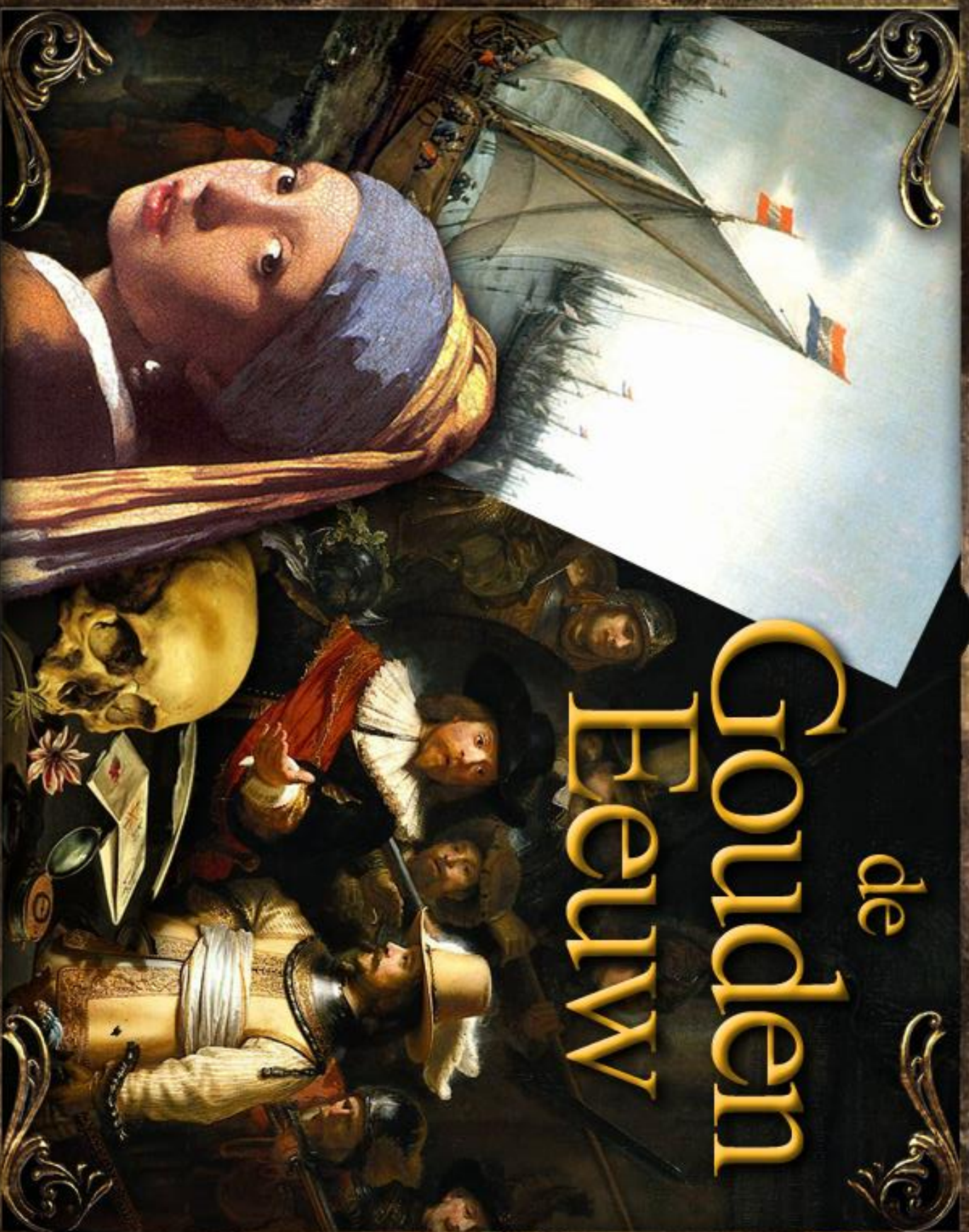


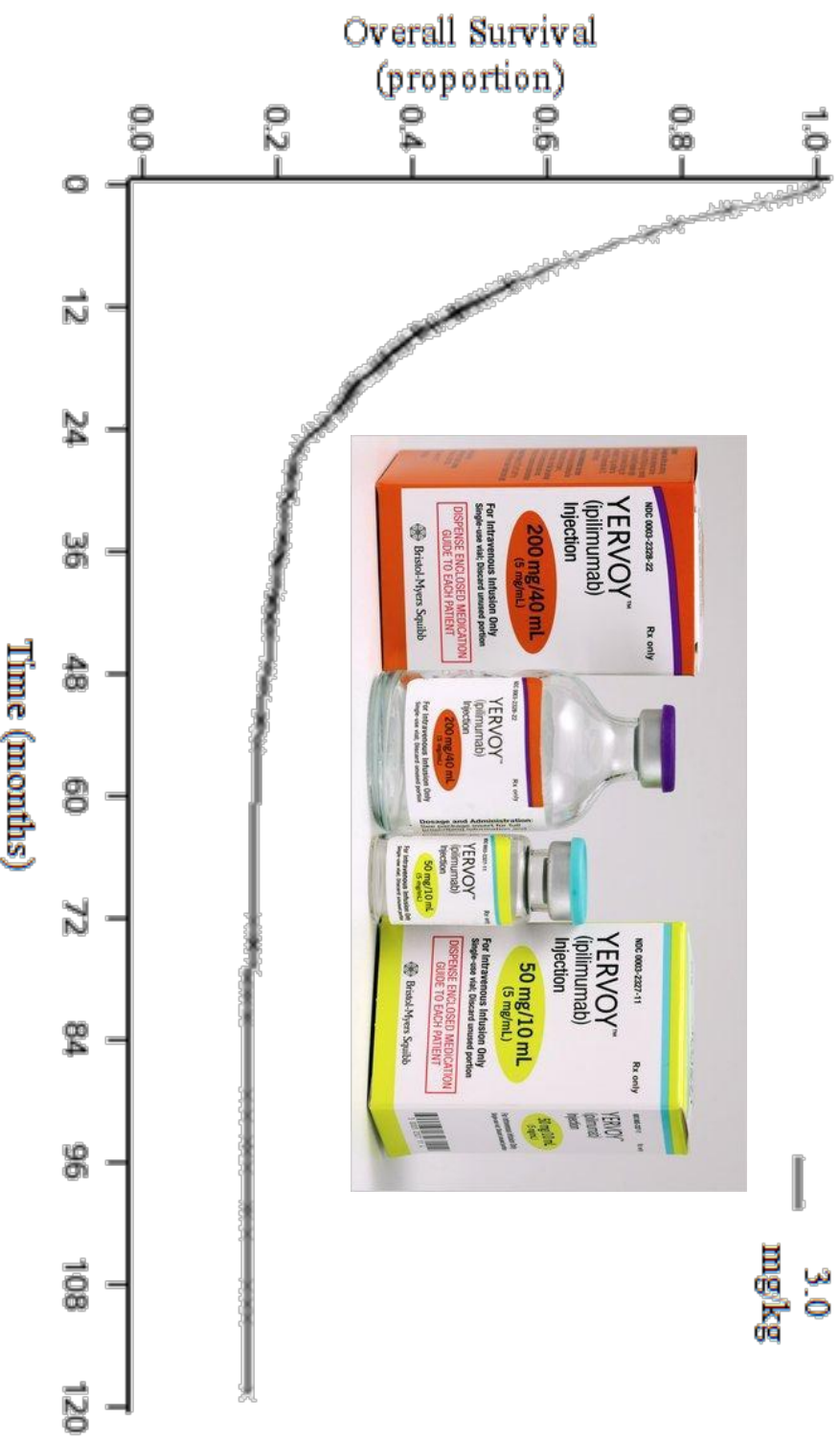


WAKING THE BODY'S DEFENDERS

For more than a century, researchers have tried to harness the human immune system to fight cancer. But high hopes, too often, have been followed by disappointment. Here, some milestones.



Melanoma: the revolution started with anti-CTLA4



Can we cure cancer?



I'Mmunotherapy™ and I'm Curing Cancer

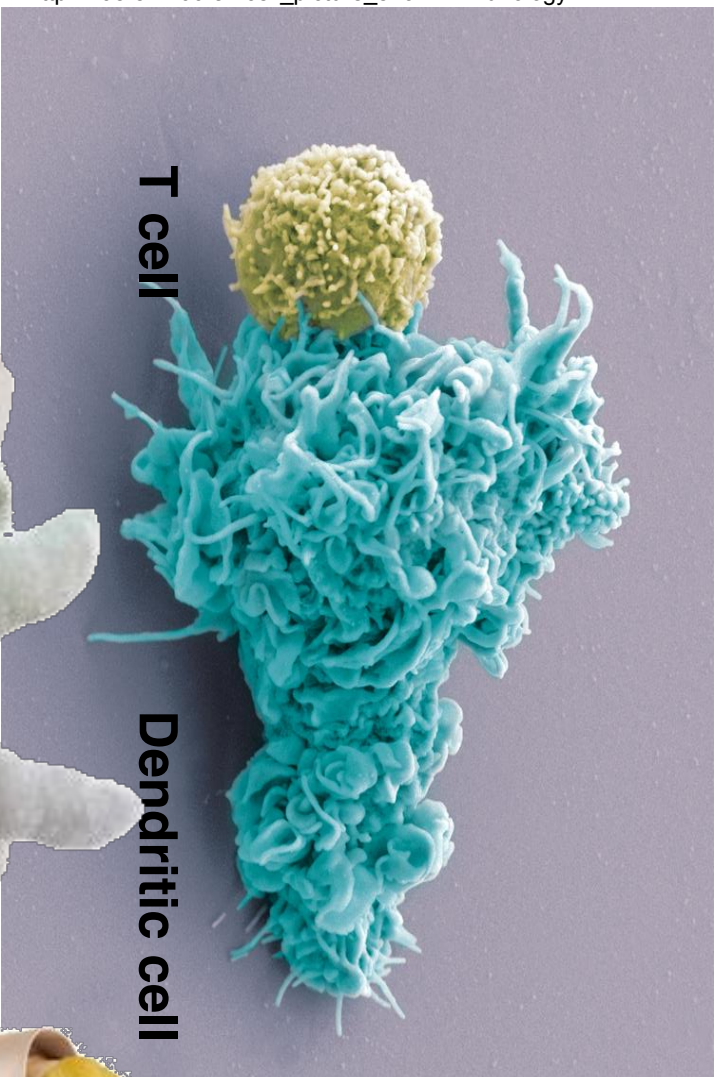
June is Cancer Immunotherapy Awareness Month. Wear white on June 7 to support cancer immunotherapy research.

Fight With White ►

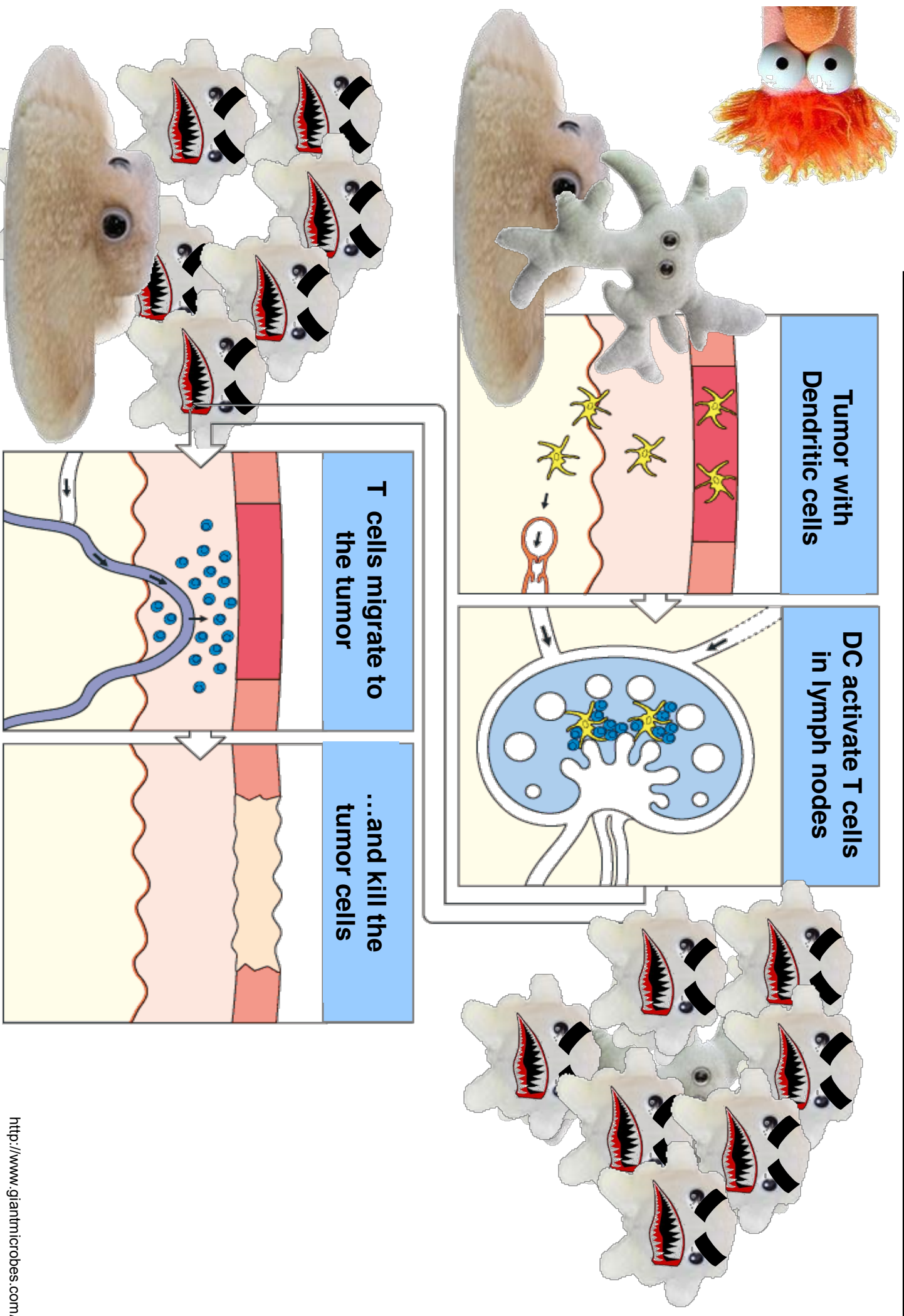
<http://www.cancerresearch.org/news-publications/our-blog/july-2013/inaugural-cancer-immunotherapy-awareness-month-a-success>

Starring...

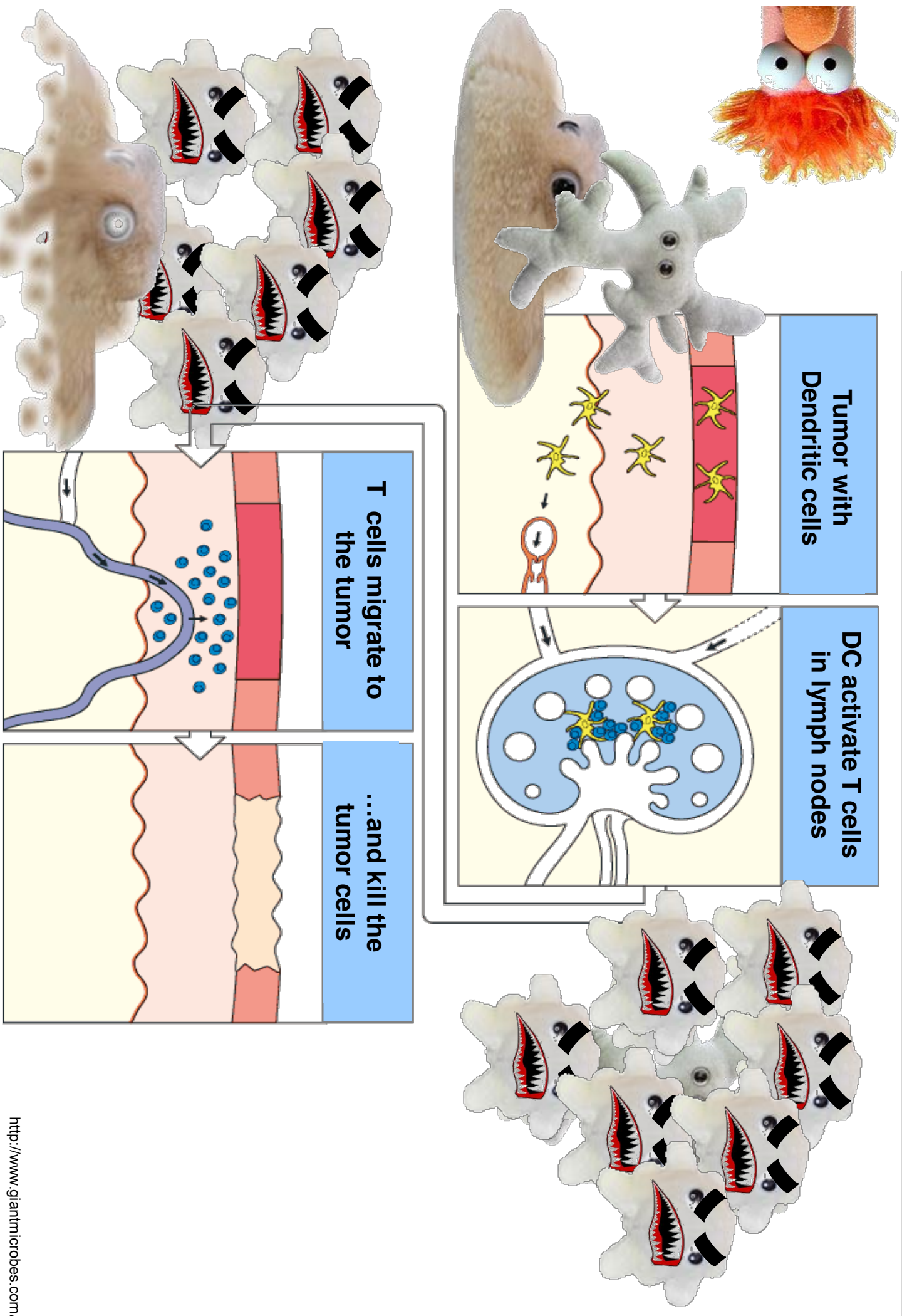
http://198.81.200.84/cell_picture_show-immunology



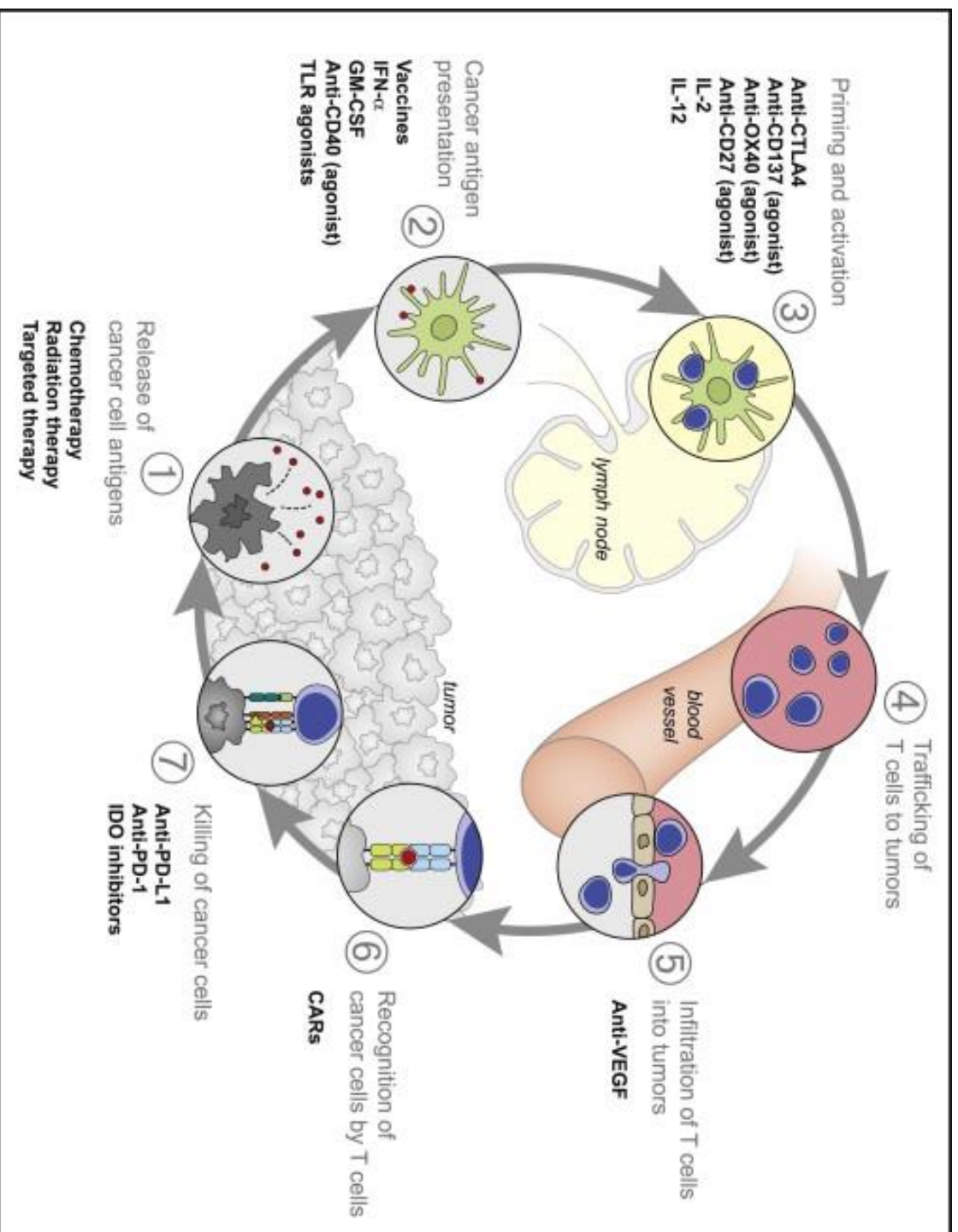
The principle of anti-tumor immunity: the Muppet version



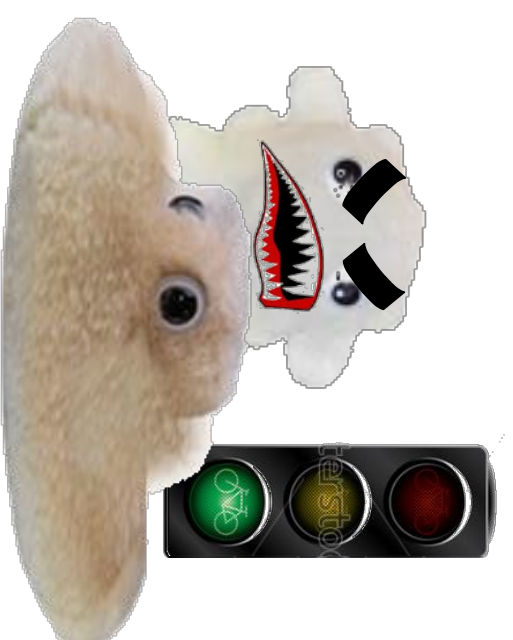
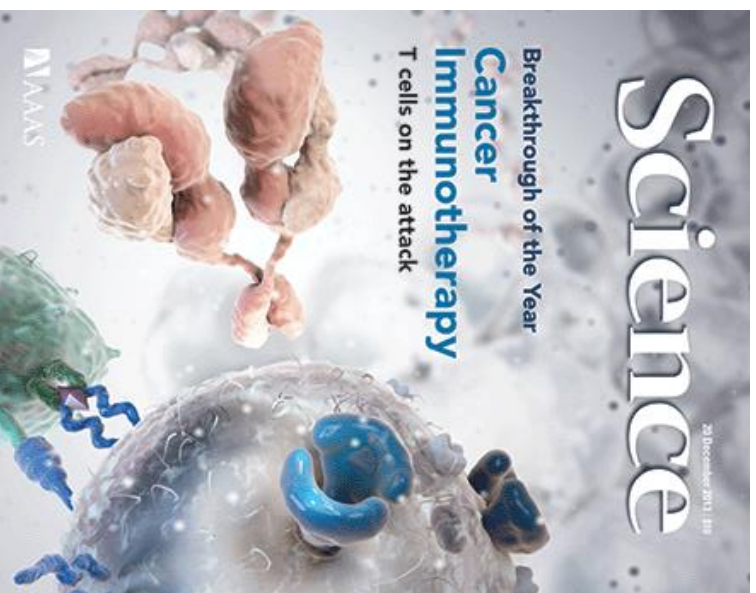
The principle of anti-tumor immunity: the Muppet version



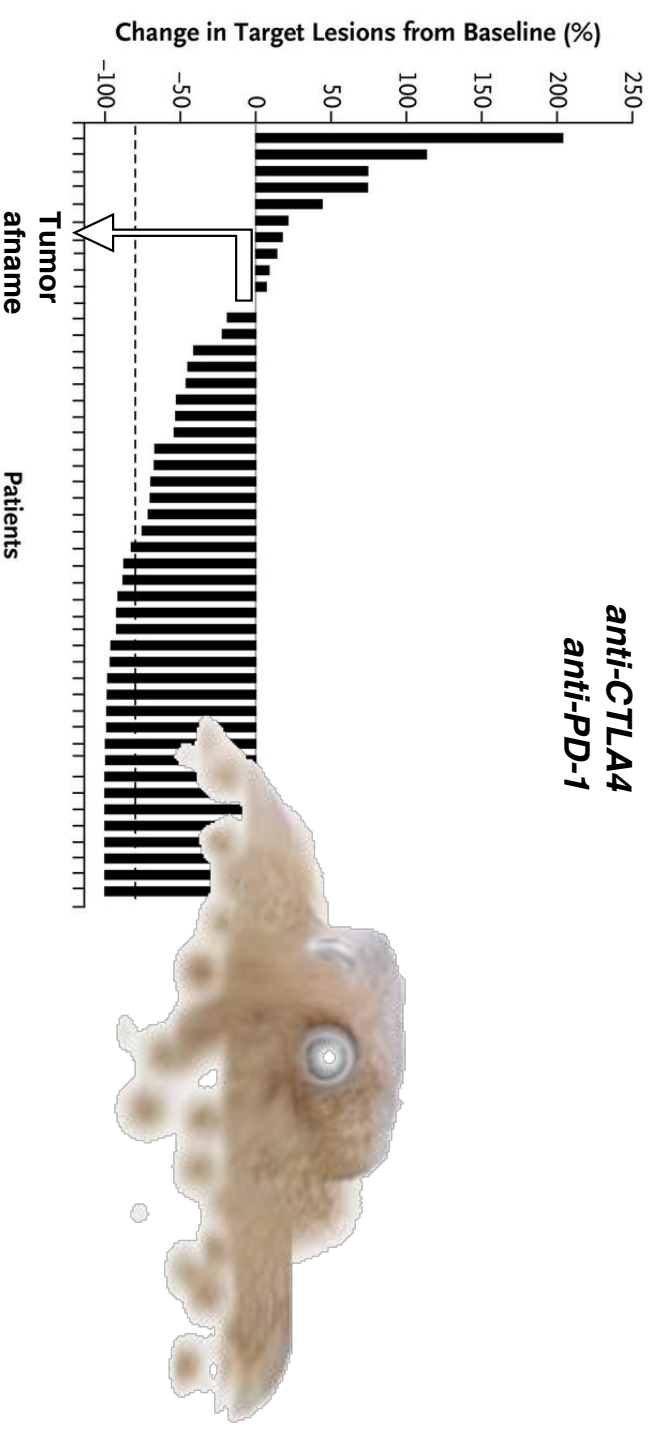
The Mellman cancer immunity cycle: slightly more scientific



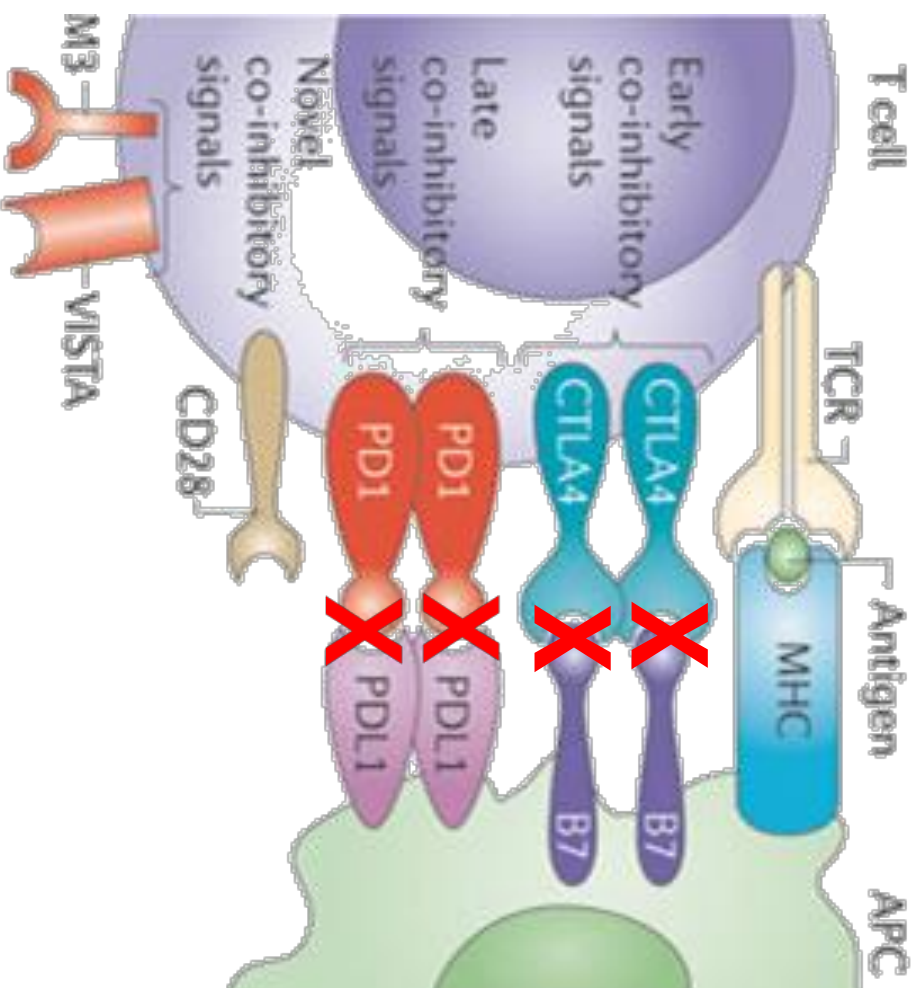
Chen et al. Immunity. 2013 Jul 25;39(1):1-10.



anti-CTLA4
anti-PD-1



PD-1 and CTLA4 expression: immune checkpoints *an important immune escape mechanism*



Sharma et al. *Nature Reviews Cancer* 11, 805-812 (November 2011)



CORRESPONDENCE



**Rapid Eradication of a Bulky Melanoma Mass
with One Dose of Immunotherapy**

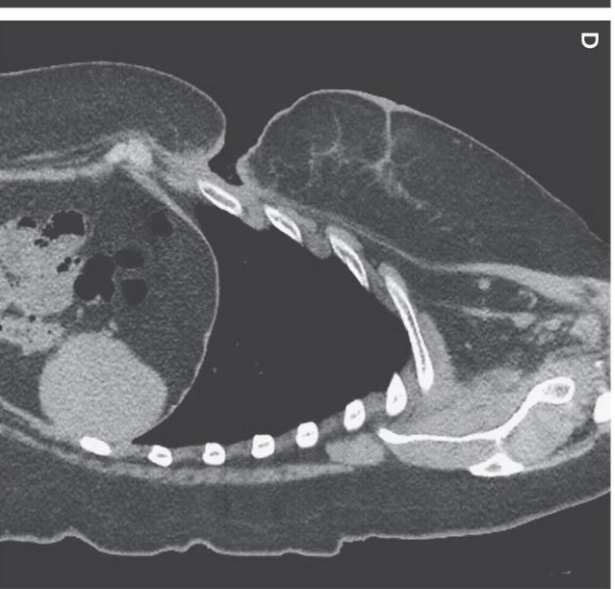
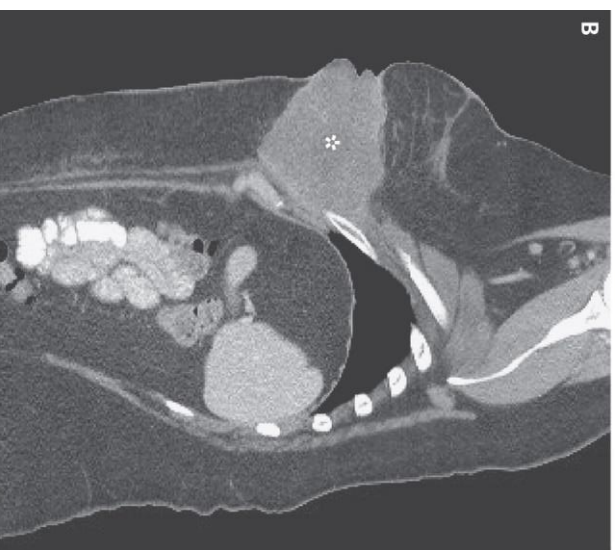
Paul B. Chapman, M.D.

Sandra P. D'Angelo, M.D.

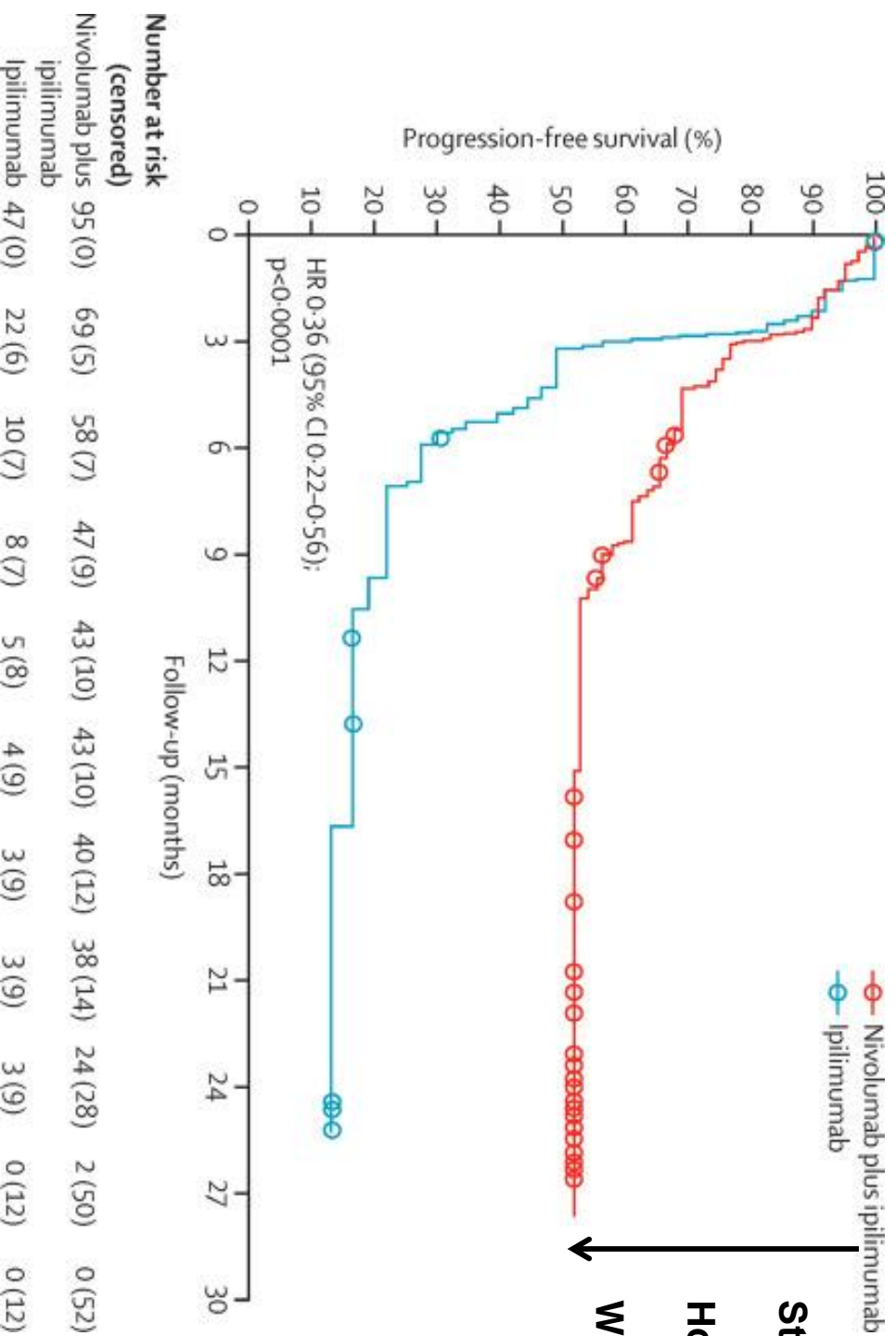
Jedd D. Wolchok, M.D., Ph.D.

Memorial Sloan Kettering Cancer Center
New York, NY

A REVOLUTION!!



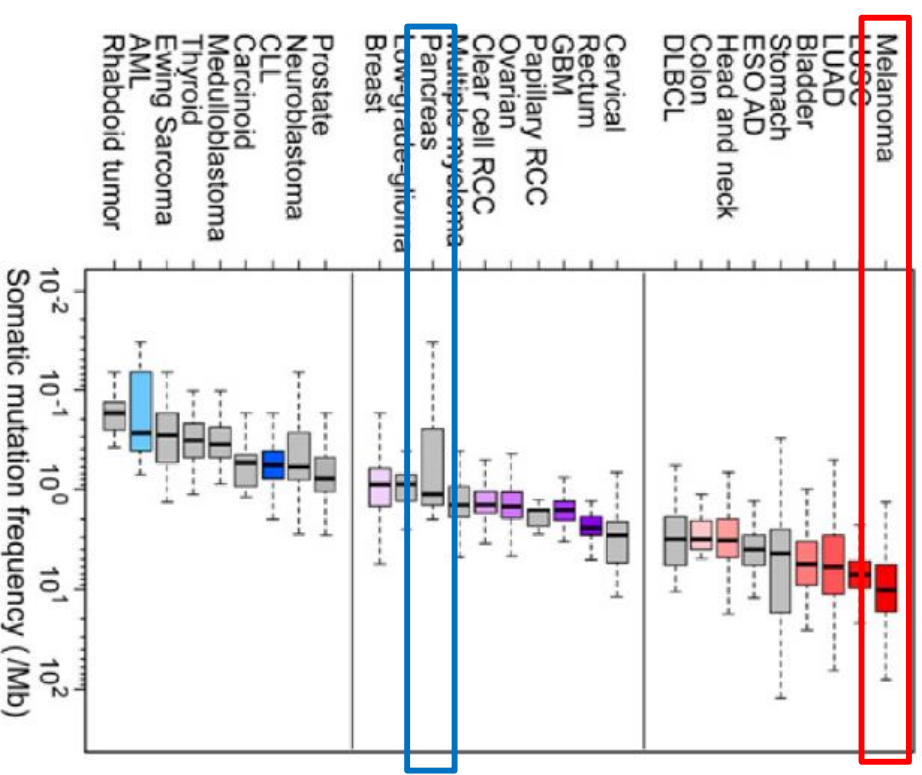
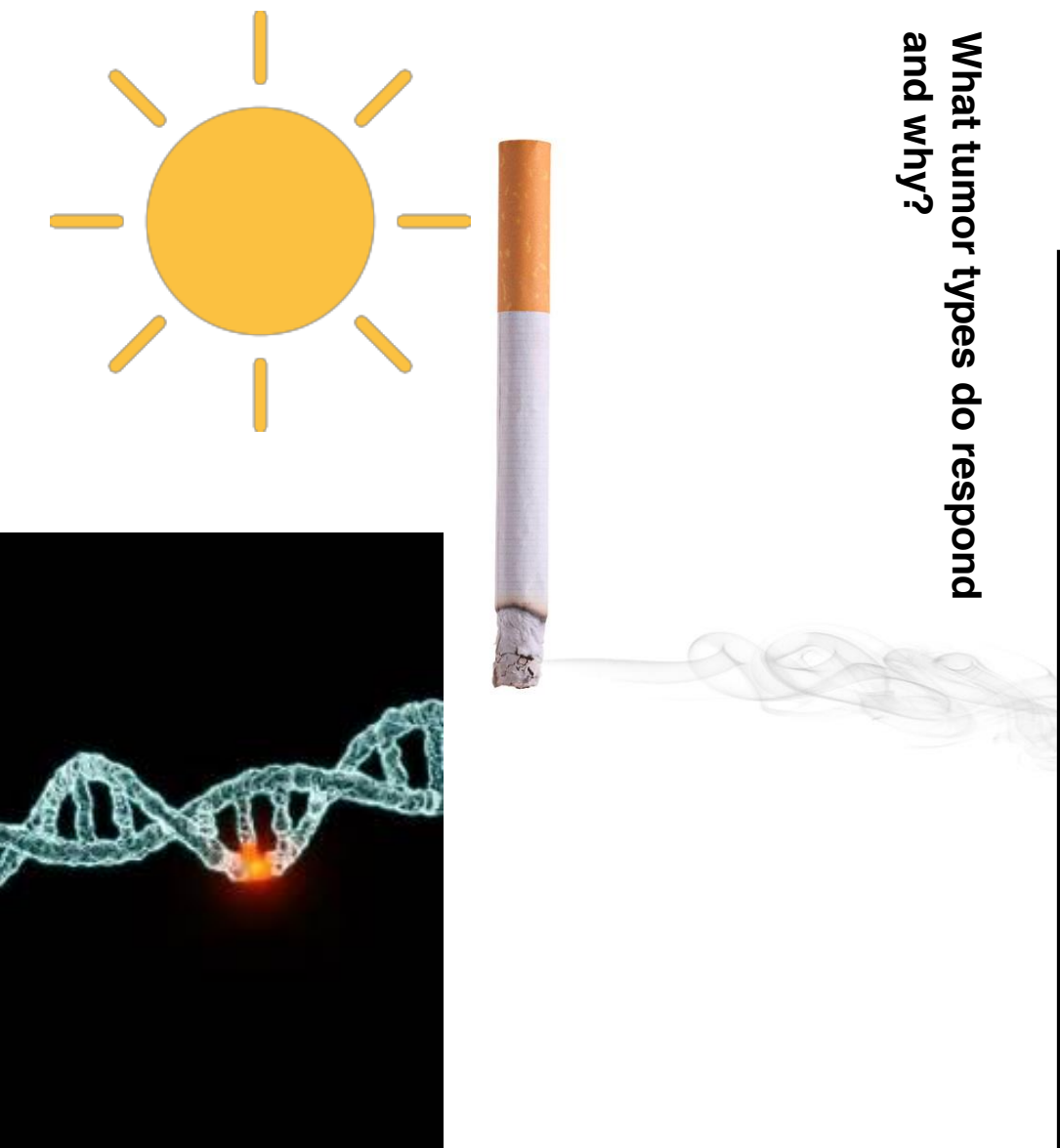
The promise of Immunotherapy: durable responses



Hodi et al. Lancet Oncol 2016

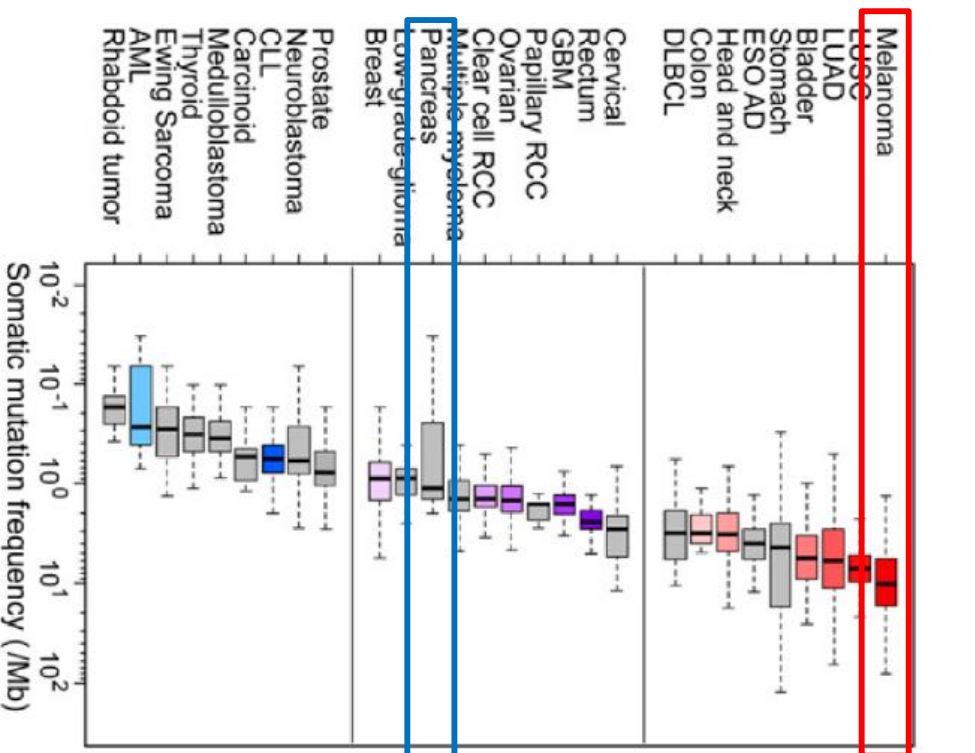
What is recognized by immune cells in tumors?

What tumor types do respond and why?

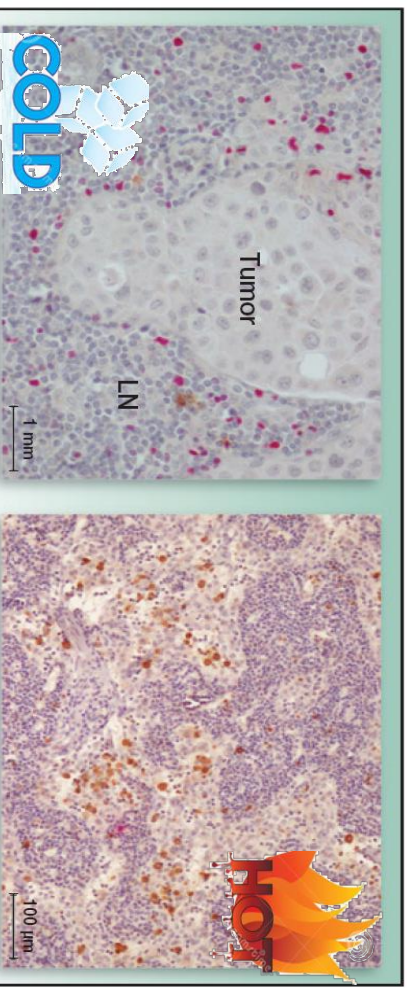


Rajasagi et al Blood 2014

High mutation load translates into hot and cold tumors...



Rajasagi et al Blood 2014

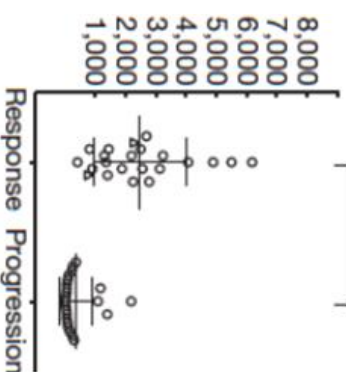


CCR Focus

© 2013 American Association for Cancer Research

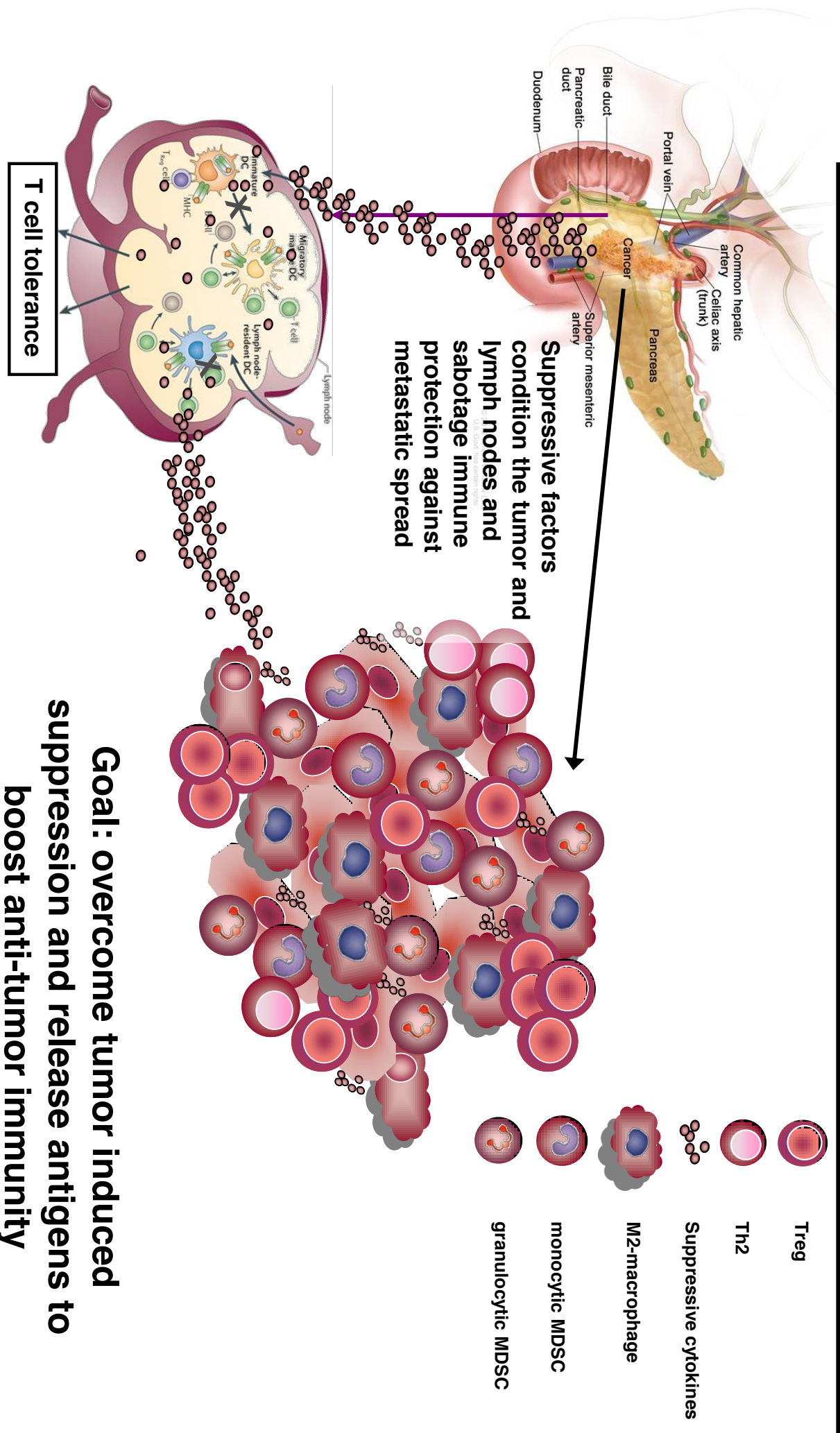
AKR

T cell numbers in tumor

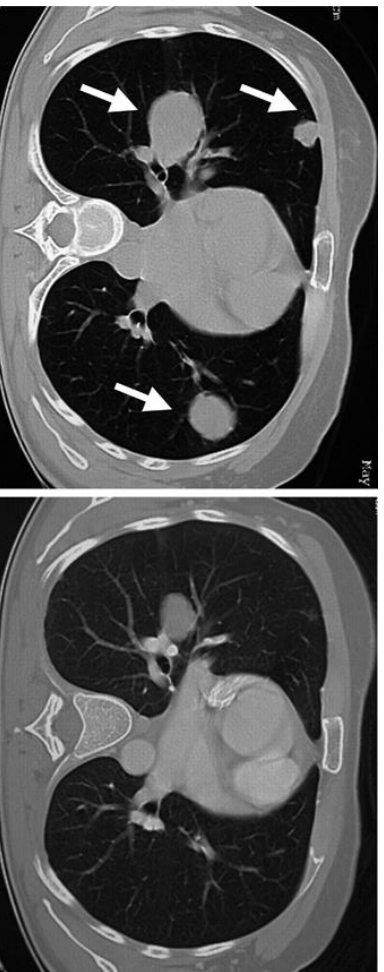
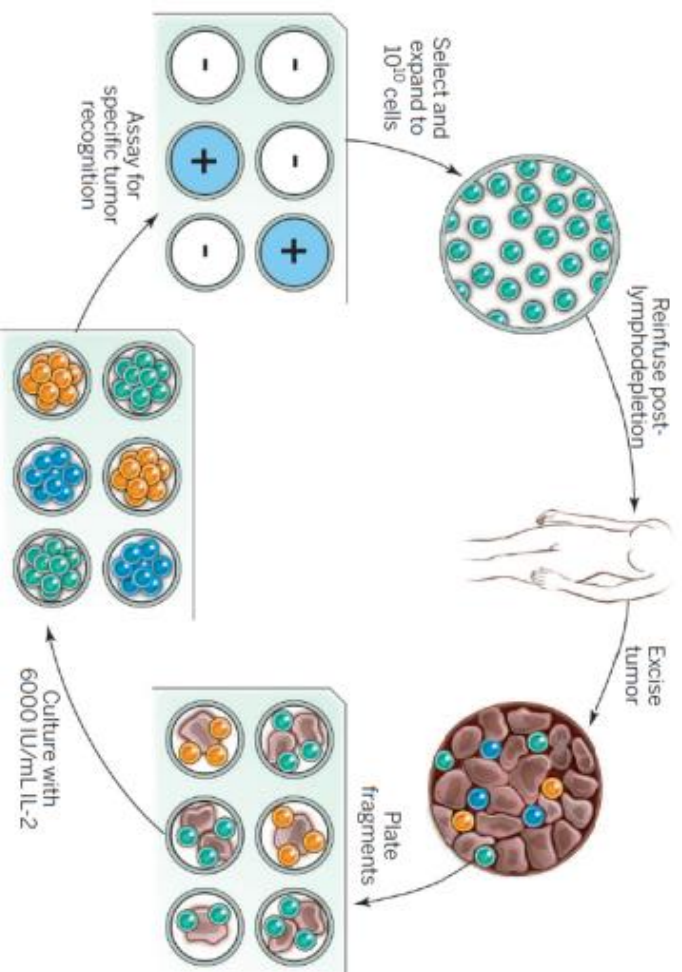


Tumeh et al Nature 2014

Tumors shape their microenvironment to escape the immune response



Can we make cold tumors (like pancreas) hot?

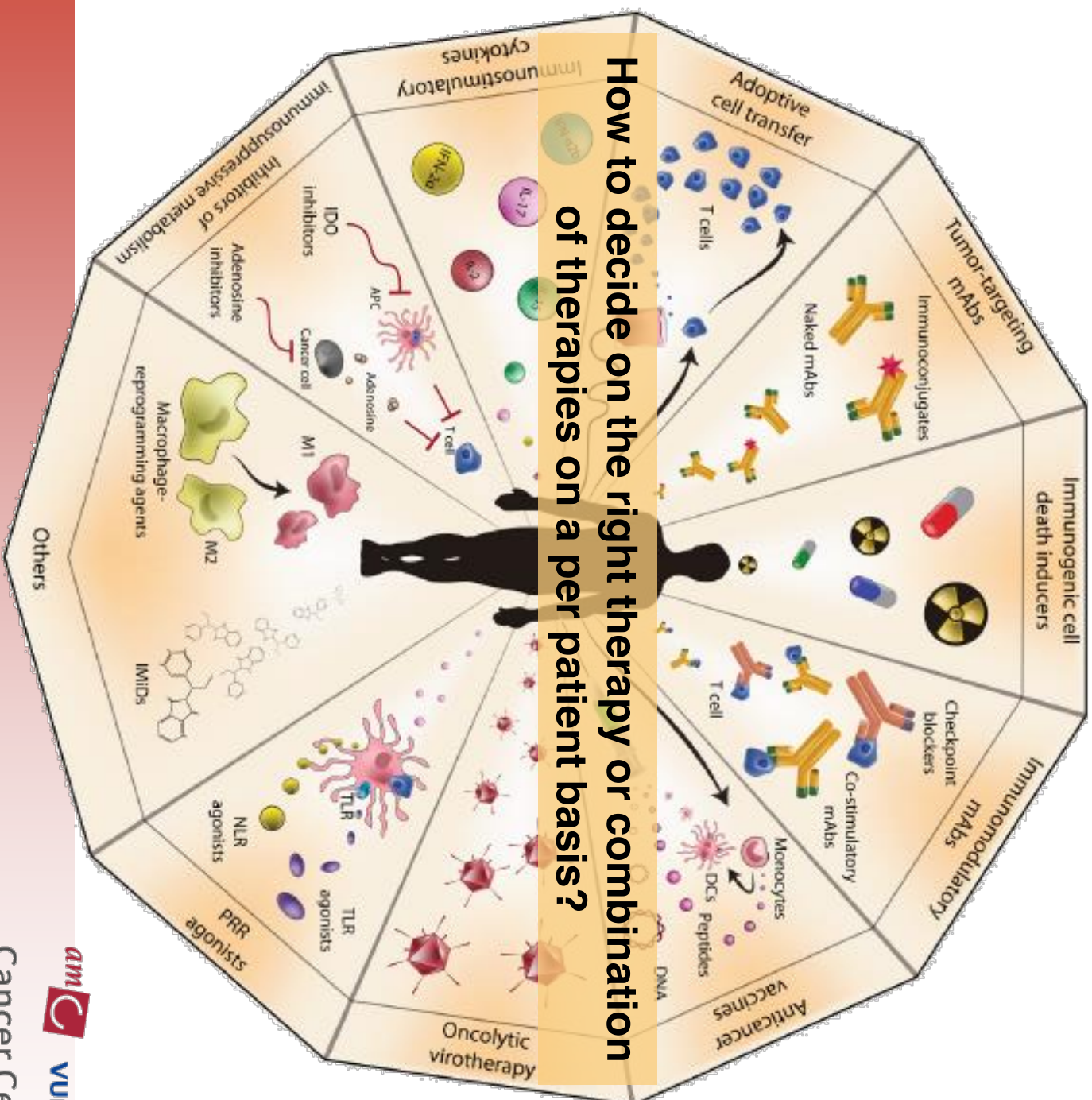


Steve Rosenberg

Approach #1: the Rosenberg strategy

A plethora of immunotherapies

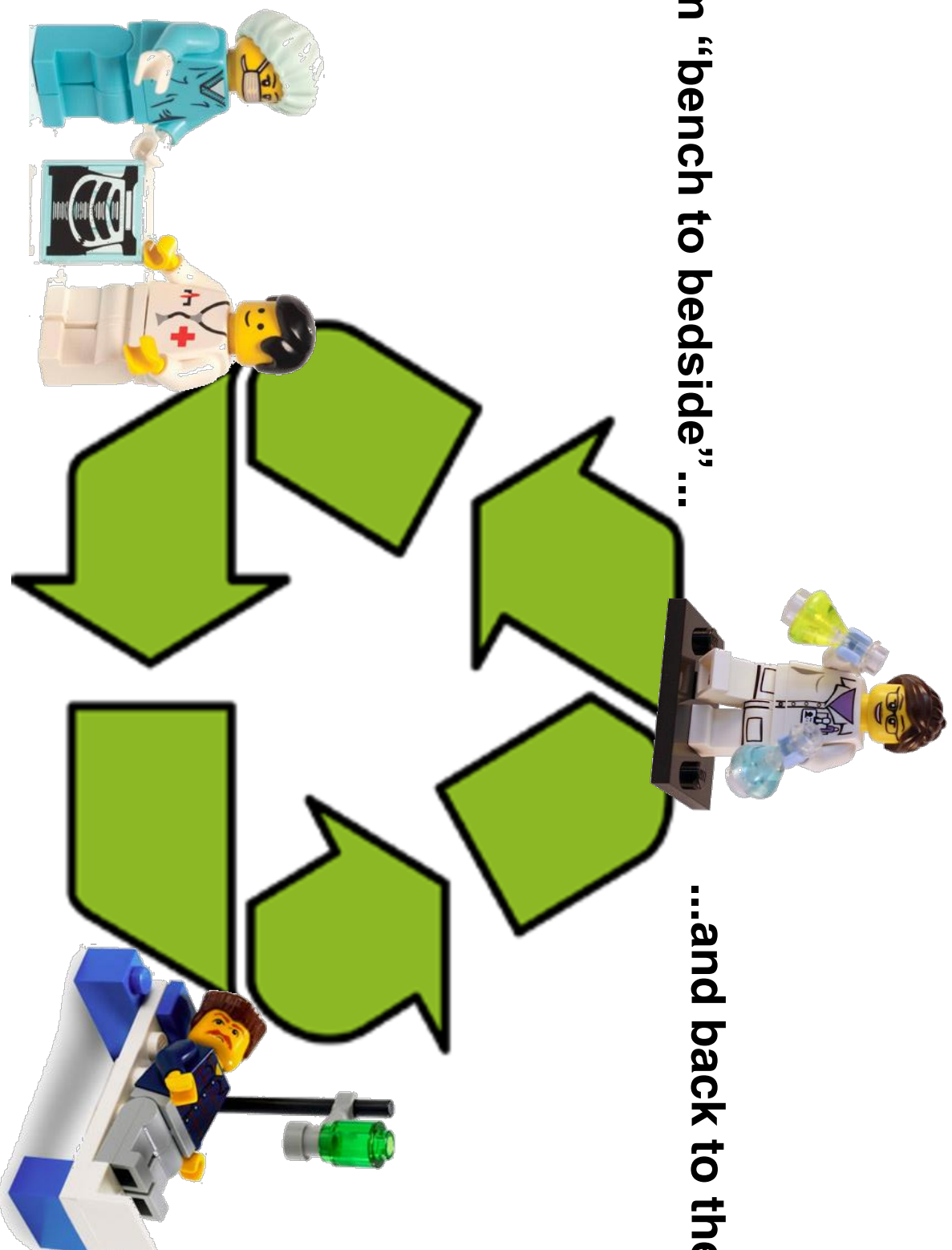
Classification of current anticancer immunotherapies



Translational Research = Recycling

From “bench to bedside” ...

...and back to the bench.



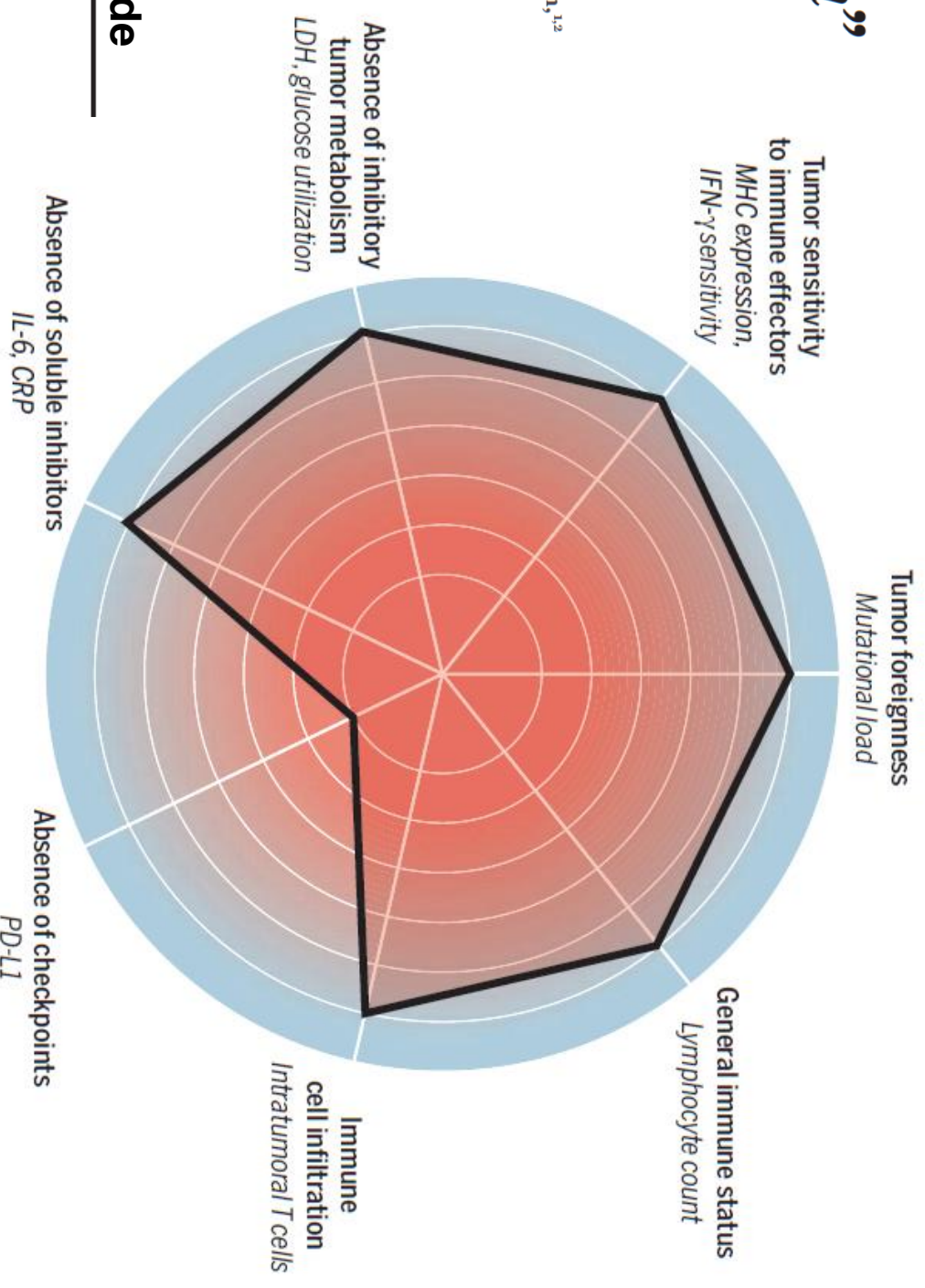
Personalized immunotherapy: the cancer immunogram

CANCER IMMUNOLOGY

The “cancer immunogram”

Visualizing the state of cancer–immune system interactions may spur personalized therapy

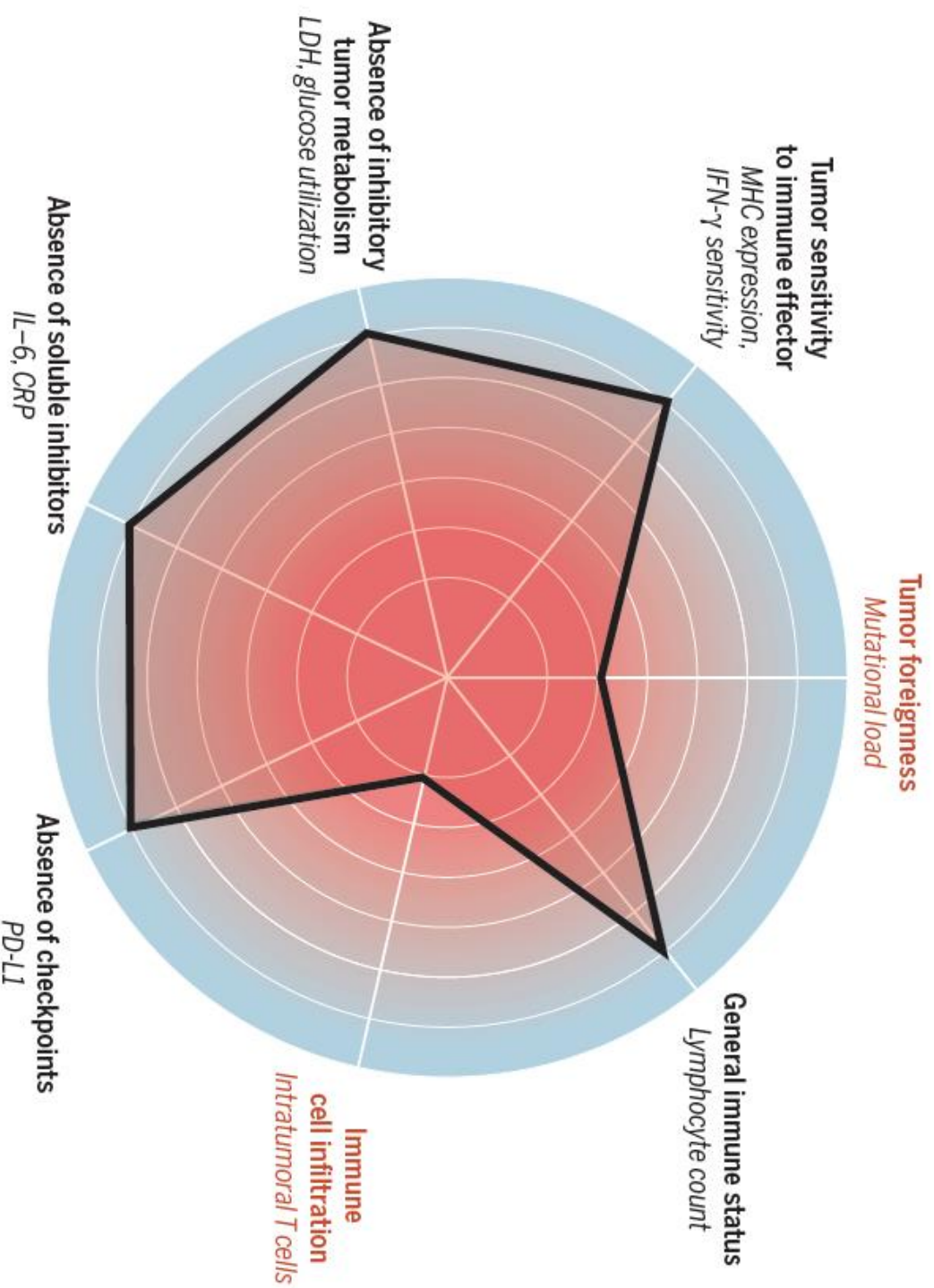
By Christian U. Blank,^{1,2} John B. Haanen,^{1,2}
Antoni Ribas,³ Ton N. Schumacher²



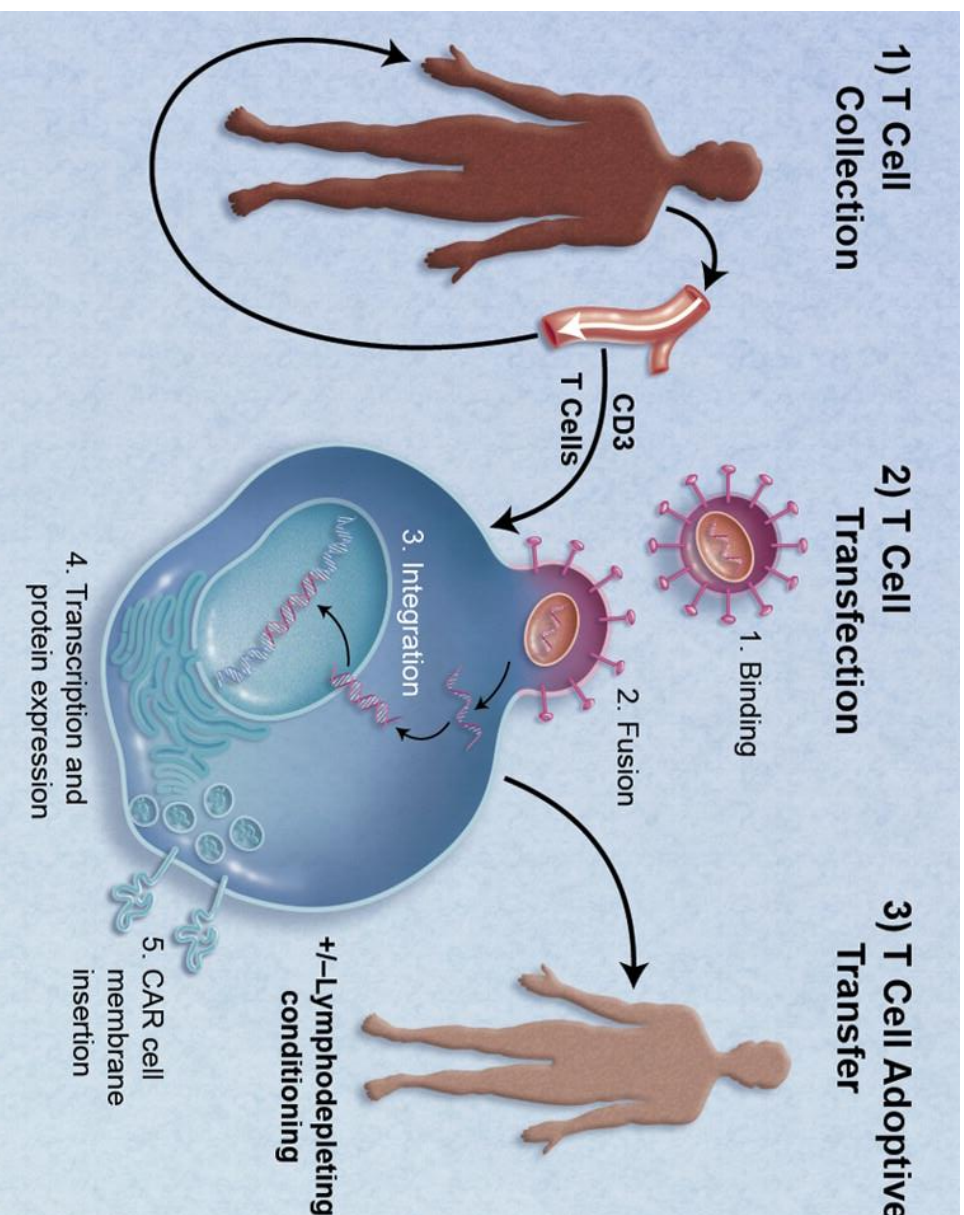
Case 1 PD-1 blockade

Case 3

CAR-T cell therapy



Can we make cold tumors (like pancreas) hot?

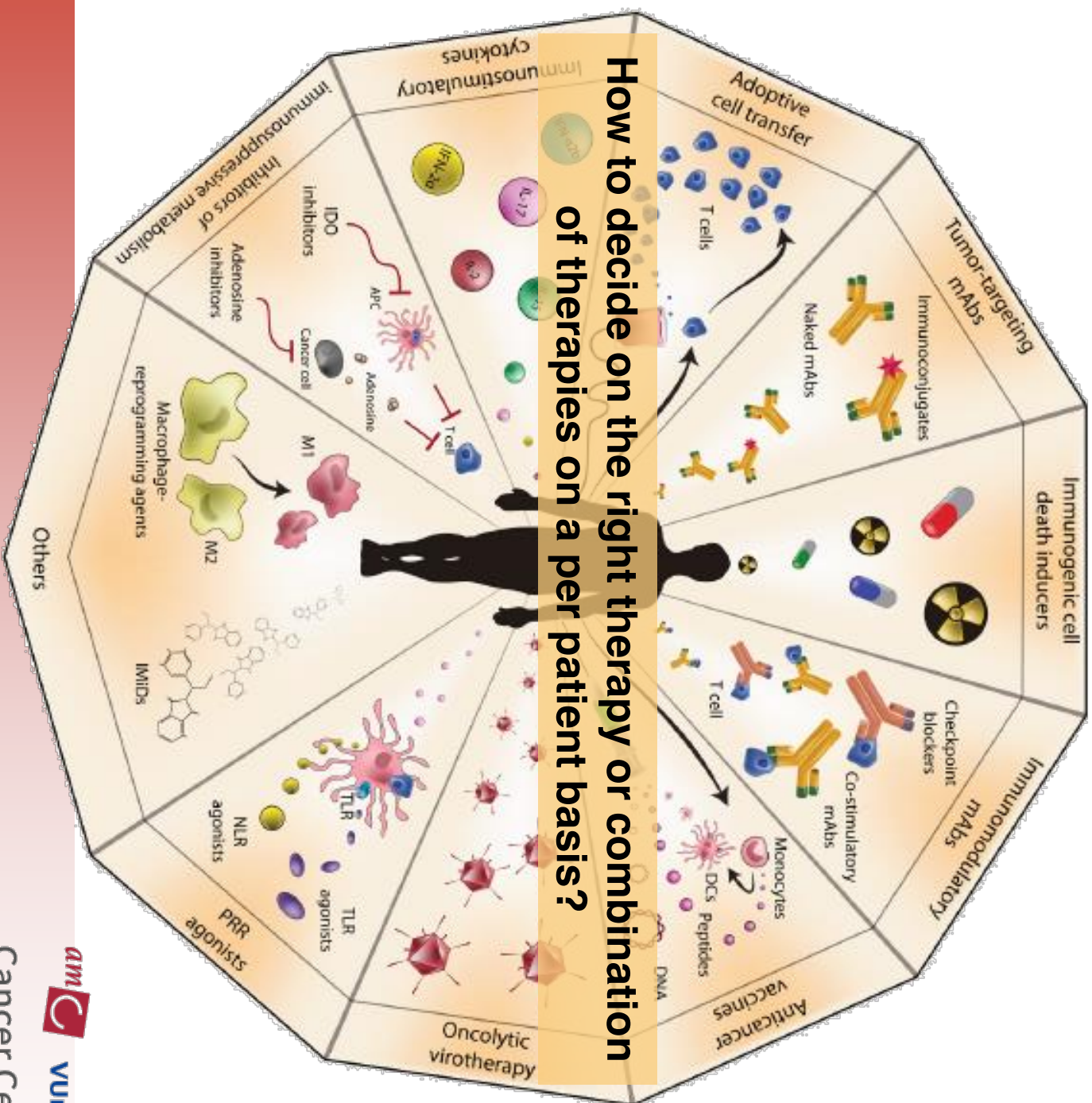


Carl June

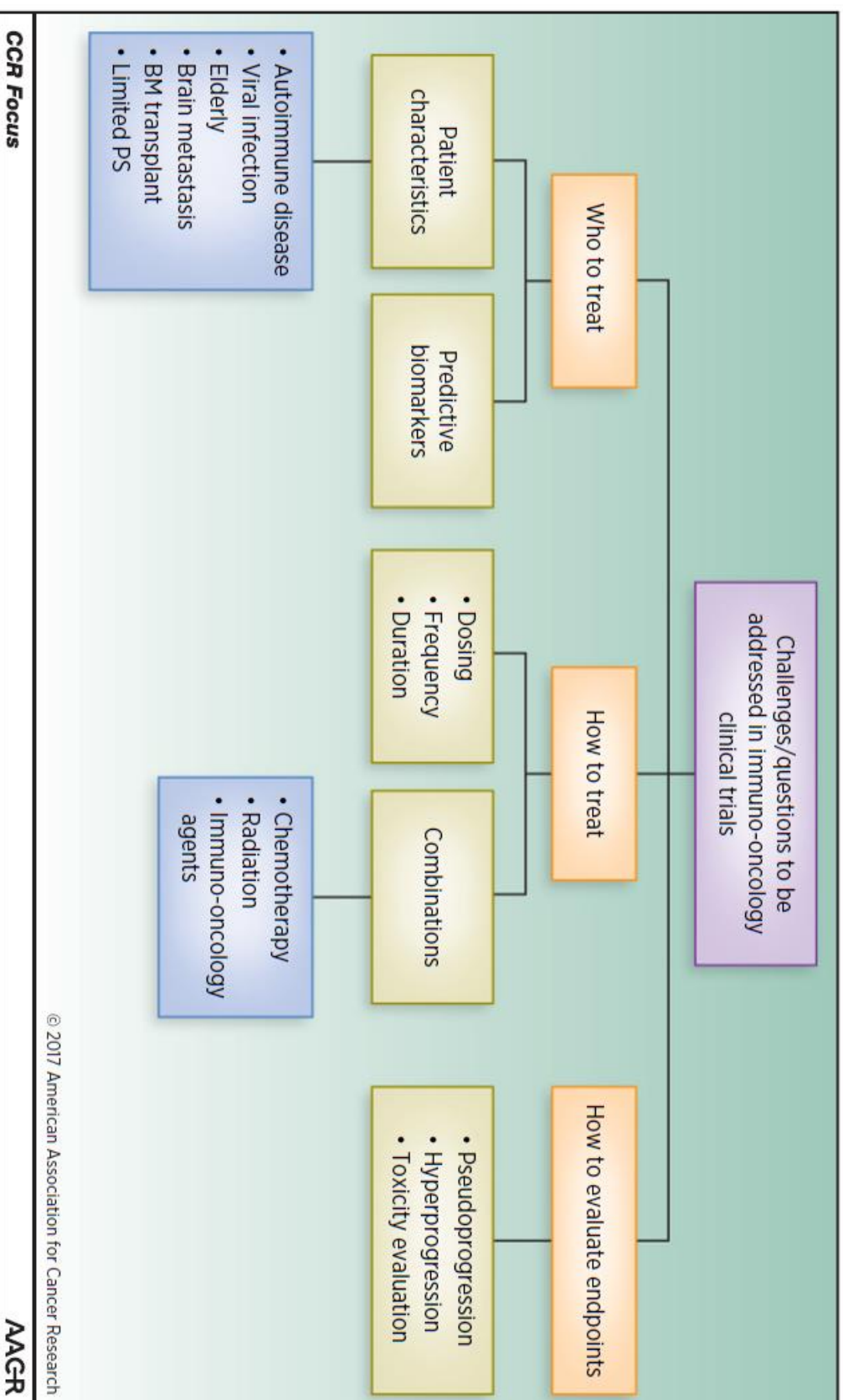
Approach #2: the June strategy

A plethora of immunotherapies

Classification of current anticancer immunotherapies

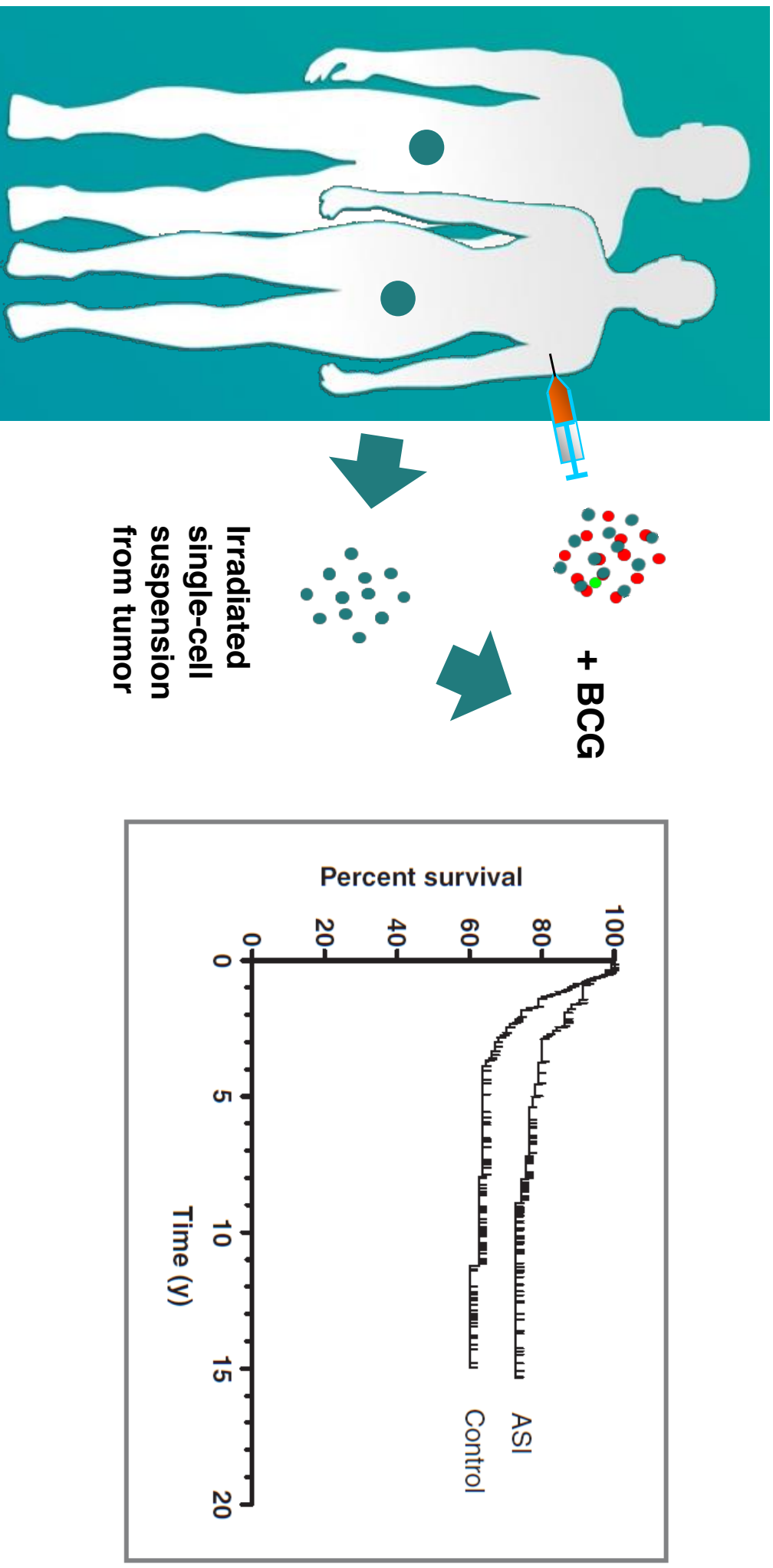


Immunotherapie trials in kanker: uitdagingen



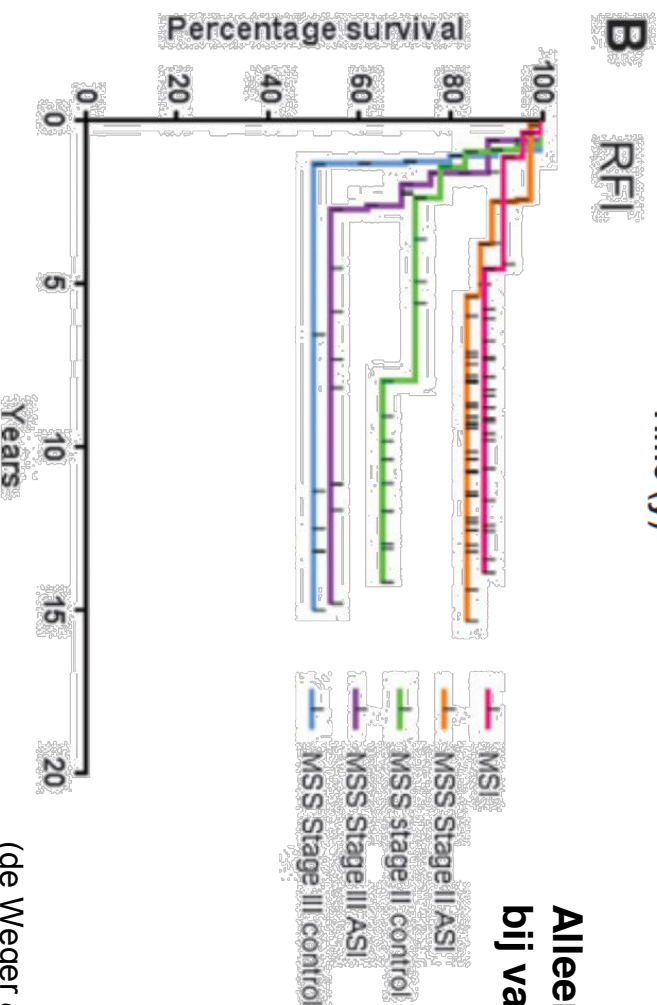
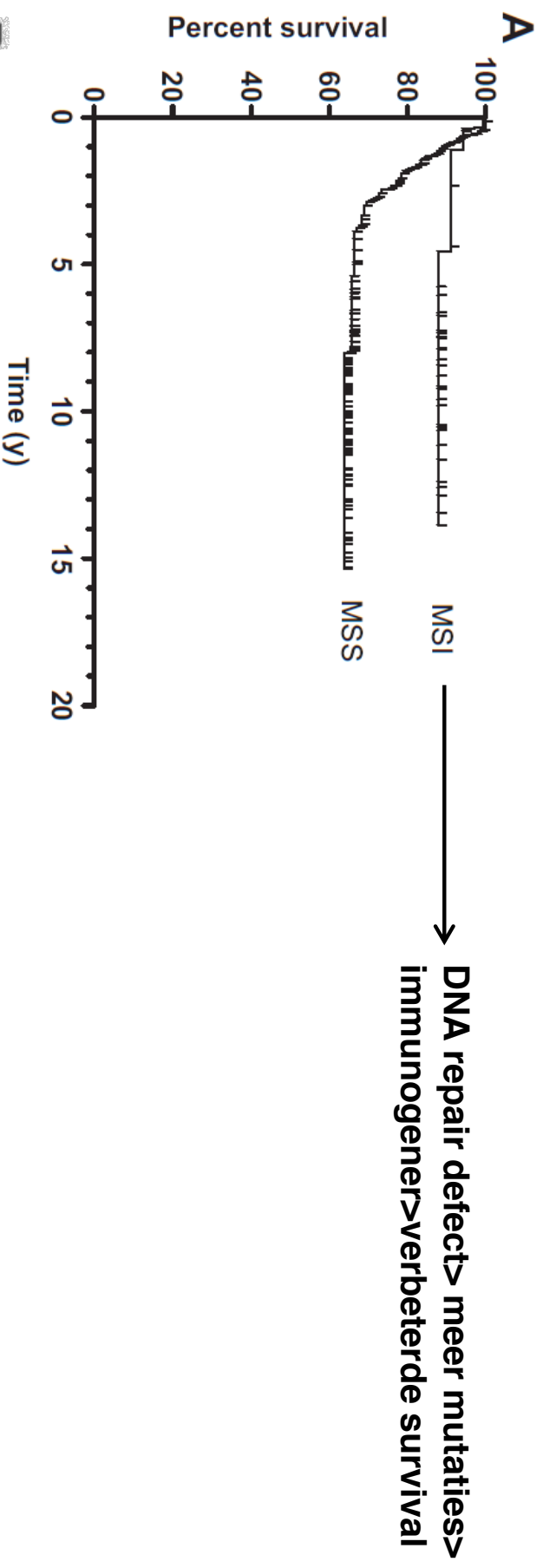
Active Specific Immunotherapy (ASI)

Active Specific Immunotherapy:



→ Shown effective in stage II colorectal cancer patients and stage III/IV melanoma patients (Vermorken *et al*, Lancet 1999 and de Weger *et al*, Clin Cancer Res 2011)

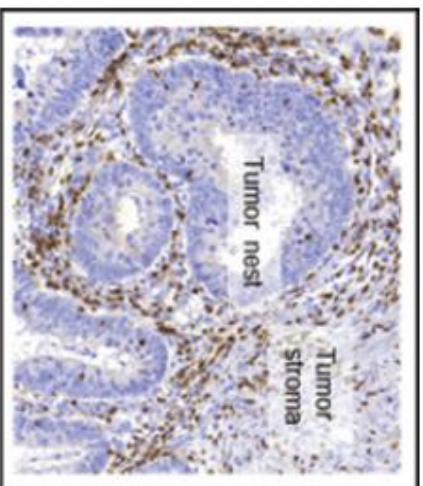
Active Specific Immunotherapy (ASI)



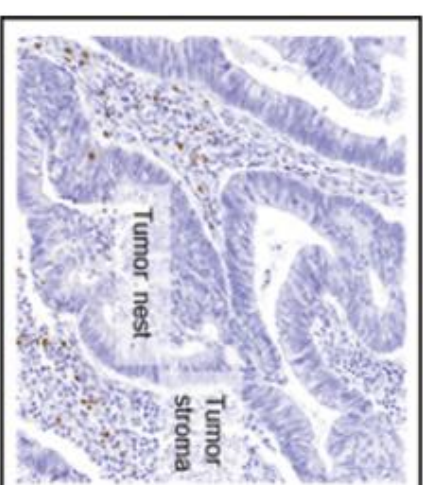
Alleen patiënten met MSS stage II hebben baat bij vaccinatie

(de Weger *et al*, Clin Cancer Res 2011; Turksma *et al*/ Clin Cancer Res 2016)

Active Specific Immunotherapy (ASI)

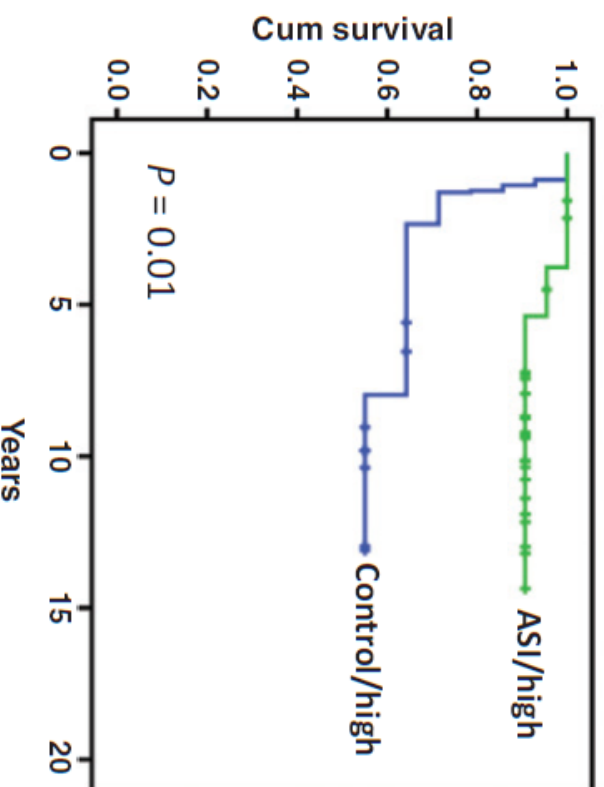


T cell
infiltratie

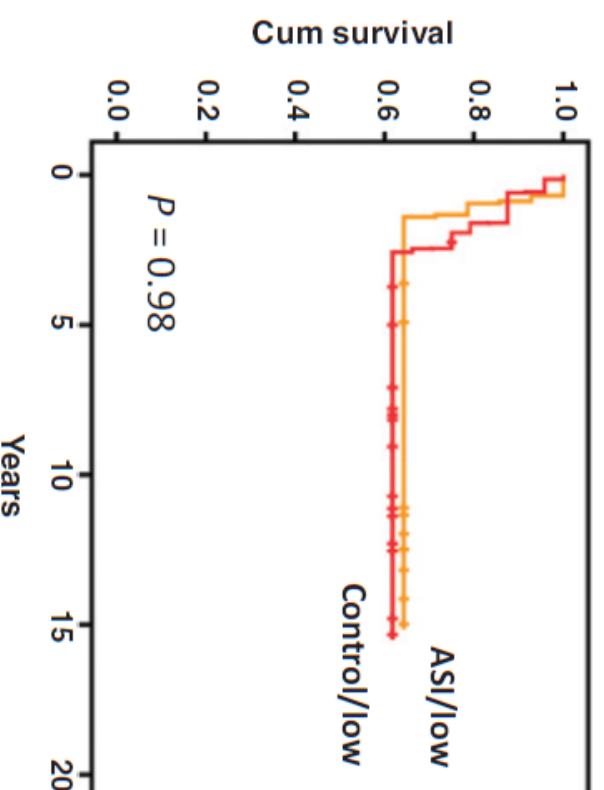


Alleen patiënten met MSS en hoge T cel infiltraten hebben baat bij vaccinatie

C RFI high

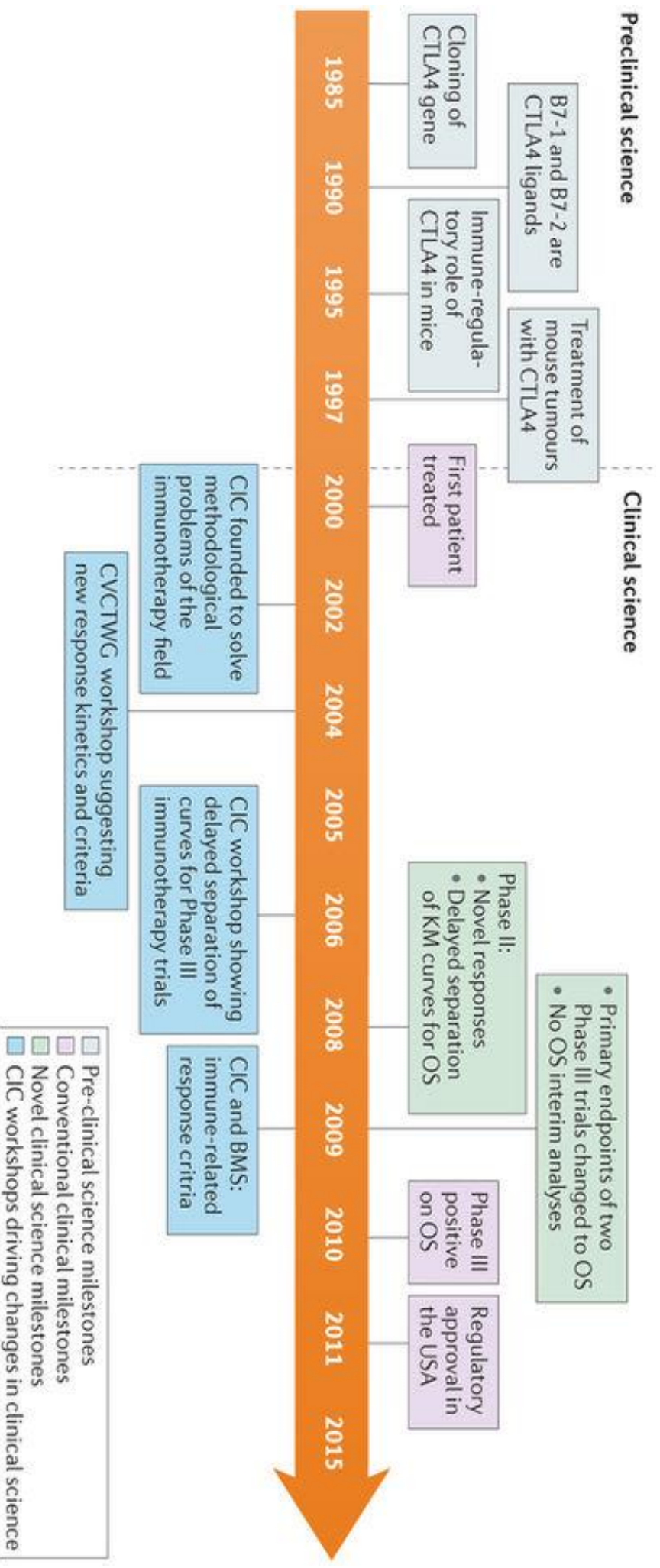


D RFI low



(Turksma et al Clin Cancer Res 2016)

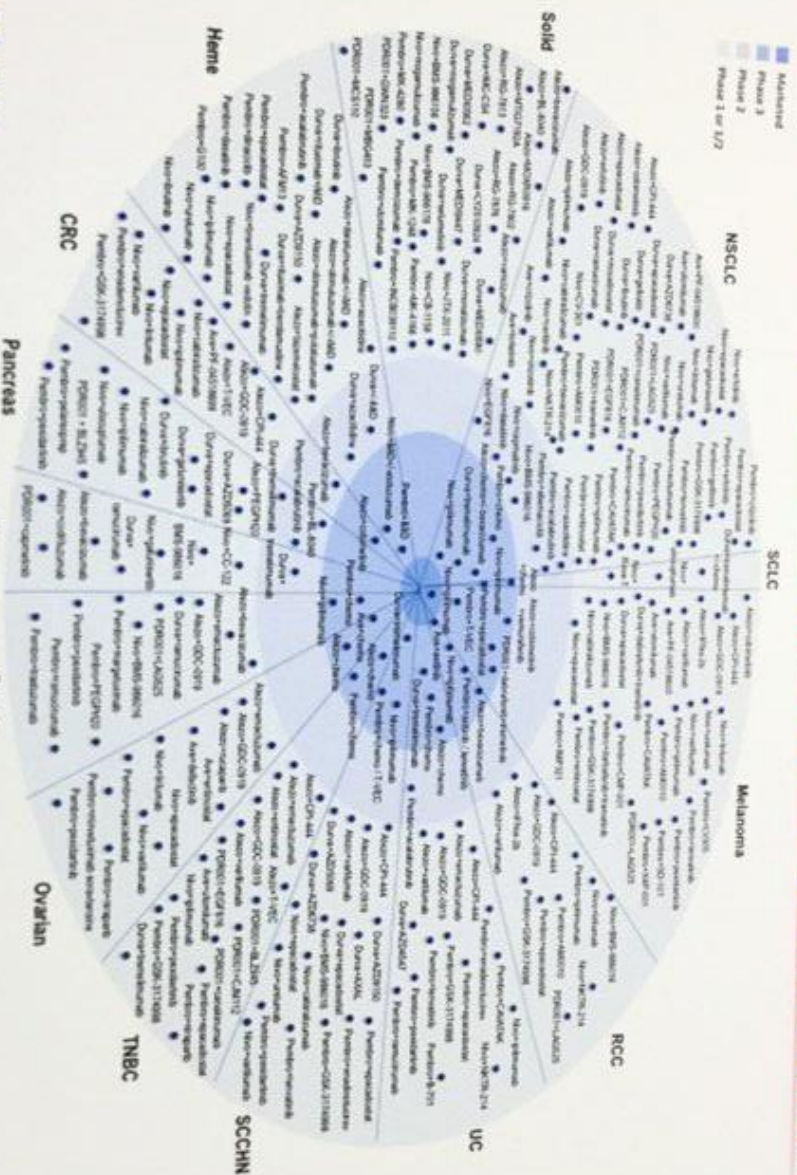
Immunotherapie trials in kanker: lange tijdslijnen



Immuntherapie trials in kanker: te veel combinaties, te weinig patiënten

16

INTENSE CIT COMBINATION LANDSCAPE EVOLVING: OVER 800+ CANCER IMMUNOTHERAPY COMBINATION STUDIES ALREADY IN THE CLINIC

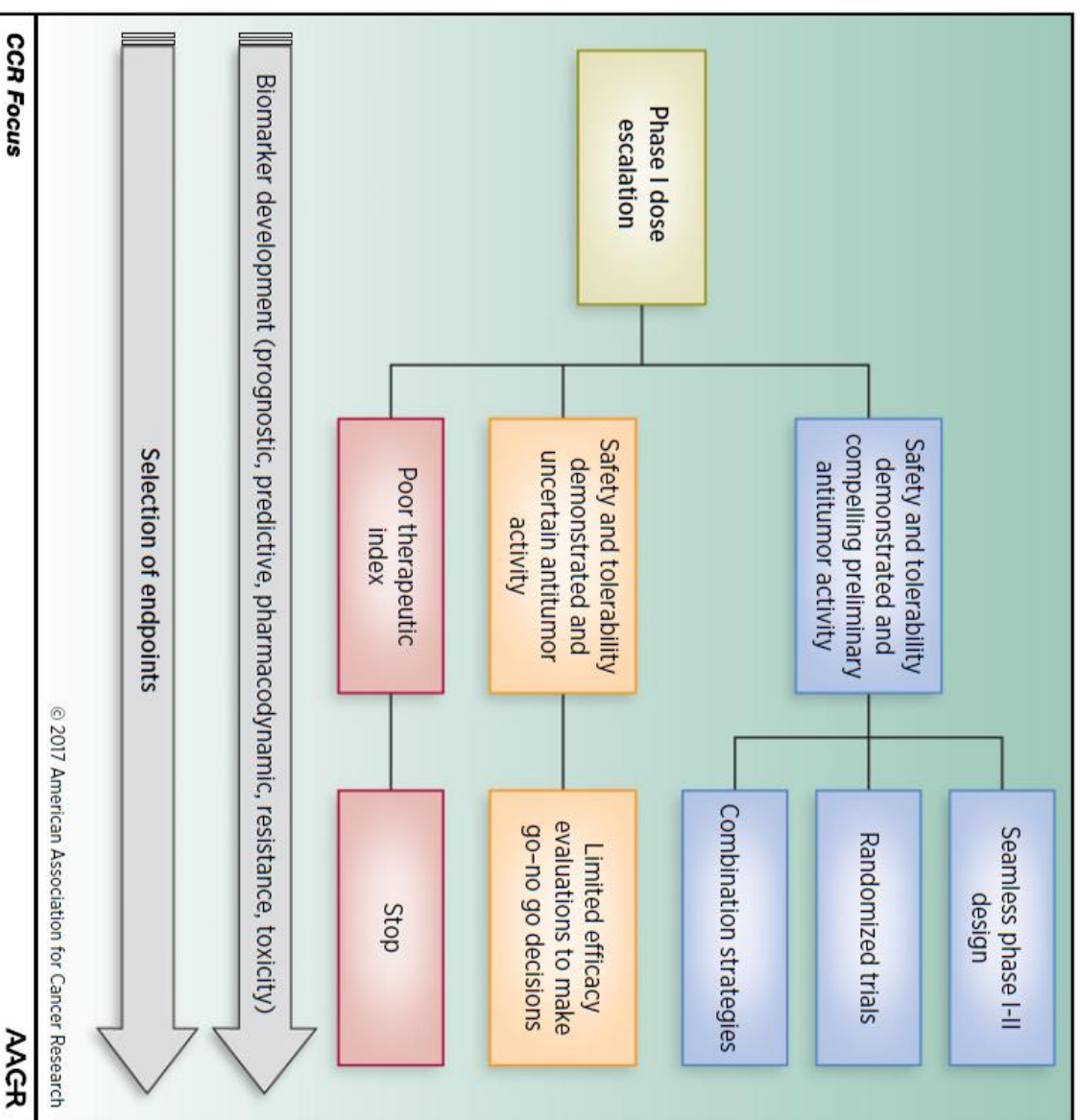


ed from Vanessa Lucey of CRI by Gergely Jarmy
and Mellman, Nature 2017

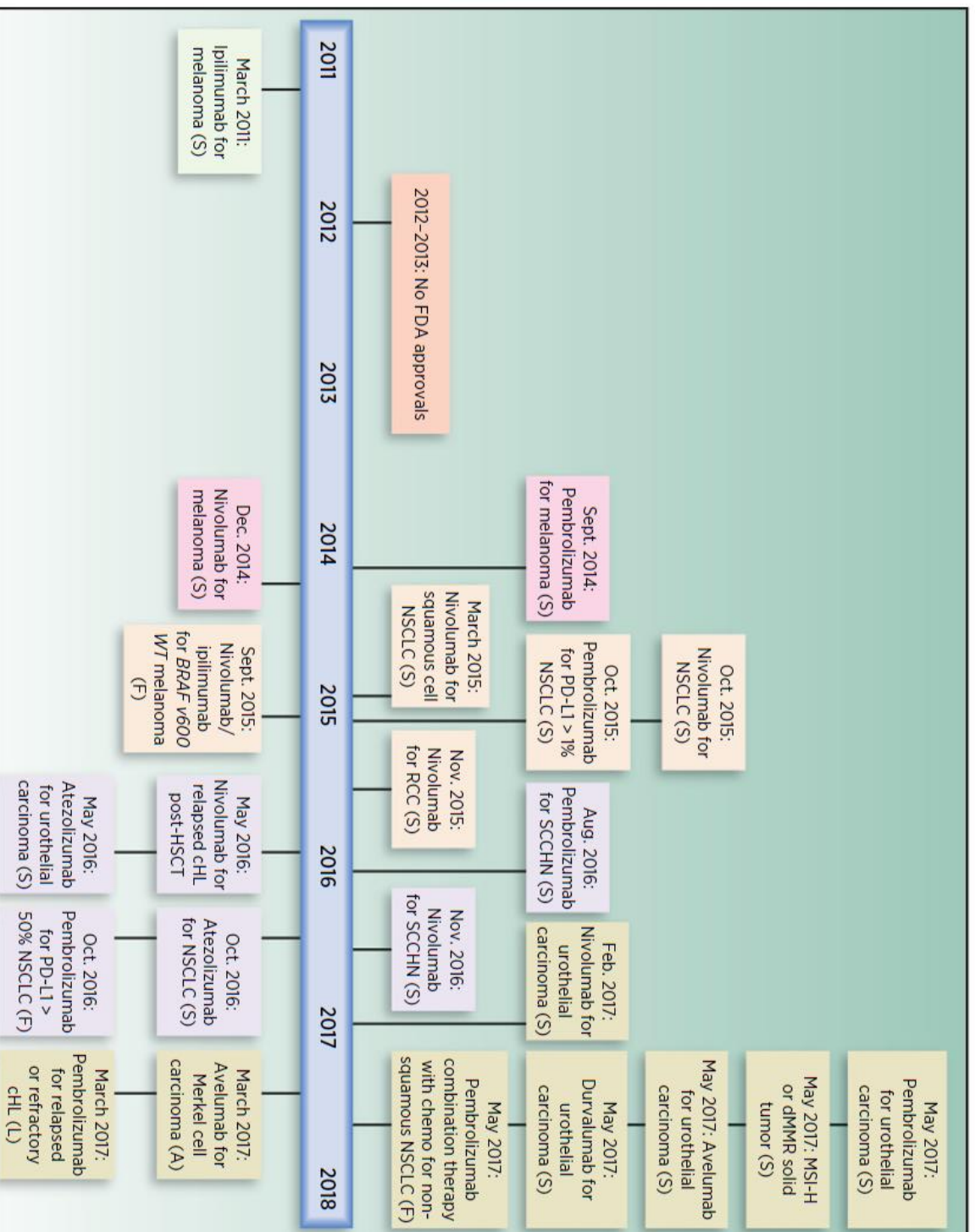
Confidential. Not for distribution.

Chen DS. AACR 2

Immuuntherapie trials in kanker: sneller schakelen



Immuuntherapie trials in kanker: steeds sneller FDA goedkeuring



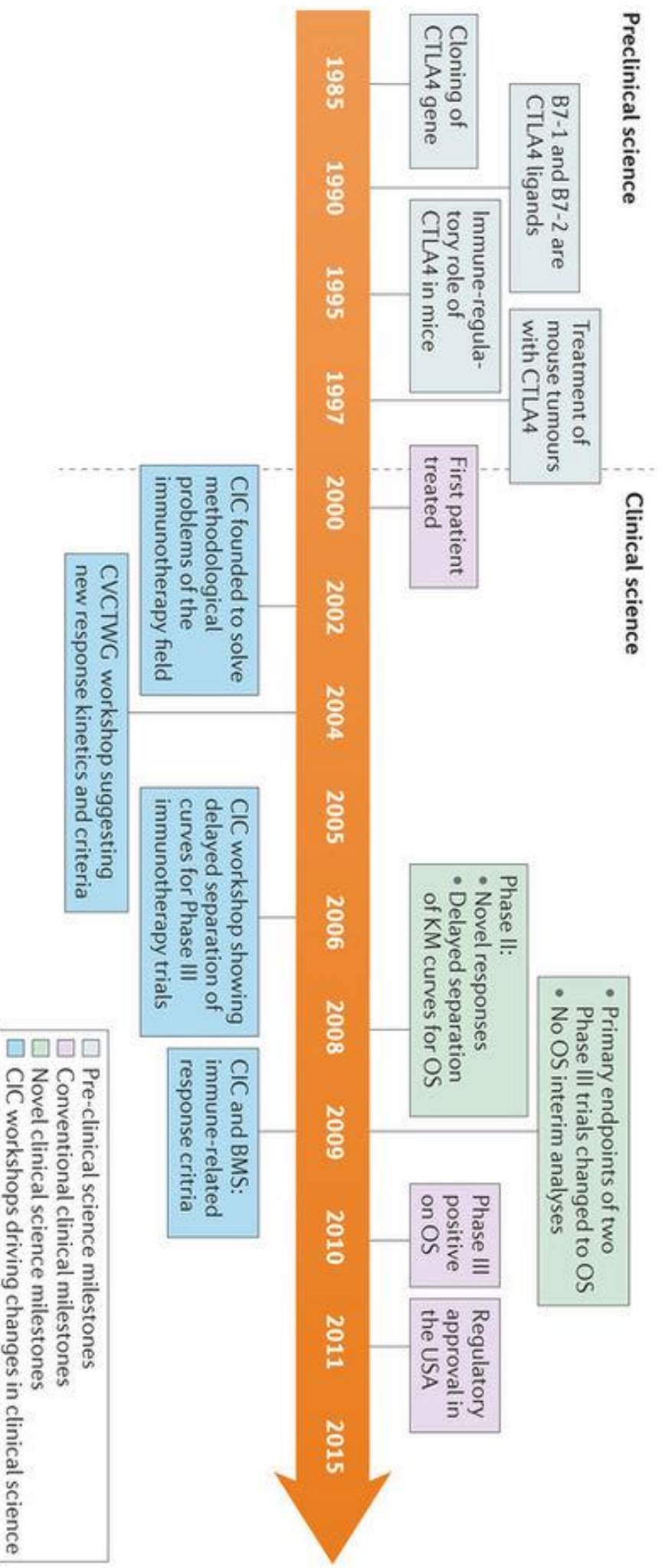
Baik *et al* Clin Cancer Res 2017

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CCR Focus

AAGR

Hoe krijgen we een immuuntherapie zo snel mogelijk bij de patiënt?



...een case studie

AD

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Dna-injectie lijkt effectief middel tegen huidkanker

Een simpele injectie met dna dat lijkt op dat van bacteriën, kan de overlevingskansen van een groep huidkankerpatiënten aanzienlijk vergroten.

Hanneke van Houwelingen 02-10-17, 06:24

[f](#) 542 [t](#) 7 [e](#)

De eerste, veelbelovende resultaten komen uit een onderzoek van het Amsterdamse VU medisch centrum onder 52 huidkankerpatiënten, die ruim tien jaar geleden met een verdachte moedervlek naar de huisarts gingen. Bij allen werd een melanoom -



Het Parool Vrij, Overvrij

[HOME](#) [AMSTERDAM](#) [OPINIE](#) [STADSGIDS](#)

Injectie kan terugkomst huidkanker mogelijk voorkomen



Cancer Center Amsterdam deed jarenlang onderzoek naar de injectie. © ANP



Een injectie kan mogelijk voorkomen dat de meest dodelijke vorm van huidkanker, melanoom, terugkeert. Dat blijkt uit onderzoek van het VUmc.

DOOR: HET PAROOL 2 OKTOBER 2017, 15:45

Melanoom is een verraderlijke ziekte...

De patient was een 58-jarige man.

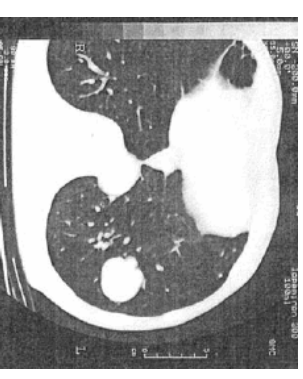
In **1976** werd een verdachte moedervlek met een diameter van 8 mm van zijn rechter middenvinger verwijderd.



Na de diagnose melanoom werd de vinger geamputeerd en de drainerende lymfeklier verwijderd en onderzocht op uitzaaiingen: deze bleek schoon.

Het melanoom had een Breslow dikte van 1.5 mm.

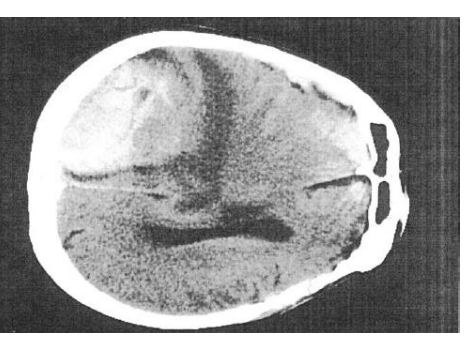
Diagnose: stadium 2 melanoom: **geen behandeling**



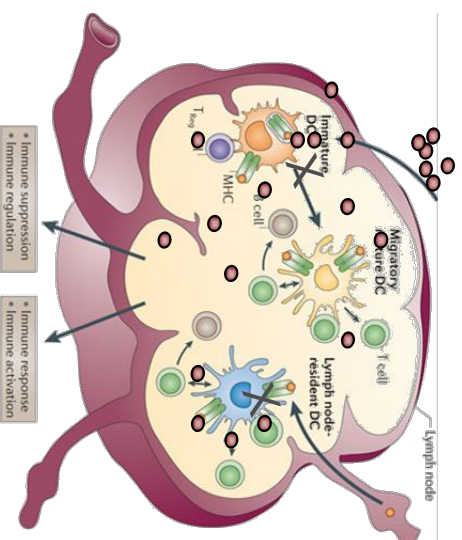
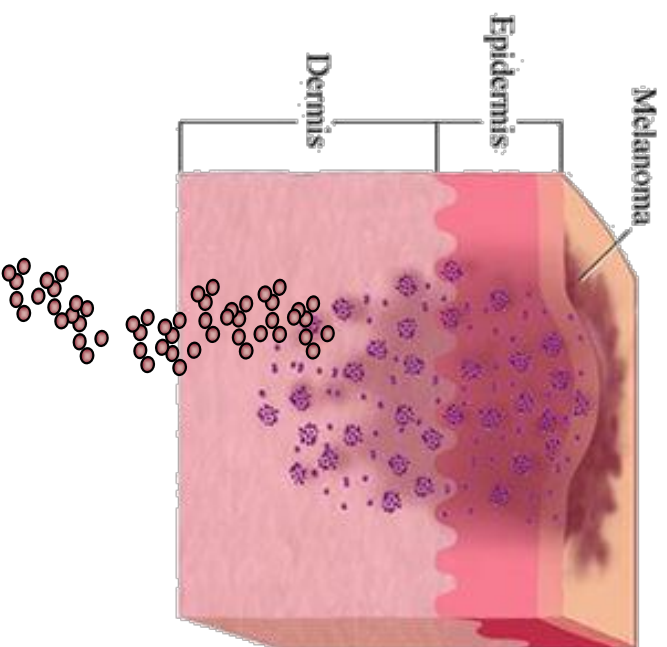
In **december 1992**, op 74-jarige leeftijd, werd een tumor in de linker long geconstateerd, die een uitzaaiing van de tumor bleek te zijn die 16 jaar eerder werd verwijderd.

Een deel van de long werd chirurgisch verwijderd in februari 1993.

Vijf maanden later overleed de man aan een bloeding van een gemetastaseerde hersentumor.

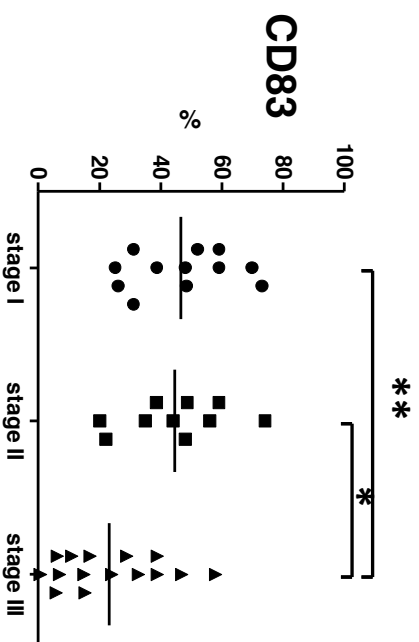


Het melanoom kan het immuunsysteem vroeg onderdrukken: vroeg metastasering

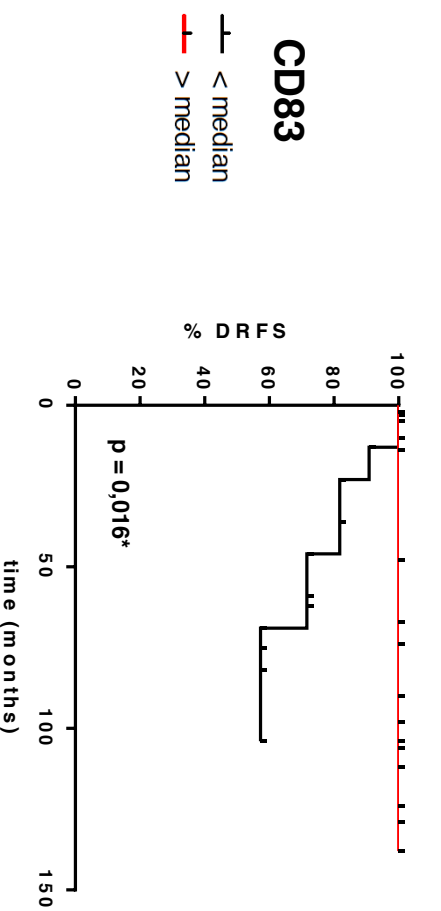


**Schildwachtklier
(SWK)**

Immunosuppressie in de SWK met uitzaaiingen

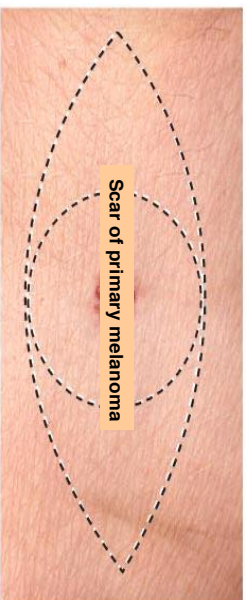


Verminderde activatie van DC in SWK met uitzaaiingen

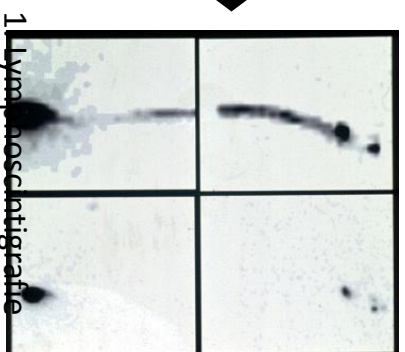


Verminderde activatie van DC in SWK is geassocieerd met het ontstaan van uitzaaiingen op afstand –soms jaren later.

Immuun stimulatie van de SWK in fase II onderzoek



1) i.d. injecties met saline / immuun stimulator op de plek van het melanoom 1 week voor de operatie



2. Patent blue



3. Gamma detection probe

2) Chirurgische verwijdering van de SWK



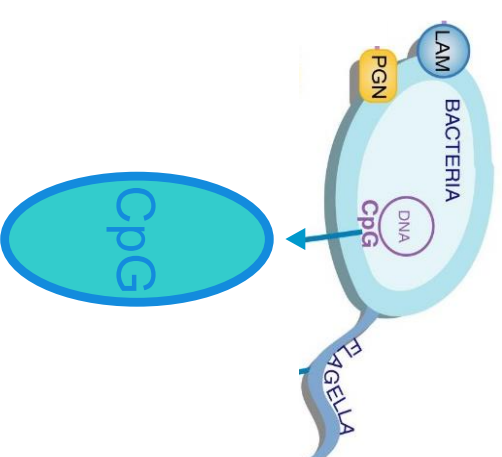
3) Immuun cellen worden uit de gehalveerde SWK geschrapt en geanalyseerd



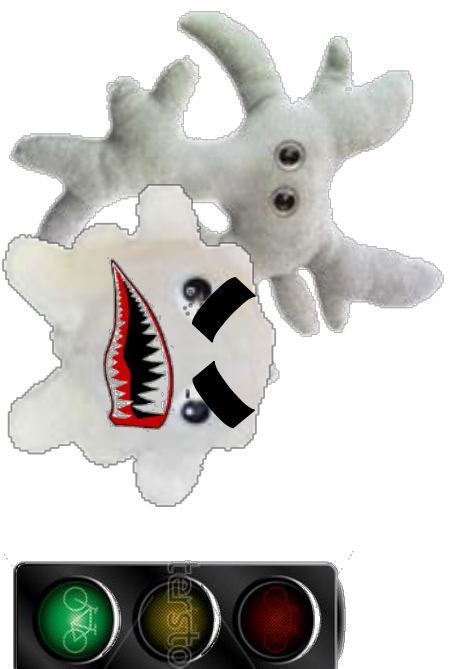
Twée studies, 22 placebo controles, 30 Cpg behandelde patiënten

Effecten van CpG op de SWK

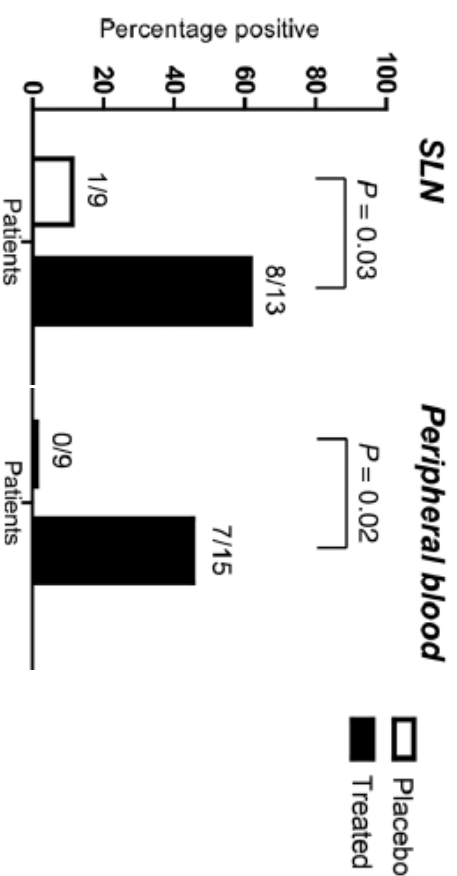
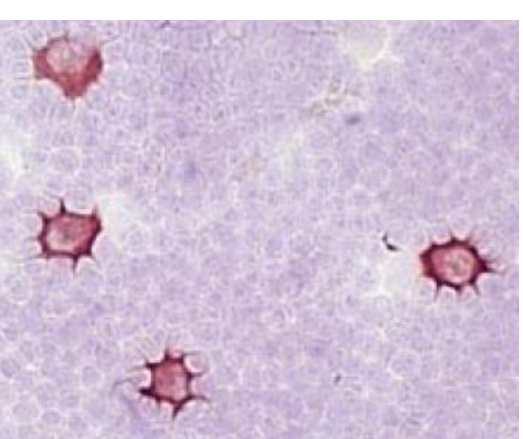
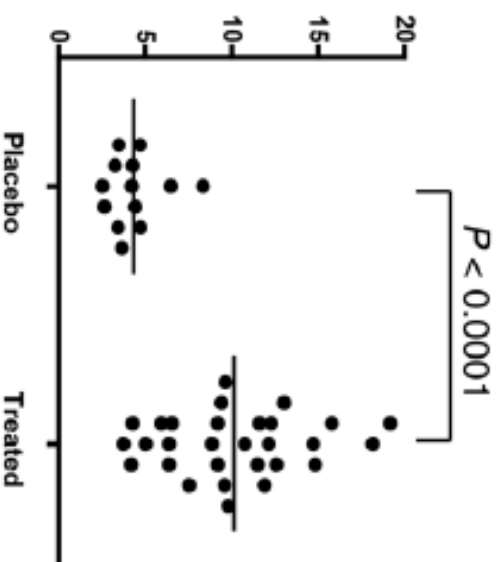
Resultaten van fase II klinische trials



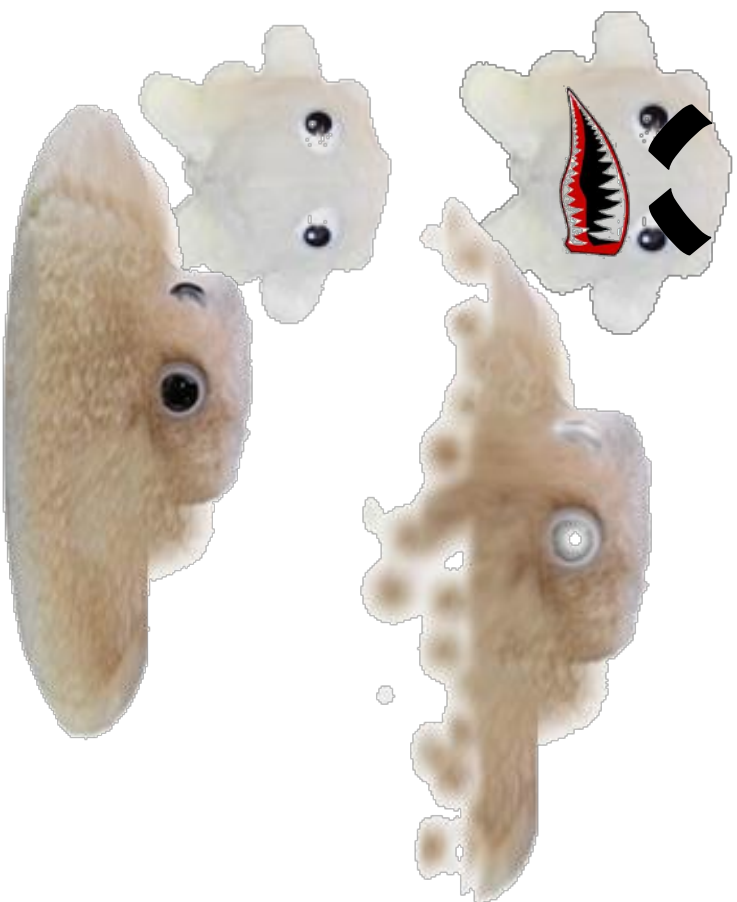
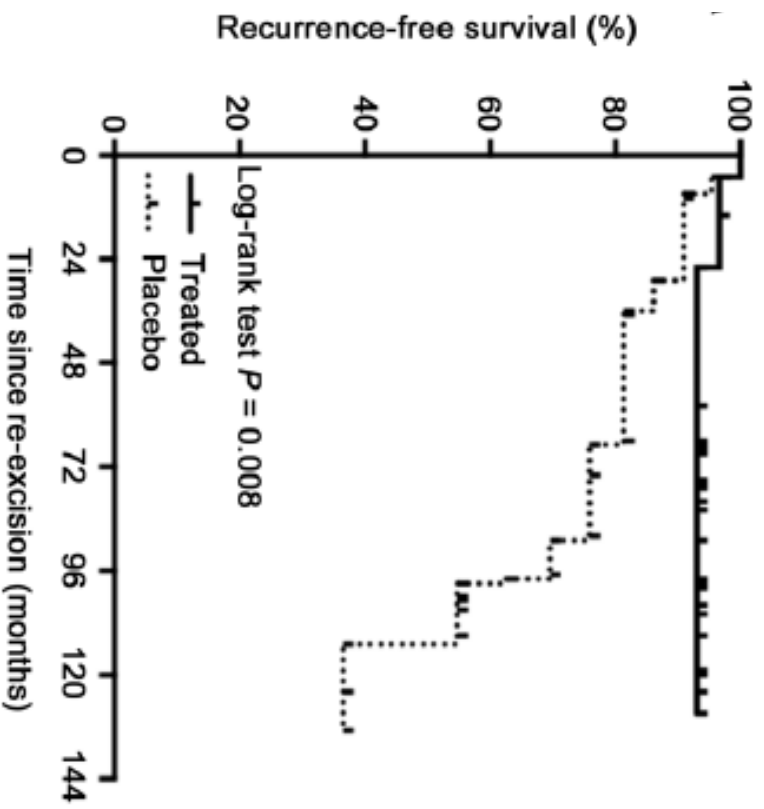
CpG: Lijkt op bacterieel DNA en activeert immuuncellen
-zowel in de SWK als in het bloed!



DC en T cel activatie



Verbeterde ziektevrije overleving!



Dept Medical Oncology

Immunotherapy Lab

Bas Koster

Kim van Pul

Rieneke van de Ven

Anita Stam

Dafni Chondronasiou

Saskia Santegeets

Sinéad Loughheed

Fons van den Eertwegh

Dept Surgical Oncology

Berbel Sluiter

Barbara Molenkamp

Lisette Te Velde

Petrousjka van den Tol

Paul van Leeuwen

Sybren Meijer

Dept Pathology

Mari van den Hout

Pepijn Wijnands

Rik Scheper



VENI
VIDI
VICI



Pfizer Inc., Vaccine Research Branch, San Diego CA
Karin Jooss

