



UNIVERSITEIT
GENT

Advanced cell therapy

BHS Educational Session

Bart Vandekerckhove
Ghent University

Advanced Therapy Medicinal Products (ATMPs)

Gene Therapy
Medicinal Products

Somatic Cell Therapy
Medicinal Products

Tissue Engineering
Products

Genetically Modified Cells




Zolgensma
NOVARTIS
avexis

NDC 7894-115-01
onasemnogene a
ZOLGENSMA
Rx ONLY
Suspension for intravenous infusion.
See enclosed prescribing information for dosage and directions for use.

Manufactured by AveXis, Inc.
Barnstable, MA 01915
US License No. 2104

 **ZOLGENSMA HAS BEEN APPROVED BY THE FDA!**



HOLOCLAR[®]
Ex vivo expanded autologous human
corneal epithelial cells containing stem cells



tisagenlecleucel
KYMRIAH[™]
NDC 0078-0846-19
Humans T-Cells - Rx only
Suspension for IV infusion
Cultured, genetically modified
For autologous use only
Dispense with Medication Guide

Target Total Volume 10mL-50mL, per bag
Dosage: See prescribing information.
Contents: 2 x 10⁸ to 2.5 x 10⁹ CD4⁺ positive viable T cells
Cryopreserved in: 31.25% (w/v) of Plasma-Lyte A, 31.25% (w/v) of 5% Dextrose/0.45% sodium chloride, 20% (w/v) of 25% HSA, 10% (w/v) of 10% Dextran 40 (LMD)/5% Dextrose and 7.5% (w/v) DMSO

Store at -120°C ; vapor phase of liquid nitrogen
Properly identify intended recipient and product
Do not use leukocyte depleting filter
Do not irradiate
Not evaluated for infectious substances

Name: John Doe
DOB: 01-JAN-2000
CIN: W1234 17 123456
Expiry: 01-JAN-2018
Batch: 12345678

Mfg. by: Novartis Pharmaceuticals Corporation
Morris Plains, NJ 07950
U.S. License # 1244 KYMRIAH.com
1-844-4KYMRIAH (1-844-429-6742)

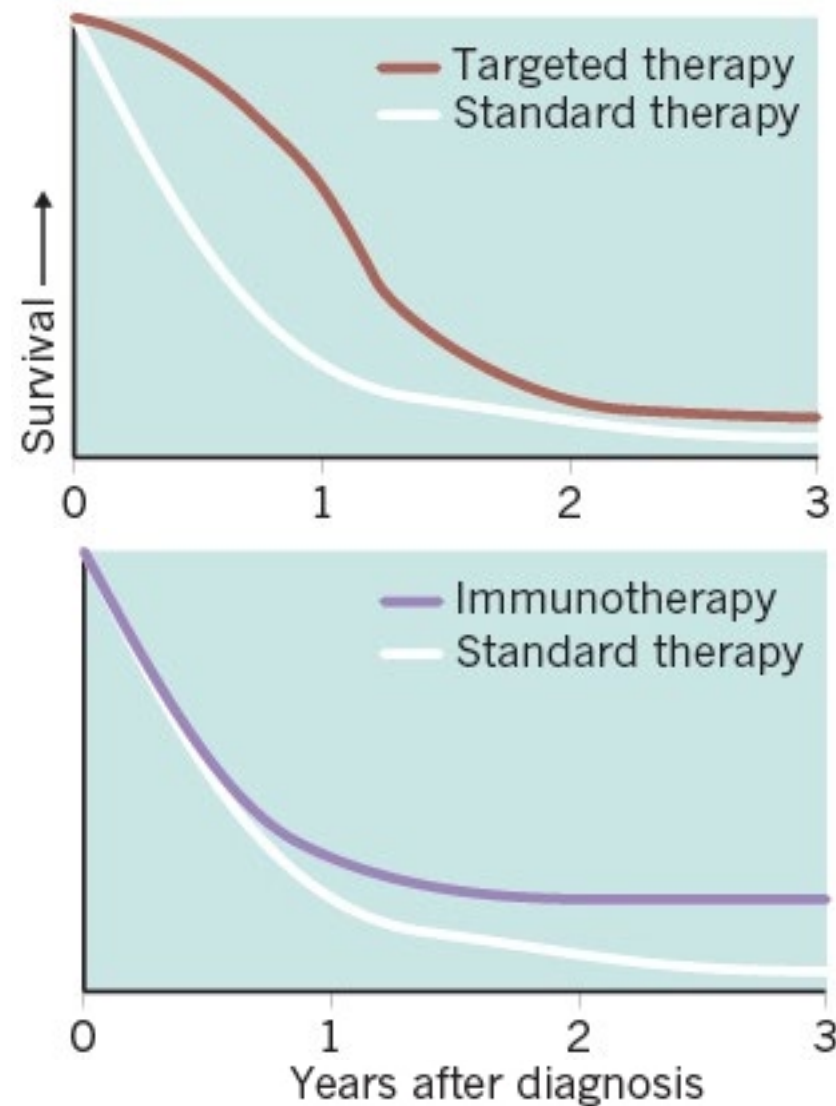
PP Material No. 8123456 For Novartis use only
PP Material No. 7123456

NOVARTIS 5004685 © Novartis

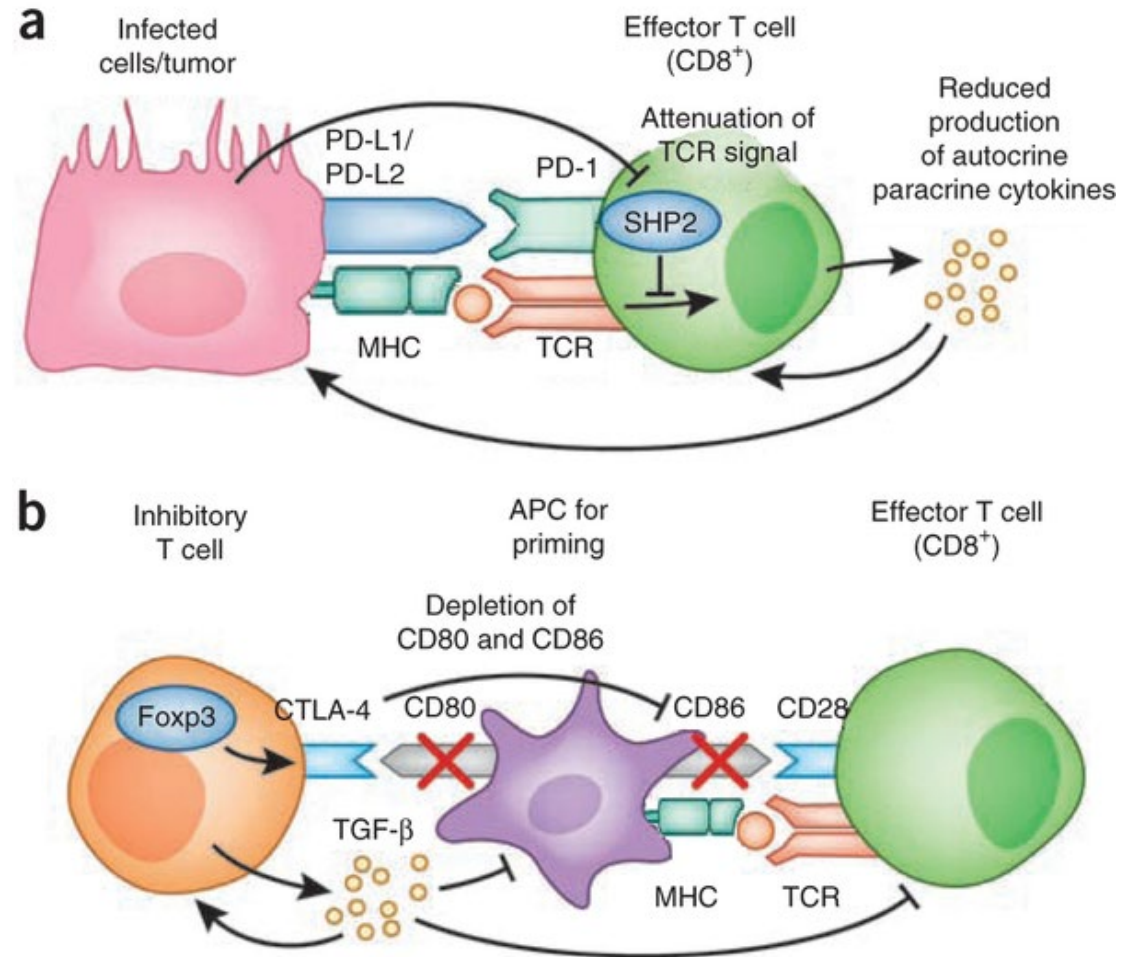


Treatment options for cancer

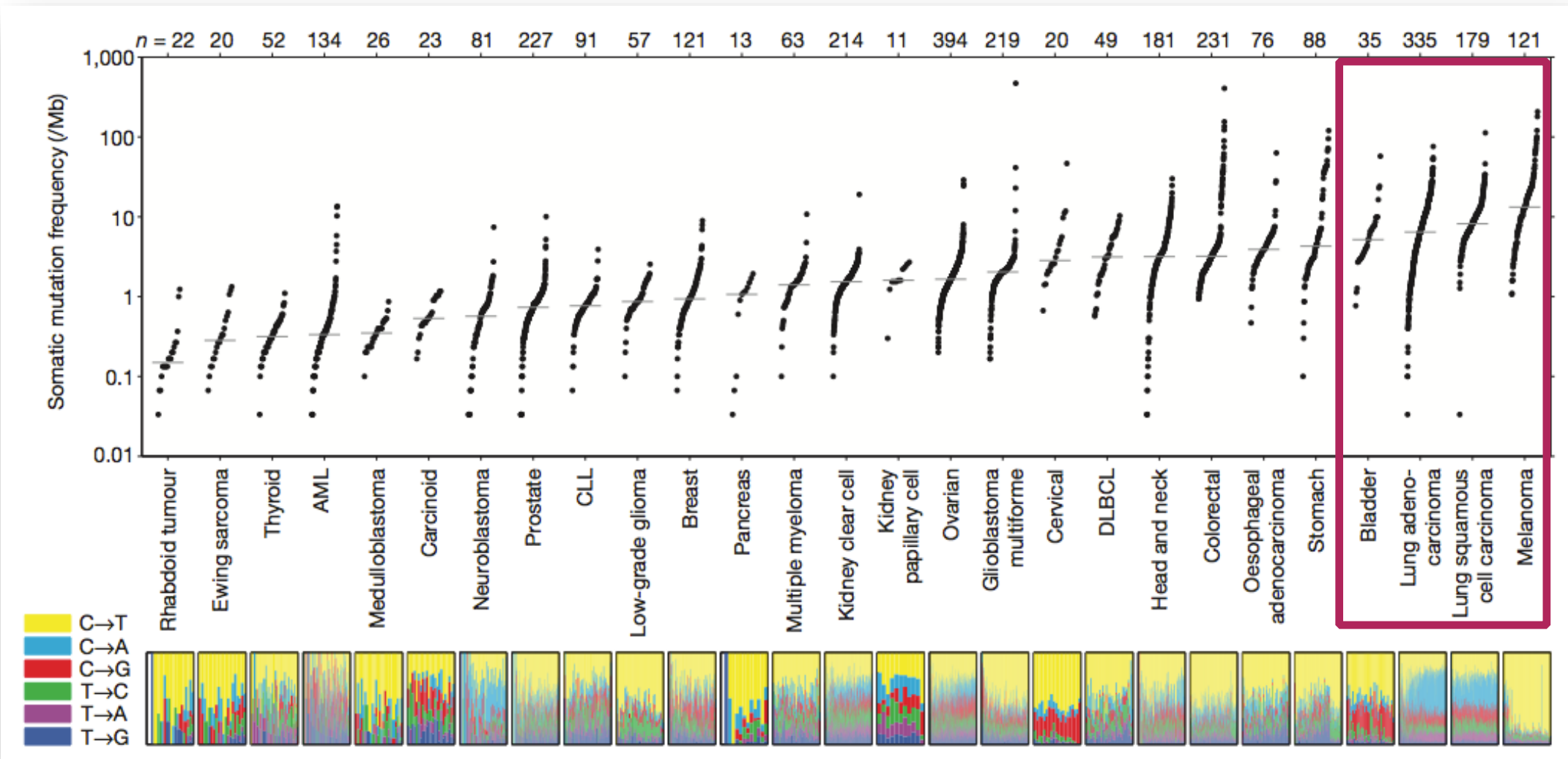
- Classic triad
 - Surgery
 - Radiotherapy
 - Chemotherapy
 - (Hormonal)
- New kids on the block
 - Targeted therapy
 - Immunotherapy



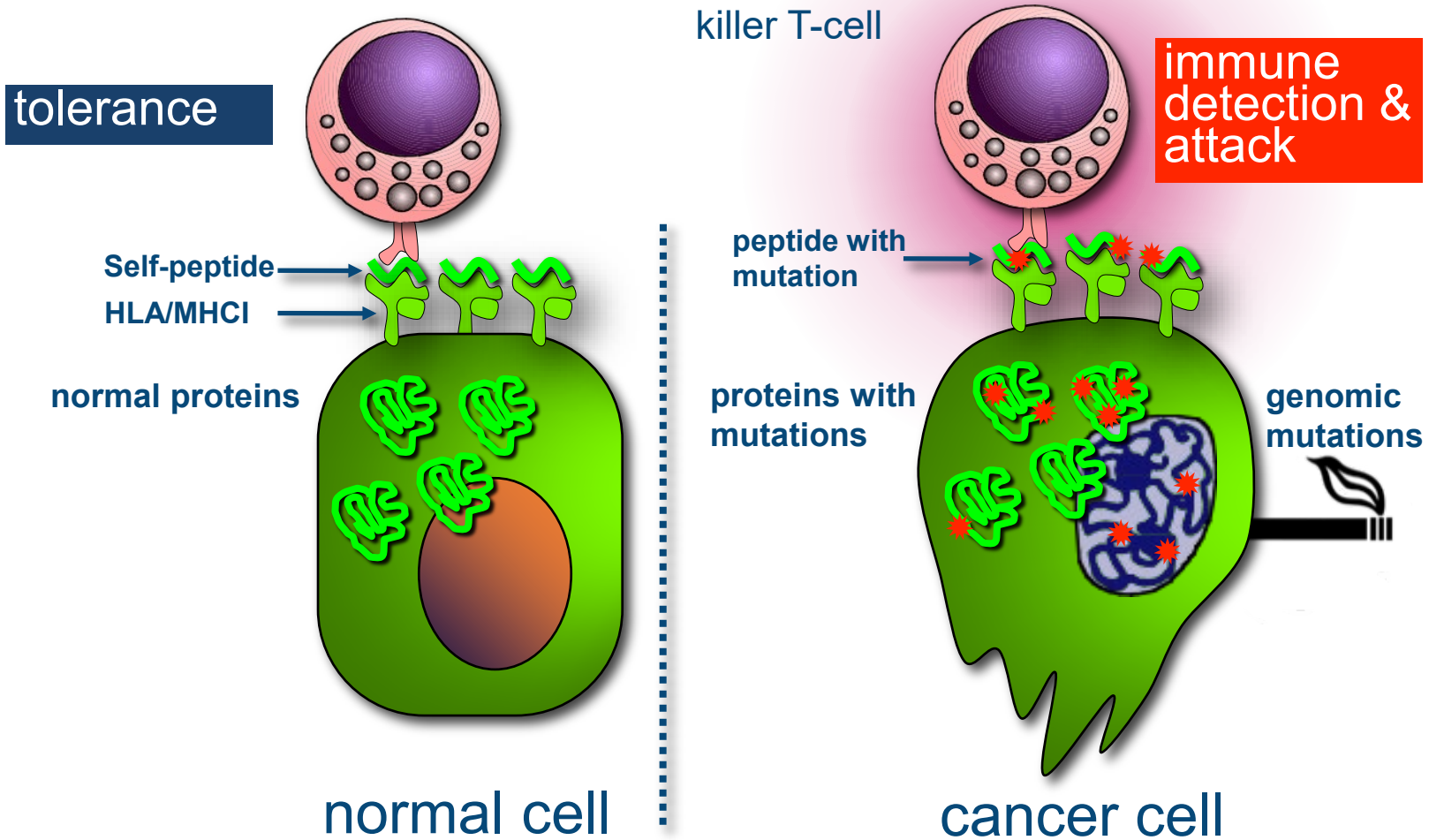
Part I Active immune therapy



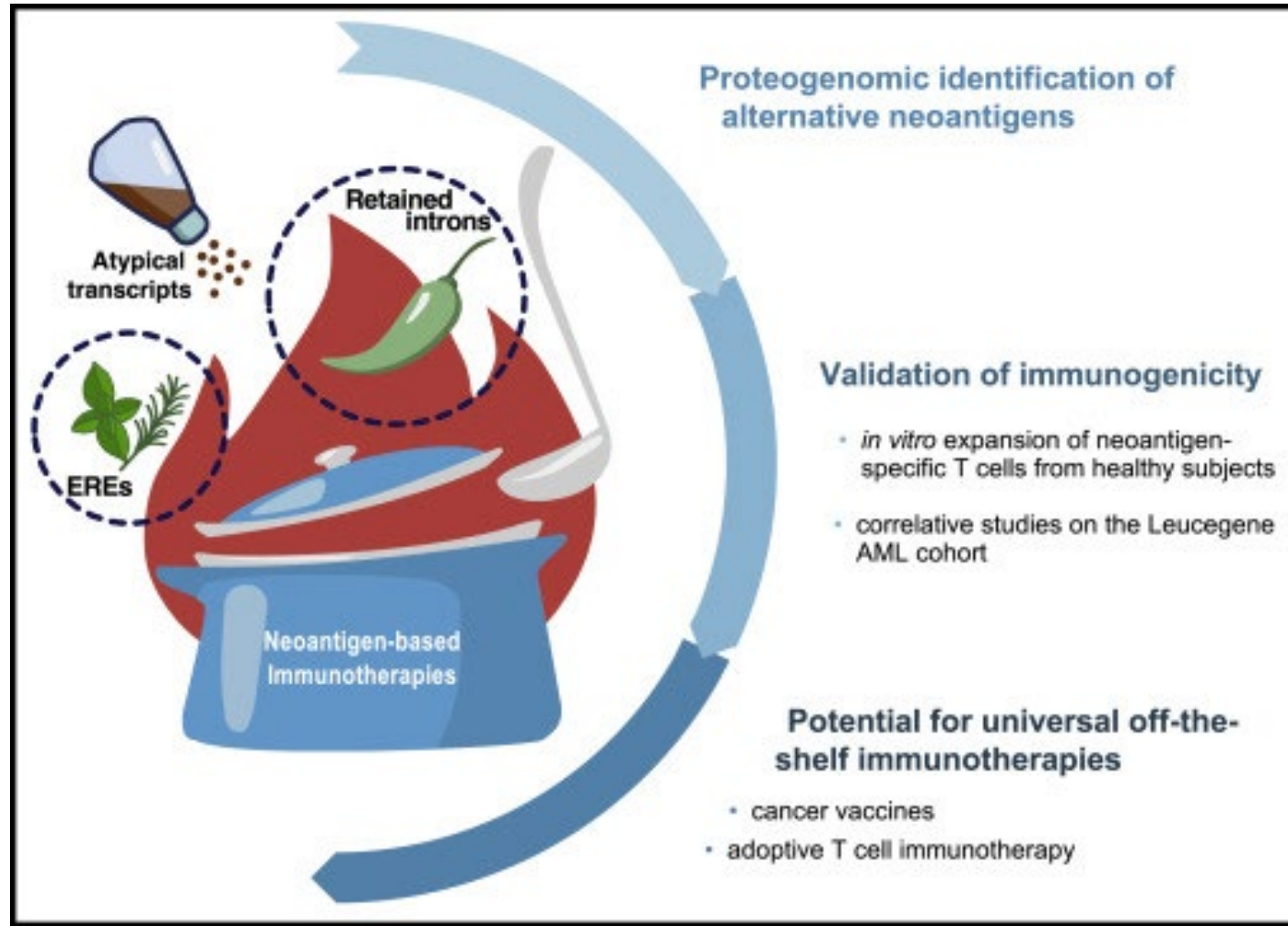
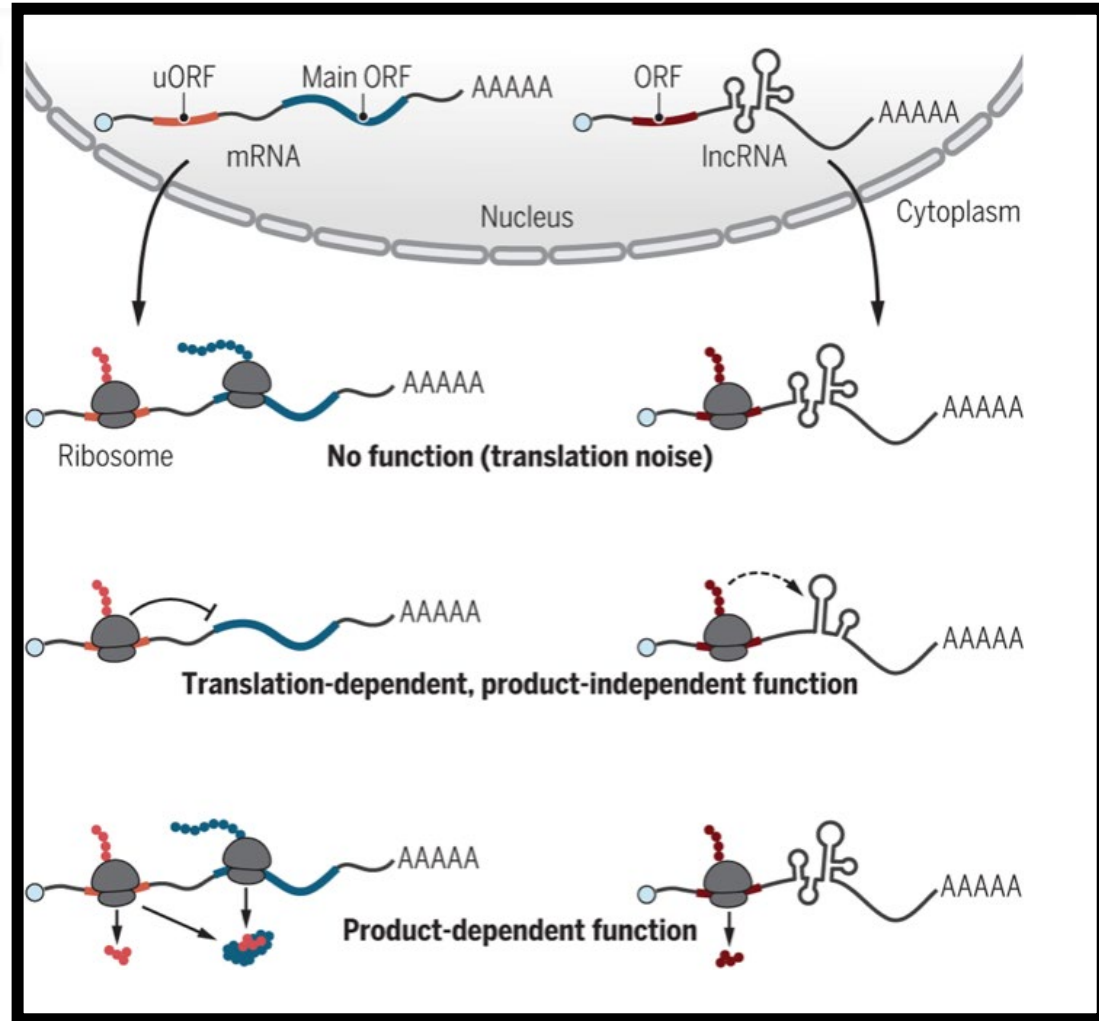
CANCER MUTATIONAL LOAD vs IMMUNOGENICITY



CANCER MUTATIONAL LOAD vs IMMUNOGENICITY



EXPRESSION AND TRANSLATION OF SILENT DNA



Wei and Guo Science 2020
Ehx Immunity 2021

TUMOR-SPECIFIC ANTIGENS

MUTATIONS

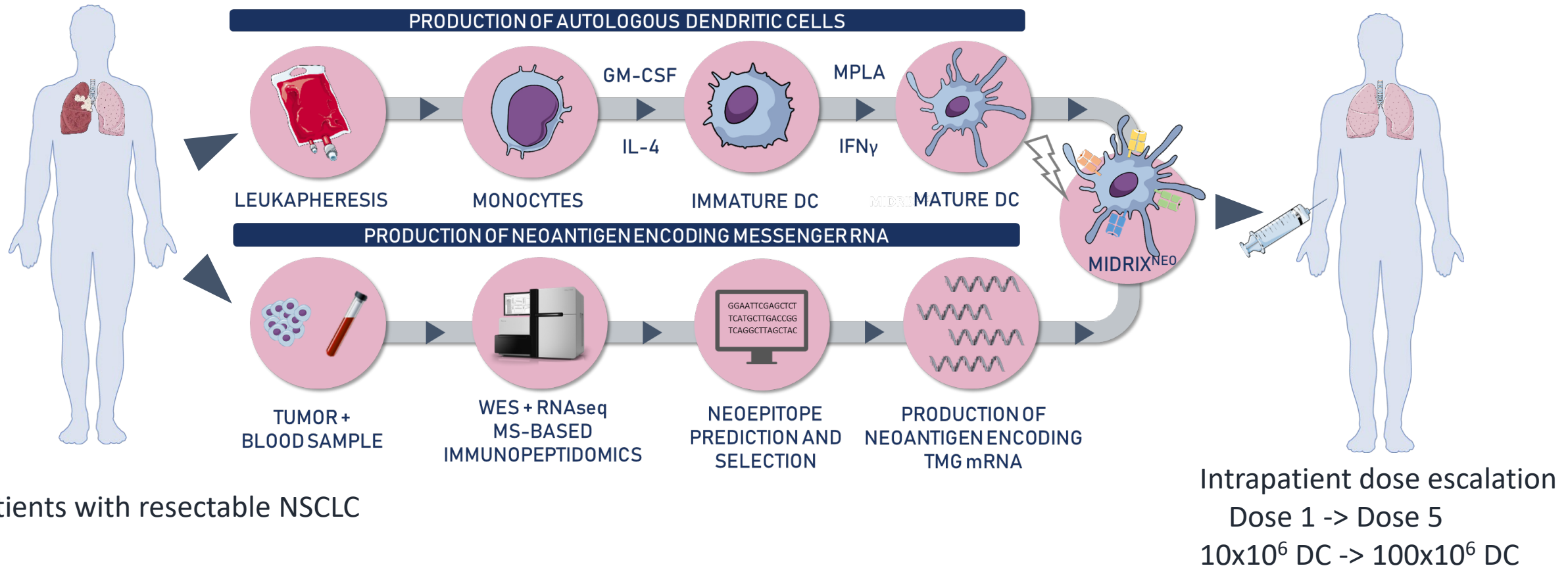
- Patient-specific
- Associated with favourable prognosis
- High expression
- Bind to MHC
- Immune “non-self”
- Immune responses
- Can induce remission

EPIGENETICS

- General expression
- ?
- Low expression
- Preferentially bind to MHC
- Immune “self” ?
- Immune responses ?
- Can induce remission ?



MIDRIX^{NEO}: ATMP Design



6 patients with resectable NSCLC

Intrapatent dose escalation
Dose 1 -> Dose 5
10x10⁶ DC -> 100x10⁶ DC

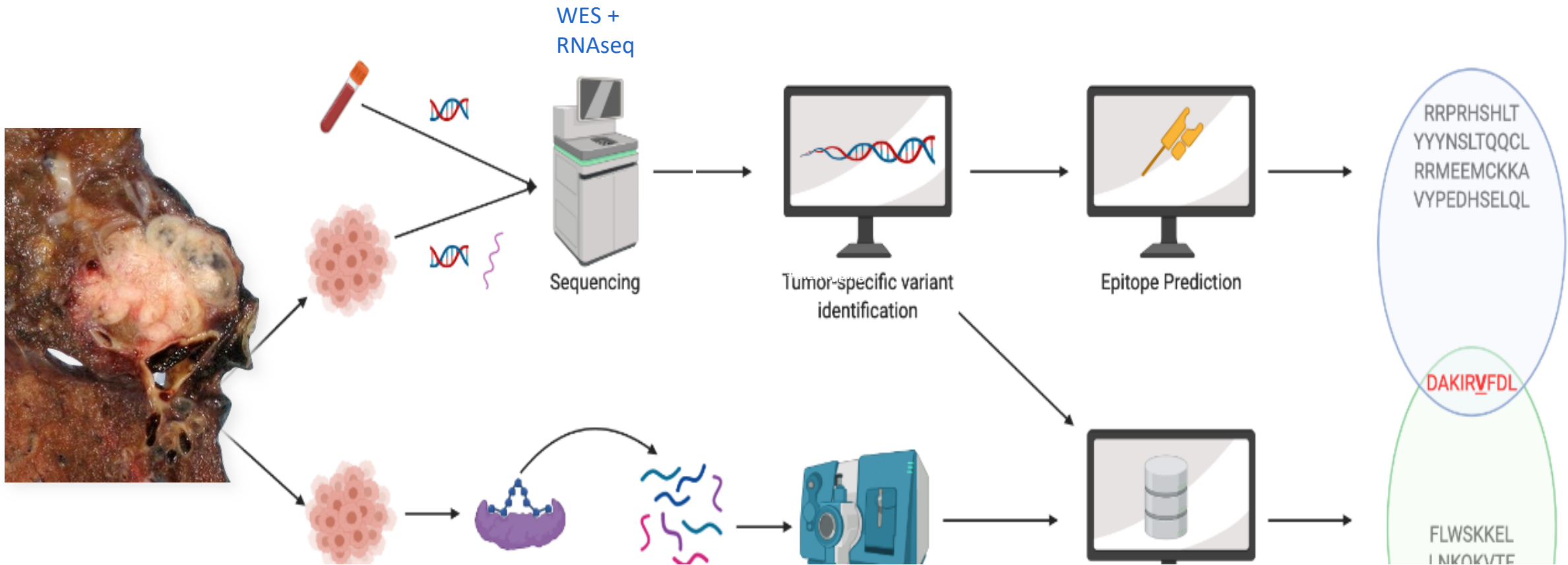
MIDRIX^{NEO}-LUNG patient case 1808-05



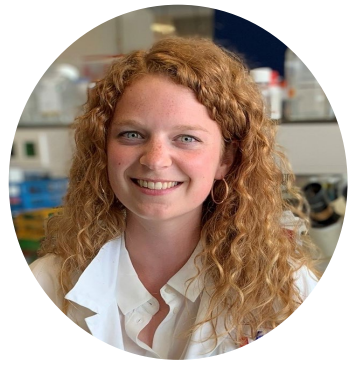
Rupert Mayer.



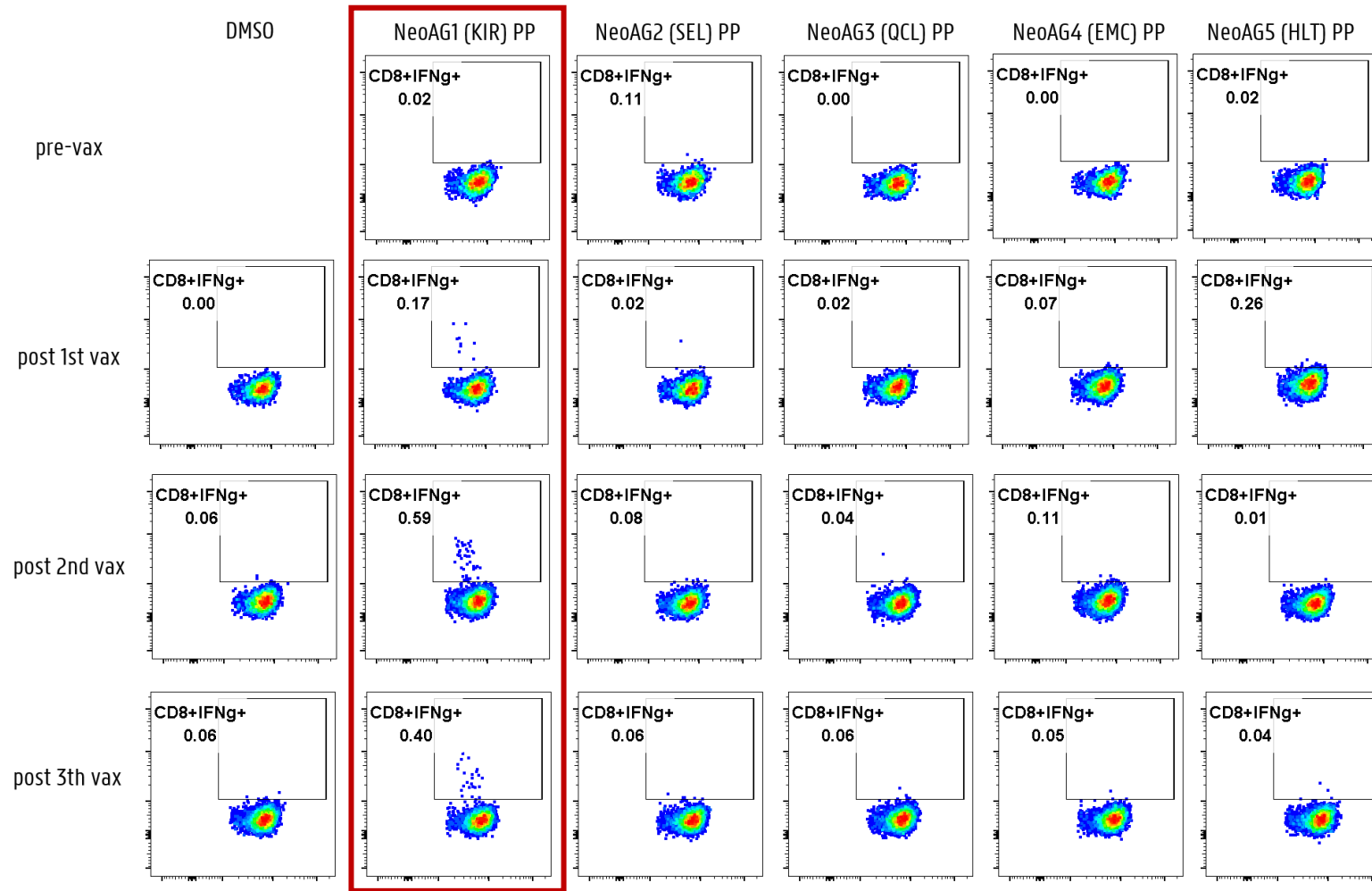
Laurenz De Cock



MIDRIX^{NEO}-LUNG patient case 1808-05



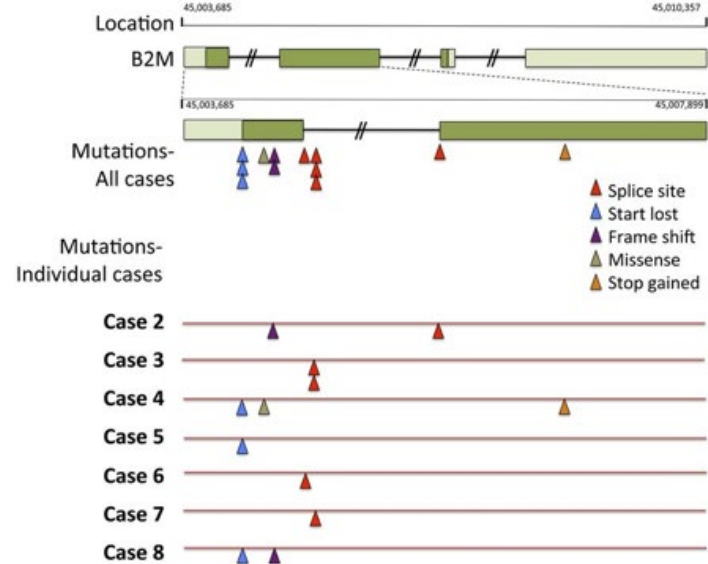
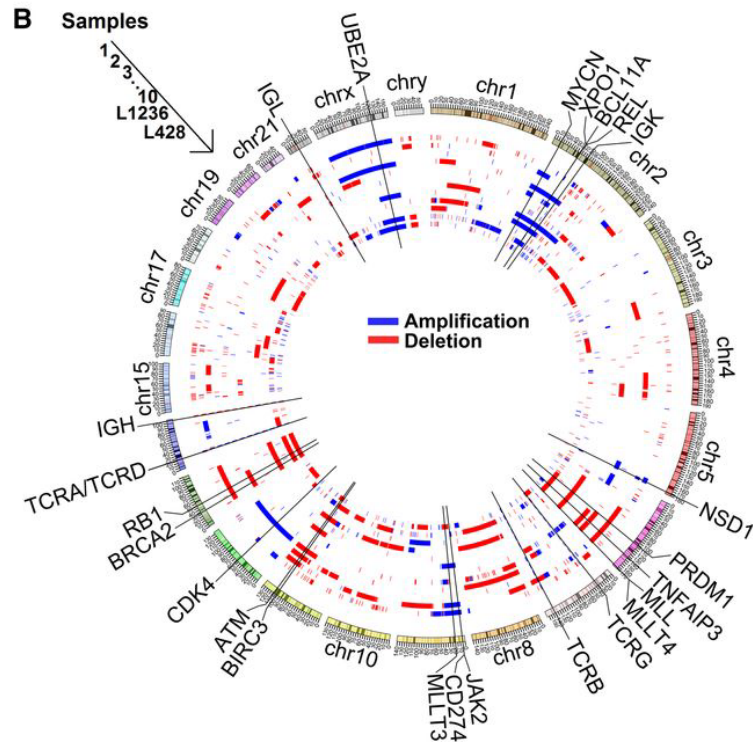
Joline Ingels



NB:

- no reactivity in TILs
- no CD4 responses in blood

Immune therapy : Hodgkin's Disease



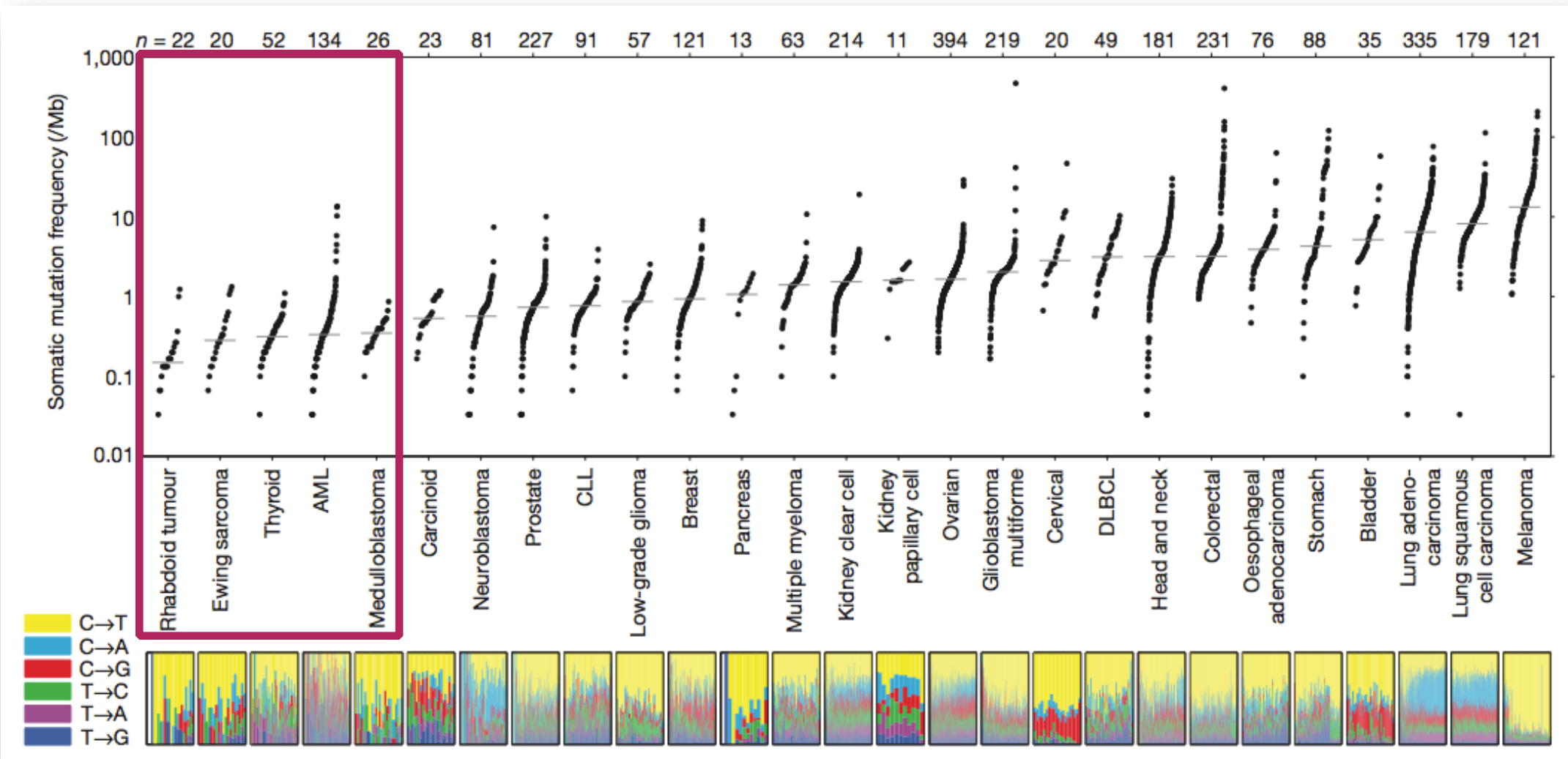
- **Chemotherapy**
- **Immune checkpoint inhibitors**
- **Combination therapy**

- **CD30 CAR-T cells**
- **EBV-specific CTL**

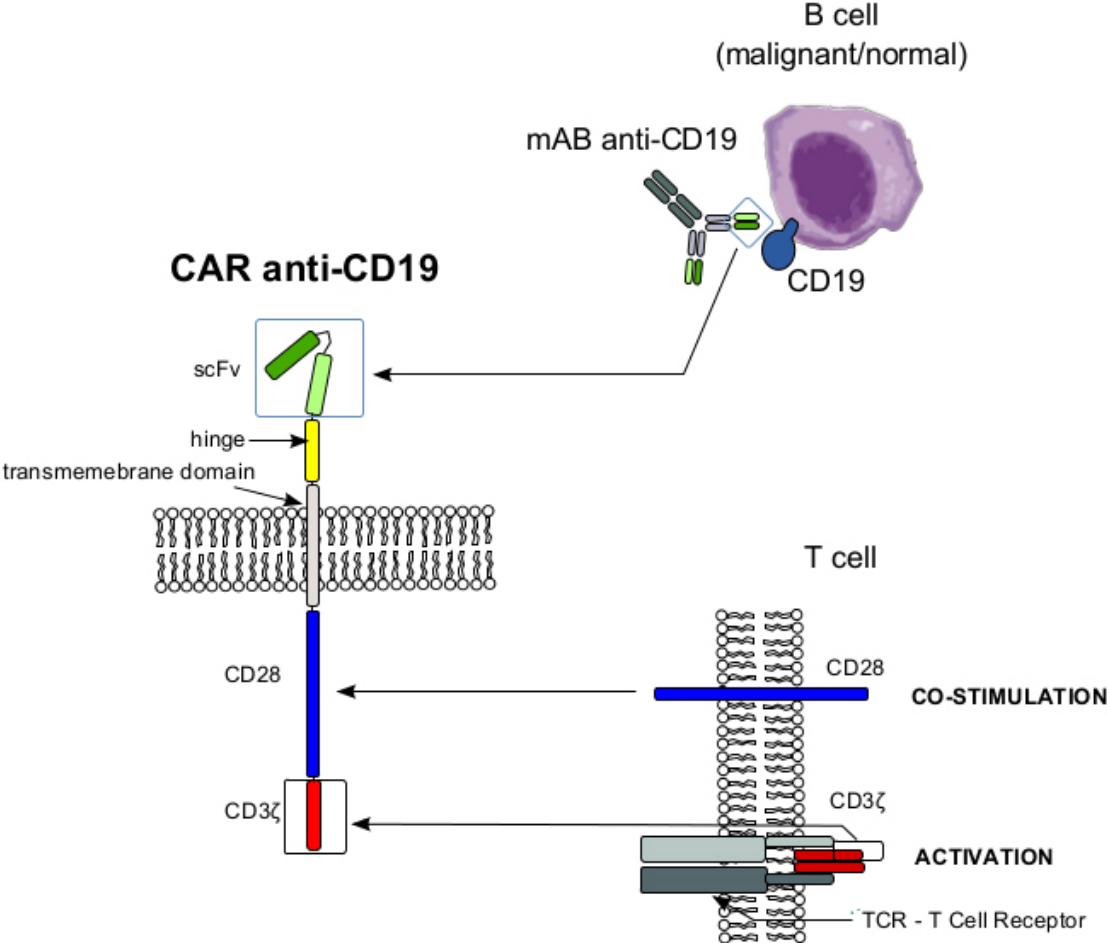
Part II Passive immune therapy



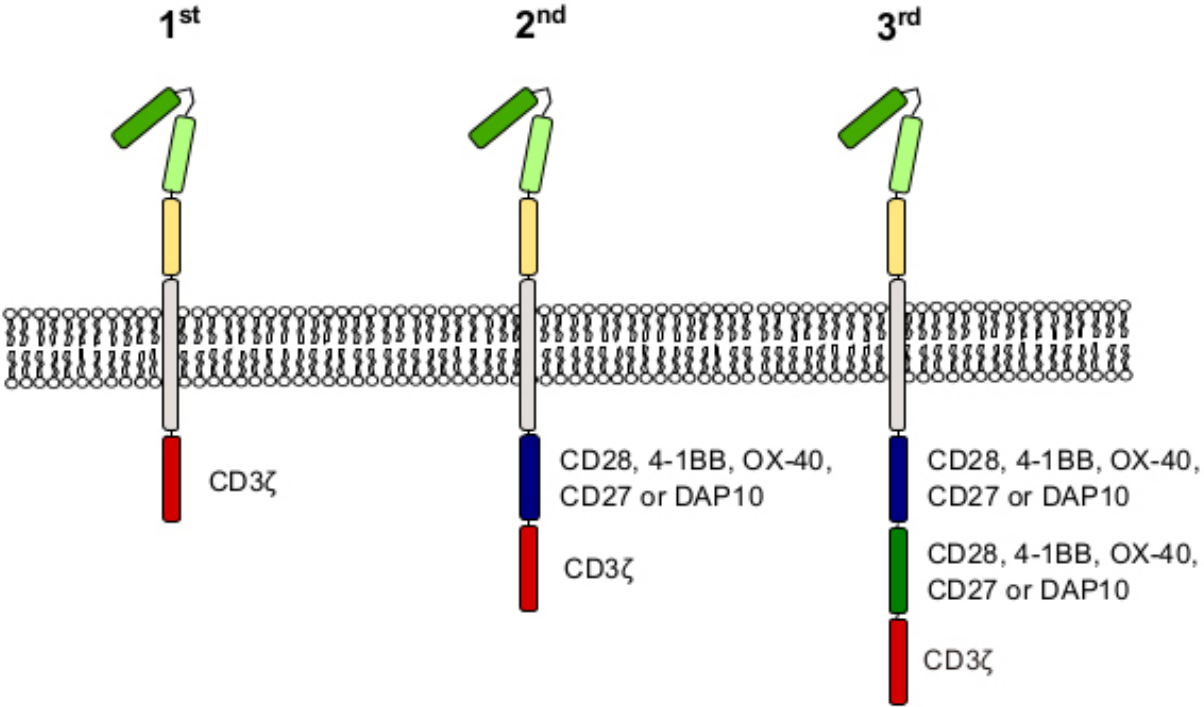
CANCER MUTATIONAL LOAD vs IMMUNOGENICITY



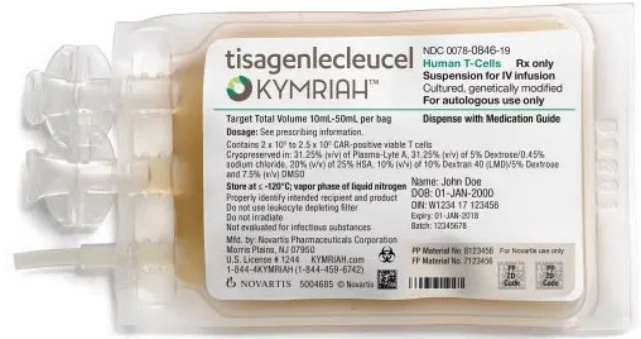
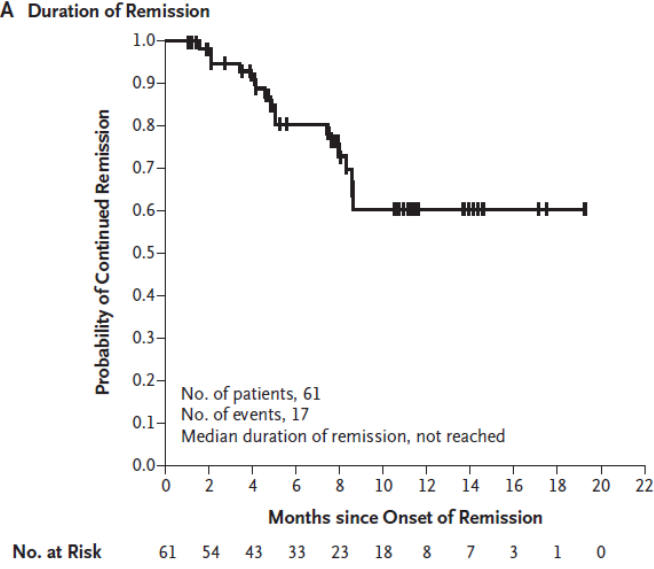
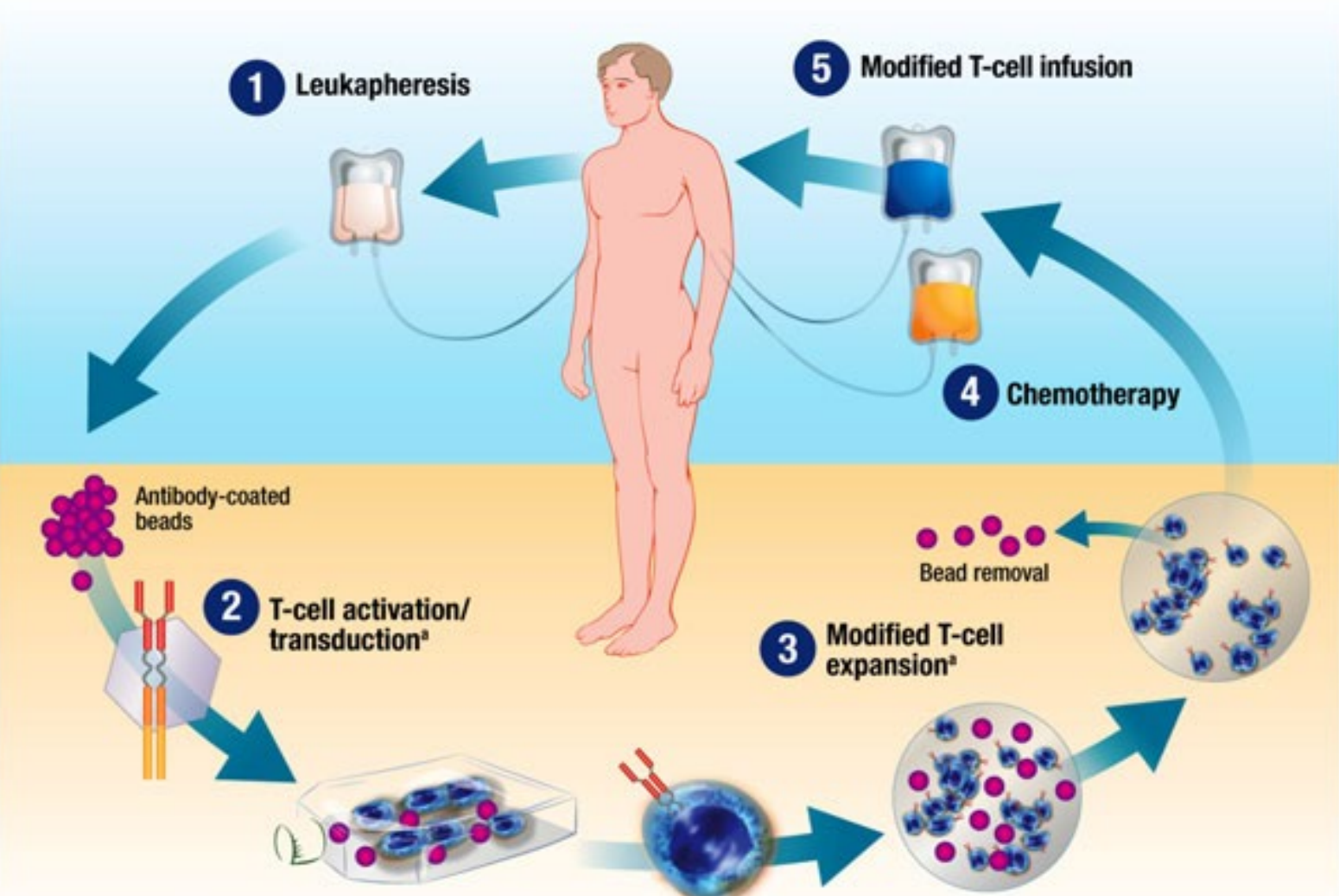
Chimeric Antigen Receptors



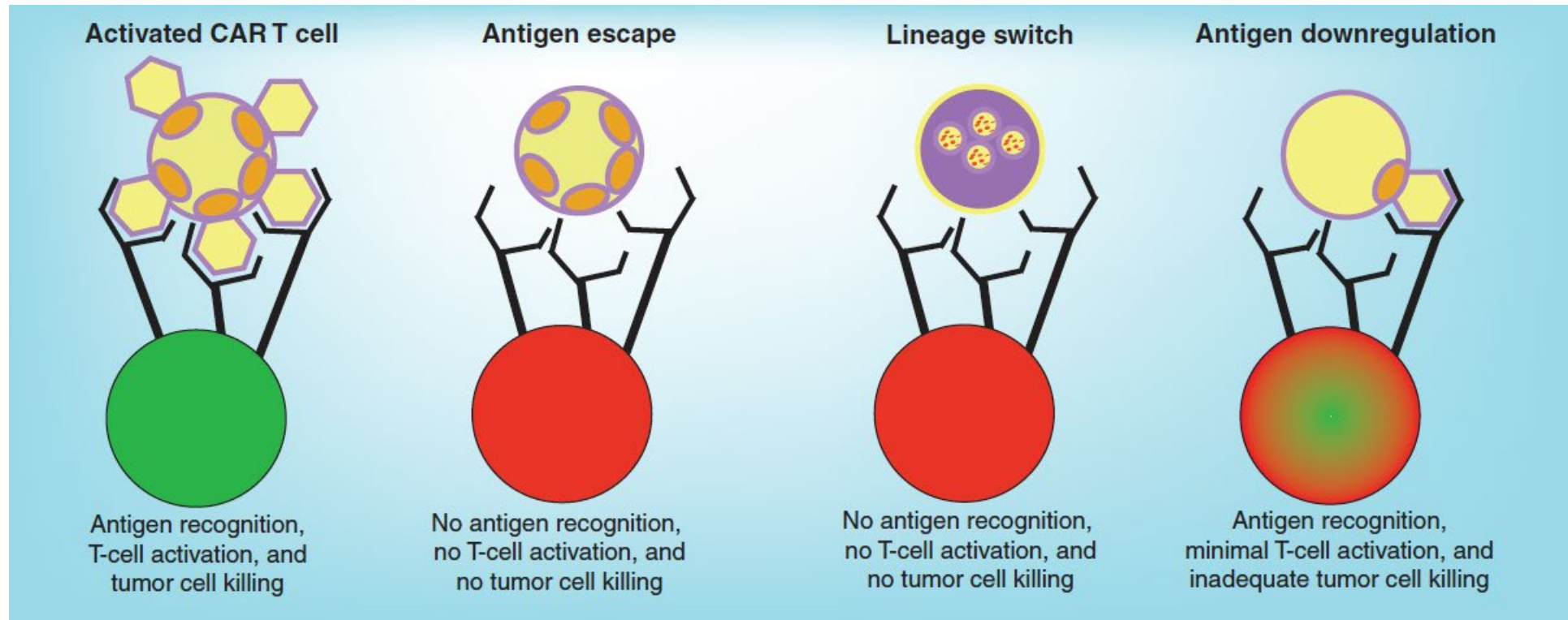
GENERATIONS OF CAR MOLECULES



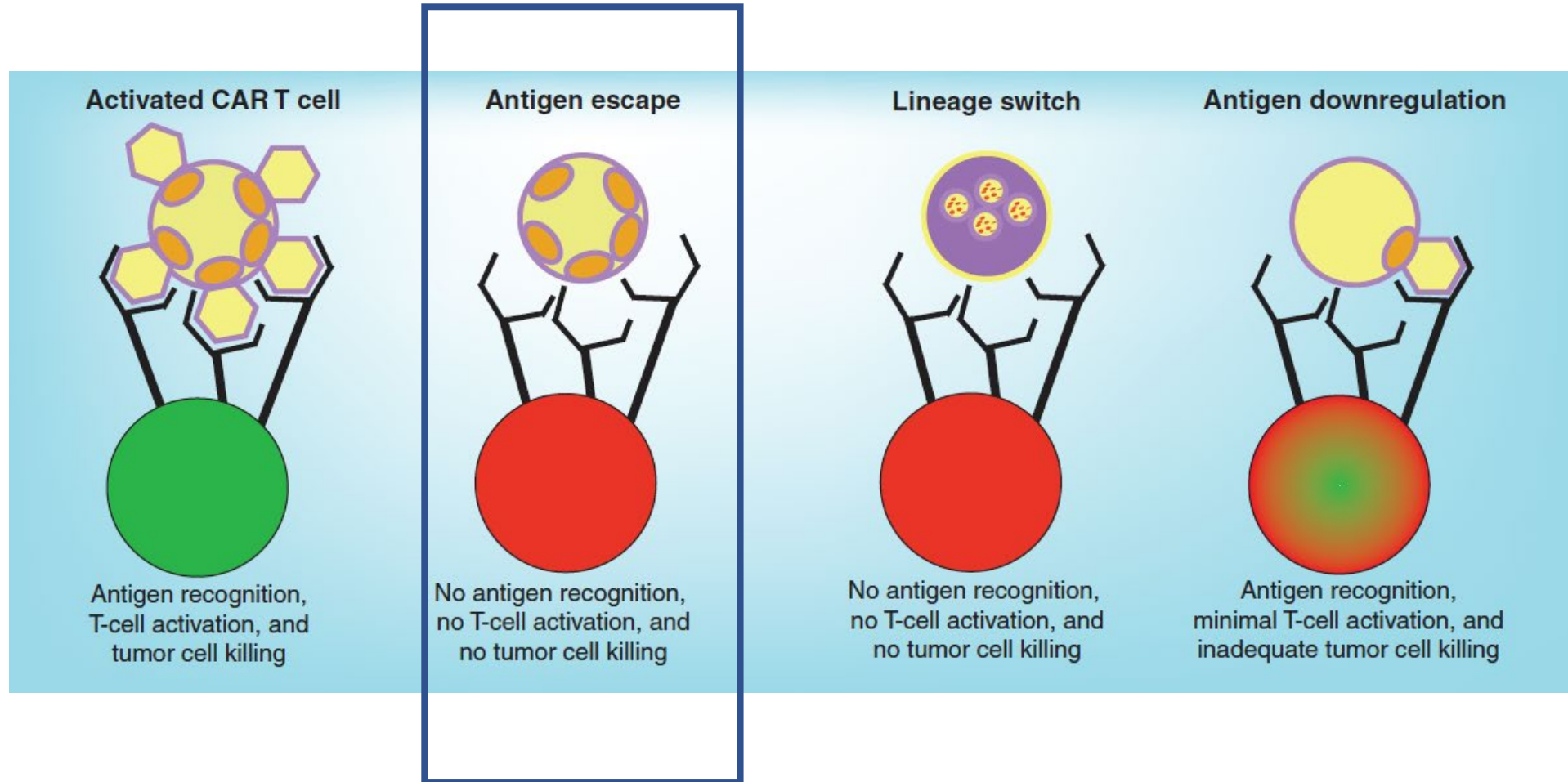
CAR-T Cell Therapy



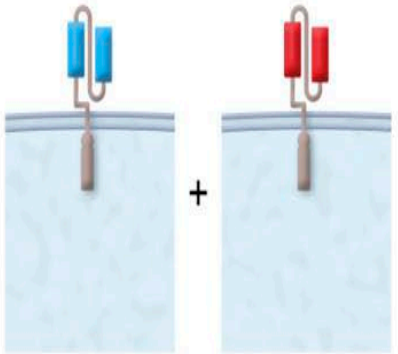
Antigen negative relapse



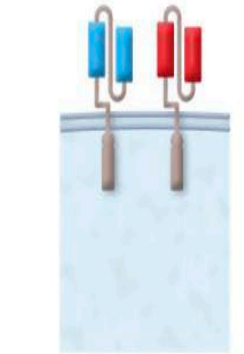
Antigen negative relapse



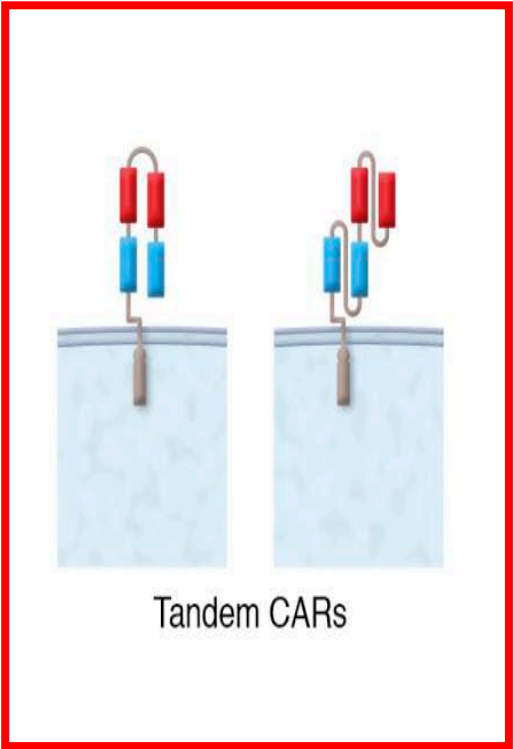
Dual-specific approaches



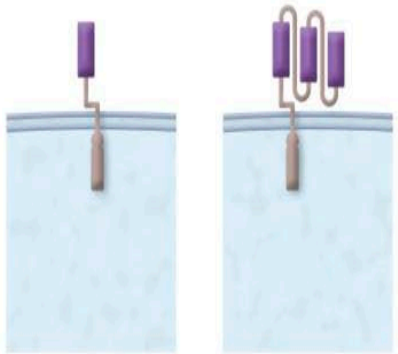
Pooled CAR populations



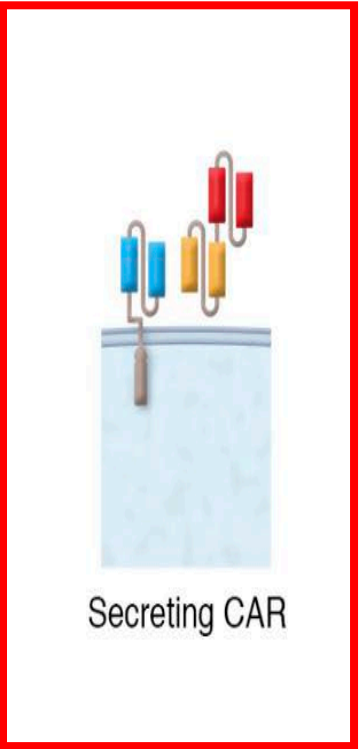
Double transduction



Tandem CARs



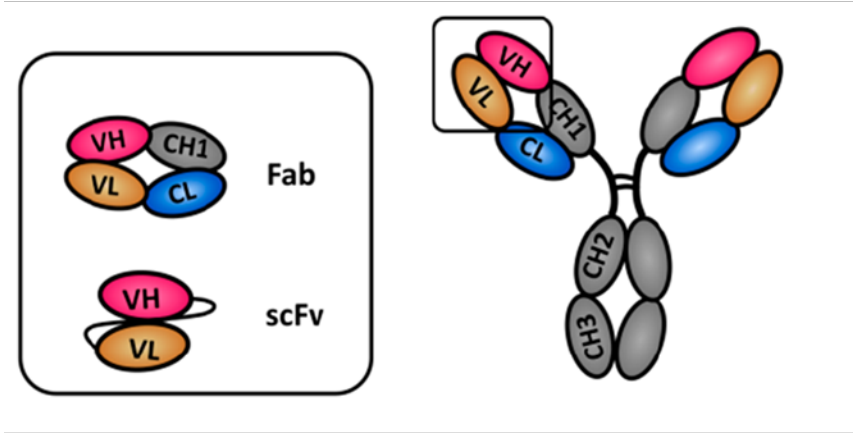
Polyspecific binding domains



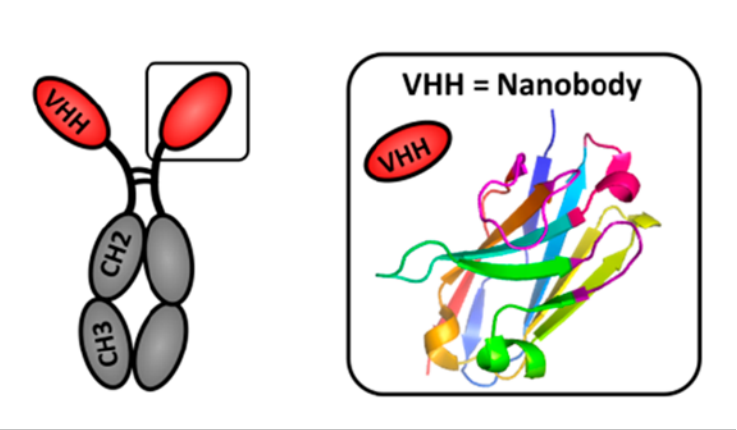
Secreting CAR

nanoCARs

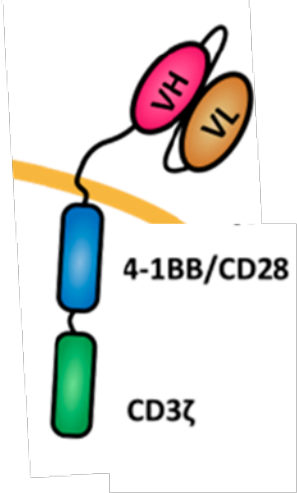
conventional antibody



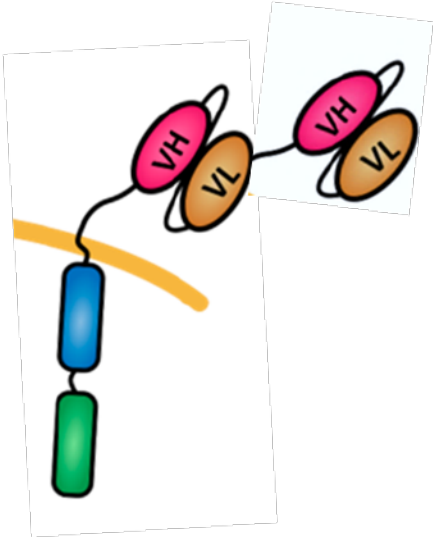
heavy chain only antibody



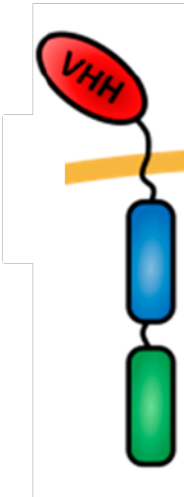
scFv based CAR



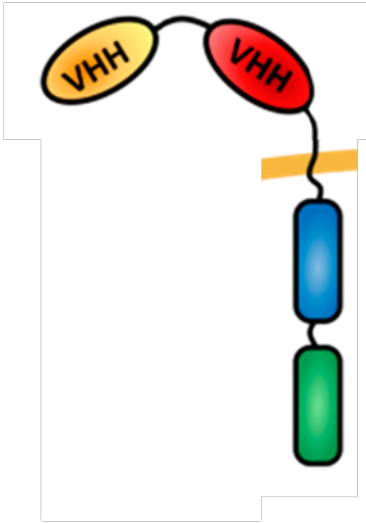
Tandem CARCAR



VHH based CAR nanoCAR



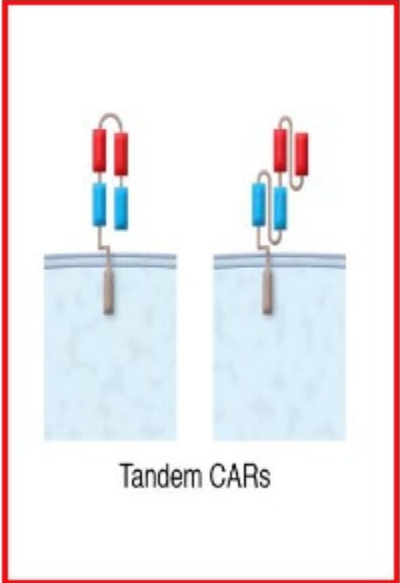
Tandem nanoCAR



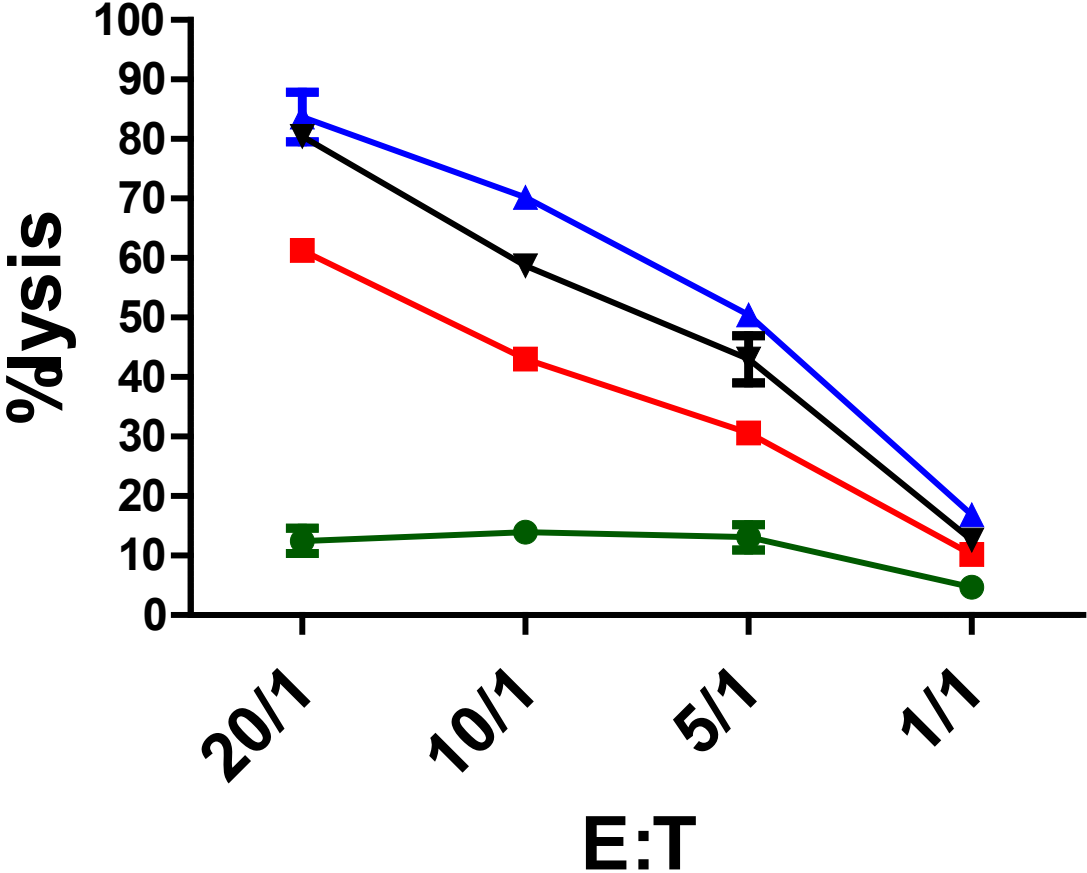
Dual-specific nanoCARs



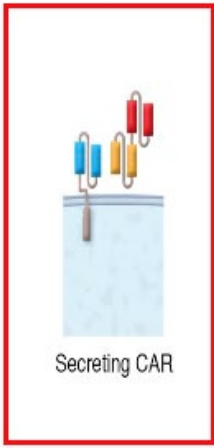
Stijn De Munter



CD20-HER2 nanoCAR



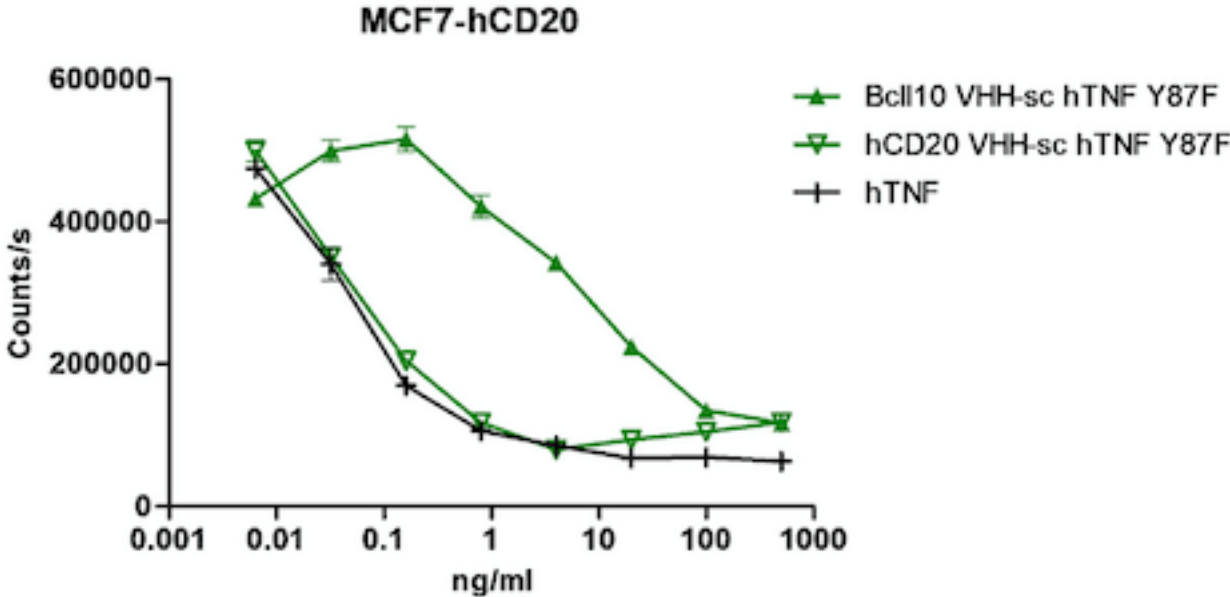
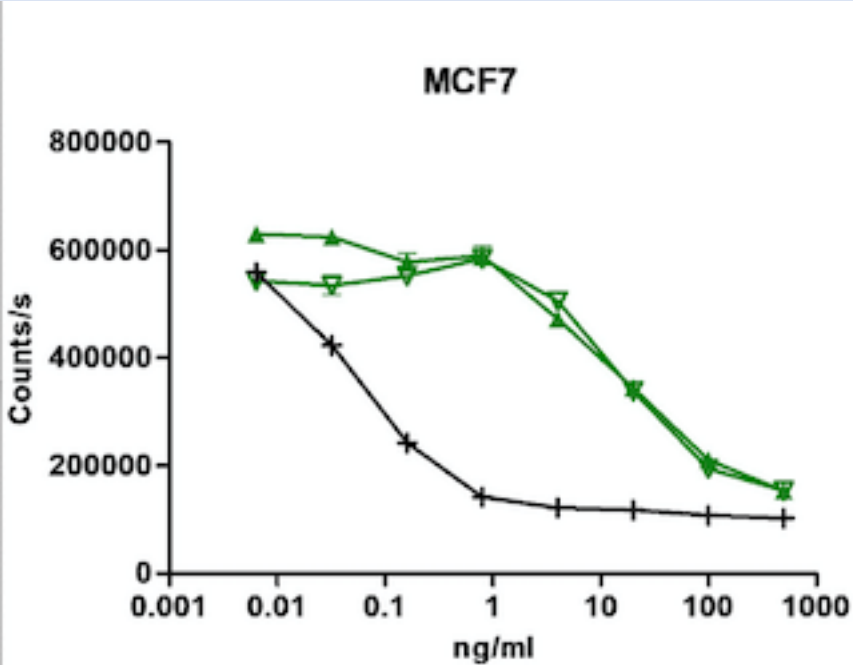
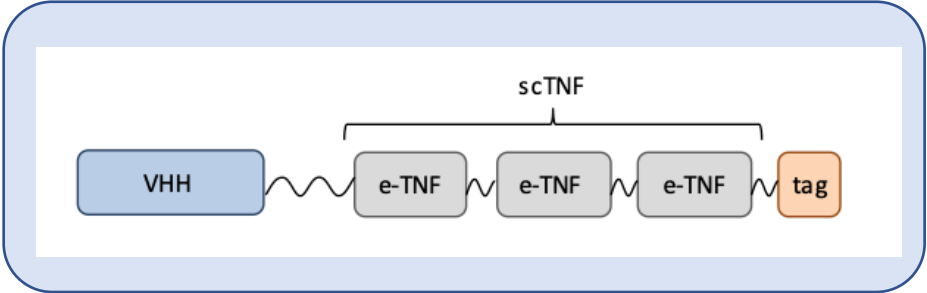
- Jurkat NTD
- Jurkat CD20⁺
- ▲ Jurkat HER2⁺
- ▼ Jurkat CD20⁺HER2⁺



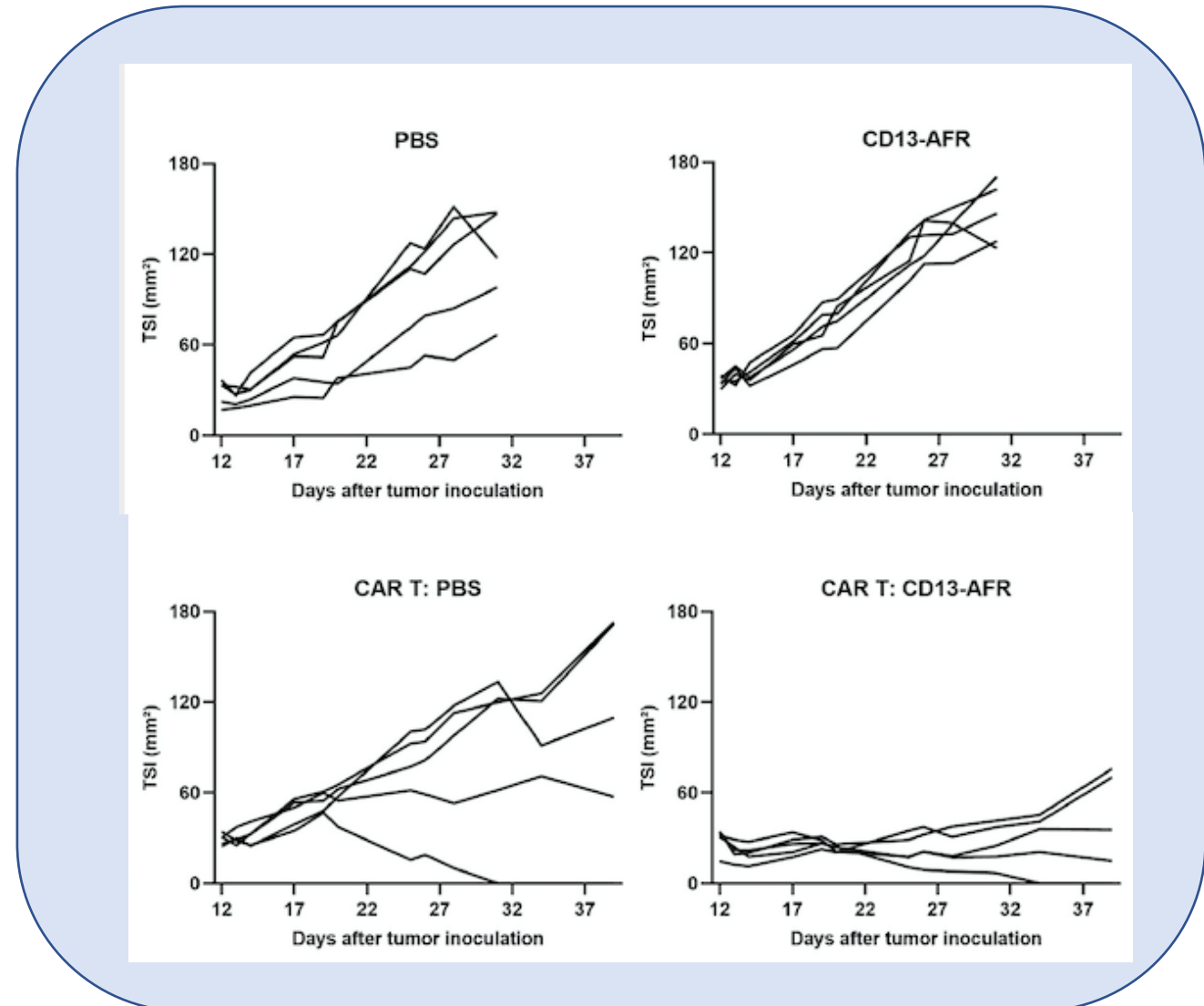
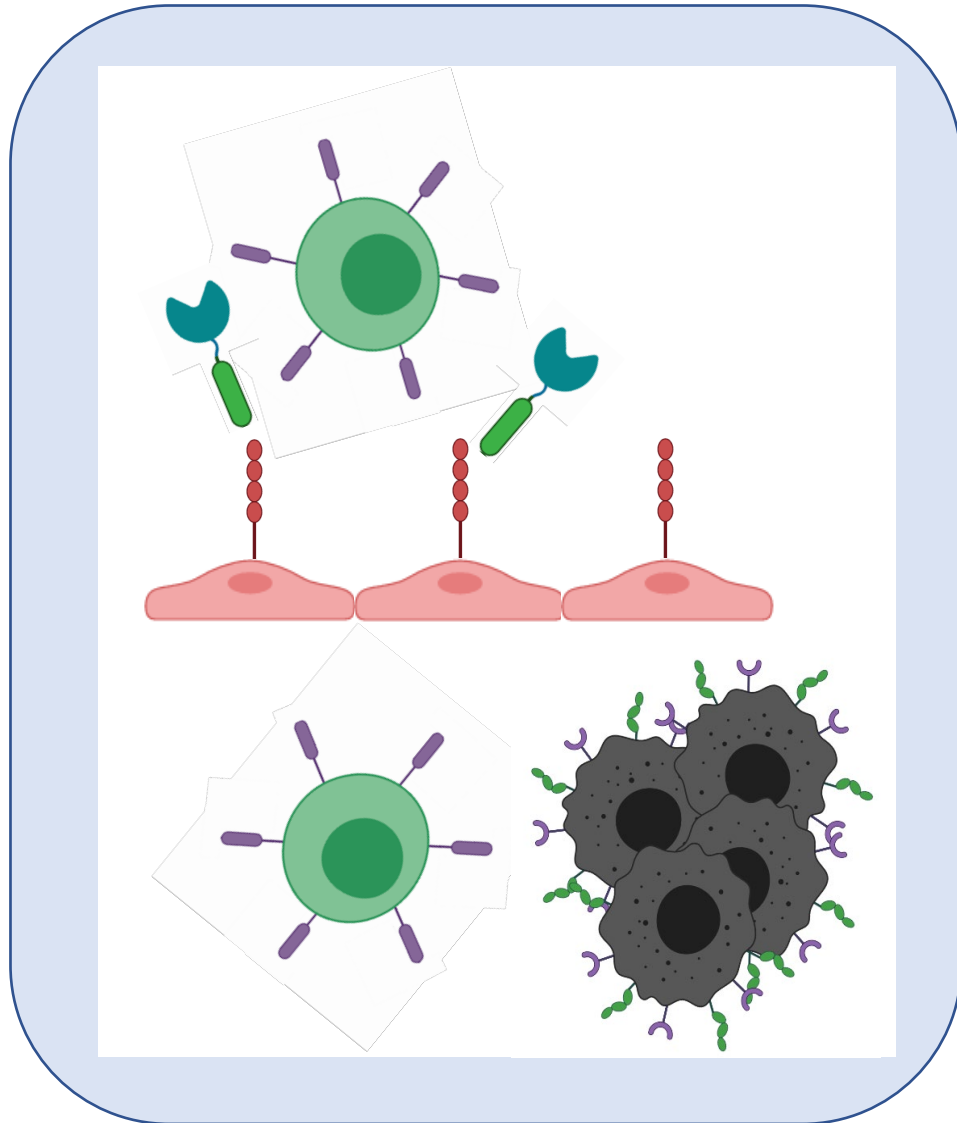
Actakines



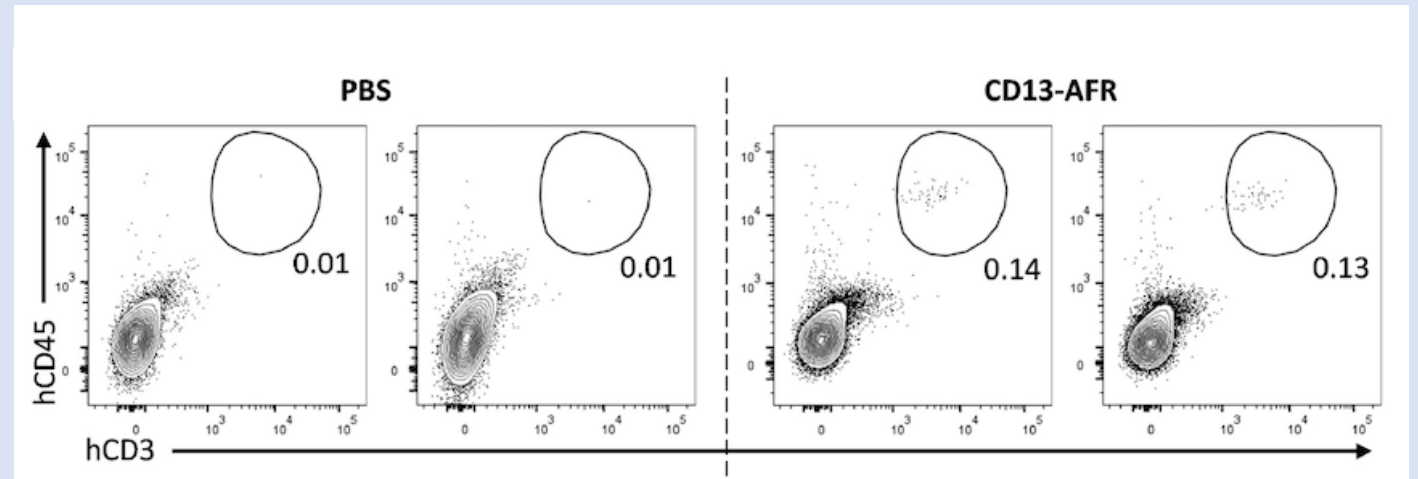
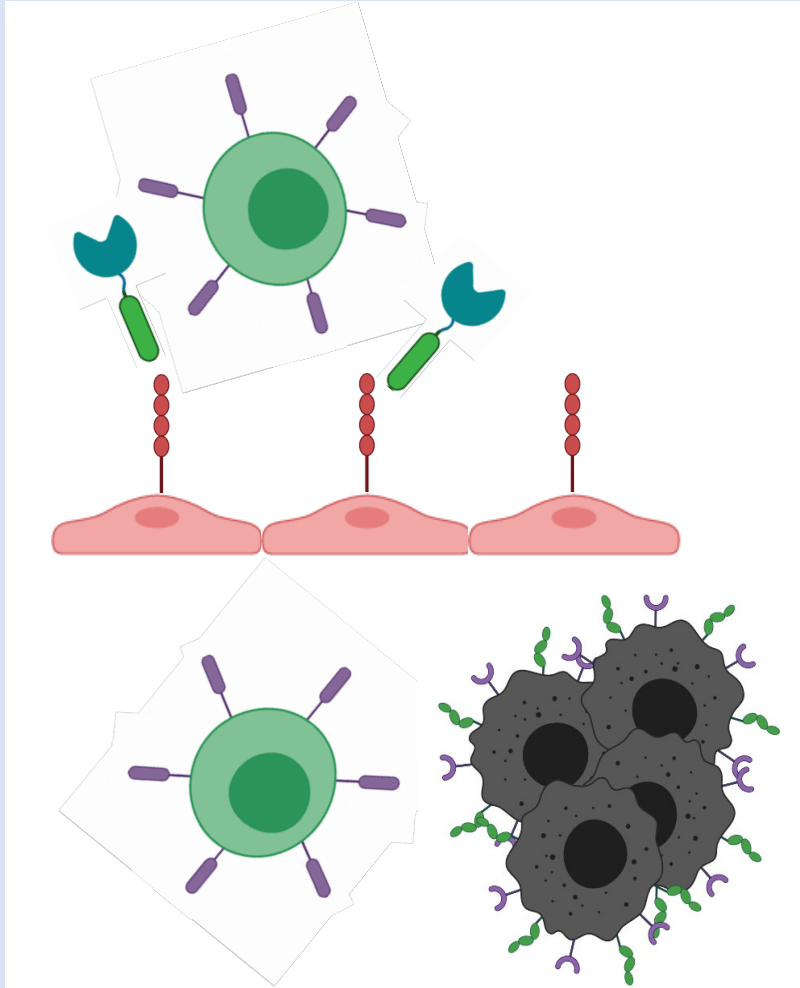
Jan Tavernier



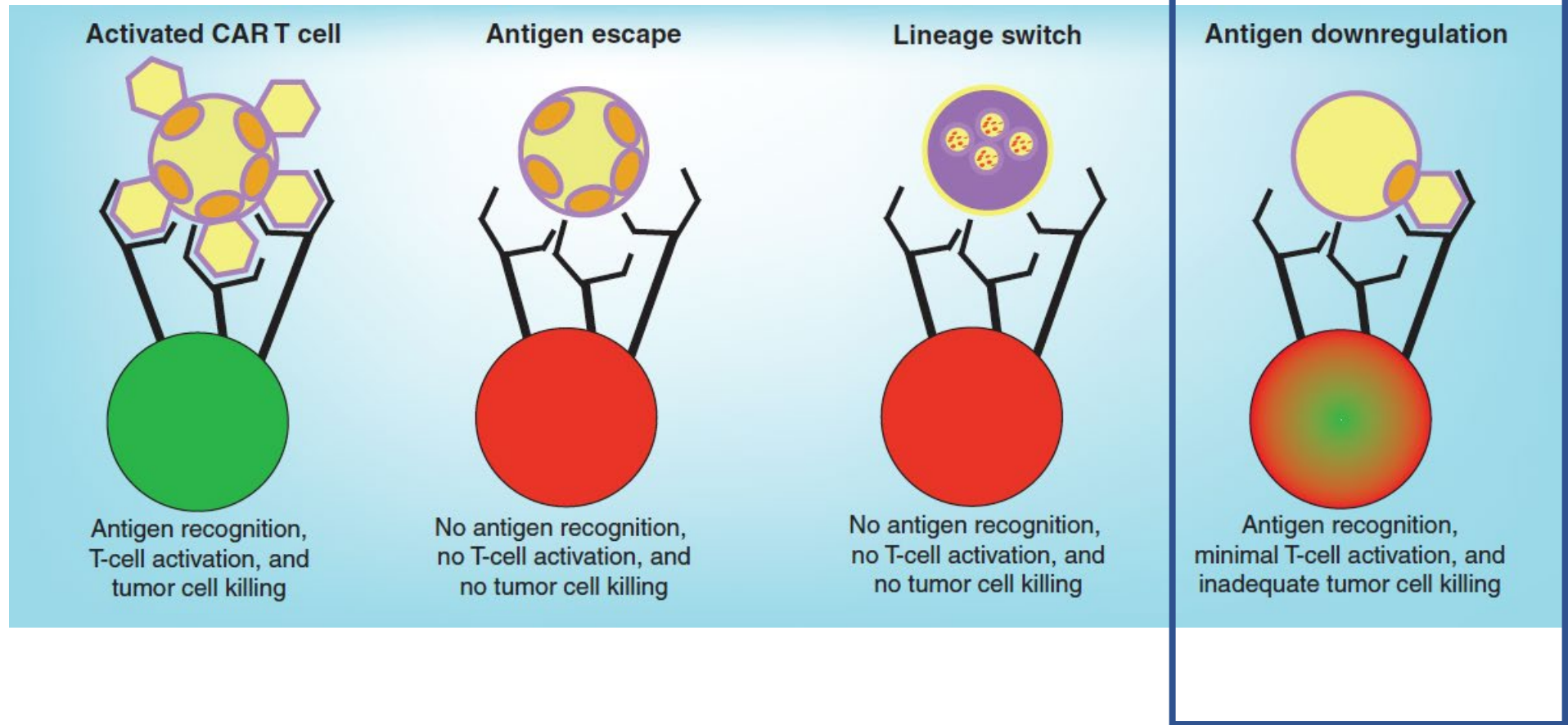
Nanobody based dual specific targeting



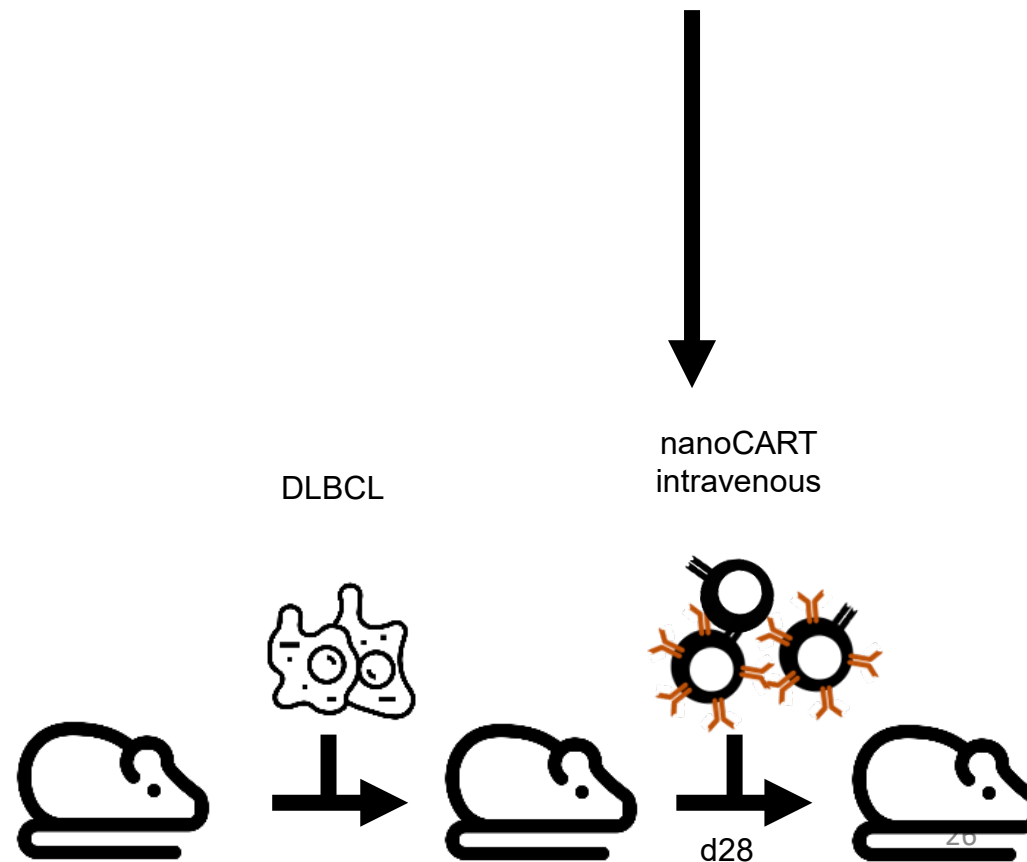
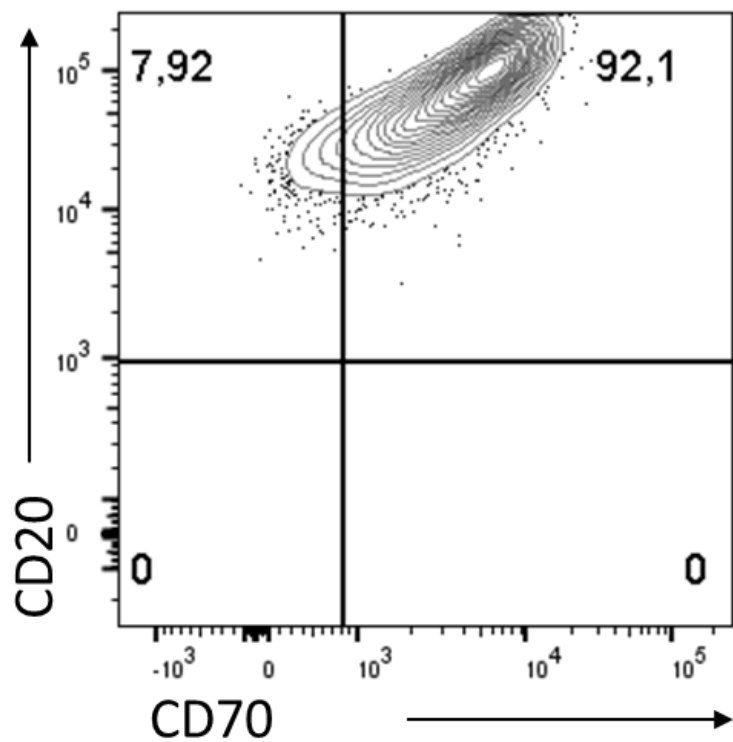
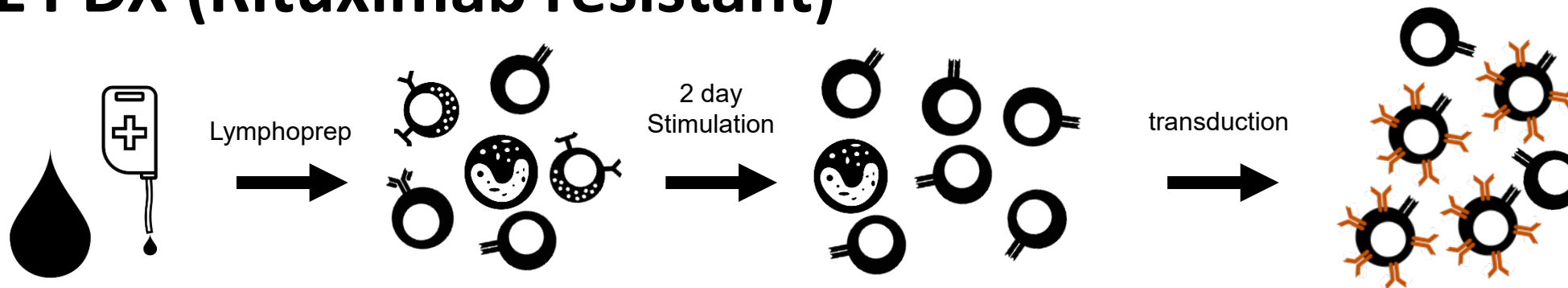
Nanobody based dual specific targeting



Antigen negative relapse



DLBCL PDX (Rituximab resistant)



Immune therapy : CAR-T

Target antigen

- Expression
- Off-target

Examples:

- CD19
- BCMA

Potency

- Checkpoint inhibitors
- Actakines/cytokines
- Dual specificity
- TCR-based CAR
- CRISPR engineered
- Off the shelf CAR
- ...

Collaborators and Team



Business Developer
Tim Desmet



Joline Ingels
Killian Raes
Stijn De Munter
Eva Pascal



Karim Vermaelen
Sandra Van Lint
Kelly Heyns



Eva Van Houtte
Saskia Desmet
Sofie Leyman
Nele Lootens
Liselotte Willems
Marieke Brusseeel



Francis Impens
Rupert Mayer
Lennart Martens



Bjorn Menten
Laurenz De Cock



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Innovatiefonds UZ Gent



Stefaan De Smedt
Heleen Dewitte
Ine Lentacker
Rein Verbeke

