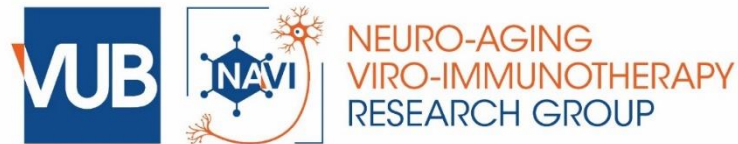
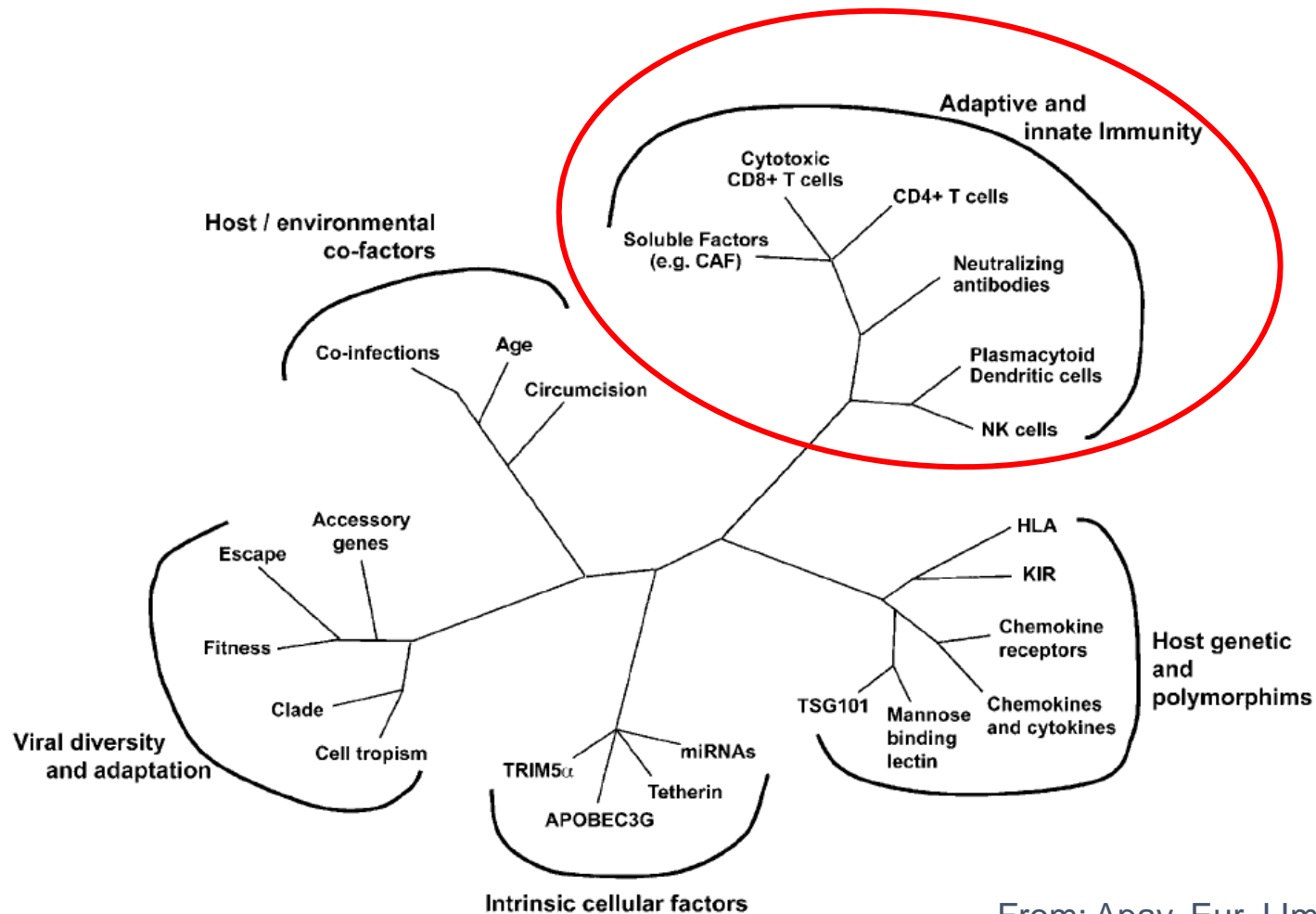


The interplay between the immune system and the HIV reservoir

Prof. Dr. Joeri Aerts

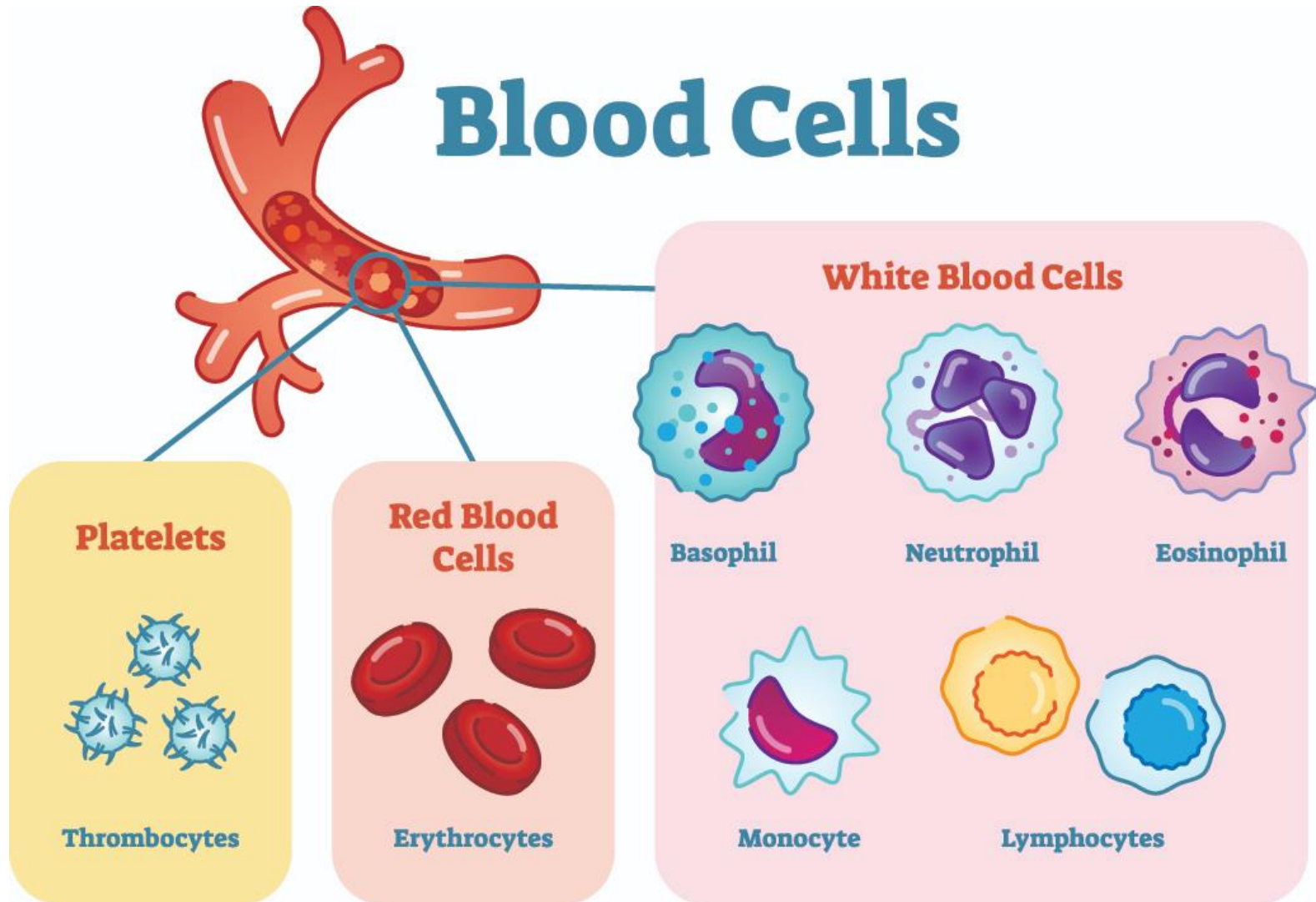


Factors influencing HIV pathogenesis

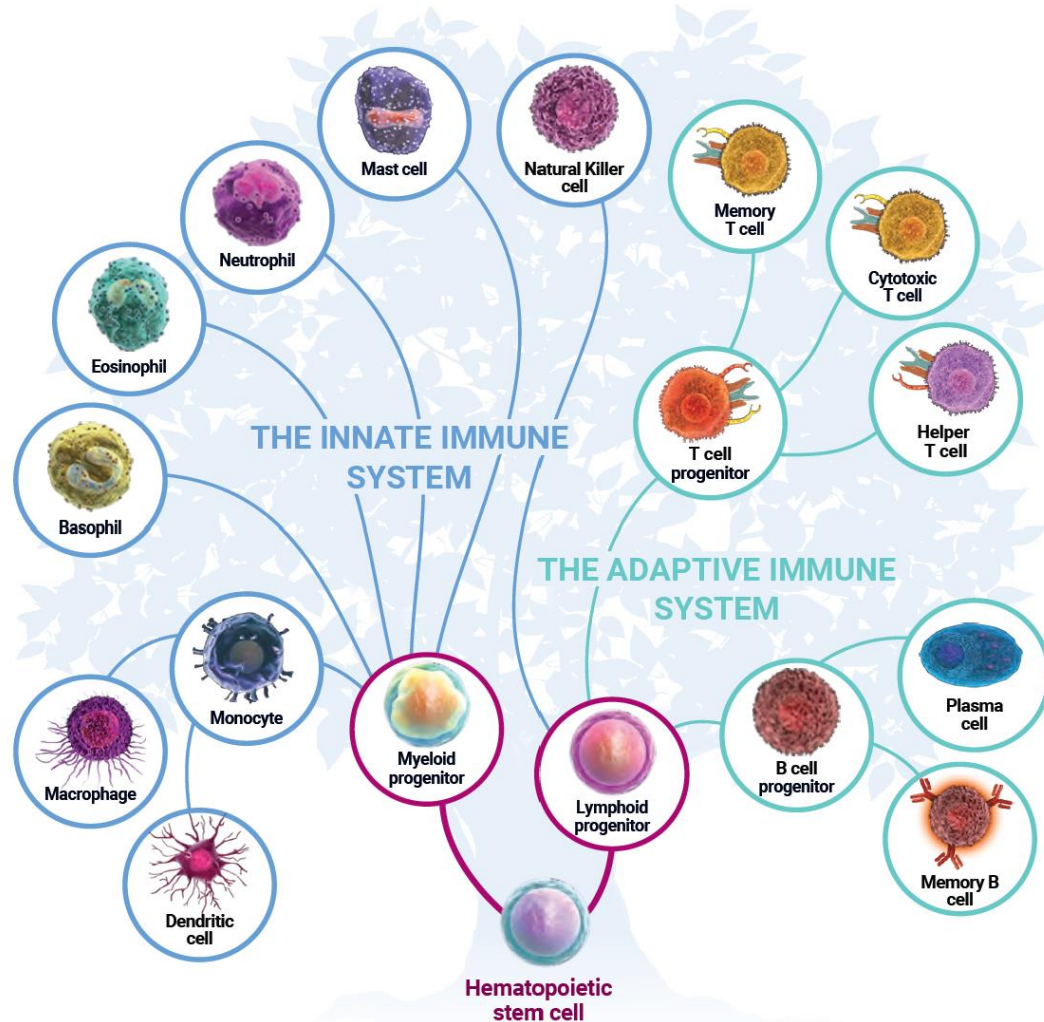


From: Apay, Eur J Immunol 2009

White blood cells are the most important immune cells in the body...



White blood cells are divided in innate and adaptive immune cells

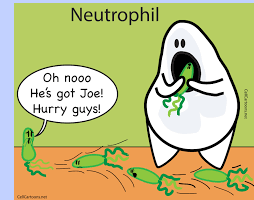


INNATE immunity

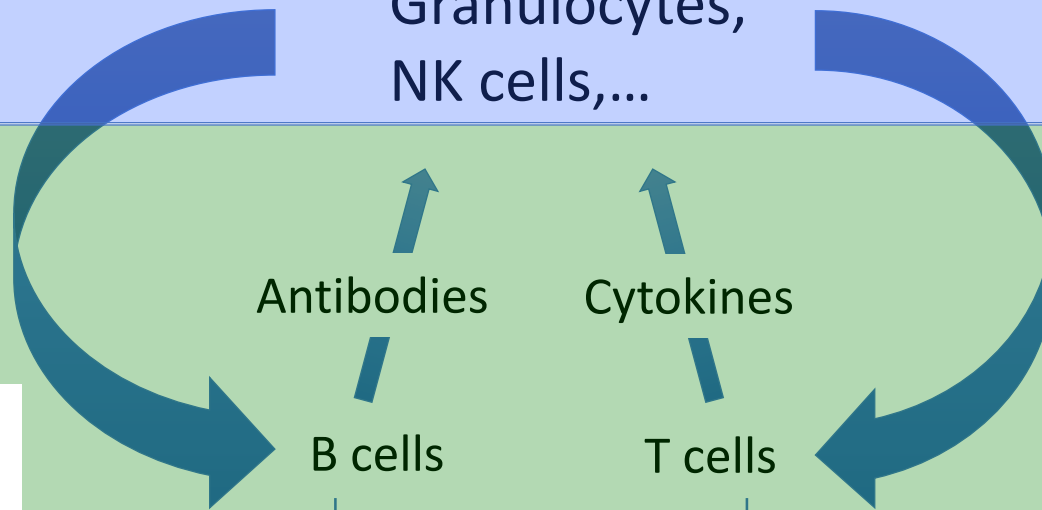
Physical barriers:
Skin, mucosa



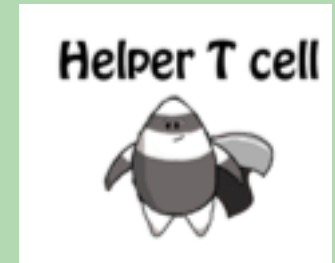
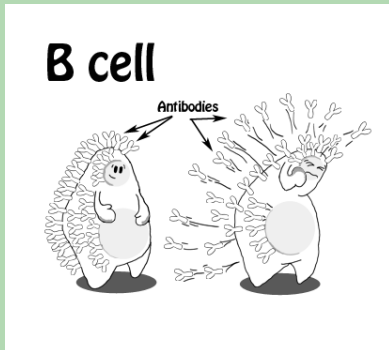
Cells:
Monocytes,
Granulocytes,
NK cells,...



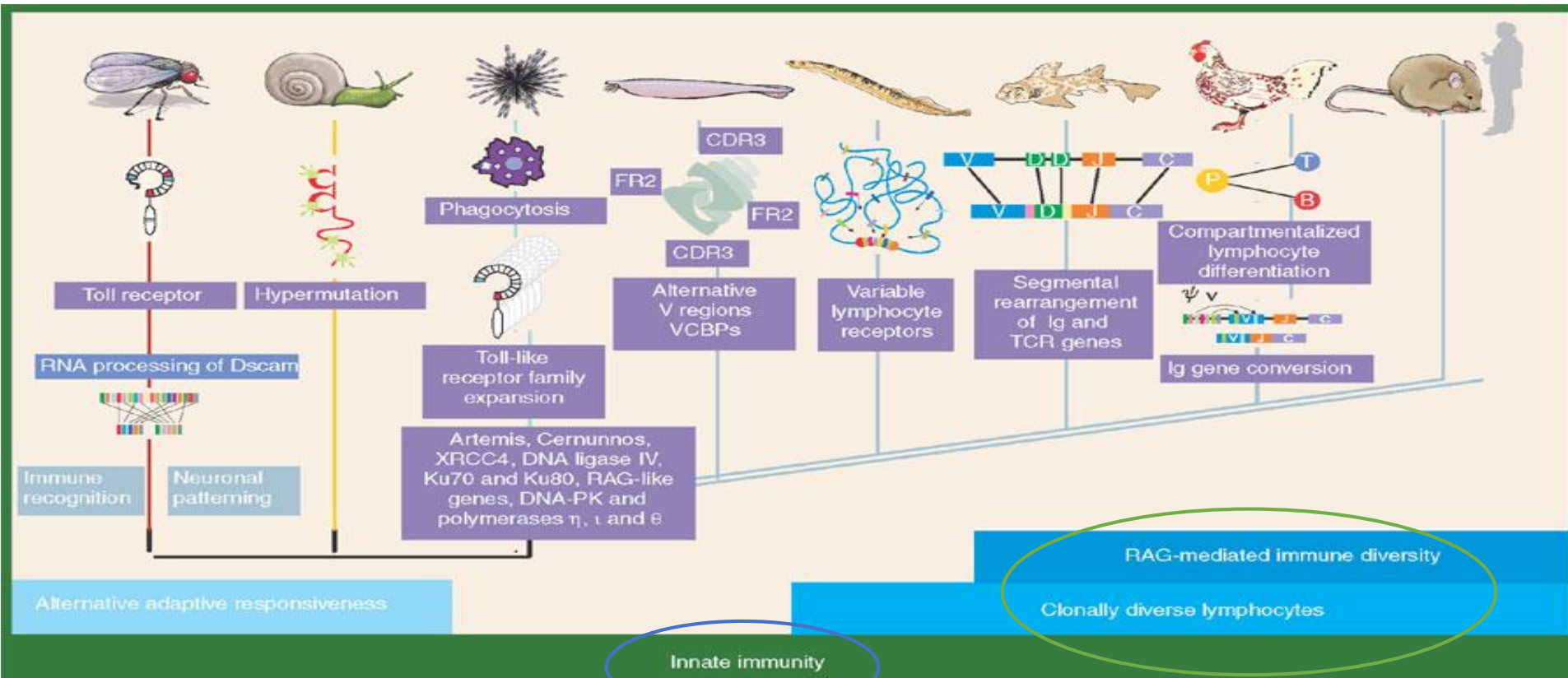
Chemical barriers:
pH, fats, enzymes



ACQUIRED immunity



Evolution of the immune system



HIV and the immune response

HIV infection is characterised by a progressive immune dysfunction:

- Quantitative:

- severely reduced number of (mainly) CD4+ T cells

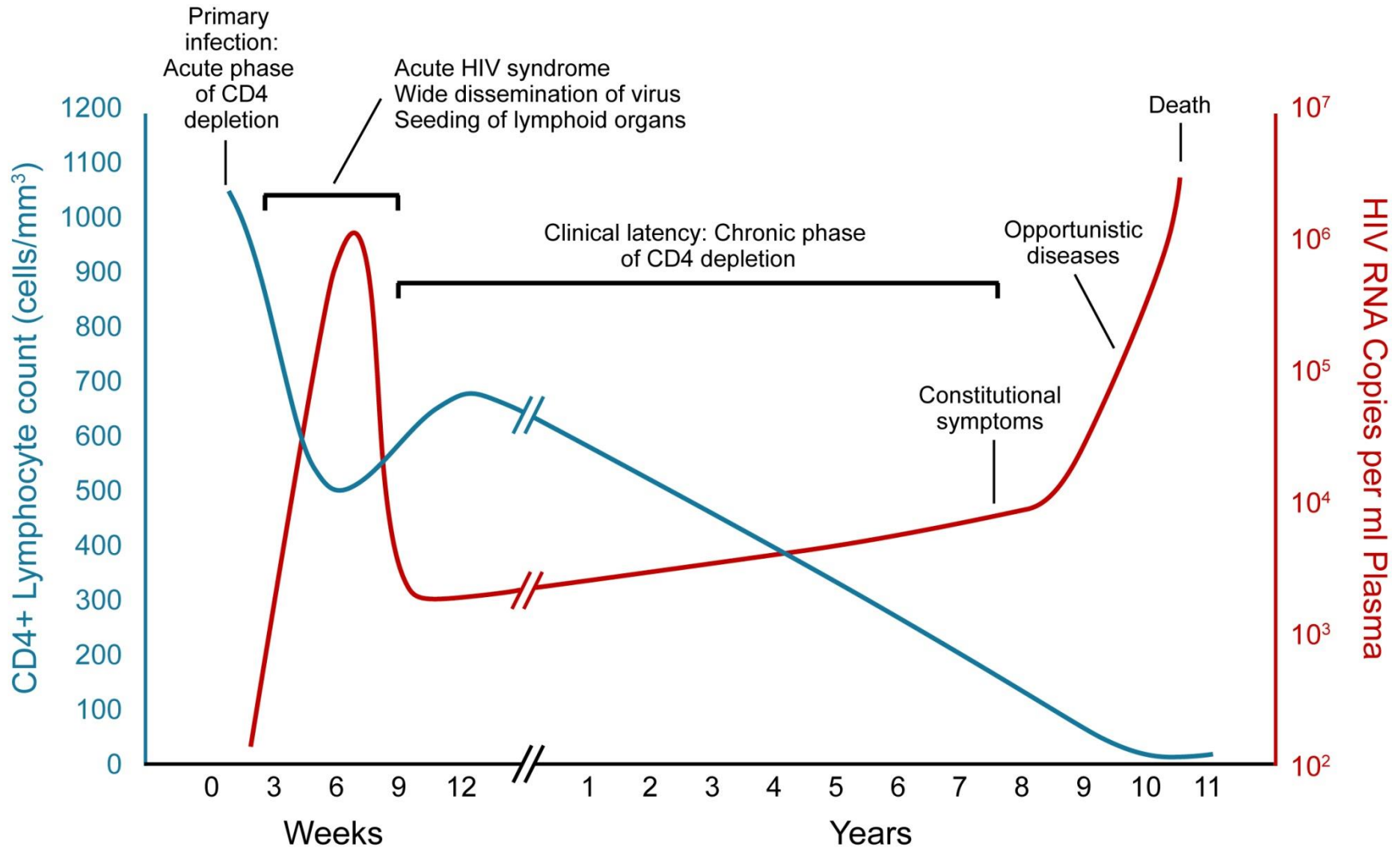
- Qualitative:

- Impaired cytokine production (monofunctional T cells)
- Impairment in cytolytic function
- Lack of T-cell proliferation
- Enhanced T-cell apoptosis
- Reduced antigen presentation
- ...

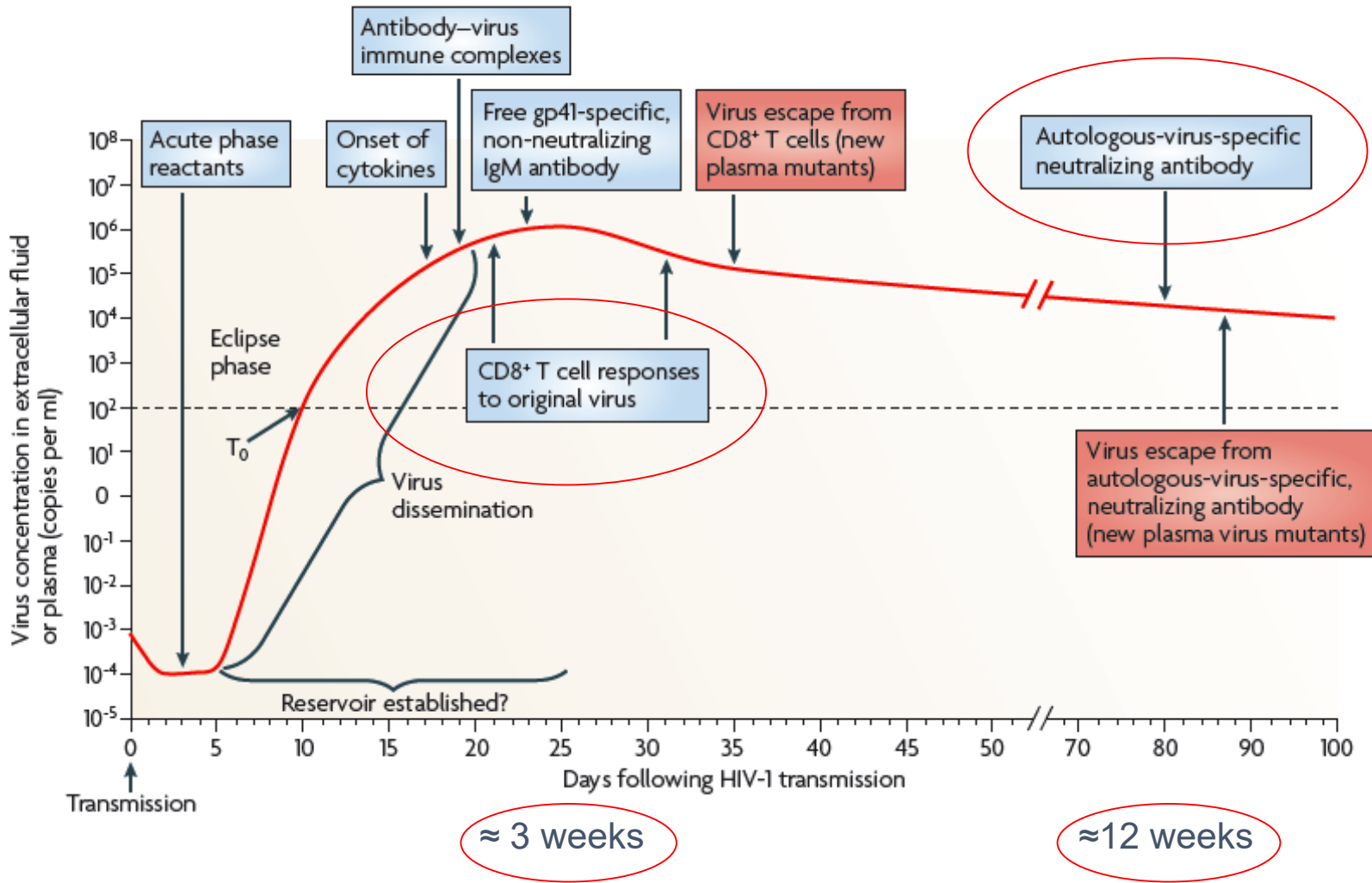
Depletion and/or dysfunction of other immune cells

Cells	Immunopathological effect
CD8+ cytotoxic T-lymphocytes (CTL)	↑ Abnormally high during acute phase ↓ Decline at later stages
Natural killer (NK) cells	↓ Impaired numbers ✗ Impaired function
Monocytes and macrophages	✗ Defects in chemotaxis ✗ Inability to promote T-cell proliferation ✗ Immune activation ✗ Defects in Fc receptor function
B-cells	↑ Production of IgG and IgA but ↓ antibody responses

CD4⁺ T cell-depletion during acute and chronic HIV infection



Natural immune responses against HIV



Correlates of protection, the holy grail for HIV research...

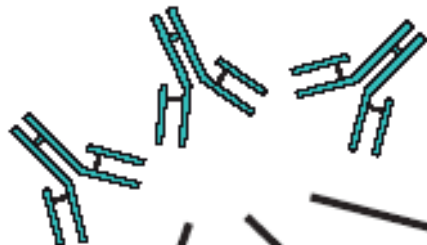
- Most viral infections: individuals exist that cleared the virus and are protected against reinfection (very often Ab titers)
- **NOT for HIV-1!**
- Surrogate models:
 - Highly exposed but uninfected individuals
 - Long term non-progressors/elite controllers
 - HIV-2 infected non-progressors
 - Acute HIV-1 seroconvertors
 - Non-human primates

Correlates of immune protection: what we know

- Neutralizing Abs: protection from *infection*
- Cell mediated immunity (= CD8⁺ T cells): protection from *disease*

Can the reservoir be recognized and eliminated by the immune system?

Virus-Specific Ab



Effective

No effect

No effect

Virus particle

Virus-Specific CTL

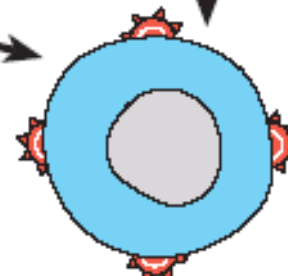


CTL

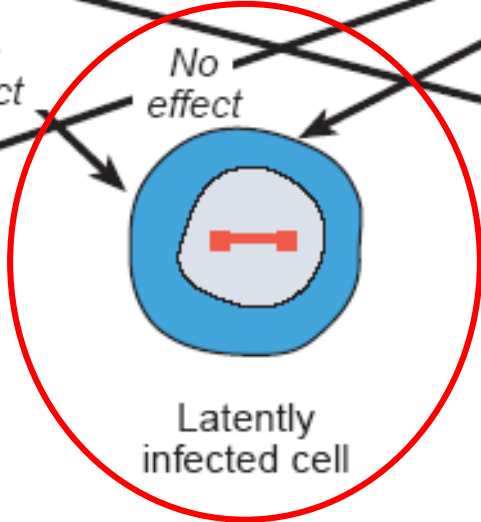
No effect

Effective

Poor effect



Virus-infected cell

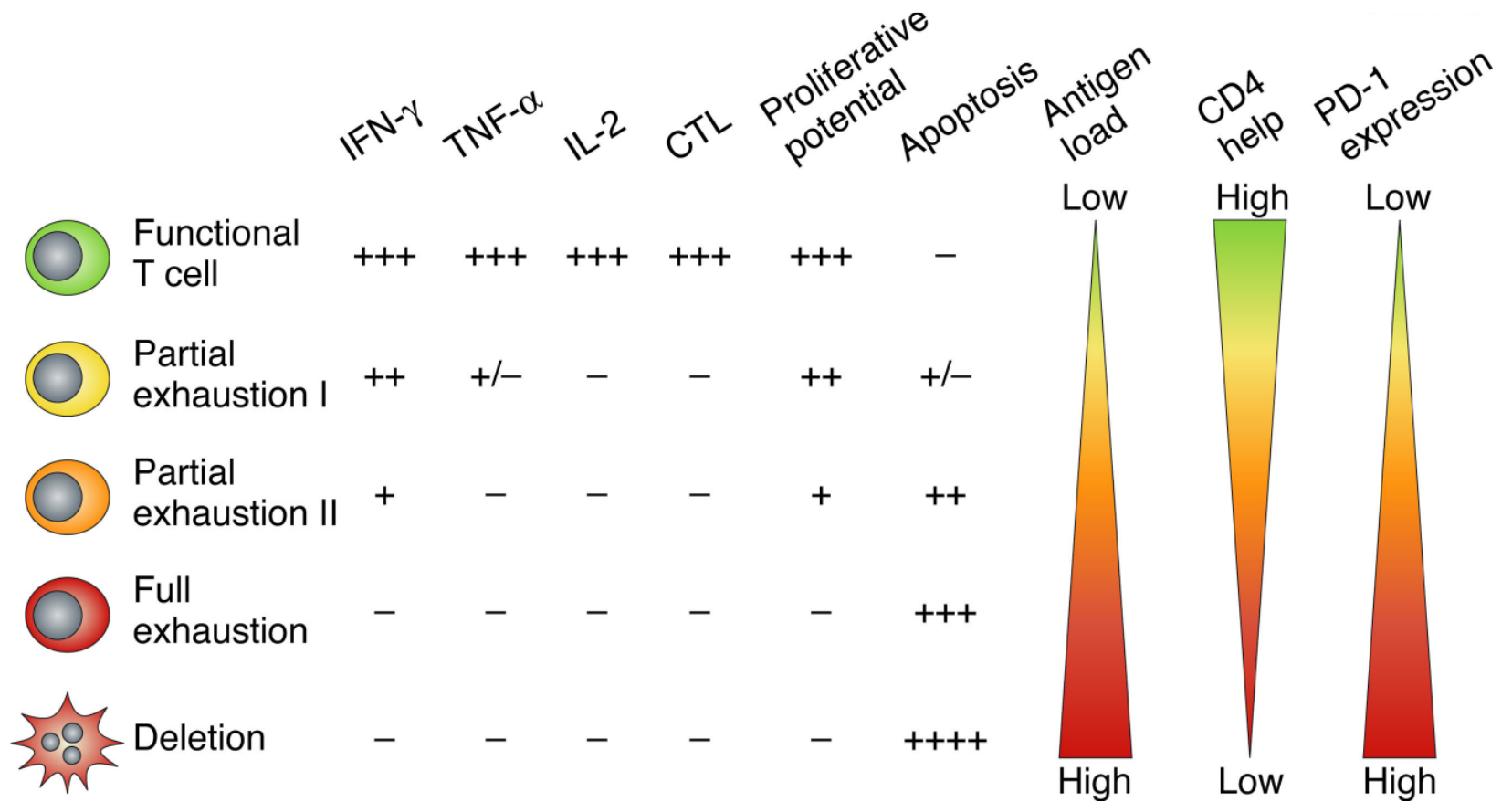


Latently infected cell

Inhibitory mechanisms limiting HIV-specific immune responses

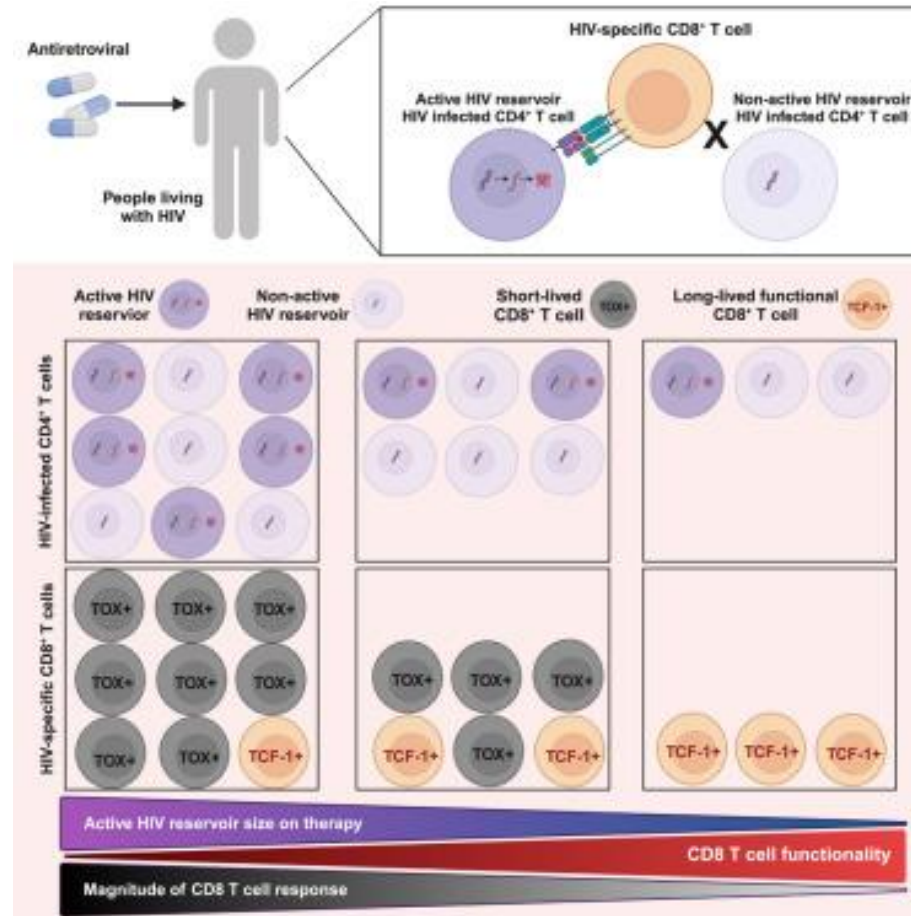
- **Exhaustion**: dysfunction and subsequent physical deletion of antigen-specific T cells during chronic HIV infection
- **Senescence**: progressive decrease in proliferative capacity due to intrinsically limited division capacity of T cells
- **Immune activation**: aspecific activation of the innate immune system driving overactivation of the adaptive immune response

Hierarchical loss of function during T cell exhaustion



From: Freeman et al., J Exp Med 2006

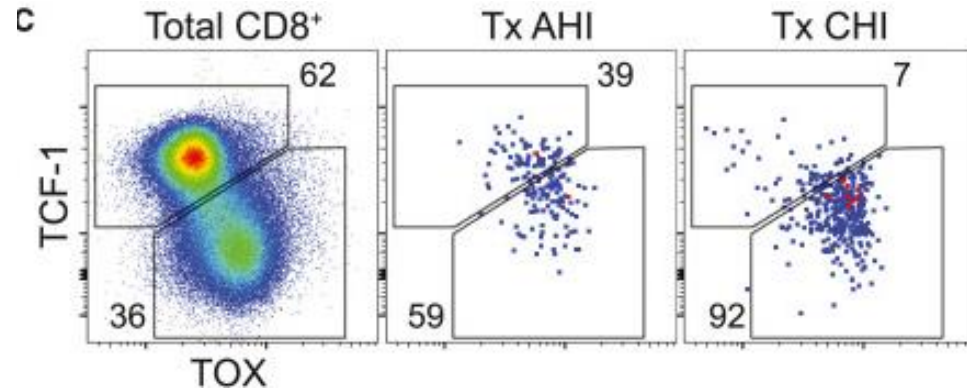
Active reservoir is associated with higher numbers but less functional (more exhausted) CD8+T cells



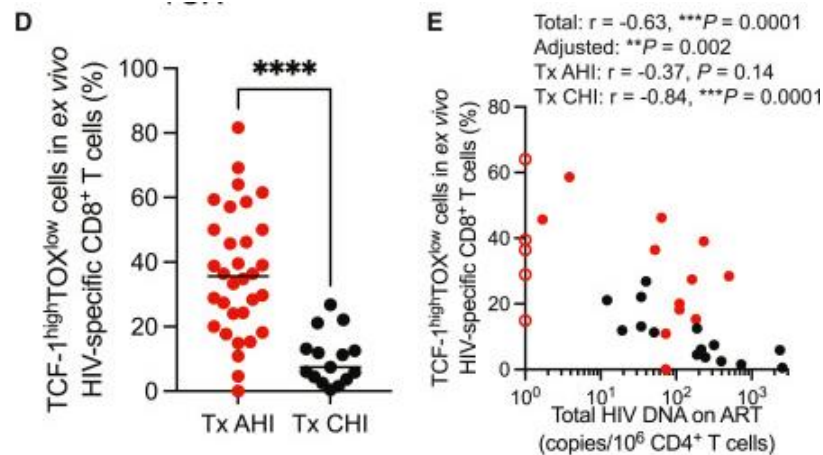
From: Takata et al., Cell Host Microbe 2022

Active reservoir is associated with higher numbers but less functional CD8+T cells

“Good” functional T cells

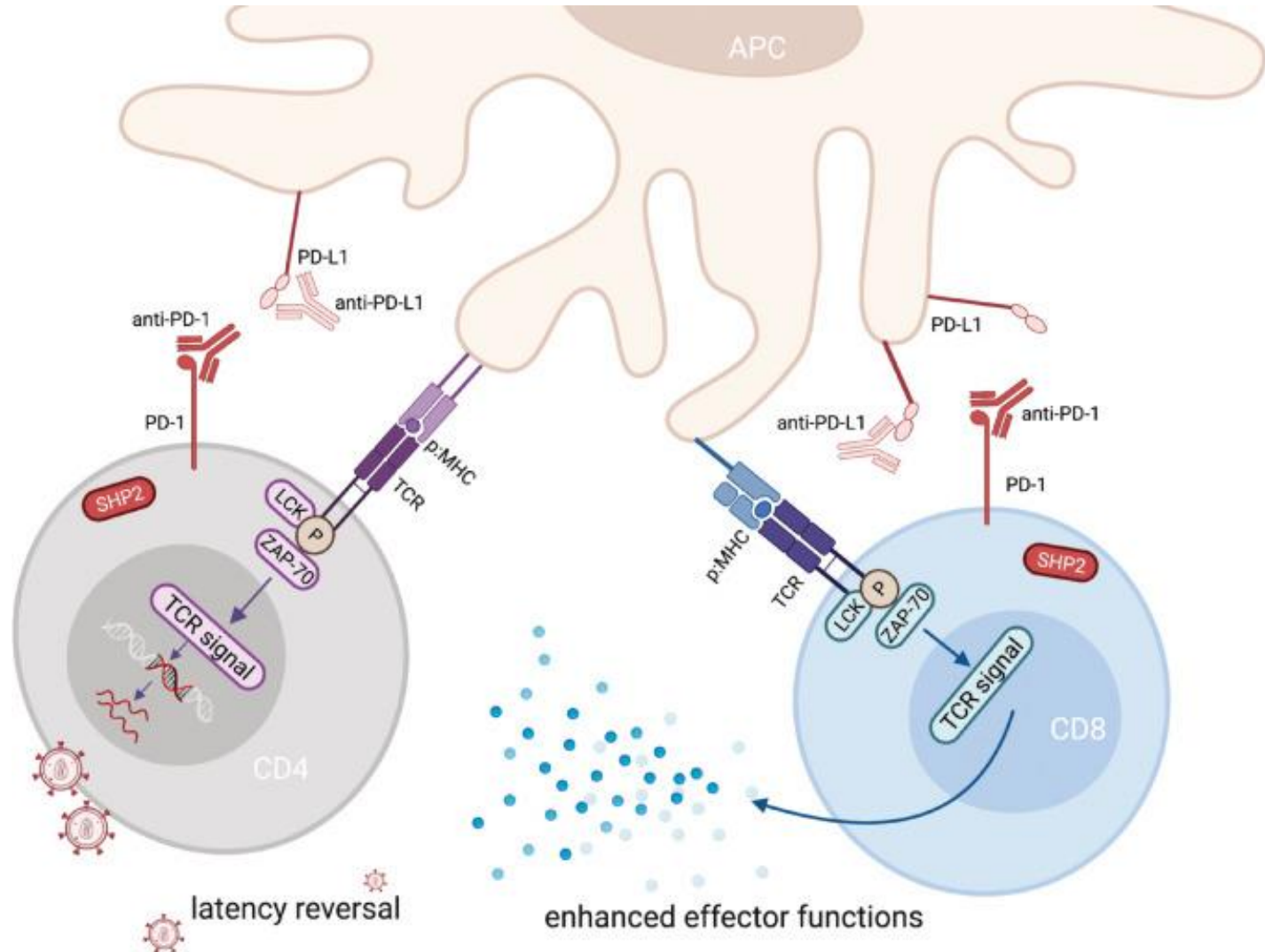


“Bad” exhausted T cells



Can we reverse T cell exhaustion?

Immune checkpoint inhibition against HIV infection



ICI approved by FDA/EMA (Oncology)

Drug	Target	Approval	Indications
Ipilimumab (Yervoy®)	CTLA-4	2011	Melanoma, renal cell carcinoma, colorectal cancer, hepatocellular carcinoma, non-small cell lung cancer, malignant pleural mesothelioma, esophageal cancer
Nivolumab (Opdivo®)	PD-1	2014	Melanoma, non-small cell lung cancer, malignant pleural mesothelioma, renal cell carcinoma, classical Hodgkin lymphoma, squamous cell carcinoma of the head and neck, urothelial carcinoma, colorectal cancer, hepatocellular carcinoma, esophageal cancer, gastric cancer, gastroesophageal junction cancer, esophageal adenocarcinoma
Pembrolizumab (Keytruda®)	PD-1	2014	Melanoma, non-small cell lung cancer, head and neck squamous cell carcinoma, classical Hodgkin lymphoma, primary mediastinal large B-cell lymphoma, urothelial carcinoma, non-muscle invasive bladder cancer, colorectal cancer, gastric cancer, esophageal cancer, cervical cancer, hepatocellular carcinoma, Merkel cell carcinoma, renal cell carcinoma, endometrial carcinoma, cutaneous squamous cell carcinoma, triple-negative breast cancer
Atezolizumab (Tecentriq®)	PD-L1	2016	Non-small cell lung cancer, small cell lung cancer, hepatocellular carcinoma, melanoma, alveolar soft part sarcoma
Durvalumab (Imfinzi®)	PD-L1	2017	Non-small cell lung cancer, small cell lung cancer, biliary tract cancer, hepatocellular carcinoma
Avelumab (Bavencio®)	PD-L1	2017	Merkel cell carcinoma, urothelial carcinoma, renal cell carcinoma
Cemiplimab (Libtayo®)	PD-1	2019	Cutaneous squamous cell carcinoma, basal cell carcinoma, non-small cell lung cancer
Dostarlimab (Jemperli®)	PD-1	2021	Endometrial cancer
Relatlimab (Opdualag®, combination with Nivolumab)	LAG-3	2022	Melanoma

Few studies with mixed results when using immune checkpoint inhibitors in PLWH...

SCIENCE TRANSLATIONAL MEDICINE | RESEARCH ARTICLE

HIV

Pembrolizumab induces HIV latency reversal in people living with HIV and cancer on antiretroviral therapy

Thomas S. Uldrick^{1,2,3*}, Scott V. Adams¹, Remi Fromentin⁴, Michael Roche^{5,6}, Steven P. Fling¹, Priscila H. Goncalves³, Kathryn Lurain³, Ramya Ramaswami³, Chia-ching Jackie Wang⁷, Robert J. Gorelick⁸, Jordan L. Welker⁸, Liz O'Donoghue¹, Harleen Choudhary¹, Jeffrey D. Lifson⁸, Thomas A. Rasmussen^{6,9}, Ajantha Rhodes⁶, Carolin Tumpach⁶, Robert Yarchoan³, Frank Maldarelli³, Martin A. Cheever^{1†}, Rafick Sékaly¹⁰, Nicolas Chomont⁴, Steven G. Deeks⁷, Sharon R. Lewin^{6,11,12*}

Open Forum Infectious Diseases

MAJOR ARTICLE



Safety and Immune Responses Following Anti-PD-1 Monoclonal Antibody Infusions in Healthy Persons With Human Immunodeficiency Virus on Antiretroviral Therapy

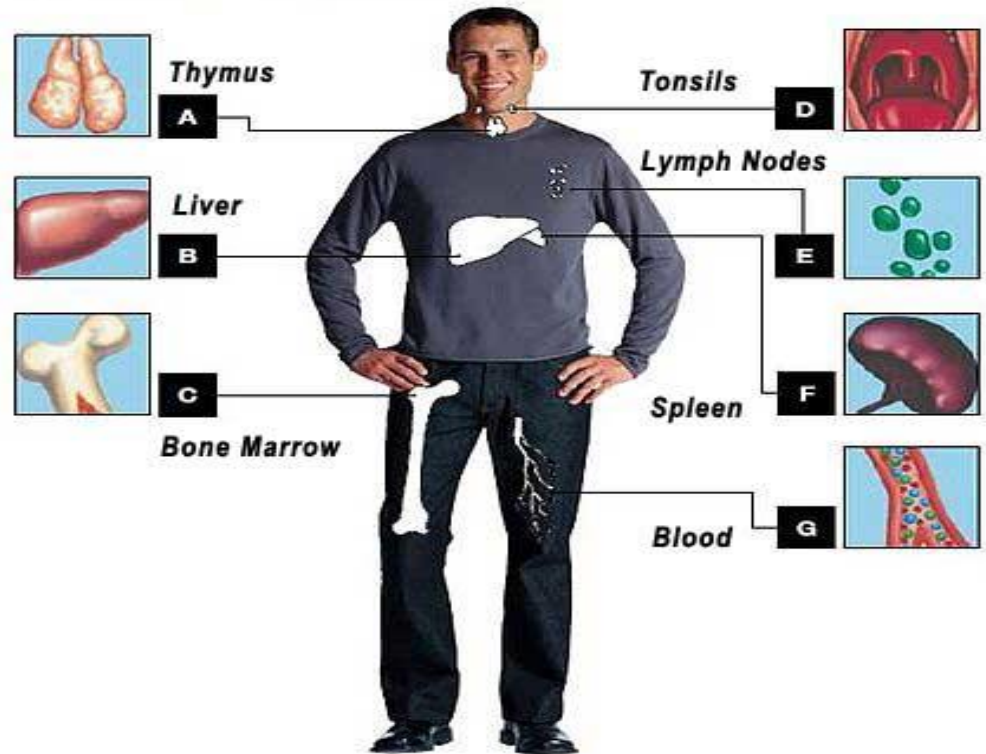
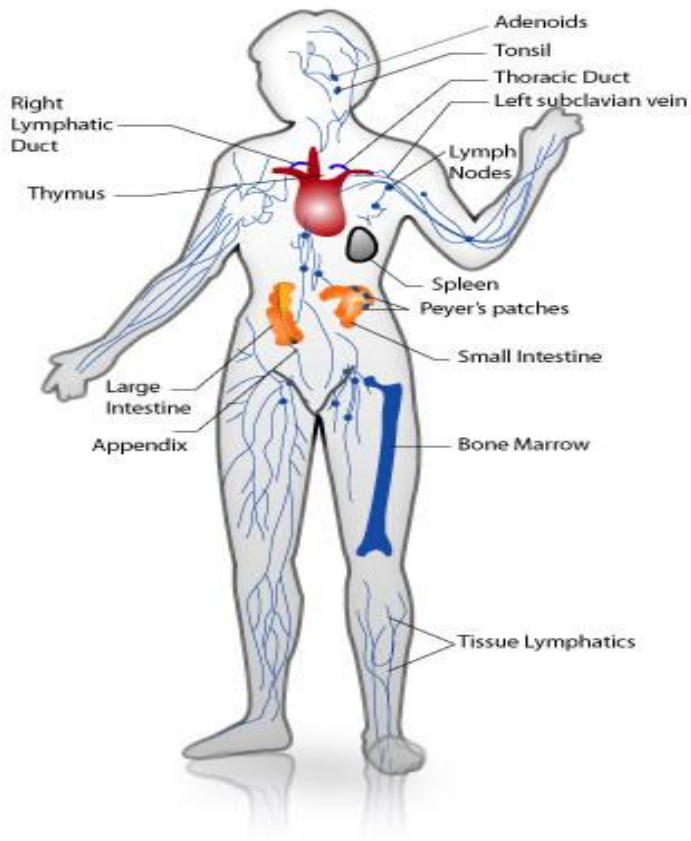
Cynthia L. Gay,^{1,6} Ronald J. Bosch,^{2,6} Ashley McKhann,² Raymond Cha,^{3,6} Gene D. Morse,^{3,6} Chanelle L. Wimbish,⁴ Danielle M. Campbell,⁵ Kendall F. Moseley,^{6,6} Steven Hendrickx,⁷ Michael Messer,^{8,6} Constance A. Benson,^{7,6} Edgar T. Overton,^{8,3,6} Anne Paccaly,^{10,6} Vladimir Jankovic,^{10,6} Elizabeth Miller,¹⁰ Randall Tressler,¹¹ Jonathan Z. Li,¹² Daniel R. Kuritzkes,^{12,6} Bernard J. C. Macatangay,^{13,6} Joseph J. Eron,^{1,6} and W. David Hardy^{14,6}, for the A5370 Team*

Only 14 studies with ICI ongoing in PLWH,
5421 in cancer...
(clinicaltrials.gov)

Can the immune system be used to target the reservoir?

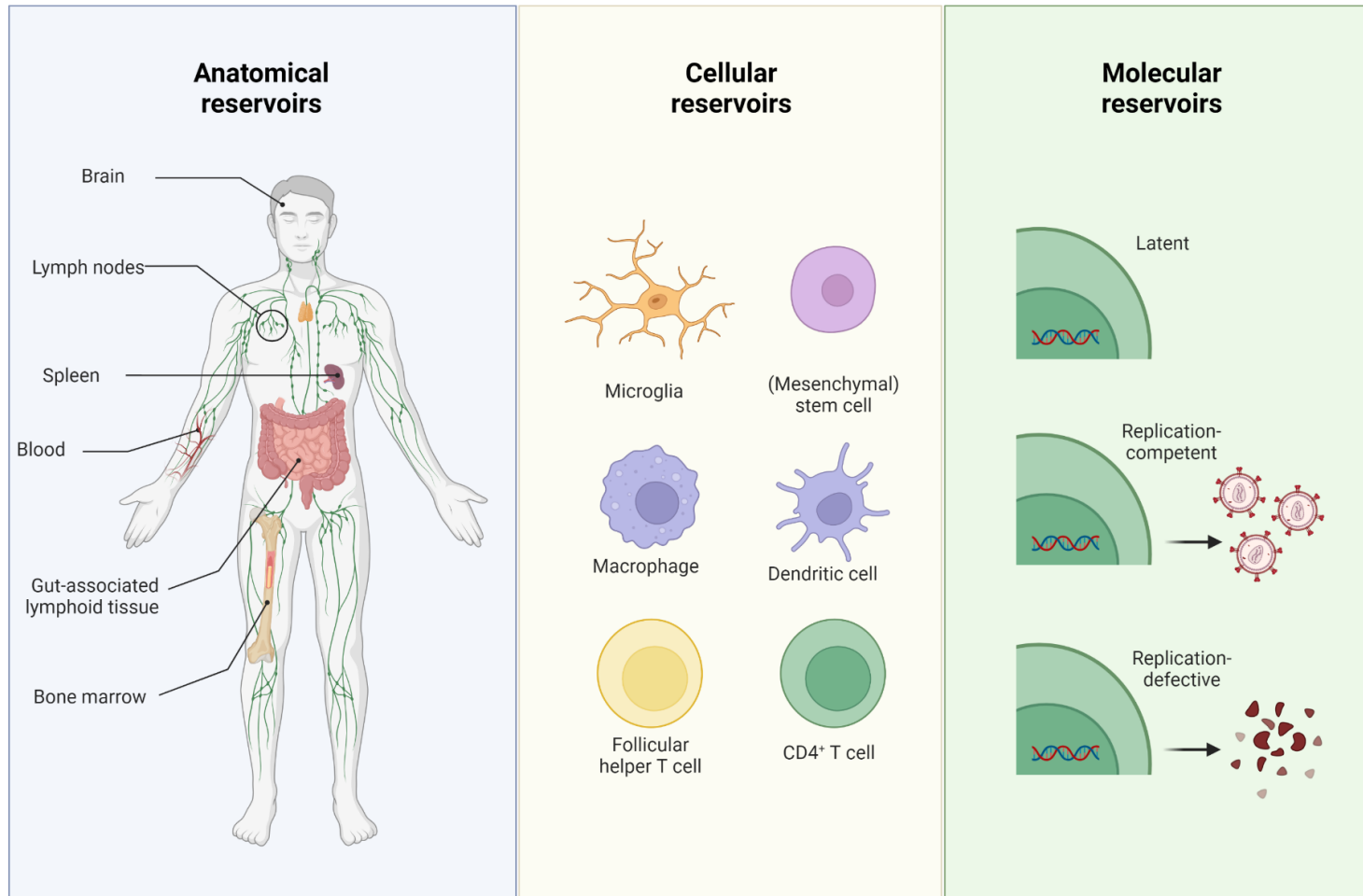
Where is the immune system?

(Almost) everywhere!



Where is the HIV reservoir?

(Almost) everywhere!



Strategies for targeting the HIV reservoir



B

The NEW ENGLAND JOURNAL of MEDICINE

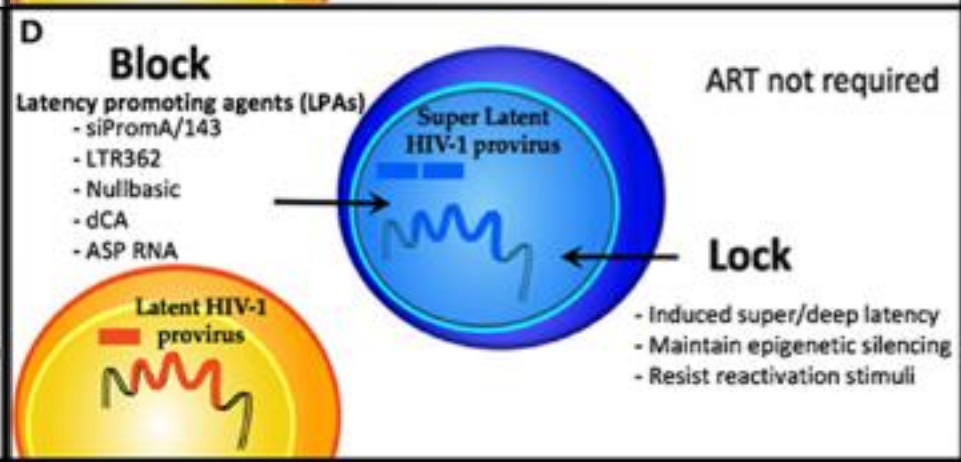
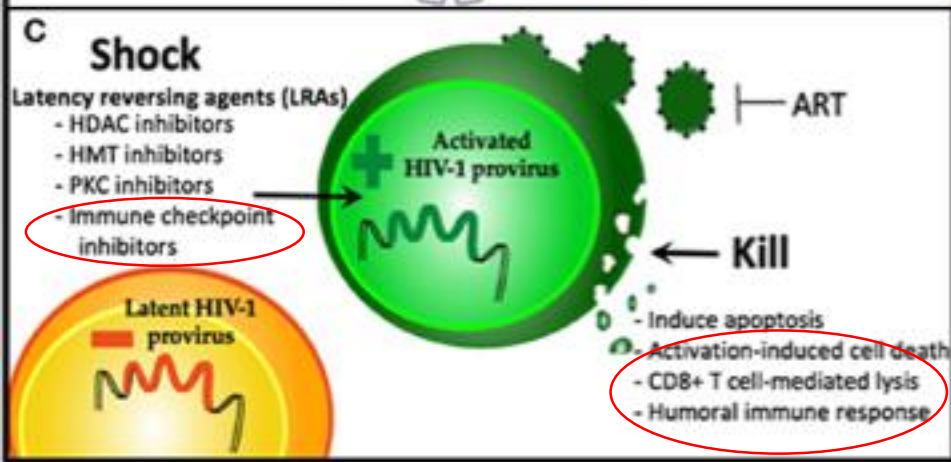
SPECIALTIES ▼ TOPICS ▼ MULTIMEDIA ▼ CURRENT ISSUE ▼ LEARNING/CME ▼ AUTHOR CENTER PUBLICATIONS ▼

ORIGINAL ARTICLE | BRIEF REPORT

CRISPR-Edited Stem Cells in a Patient with HIV and Acute Lymphocytic Leukemia

Authors: Lei Xu, M.D., Ph.D., Jun Wang, M.D., Ph.D., Yulin Liu, B.S., Liangfu Xie, B.S., Bin Su, Ph.D., Danlei Mou, M.D., Ph.D., Longteng Wang, B.S., and Hu Chen, M.D., Ph.D. [Author Info & Affiliations](#)

Published September 11, 2019 | N Engl J Med 2019;381:1240-1247 | DOI: 10.1056/NEJMoa1817426
VOL. 381 NO. 13



Therapeutic vaccination to obtain functional cure

WHAT'S THE DIFFERENCE?

A brief overview of what a "functional" HIV cure and a "sterilizing" HIV cure is.

FUNCTIONAL CURE

When the level of HIV particles in an infected person's body has been reduced to such an extremely low level that the person can stop treatment and not worry about the disease rebounding and damaging his immune system or body.



STERILIZING CURE

Eradication of HIV

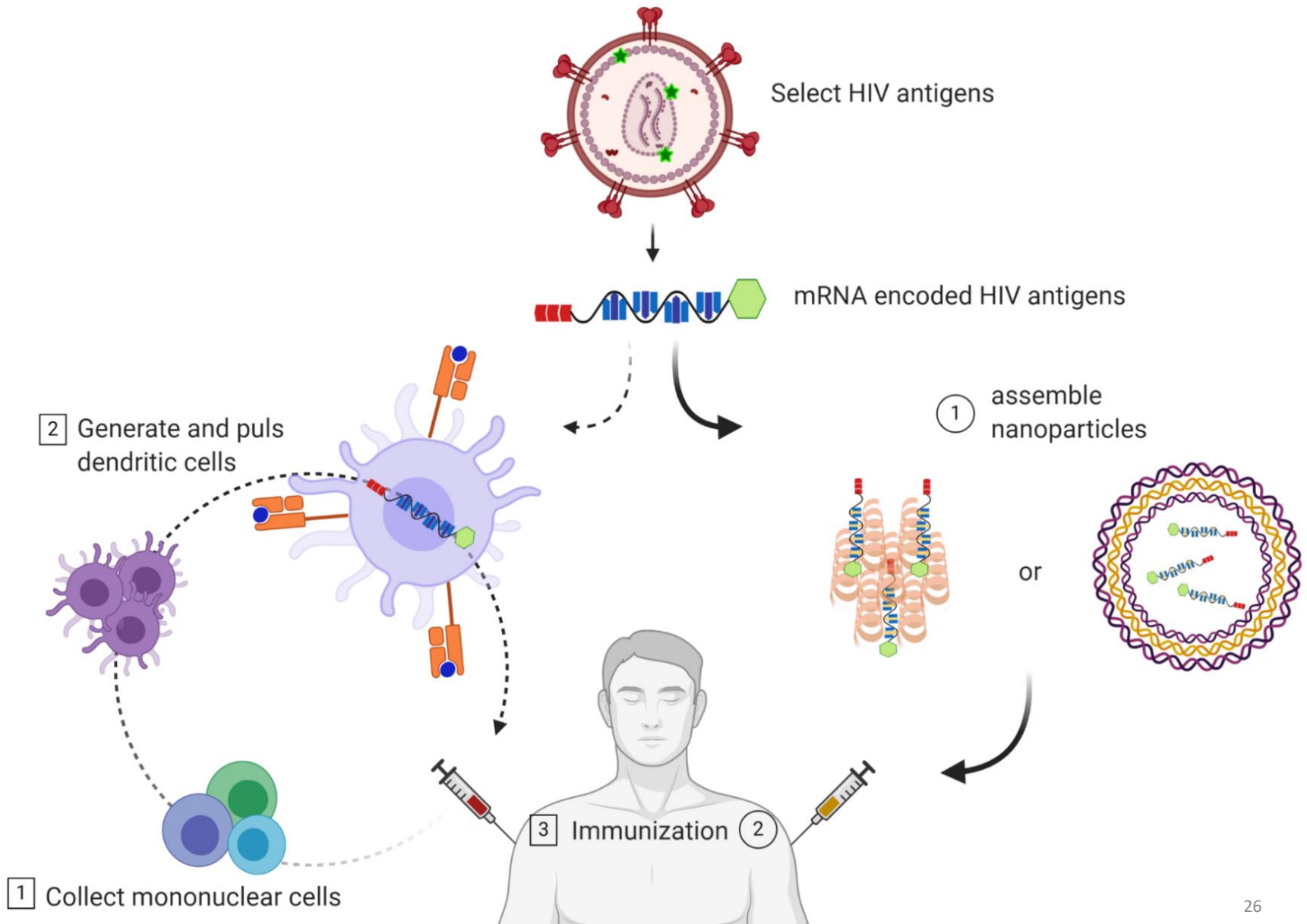
When every last particle of HIV has been destroyed or cleared out from an infected person's body.



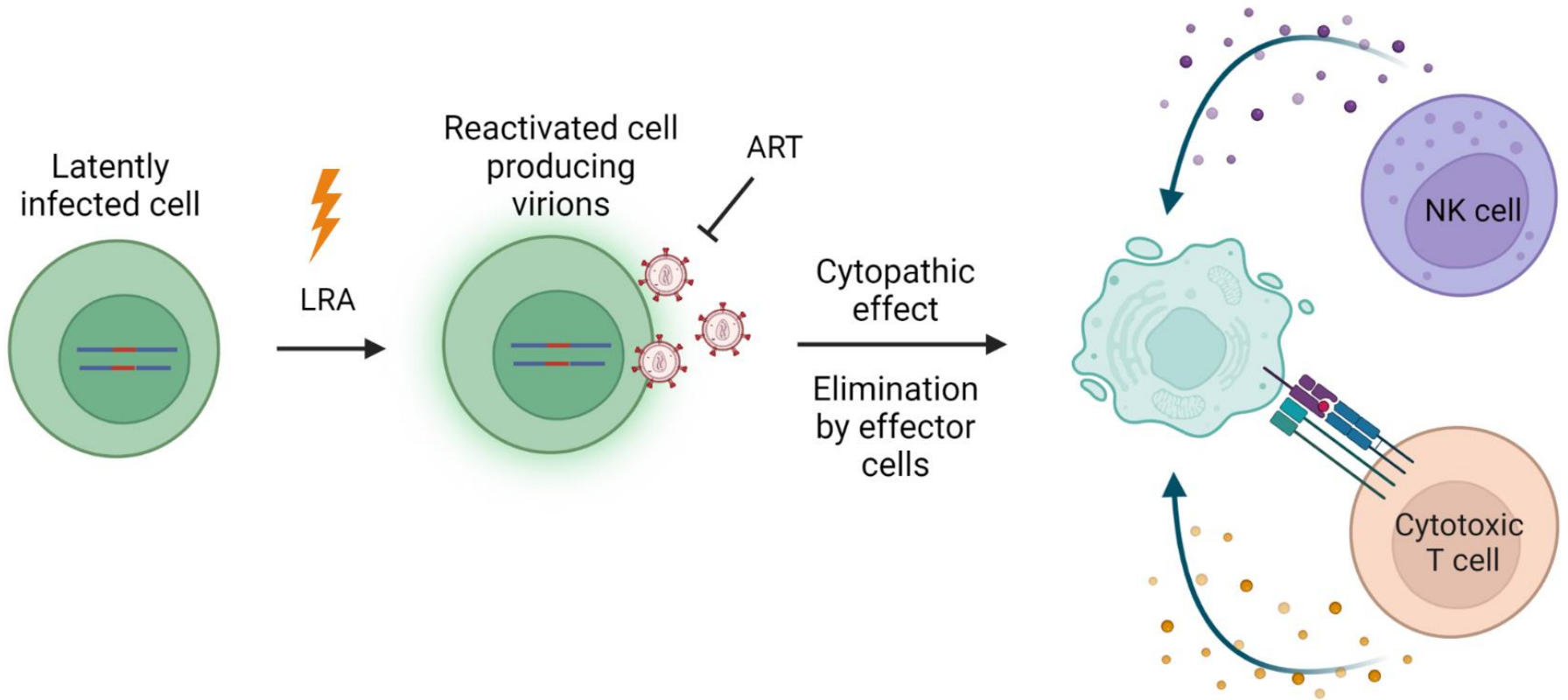
AIDS Action Committee | www.aac.org | [@AIDSActionCommittee](#) | [@AIDSAction](#)

For more information about HIV/AIDS and hepatitis B and C, check out our online Health Library: aac.org/health.

mRNA as a tool for therapeutic vaccination



Going for the *Kick and Kill* by combining LRAs and the immune system



Boosting therapeutic vaccination by adding LRAs

THE LANCET
HIV

Combined effect of Vacc-4x, recombinant human granulocyte macrophage colony-stimulating factor vaccination, and romidepsin on the HIV-1 reservoir (REDUC): a single-arm, phase 1B/2A trial

Dr Steffen Leth, MD   • Mariane H Schleimann, PhD • Sara K Nissen, MS • Jesper F Højen, MD • Rikke Olesen, PhD • Mette E Graversen, MD • Sofie Jørgensen, BSs • Anne Sofie Kjær, MD • Paul W Denton, PhD • Alejandra Mørk, PhD • Maja A Sommerfelt, PhD • Kim Krogsgaard, DMSc • Prof Lars Østergaard, DMSc • Thomas A Rasmussen, PhD • Martin Tolstrup, PhD • Dr Ole Schmeltz Søgaard, PhD   • [Show less](#)

 frontiers
in Immunology

ORIGINAL RESEARCH
published: 06 May 2020
doi: 10.3389/fimmu.2020.00323



HIVconsV Vaccines and Romidepsin in Early-Treated HIV-1-Infected Individuals: Safety, Immunogenicity and Effect on the Viral Reservoir (Study BCN02)

OPEN ACCESS

Edited by:

Carolina Garrido,
University of North Carolina at
Chapel Hill, United States

Reviewed by:

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University of Nebraska Omaha,
United States
Jonathan Li,
Brigham and Women's Hospital,
United States

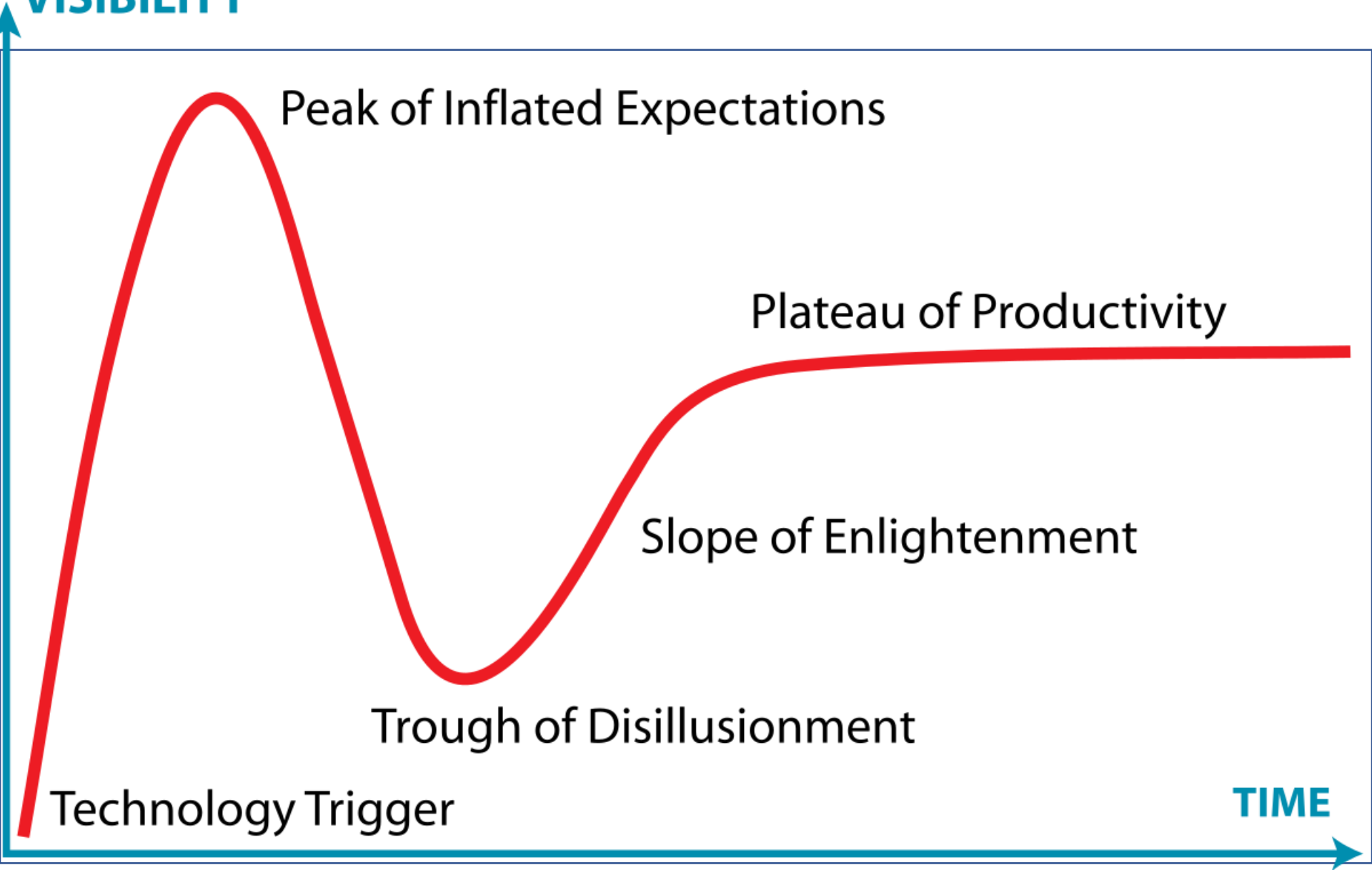
Beatriz Mothe^{1,2,3*}, Miriam Rosás-Umber^{1,4†}, Pep Coll¹, Christian Manzano⁵, Maria C. Puertas¹, Sara Morón-López¹, Anuska Llano¹, Cristina Miranda², Samantha Cedeño¹, Miriam López², Yovaninna Alarcón-Soto⁶, Guadalupe Gómez Melis⁶, Klaus Langohr⁶, Ana M. Barriocanal^{4,7}, Jessica Toro², Irene Ruiz², Cristina Rovira⁵, Antonio Carrillo¹, Michael Meulbroek⁸, Alison Crook⁹, Edmund G. Wee⁹, Jose M. Miró⁵, Bonaventura Clotet^{1,2,3,4}, Marta Valle^{4,10}, Javier Martínez-Picado^{1,3,11}, Tomás Hanke^{8,12}, Christian Brander^{1,3,11†}, José Moltó^{2,7†} and the BCN02 Study Investigators

→ Only very modest effects observed for active immunization approaches combined with LRAs

Can the immune system directly recognize (and eliminate) reservoir cells?

A seminal report identifying a reservoir-specific marker

VISIBILITY



Peak of Inflated Expectations

Plateau of Productivity

Slope of Enlightenment

Trough of Disillusionment

Technology Trigger

TIME

The trough of disillusionement: nobody can reproduce these results...

SCIENCE TRANSLATIONAL MEDICINE | RESEARCH ARTICLE

HIV

CD32 is expressed on cells with transcriptionally active HIV but does not enrich for HIV DNA in resting T cells

Mohamed Abdel-Mohsen,^{1*} Leticia Kuri-Cervantes,^{2*} Judith Grau-Exposito,^{3*} Adam M. Spivak,⁴ Racheal A. Nell,⁴ Costin Tomescu,¹ Surya Kumari Vadrevu,¹ Leila B. Giron,¹ Carla Serra-Peinado,³ Meritxell Genescà,³ Josep Castellví,⁵ Guoxin Wu,⁶ Perla M. Del Rio Estrada,⁷ Mauricio González-Navarro,⁷ Kenneth Lynn,^{1,2,8} Colin T. King,⁹ Sai Vemula,⁶ Kara Cox,⁶ Yanmin Wan,¹⁰ Qingsheng Li,¹⁰ Karam Mounzer,⁸ Jay Kostman,⁸ Ian Frank,² Mirko Paiardini,⁹ Daria Hazuda,⁶ Gustavo Reyes-Terán,⁷ Douglas Richman,¹¹ Bonnie Howell,⁶ Pablo Tebas,² Javier Martínez-Picado,^{12,13,14} Vicente Planelles,⁴ Maria J. Buzon,^{3†} Michael R. Betts,^{2†} Luis J. Montaner^{1†}

BRIEF COMMUNICATIONS ARISING

Conflicting evidence for HIV enrichment in CD32⁺ CD4 T cells

ARISING FROM B. Descours et al. *Nature* **543**, 564–567 (2017); <https://doi.org/10.1038/nature21710>

RESEARCH

HIV

Induction of durable remission by dual immunotherapy in SHIV-infected ART-suppressed macaques

So-Yon Lim^{1†}, Jina Lee^{1†}, Christa E. Osuna¹, Pratik Vikhe¹, Dane R. Schalk², Elsa Chen¹, Emily Fray³, Mithra Kumar³, Nancy Schultz-Darken², Eva Rakasz², Saverio Capuano², Ruby A Ladd^{2†}, Hwi Min Gil², David T. Evans², Emily K. Jeng⁴, Michael Seaman¹, Malcolm Martin⁵, Christiaan Van Dorp^{6,5}, Alan S. Perelson^{6,7}, Hing C. Wong⁴, Janet D. Siliciano³, Robert Siliciano^{3,8}, Jeffrey T. Safritz⁹, Douglas F. Nixon¹⁰, Patrick Soon-Shiong⁹, Michel Nussenzweig^{11,12}, James B. Whitney^{1,13*}



ARTICLE

DOI: 10.1038/s41467-018-05157-w OPEN

CD32 expression is associated to T-cell activation and is not a marker of the HIV-1 reservoir

Roger Badia¹, Ester Ballana¹, Marc Castellví¹, Ederne García-Vidal¹, Maria Pujantell¹, Bonaventura Clotet¹, Julia G. Prado¹, Jordi Puig¹, Miguel A. Martínez¹, Eva Riveira-Muñoz¹ & José A. Esté¹



ORIGINAL RESEARCH
published: 04 May 2018
doi: 10.3389/fimmu.2018.00328



CD32-Expressing CD4 T Cells Are Phenotypically Diverse and Can Contain Proviral HIV DNA

Genevieve E. Martin^{1†}, Matthew Pace^{1†}, John P. Thornhill^{1,2†}, Chansavath Phetsouphanh¹, Jodi Meyerowitz¹, Morgane Gossez¹, Helen Brown¹, Natalia Olejniczak¹, Julianne Lwanga¹, Gita Ramjee¹, Pontiano Kaleebu¹, Kholoud Porter¹, Christian B. Willberg^{1,2}, Paul Klenerman^{1,2}, Nneka Nwokolo^{1,3}, Julie Fox^{1,4},
[†]On Behalf of the CHERUB Investigators

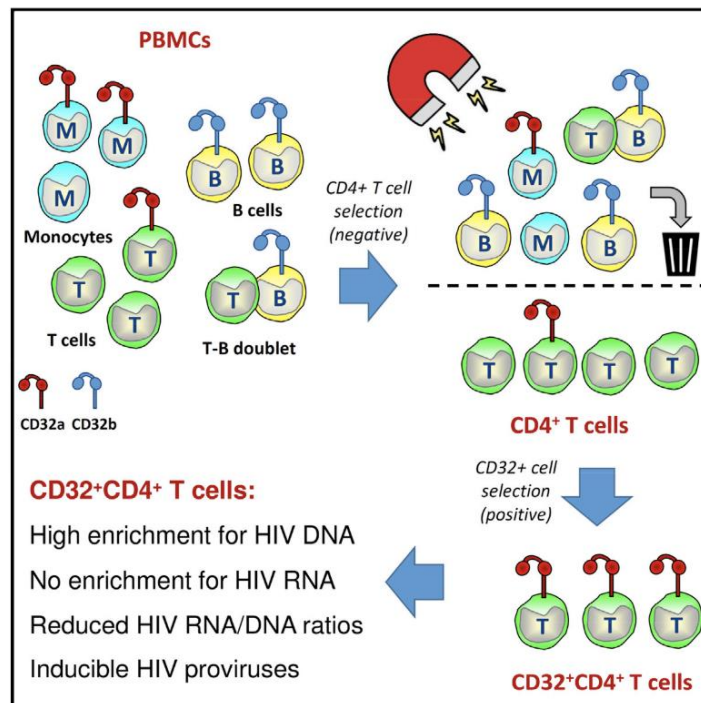
With some persistence, CD32 can indeed be specifically linked to latent infection of CD4+ T cells...

Article

Cell Reports

CD32⁺CD4⁺ T Cells Are Highly Enriched for HIV DNA and Can Support Transcriptional Latency

Graphical Abstract



Authors

Gilles Darcis, Neeltje A. Kootstra, Berend Hooibrink, ..., Carine van Lint, Ben Berkhout, Alexander O. Pasternak

Correspondence

gdarcis@chuliege.be (G.D.), a.o.pasternak@amsterdamumc.nl (A.O.P.)

In Brief

CD32a was recently proposed to mark the HIV reservoir, but this finding was subsequently challenged. By using a sequential cell-sorting protocol to purify bona fide CD32⁺CD4⁺ cells, Darcis et al. demonstrate HIV DNA enrichment and *ex vivo* reactivation-mediated virus production in these cells, reinforcing CD32 as an HIV reservoir marker.

With some persistence, CD32 can indeed be specifically linked to latent infection of CD4+ T cells...

iScience

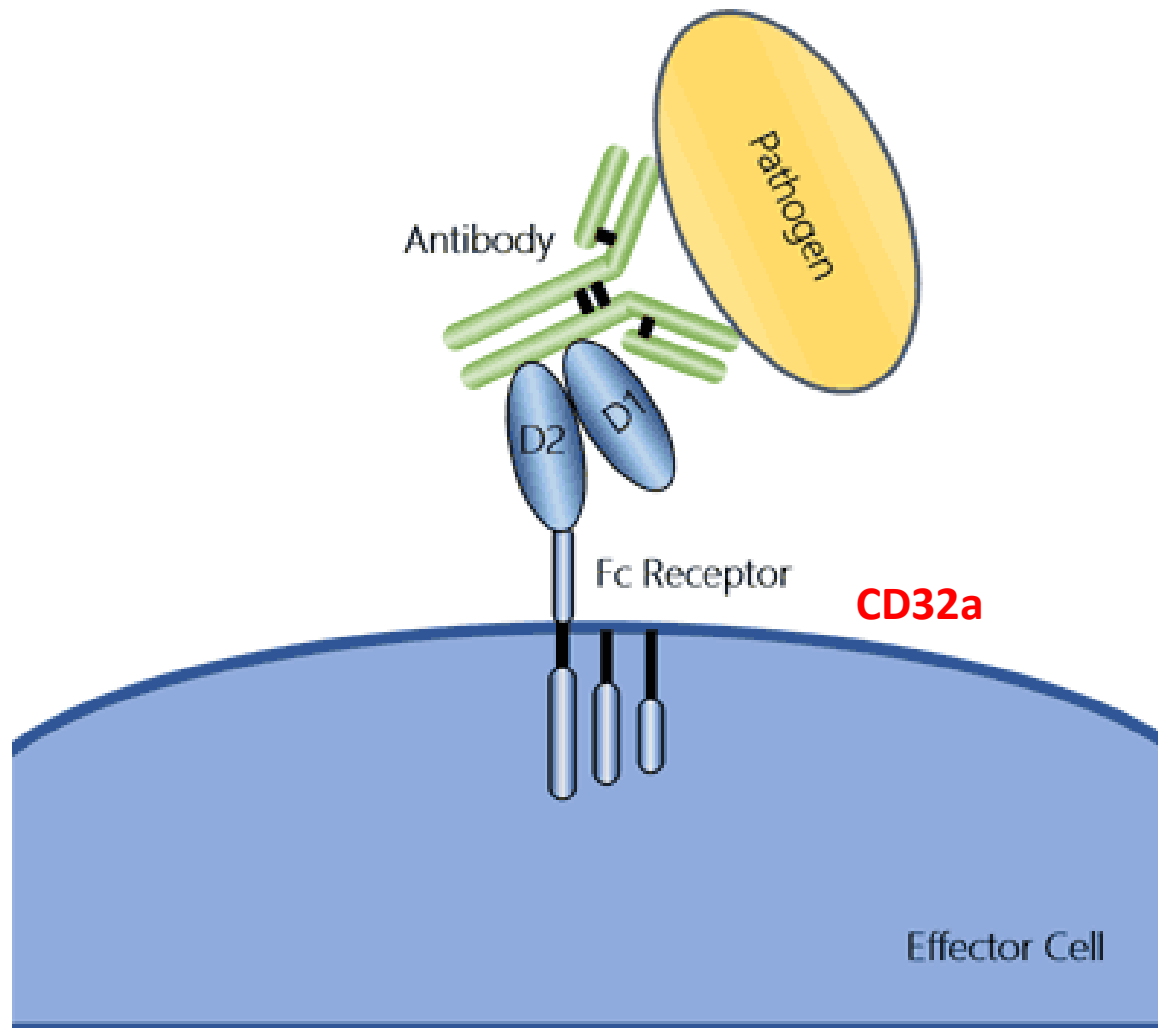
 **CellPress**
OPEN ACCESS

Article

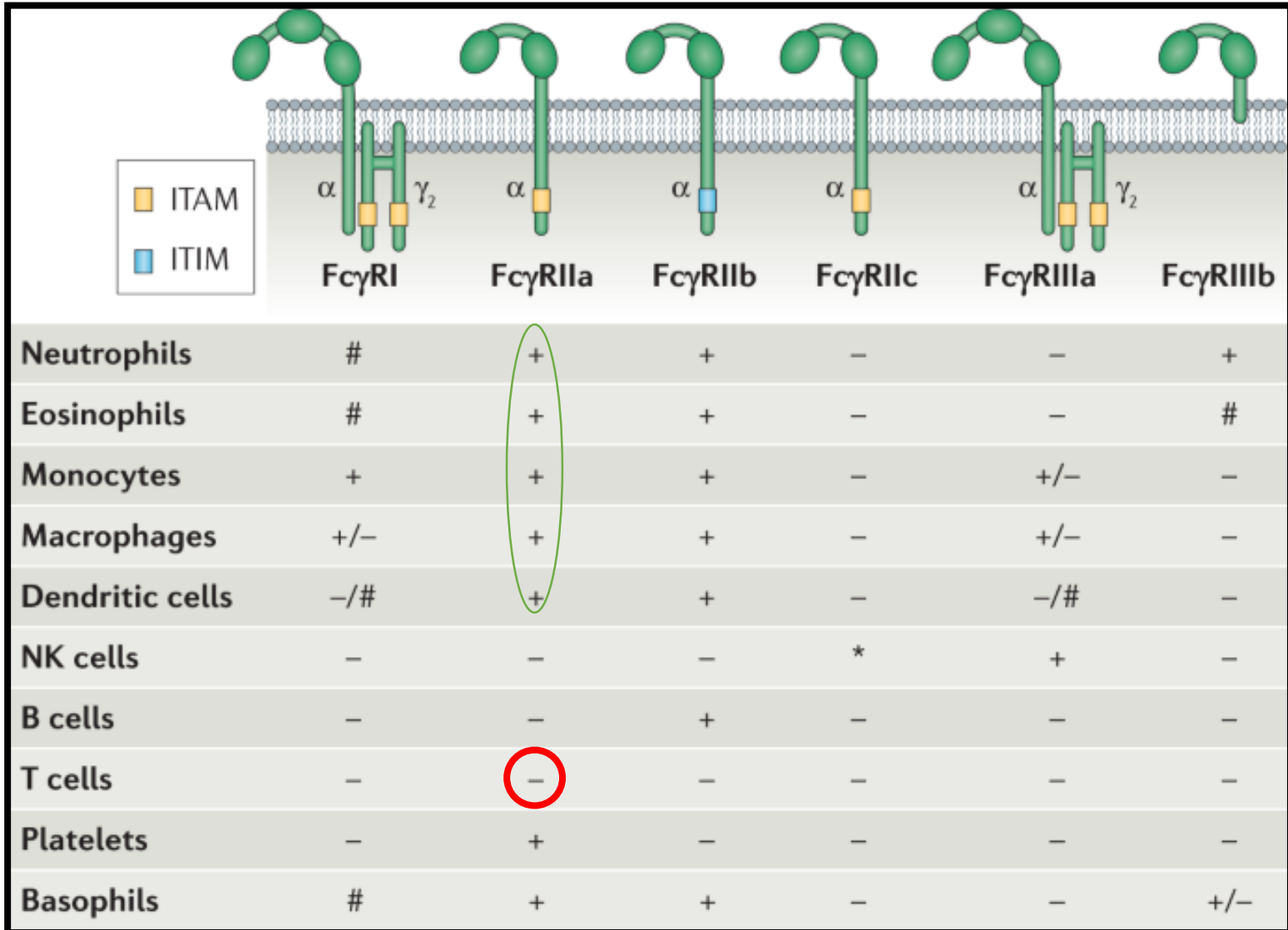
CD32⁺CD4⁺ memory T cells are enriched for total HIV-1 DNA in tissues from humanized mice

Philipp Adams,^{1,2,3,8} Virginie Fievez,^{1,8} Rafaëla Schober,¹ Mathieu Amand,¹ Gilles Iserentant,¹ Sofie Rutsaert,⁴ Géraldine Dessilly,⁵ Guido Vanham,^{2,3} Fanny Hedin,⁶ Antonio Cosma,⁶ Michel Moutschen,⁷ Linos Vandekerckhove,⁴ and Carole Seguin-Devaux^{1,9,*}

Can the immune system directly recognize (and eliminate) reservoir cells?



Can the immune system directly recognize (and eliminate) reservoir cells?



With some help from ChatGPT...

Are there other surface markers than CD32 for identifying the latent HIV reservoir?



Yes, there are several surface markers other than CD32 that have been explored for identifying the latent HIV reservoir. Identifying these markers is critical for targeting and potentially eliminating latent HIV-infected cells. Some of these markers include:

It's important to note that no single marker is universally specific for the latent HIV reservoir. Often, a combination of markers is used to better identify and characterize these cells. Additionally, research is ongoing to validate and discover new markers that can more accurately pinpoint latent reservoirs for effective HIV cure strategies.



Are there other surface markers than CD32 for identifying the latent HIV reservoir?

- 1. PD-1 (Programmed Cell Death Protein 1):** PD-1 is an inhibitory receptor commonly upregulated on exhausted T cells, including those harboring latent HIV. It has been associated with a higher frequency of HIV DNA and RNA in infected individuals.
- 2. LAG-3 (Lymphocyte-Activation Gene 3):** Similar to PD-1, LAG-3 is another exhaustion marker that has been found on T cells with latent HIV infection.
- 3. TIGIT (T cell Immunoreceptor with Ig and ITIM domains):** TIGIT is another inhibitory receptor associated with T cell exhaustion and has been linked to the presence of latent HIV.
- 4. CXCR5 (C-X-C Chemokine Receptor Type 5):** CXCR5 is a chemokine receptor involved in the homing of T cells to lymphoid follicles. It has been found on a subset of CD4+ T cells that may serve as a reservoir for latent HIV.
- 5. CD30 (TNF Receptor Superfamily Member 8):** CD30 is expressed on activated T cells and has been associated with cells harboring latent HIV.
- 6. HLA-DR (Human Leukocyte Antigen – DR isotype):** HLA-DR is a marker of immune activation, and higher expression has been observed in cells with latent HIV.
- 7. CD20 (B cell marker):** Some studies have identified CD20 on a subset of T cells with latent HIV, although its role is less established compared to others.
- 8. CD2, CD69, and CD25:** These activation markers are also associated with a subset of CD4+ T cells that can harbor latent HIV.
- 9. CD27 and CD45RO:** Memory T cell markers that are used to identify central and effector memory T cells, which are primary reservoirs for latent HIV.
- 10. CCR5 and CXCR4 (Chemokine Receptors):** While these are primarily entry co-receptors for HIV, their expression patterns on different T cell subsets can help identify potential reservoirs.

Can the immune system directly recognize (and eliminate) reservoir cells?

Are there other surface markers than CD32 for identifying the latent HIV reservoir?



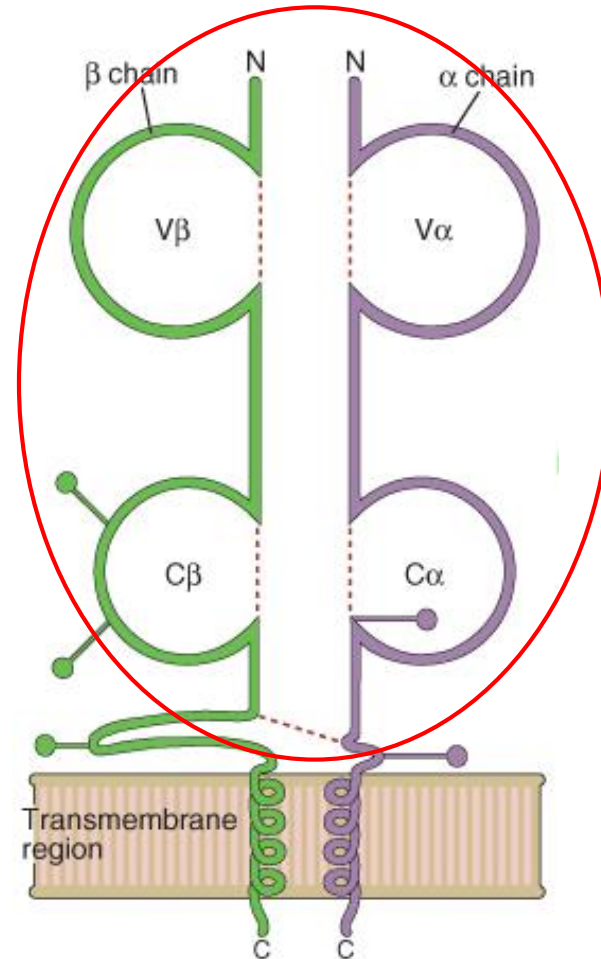
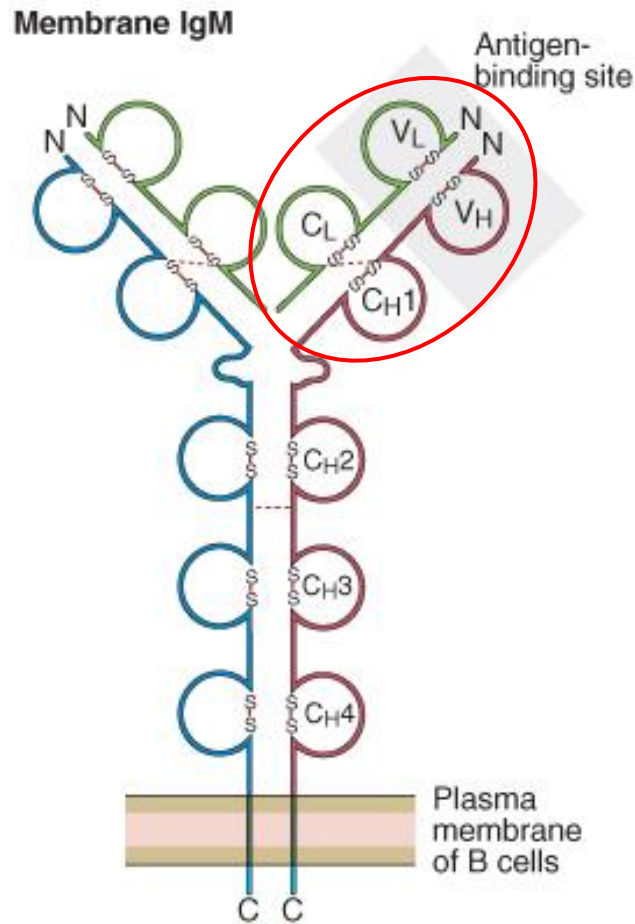
Yes, there are several surface markers other than CD32 that have been explored for identifying the latent HIV reservoir. Identifying these markers is critical for targeting and potentially eliminating latent HIV-infected cells. Some of these markers include:

Chimeric antigen receptors
(CARs) to the rescue?

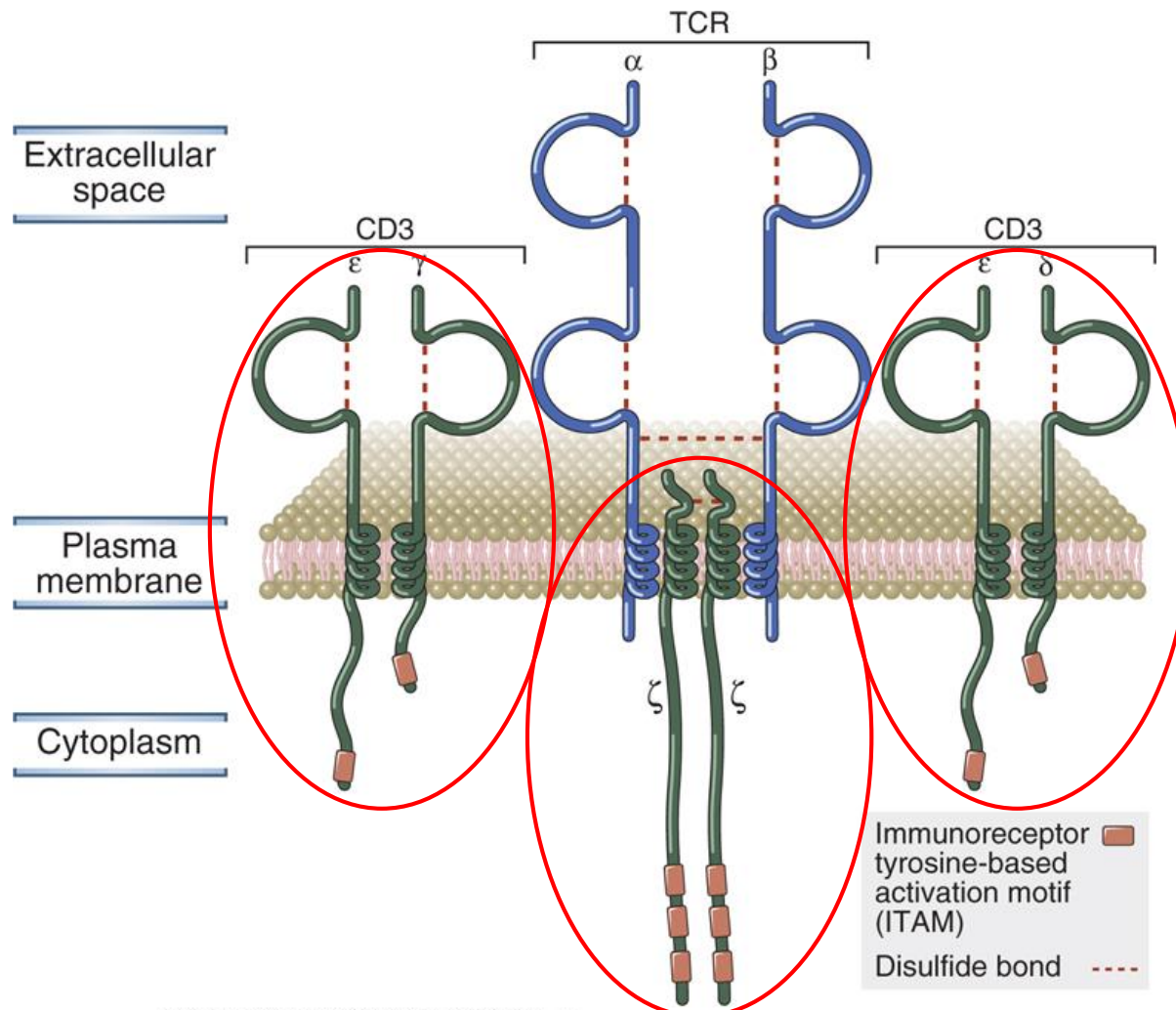
Similarity between TCR and antibody structure

Antibody

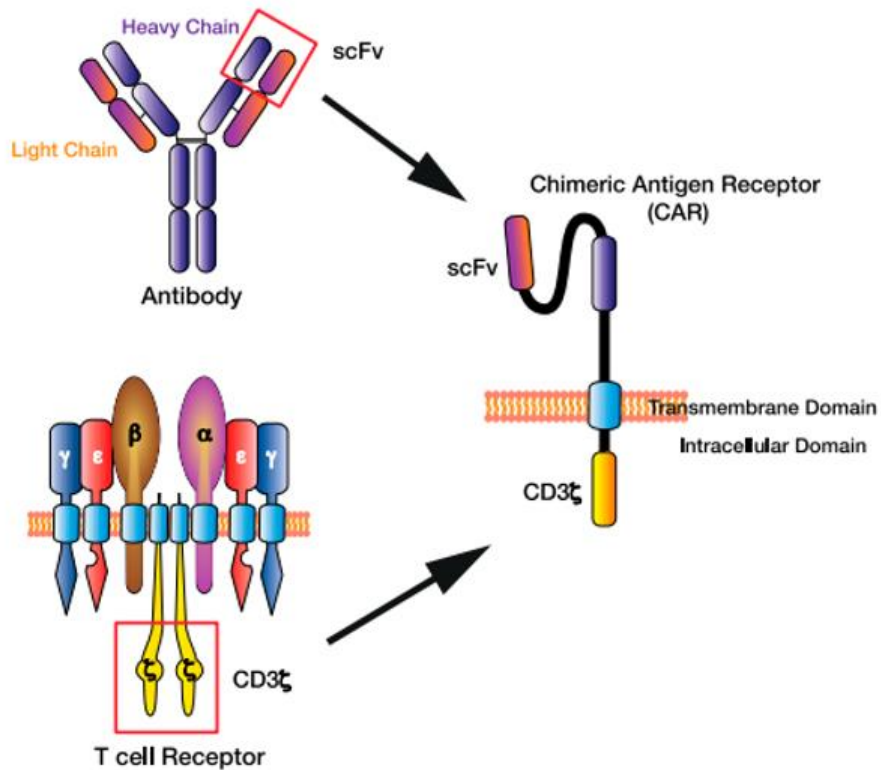
T cell receptor



TCR signaling is mediated by the CD3 chain

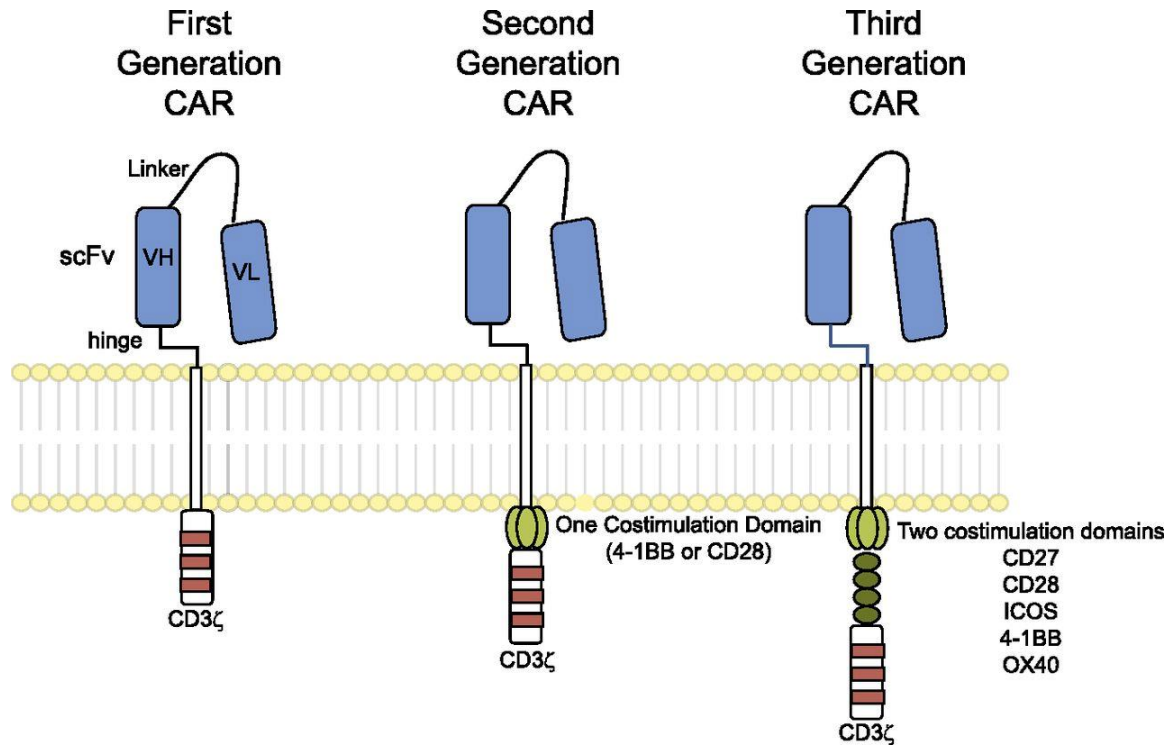


The egg of Columbus...

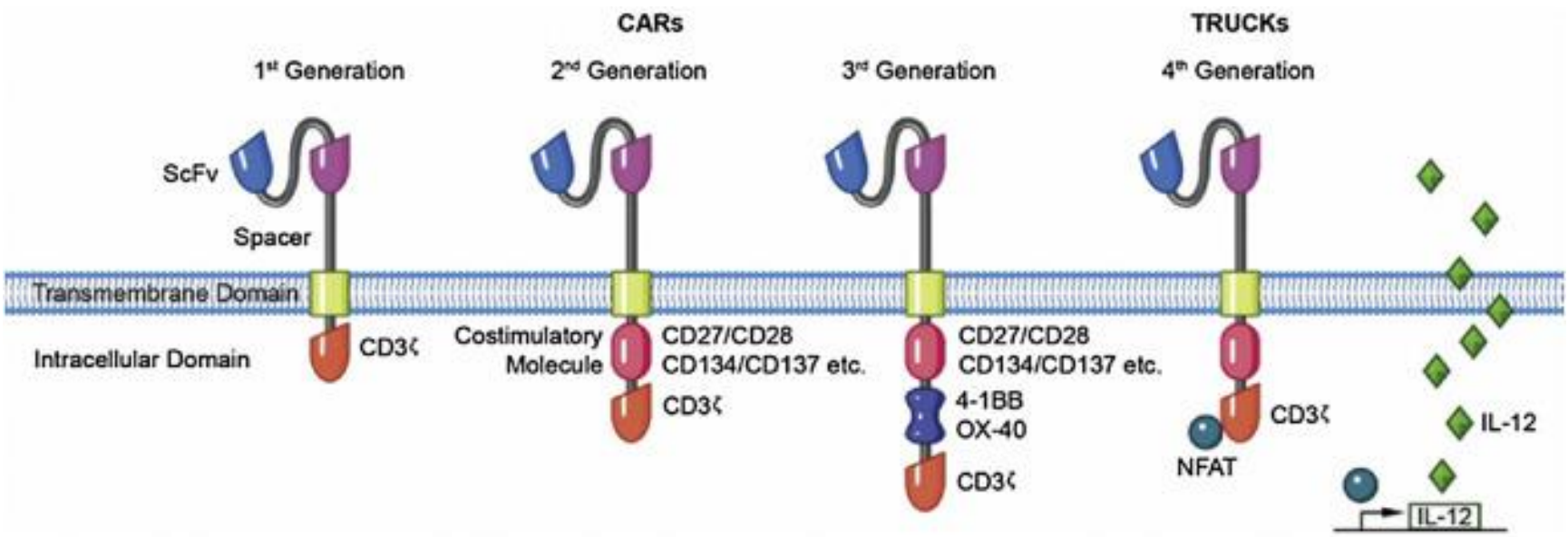


How do we use the potency of cytotoxic T cells to kill virally infected cells, and expand the recognition capacity without losing too much specificity?

The evolution of CARs

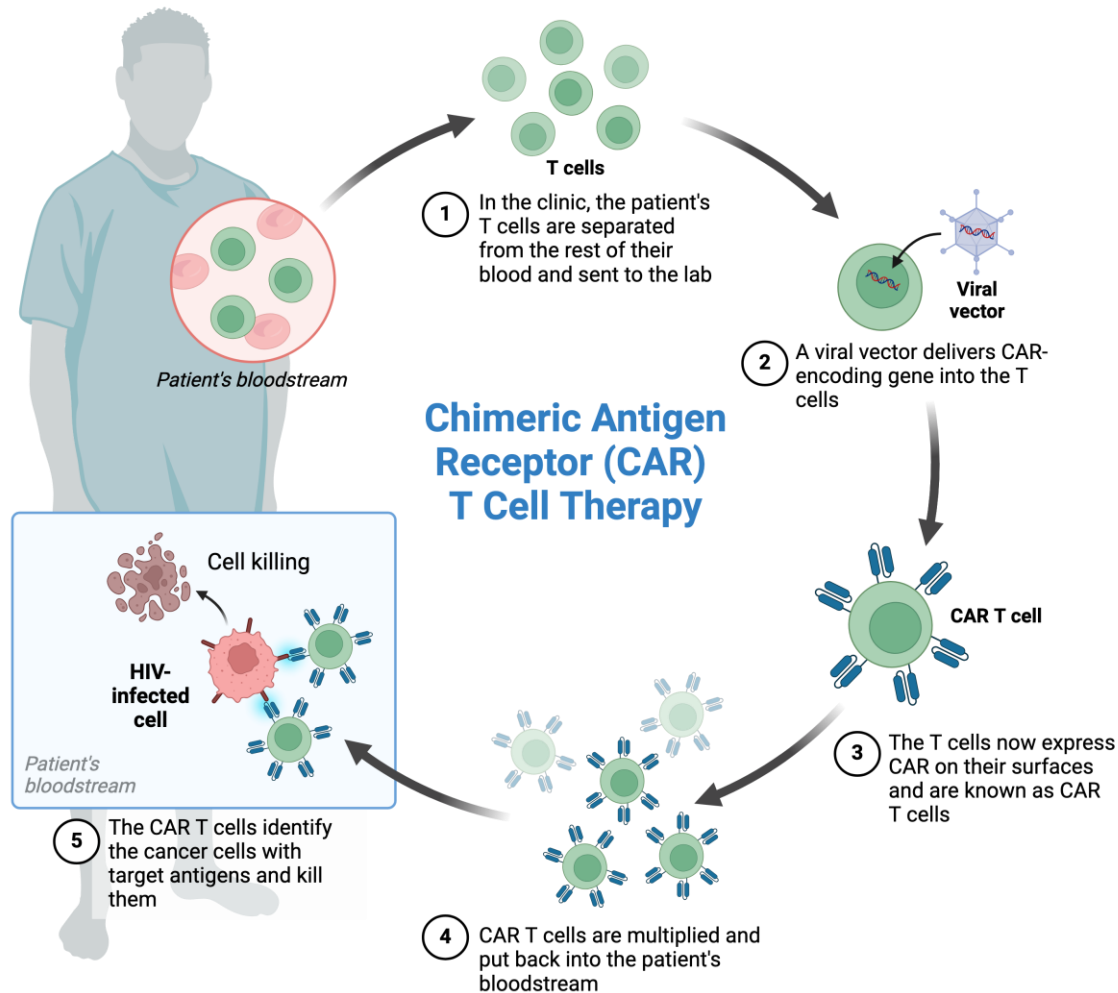


And TRUCKs...








TRUCKs = T cells redirected for antigen-unrestricted cytokine-initiated killing

How do we bring this to the patient?



CAR T-cell products approved by EMA in (hemato)oncology

Name	Company	Type	EMA Market authorization	Indication
Kymriah	 NOVARTIS	GTMP (CAR-T)	2018	B-ALL
Yescarta	 Kite A GILEAD Company	GTMP (CAR-T)	2018	B-cell lymphoma
Tecartus	 Kite A GILEAD Company	GTMP (CAR-T)	2020	Mantle cell lymphoma
Abecma	 Bristol Myers Squibb	GTMP (CAR-T)	2021	Multiple myeloma
Breyanzy	 Bristol Myers Squibb	GTMP (CAR-T)	2022	B-cell tumors

Many promising reports show the potential of CAR-T cells to kill HIV-infected cells

The Journal of Clinical Investigation

RESEARCH ARTICLE

Mao et al. *Cell Discovery* (2024)10:49
<https://doi.org/10.1038/s41421-024-00658-z>

Cell Discovery
www.nature.com/celldisc

Anti-PD-1 chimeric antigen receptor T cells efficiently target SIV-infected CD4⁺ T cells in germinal centers

Karsten Eichholz,¹ Yoshinori Fukazawa,² Christopher W. Peterson,^{3,4} Françoise Haeseleer,^{1,4,5} Manuel Medina,² Shelby Hoffmeister,² Derick M. Duell,² Benjamin D. Varco-Merth,² Sandra Dross,^{6,7} Haesun Park,² Caralyn S. Labriola,² Michael K. Axthelm,² Robert D. Murnane,⁸ Jeremy V. Smedley,² Lei Jin,¹ Jiaxin Gong,¹ Blake J. Rust,³ Deborah H. Fuller,^{6,7} Hans-Peter Kiem,^{1,3,5} Louis J. Picker,² Afam A. Okoye,² and Lawrence Corey^{4,5}

¹Vaccine and Infectious Disease Division, Fred Hutchinson Cancer Center, Seattle, Washington, USA. ²Vaccine and Gene Therapy Institute and Oregon National Primate Research Center (ONPRC), Oregon Health & Science University, Beaverton, Oregon, USA. ³Stem Cell and Gene Therapy Program, Fred Hutchinson Cancer Center, Seattle, Washington, USA. ⁴Department of Laboratory Medicine and ⁵Department of Medicine, University of Washington, Seattle, Washington, USA. ⁶Washington National Primate Research Center (WanPRC), Seattle, Washington, USA. ⁷Department of Microbiology, University of Washington, Seattle, Washington, USA.

ARTICLE

Open Access

Efficacy and safety of novel multifunctional M10 CAR-T cells in HIV-1-infected patients: a phase I, multicenter, single-arm, open-label study

Yunyu Mao¹, Qibin Liao¹, Youwei Zhu¹, Mingyuan Bi², Jun Zou³, Nairong Zheng¹, Lingyan Zhu¹, Chen Zhao¹, Qing Liu², Li Liu¹, Jun Chen¹, Ling Gu¹, Zhuoqun Liu¹, Xinghao Pan¹, Ying Xue¹, Meiqi Feng¹, Tianlei Ying¹, Pingyu Zhou⁴, Zhanshuai Wu⁵, Jian Xiao⁵, Renfang Zhang^{1,8,9}, Jing Leng^{5,8,9}, Yongtao Sun^{2,8,9}, Xiaoyan Zhang^{1,8,9} and Jianqing Xu^{1,8,9}

ARTICLES

<https://doi.org/10.1038/s41591-020-1039-5>

nature
medicine

Check for updates

Dual CD4-based CAR T cells with distinct costimulatory domains mitigate HIV pathogenesis in vivo

Colby R. Maldini^{1,6}, Daniel T. Claiborne^{2,4}, Ken Okawa⁷, Tao Chen², Derrick L. Dopkin³, Xiaochuan Shan³, Karen A. Power², Radiana T. Trifonova^{1,2}, Katharine Krupp², Meredith Phelps^{1,2}, Vladimir D. Vrbancac^{2,4}, Serah Tanno^{2,4}, Timothy Bateson², George J. Leslie⁶, James A. Hoxie⁵, Christian L. Boutwell⁸, James L. Riley^{1,7,8,9} and Todd M. Allen^{1,7,8,9}

JCI INSIGHT

RESEARCH ARTICLE

In vivo killing of primary HIV-infected cells by peripheral-injected early memory-enriched anti-HIV duoCAR T cells

Kim Anthony-Gonda,^{1,2} Alex Ray,³ Hang Su,³ Yuge Wang,² Ying Xiong,^{1,2} Danica Lee,³ Arielle Block,³ Vanessa Chilunda,⁴ Jessica Weiselberg,⁴ Lily Zemelko,⁵ Yen Y. Wang,⁵ Sarah Kleinsorge-Block,⁶ Jane S. Reese,⁶ Marcos de Lima,⁶ Christina Ochsenbauer,⁷ John C. Kappes,^{7,8} Dimitar S. Dimitrov,⁹ Rimas Orentas,^{1,10} Steven G. Deeks,⁵ Rachel L. Rutishauser,⁵ Joan W. Berman,^{3,4} Harris Goldstein,^{3,11} and Boro Dropulic^{1,2}

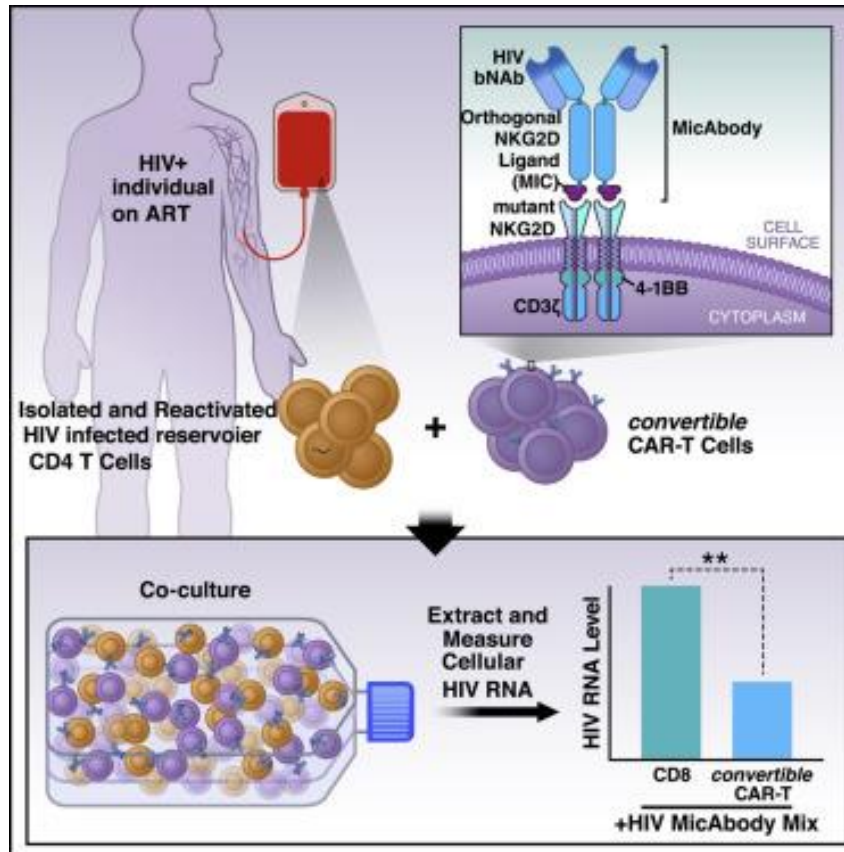
And even affect the reservoir...

Cell

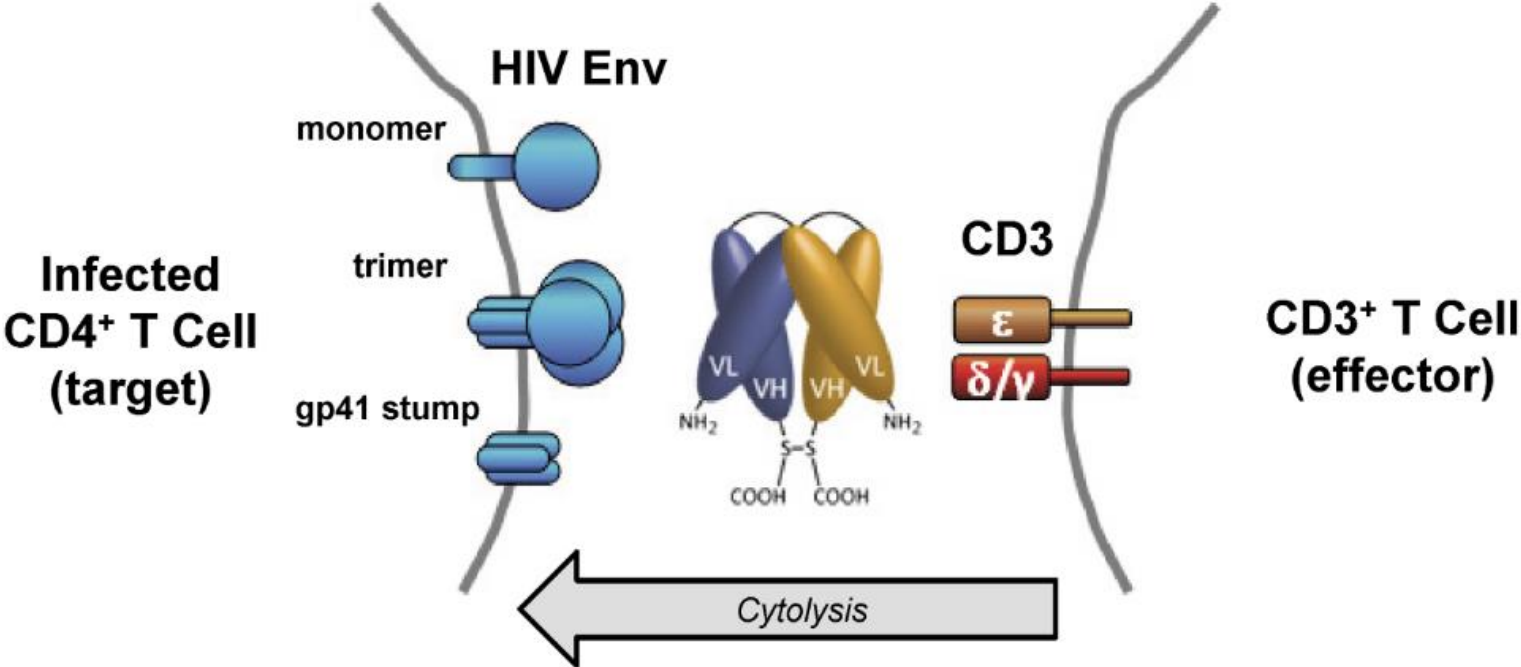
Article

Attacking Latent HIV with *convertible*CAR-T Cells, a Highly Adaptable Killing Platform

Eytan Herzog,^{1,2} Kaman Chan Kim,³ Thomas A. Packard,^{1,2} Noam Vardi,^{4,5} Roland Schwarzer,^{1,2} Andrea Gramatica,^{1,2} Steven G. Deeks,⁶ Steven R. Williams,³ Kyle Landgraf,³ Nigel Killeen,³ David W. Martin,³ Leor S. Weinberger,^{1,4,5} and Warner C. Greene^{1,2,7,*}



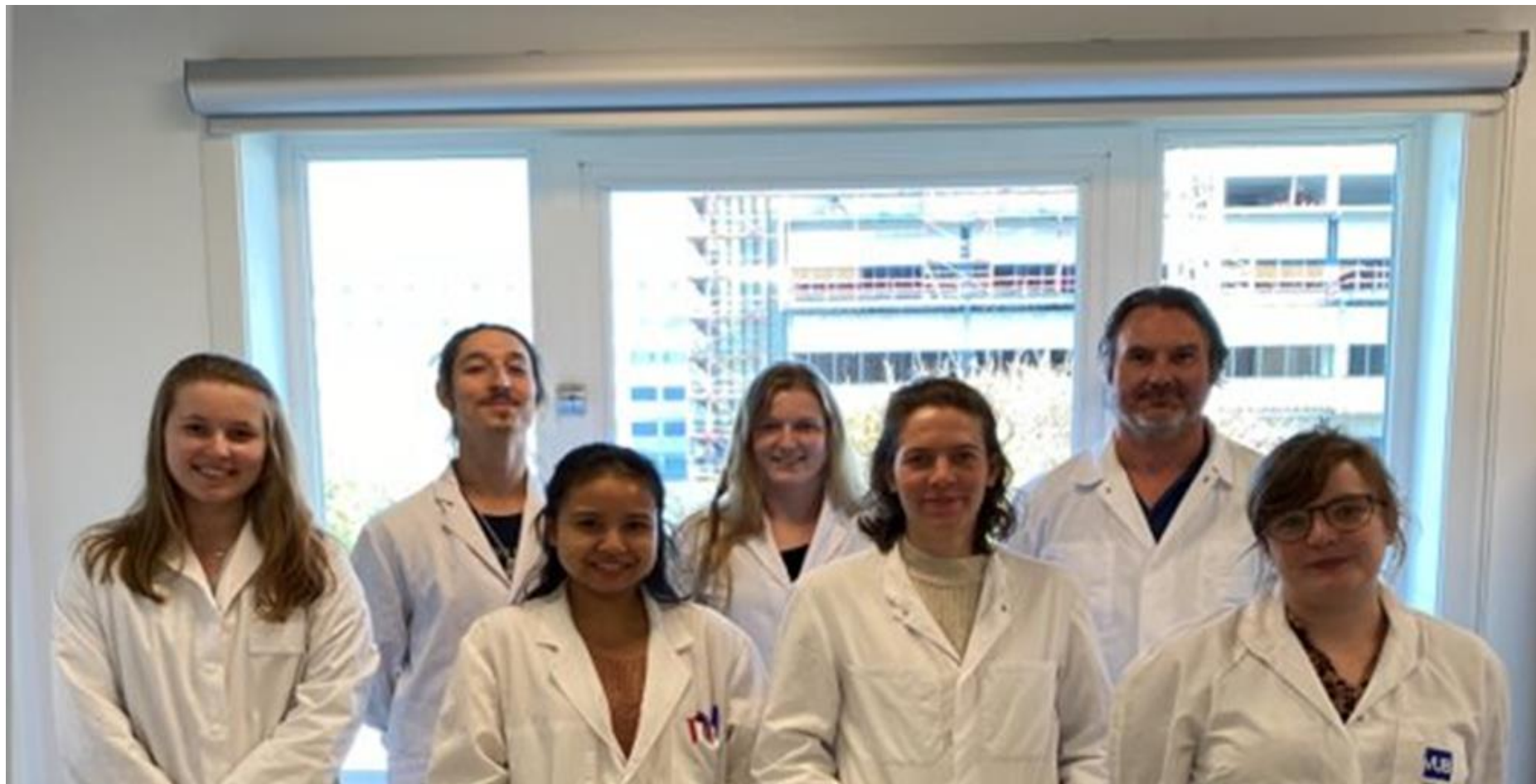
Bispecific antibody modalities to overcome patient specificity



Take home messages

- HIV infection presents unique challenges for the immune system
- The immune system plays a crucial role in controlling HIV infection, as well as the size and of the type of reservoir
- The reservoir in turn influences the quality of the immune system
- Many efforts have been made to boost the immune system against HIV (and the reservoir) through immunotherapy
- Many dysfunctions observed in HIV infection are reminiscent of those observed in cancer
- Thanks to breakthroughs in cancer immunotherapy and COVID-19 vaccine development, novel immunotherapeutic approaches are now being tested in PLWH as well

Thank you!



Utilizing the immune system to target the reservoir

