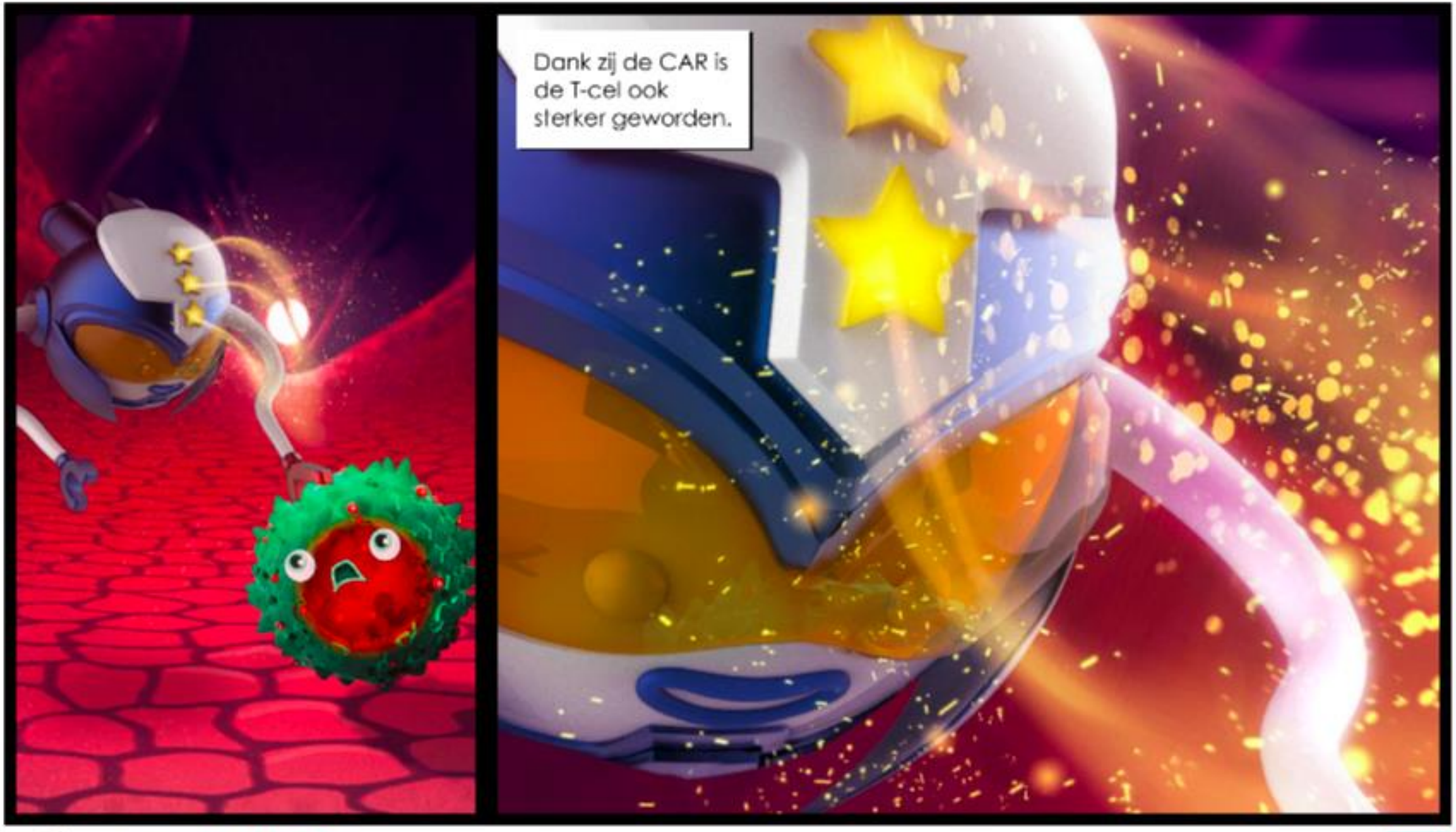
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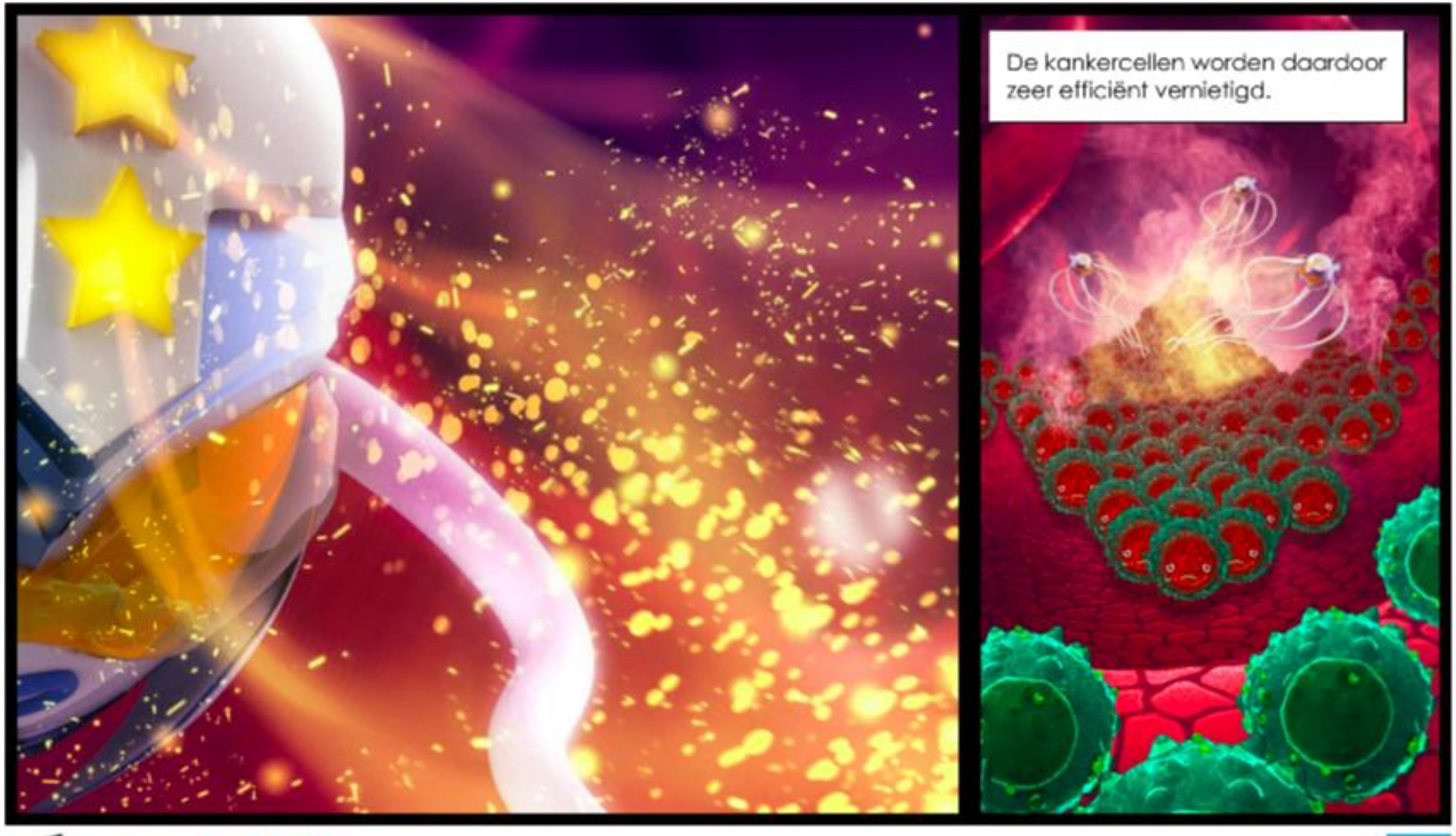
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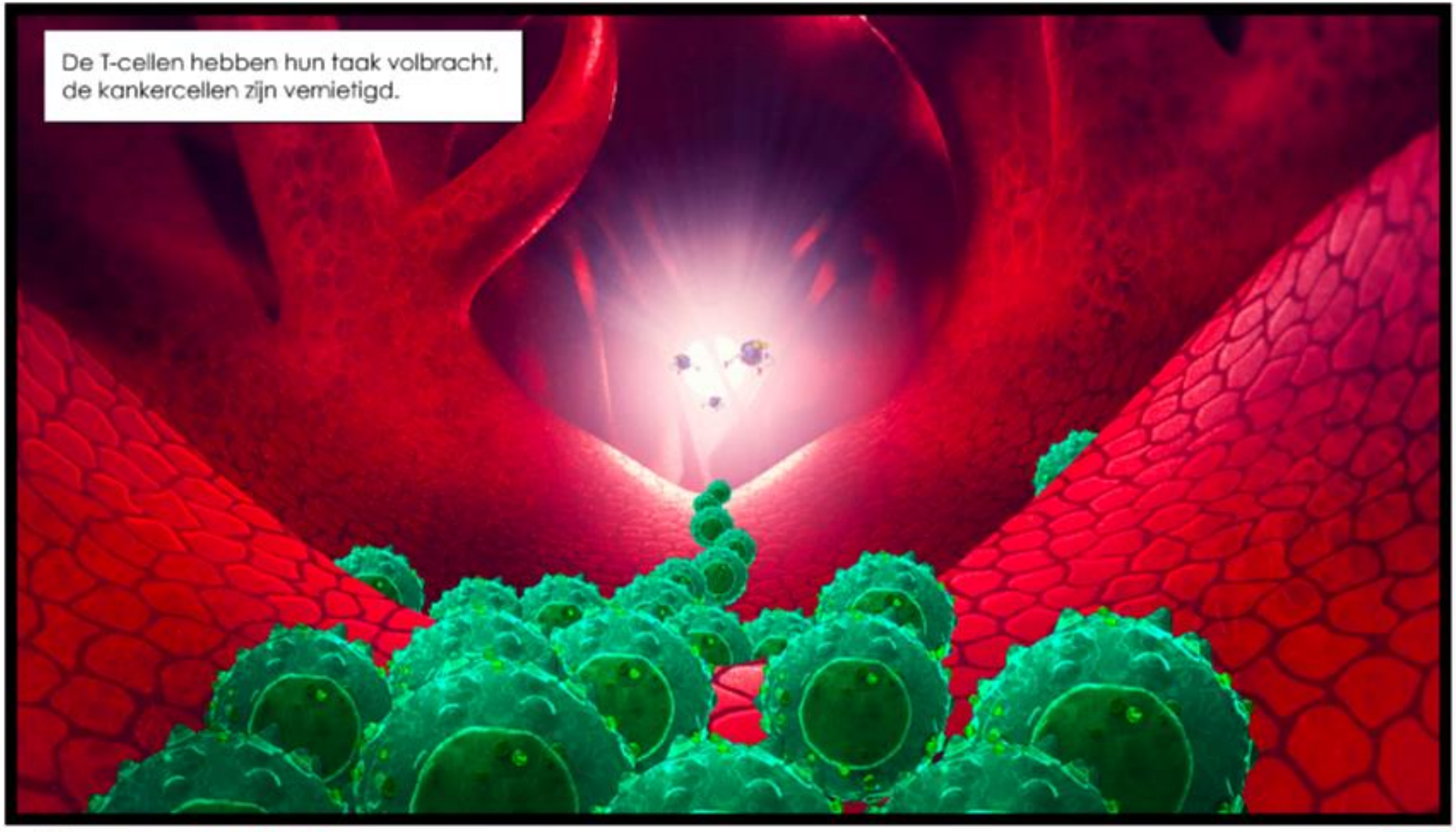
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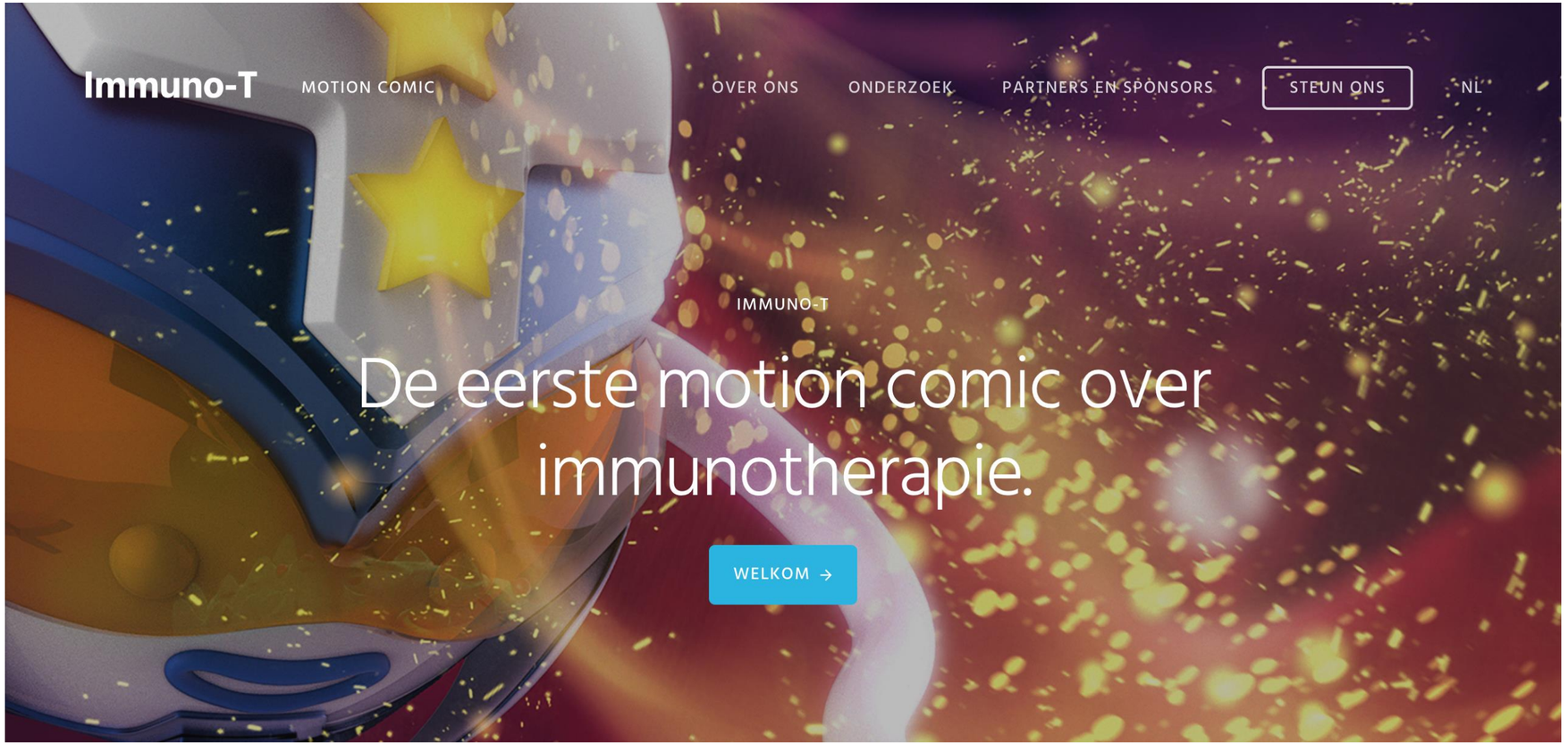
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IMMUNO-T: WAAR STAAN WE NU EN WAAR GAAN WE HEEN?

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IMMUNO-T: WAAR STAAN WE NU?

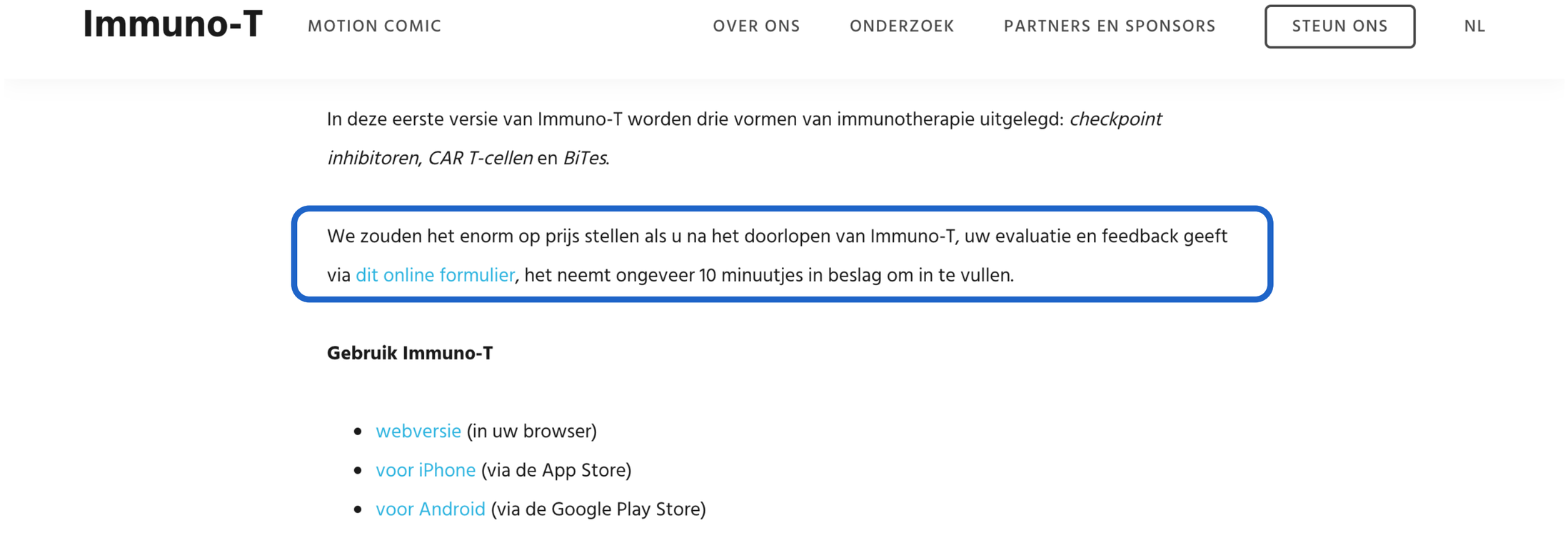
- Website Immuno-T.inmotion.care
- Vanop website kan je Immuno-T gratis downloaden



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IMMUNO-T: WAAR STAAN WE NU?

- Website Immuno-T.inmotion.care
- Warme oproep tot het bekijken van Immuno-T en **invullen van het evaluatieformulier**



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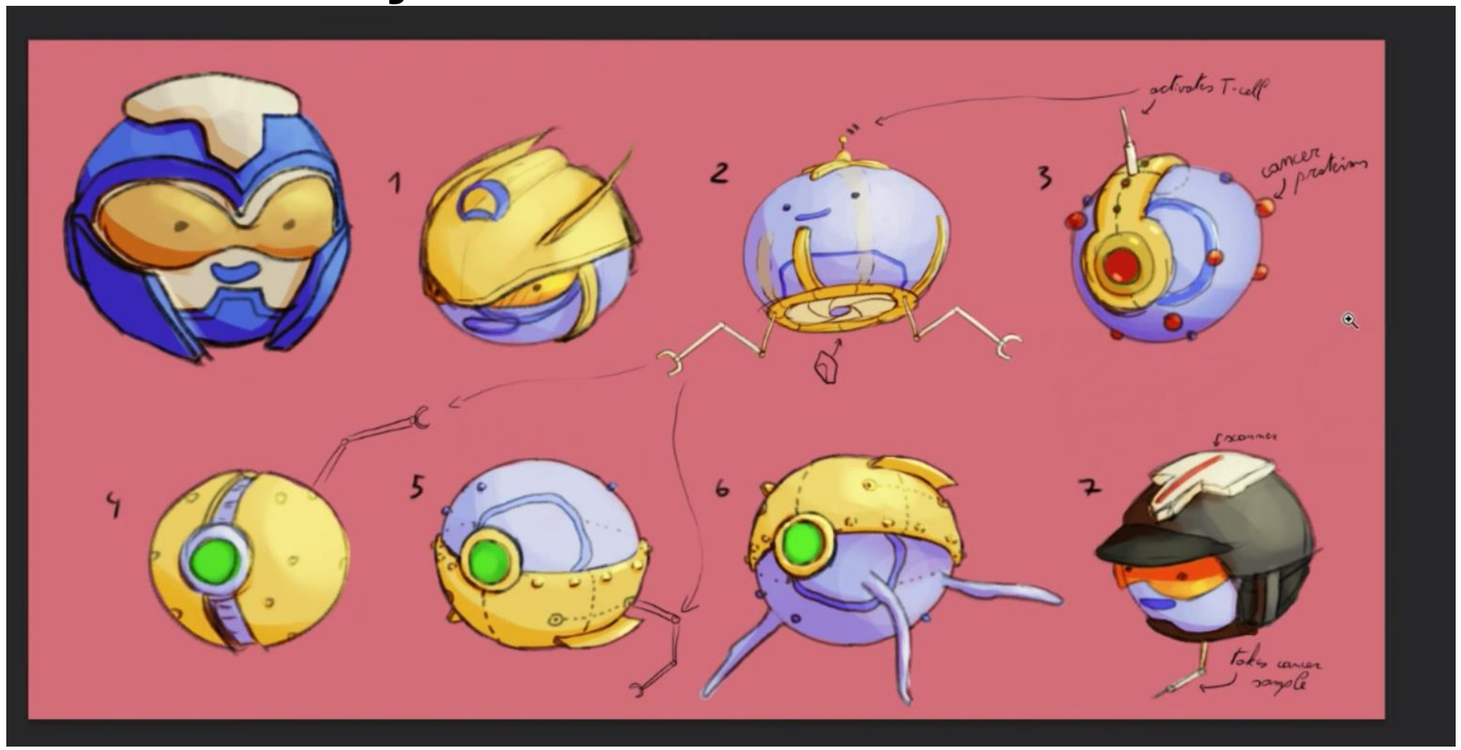
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IMMUNO-T: TOEKOMSTPLANNEN

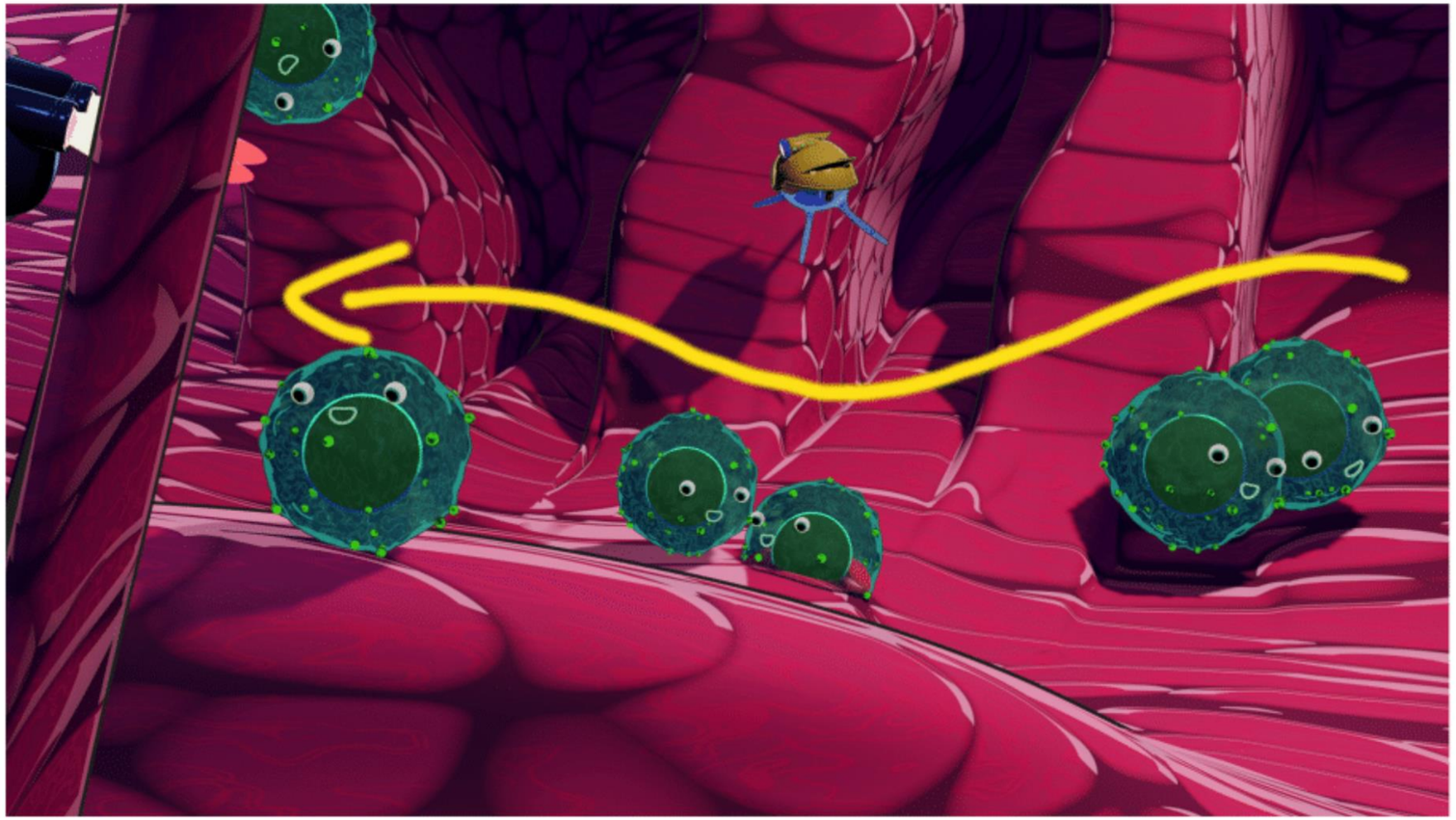
- Uitbreiding Immuno-T:
  - Inleiding: aanvullen met dendritische cellen
  - Extra flesje: vaccinatie



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IMMUNO-T: TOEKOMSTPLANNEN

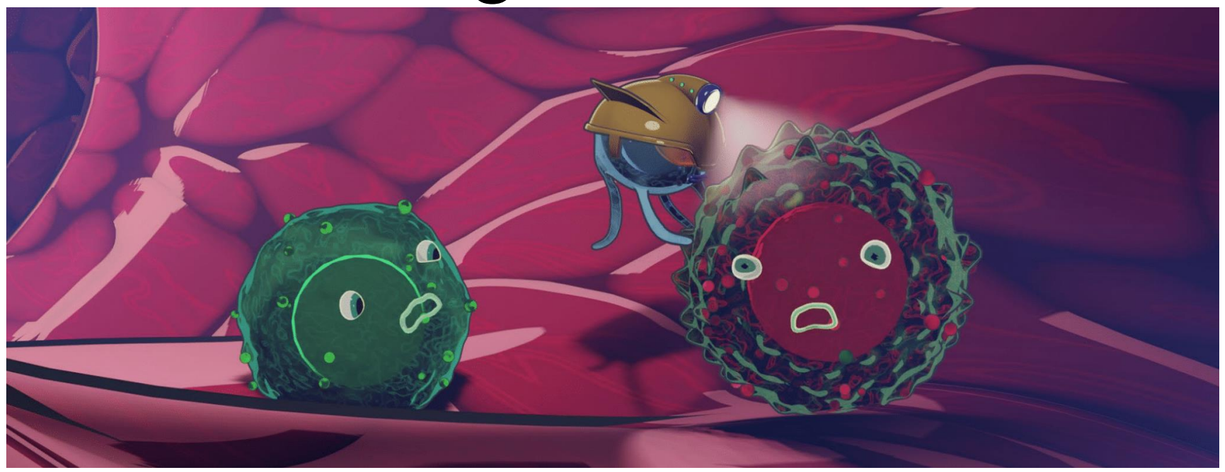
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  - Extra flesje: vaccinatie

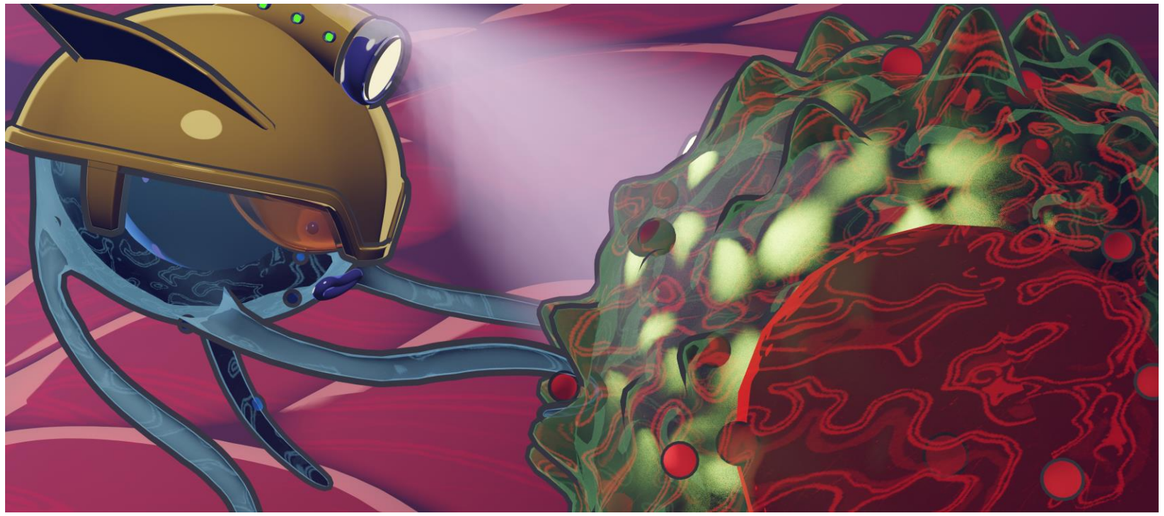


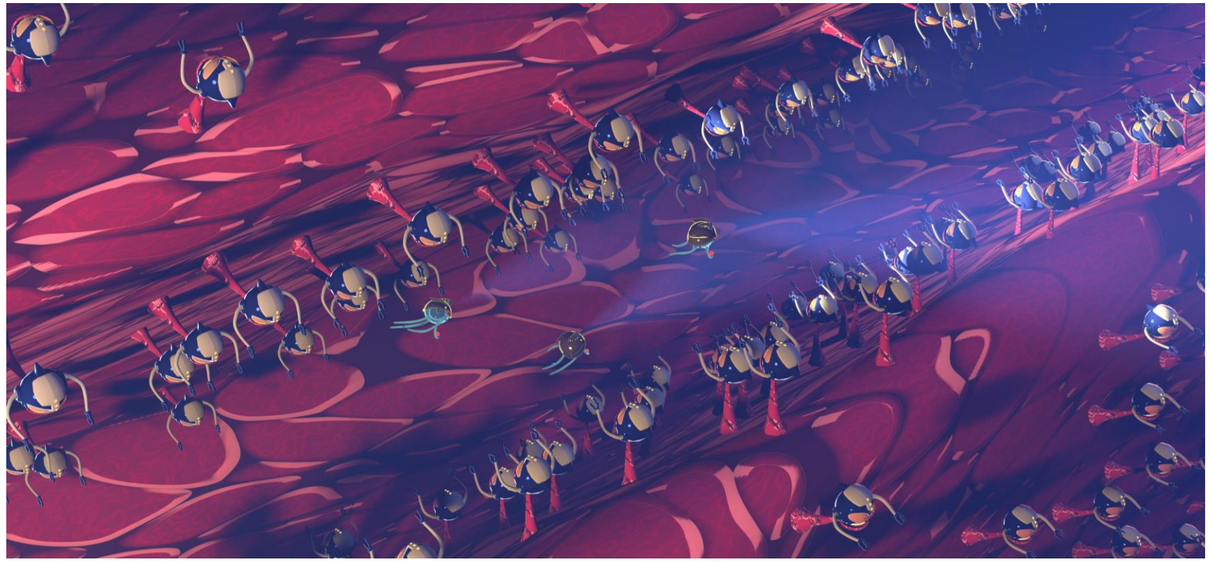
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IMMUNO-T: TOEKOMSTPLANNEN

- Uitbreiding Immuno-T:
  - Inleiding: aanvullen met dendritische cellen



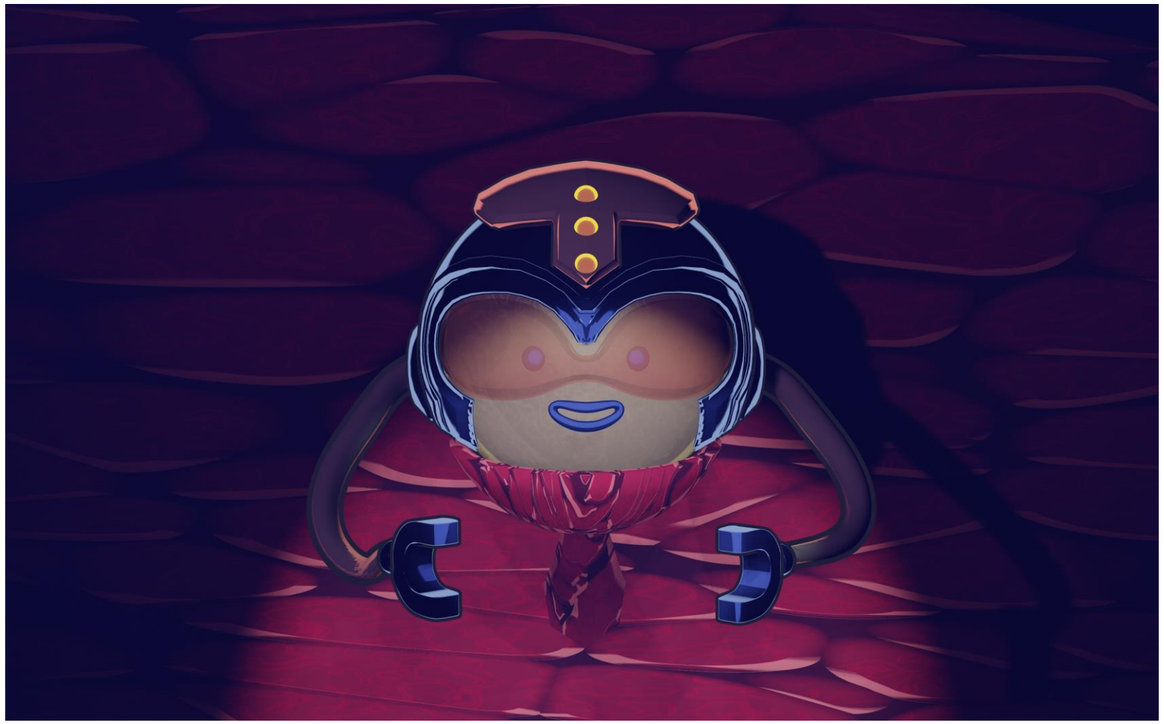


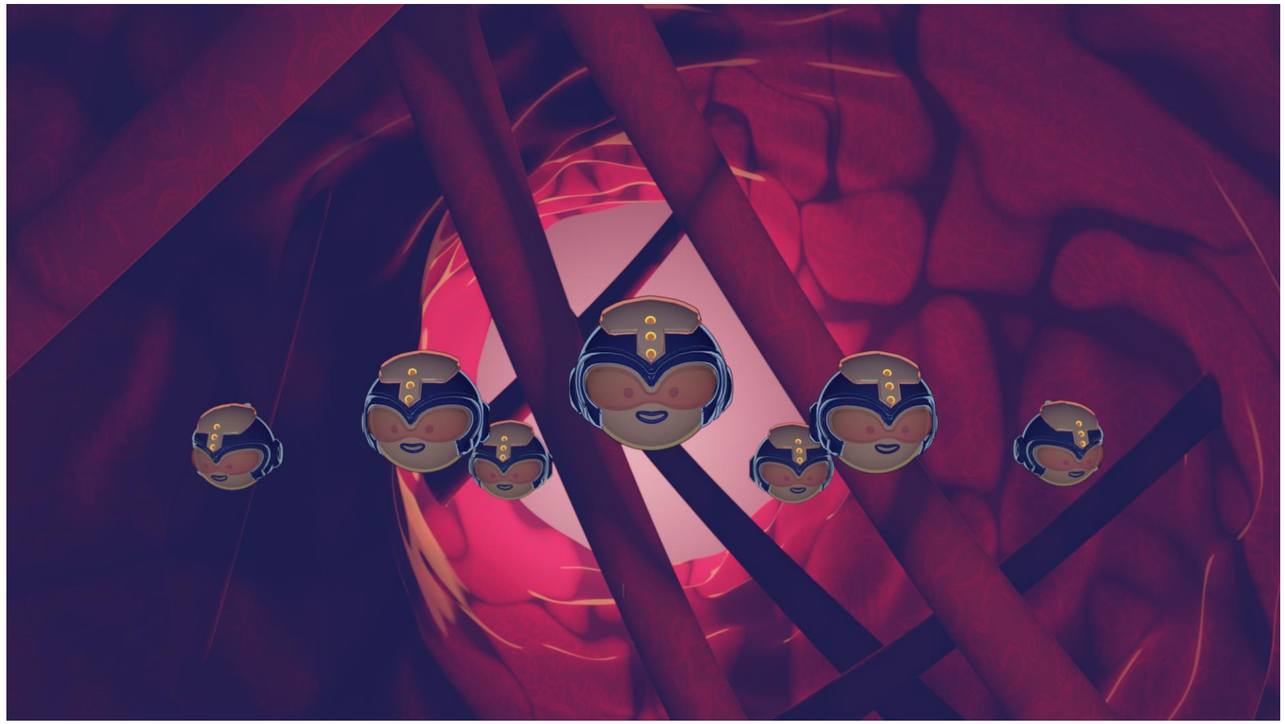




IMMUNO-T: TOEKOMSTPLANNEN

- Uitbreiding Immuno-T:
  - Inleiding: aanvullen met dendritische cellen





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IMMUNO-T: TOEKOMSTPLANNEN

- Uitbreiding Immuno-T:
  - Vierde flesje: vaccinatie



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IMMUNO-T: TOEKOMSTPLANNEN

- Uitbreiding Immuno-T:
  - Vijfde flesje: allogene stamceltransplantatie



PACE AWARD BHS 2024

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IMMUNO-T: TOEKOMSTPLANNEN

- Een tool rond herkennen van bijwerkingen voor patiënten

- Pakketten voor onderwijs, voor leerkracht en klasgenootjes van kind met kanker dat immunotherapie krijgt

- Nog meer vertalingen:
  - Turks
  - Arabisch

- 3D versie – VR bril

EN OOK…

- **Andere motion comics**:
  - **Chemo-T** (over chemotherapie)
  - **Radio-T** (over radiotherapie)
  - **Transplant-T** (over stamceltransplantatie)→ 5de flesje
  - nieuwe behandelingen uitleggen (in samenwerking met CRIG)
  - …

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IMMUUN VOOR KANKER





ACADEMIA
PRESS

Lannoo

FACULTEIT GENEESKUNDE EN GEZONDHEIDSWETENSCHAPPEN

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