Immunotherapy of Cancer

OLLI, Fall 2020, Lecture 4

Ed Roy, Instructor

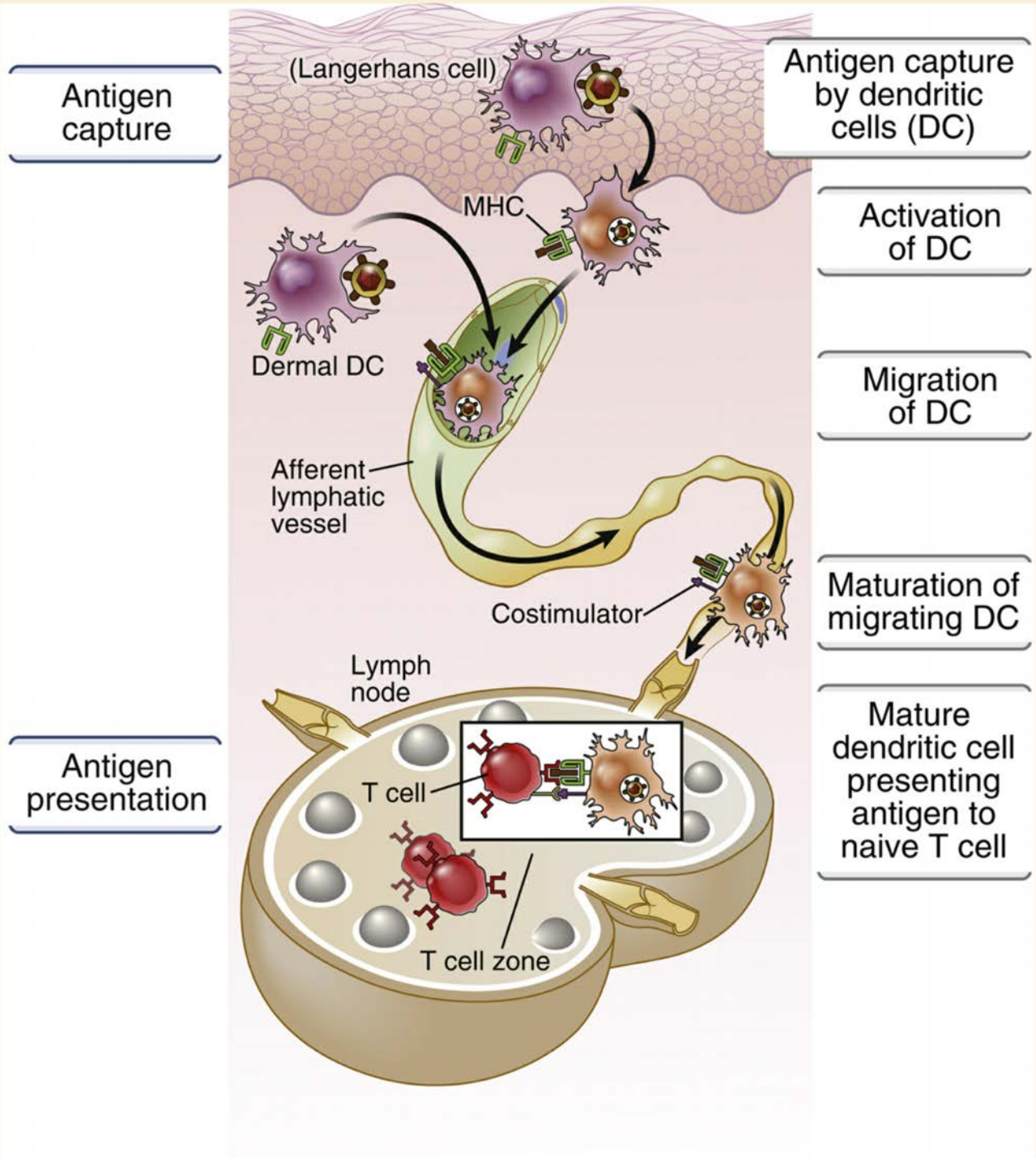
Marie Roy, Chief Investigative Reporter

eroy@illinois.edu


Where the heck are my students?
That's the microwave, Bob.
Retired teachers helping online classes.😊

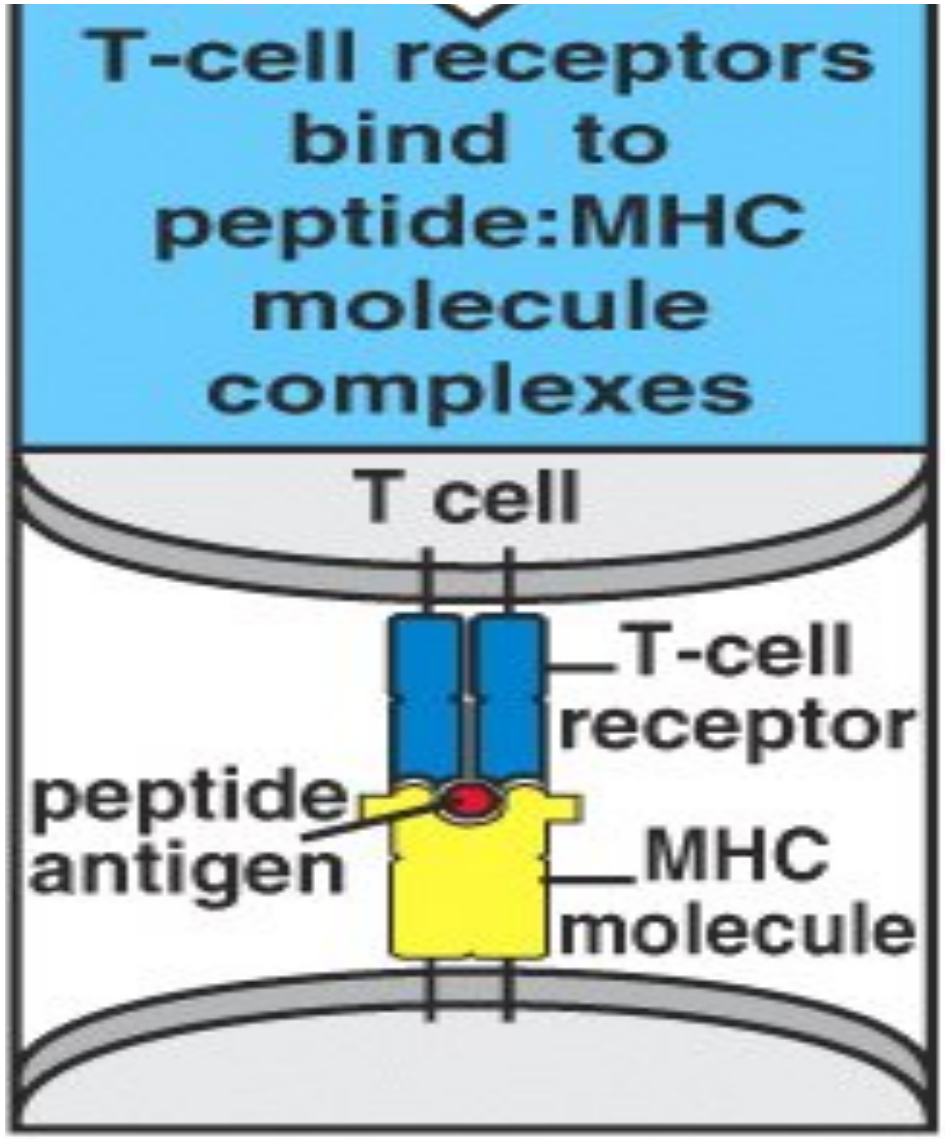
Review

- Antibodies and T cell receptors can specifically target cancer cells
- Cancer cells have mutations that are potential targets
- T cells have the advantage of being actively mobile
- Cancers make use of normal physiological processes that shut off an immune response, like checkpoints: antibodies that block checkpoints, like anti-CTLA-4 and anti-PD-1, encourage a T cell response against tumors
- Checkpoint inhibitors have the disadvantage that they increase autoimmune responses as well as anti-cancer responses
- T cells recognize peptides bound by MHC on antigen presenting cells and tumor cells

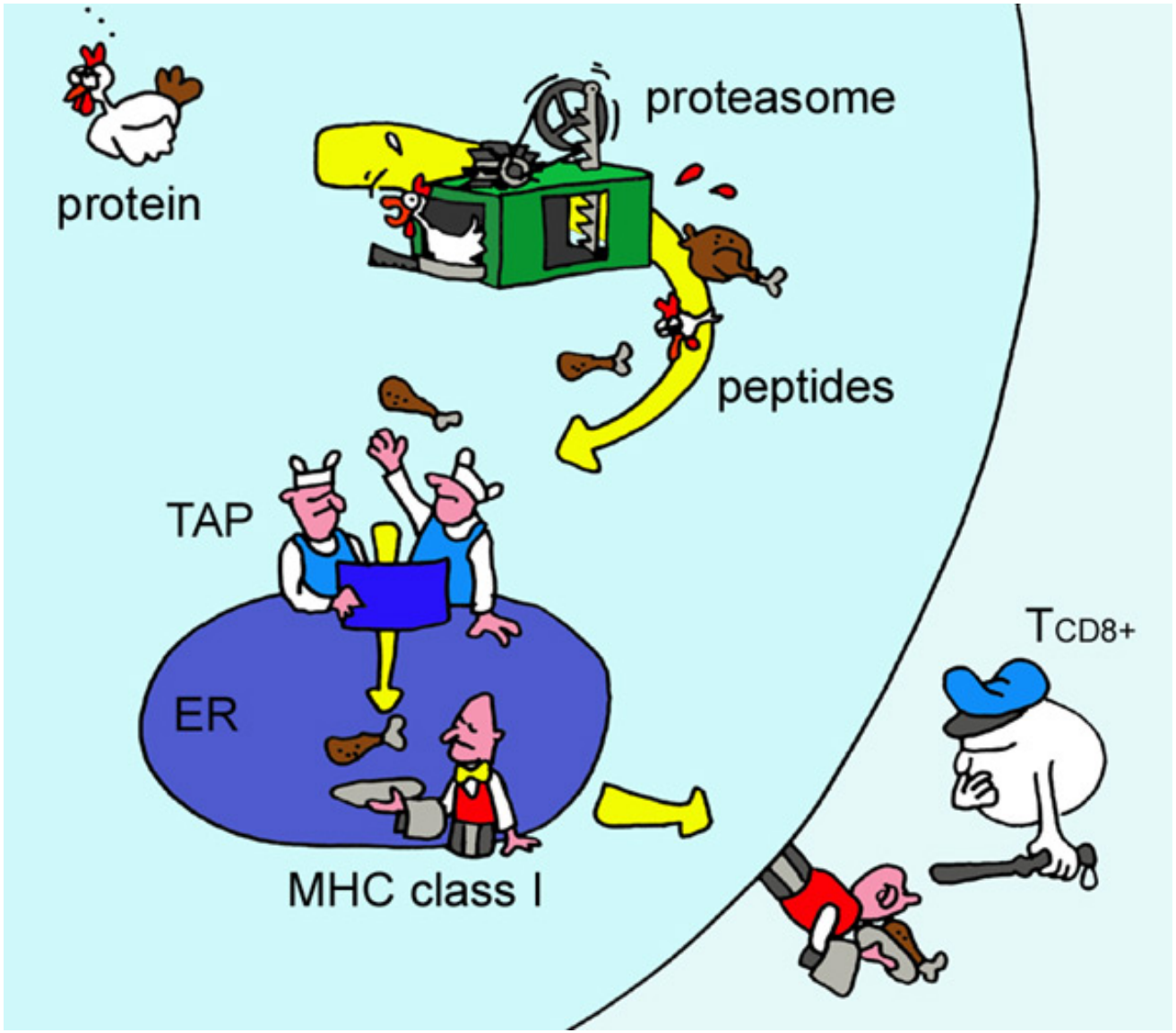

Antigen capture
Antigen presentation
(Langerhans cell)
MHC
Dermal DC
Afferent lymphatic vessel
Costimulator
Lymph node
T cell
T cell zone
Antigen capture by dendritic cells (DC)
Activation of DC
Migration of DC
Maturation of migrating DC
Mature dendritic cell presenting antigen to naive T cell

Fig

MHC molecule- the receptor responsible for presenting peptide antigen to T cells. Also called Human Leukocyte Antigen (HLA) in humans.



Cartoon of MHC Class I Presentation.



Take-home about MHC:

- The T cell receptor binds tumor peptides, fragments of proteins, bound to MHC, not proteins directly. This allows T cells to recognize proteins besides cell-surface proteins.

Learning Objectives

Learn about vaccination as a strategy to promote a T cell response against tumors

Learn about adoptive cell therapies: tumor infiltrating lymphocytes, engineered T cells, chimeric antigen receptor T cells

Learn about the tumor microenvironment

Learn a little about the economics of immunotherapy

Hear some predictions for future directions

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Cancer Vaccines

- Prophylactic vaccines that prevent viral infections that lead to cancer (human papilloma virus causes cervical cancer)
- Therapeutic vaccines after cancer is already present
- Goal of Cancer vaccines is to generate T cell response (most successful prophylactic vaccines primarily generate antibody response)

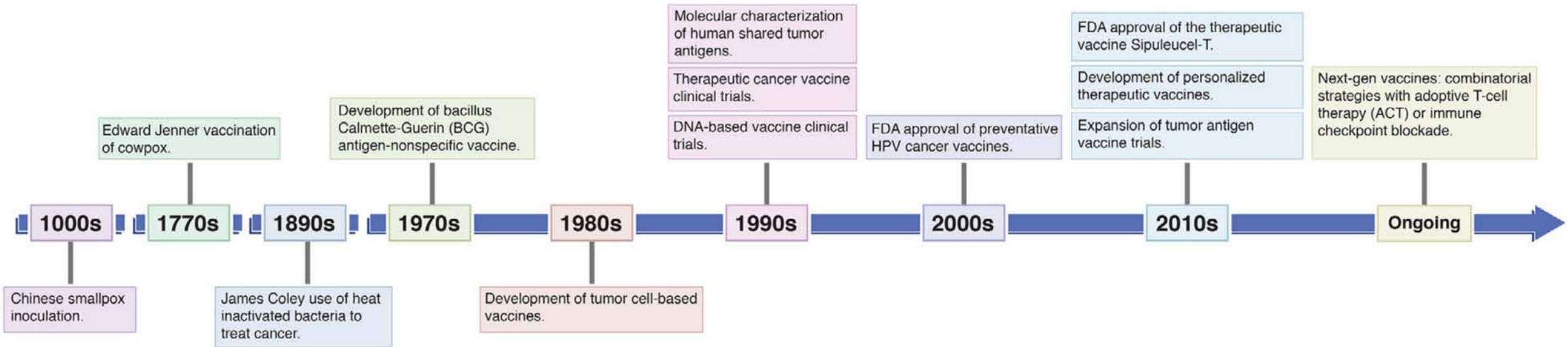
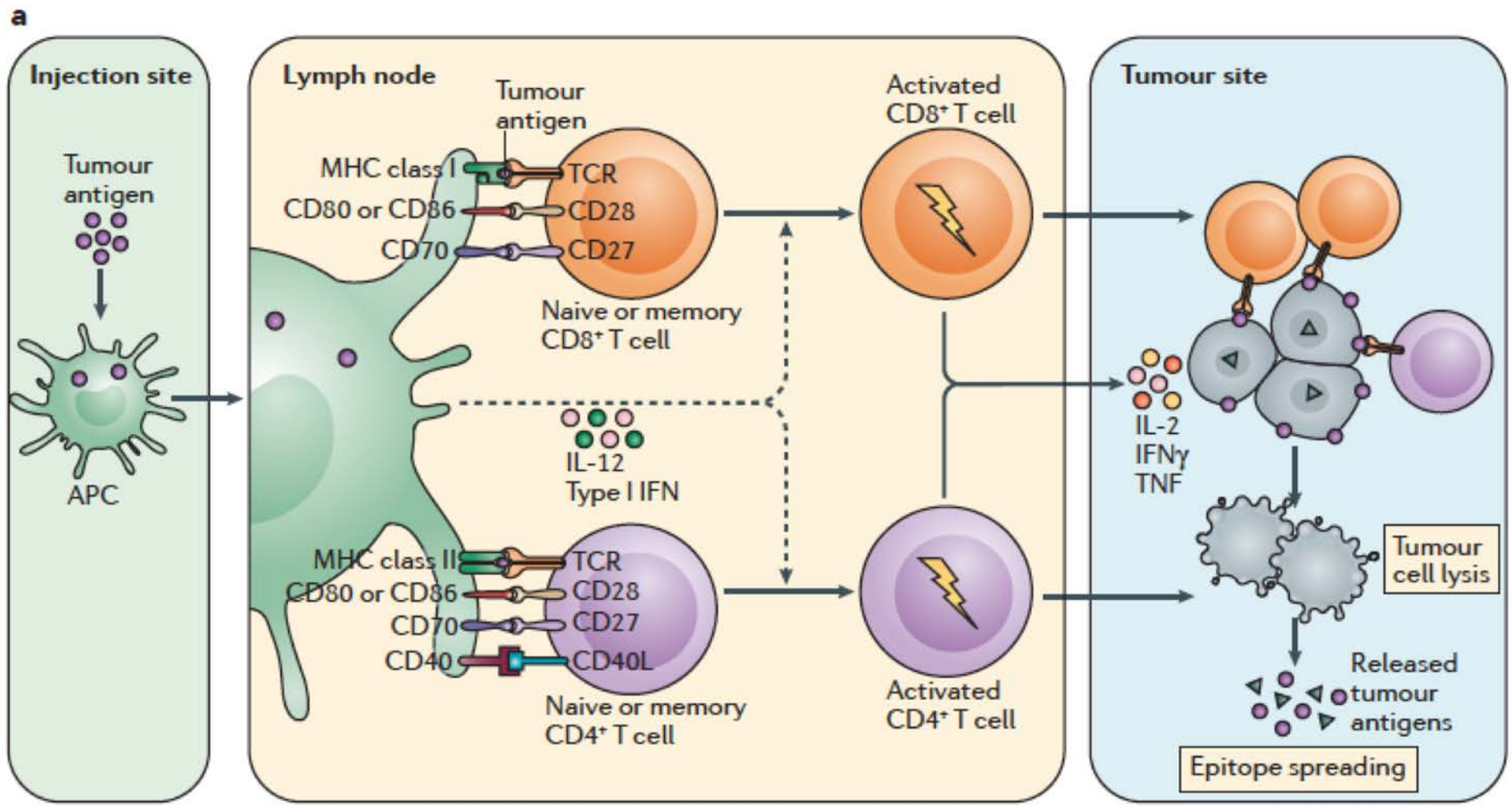
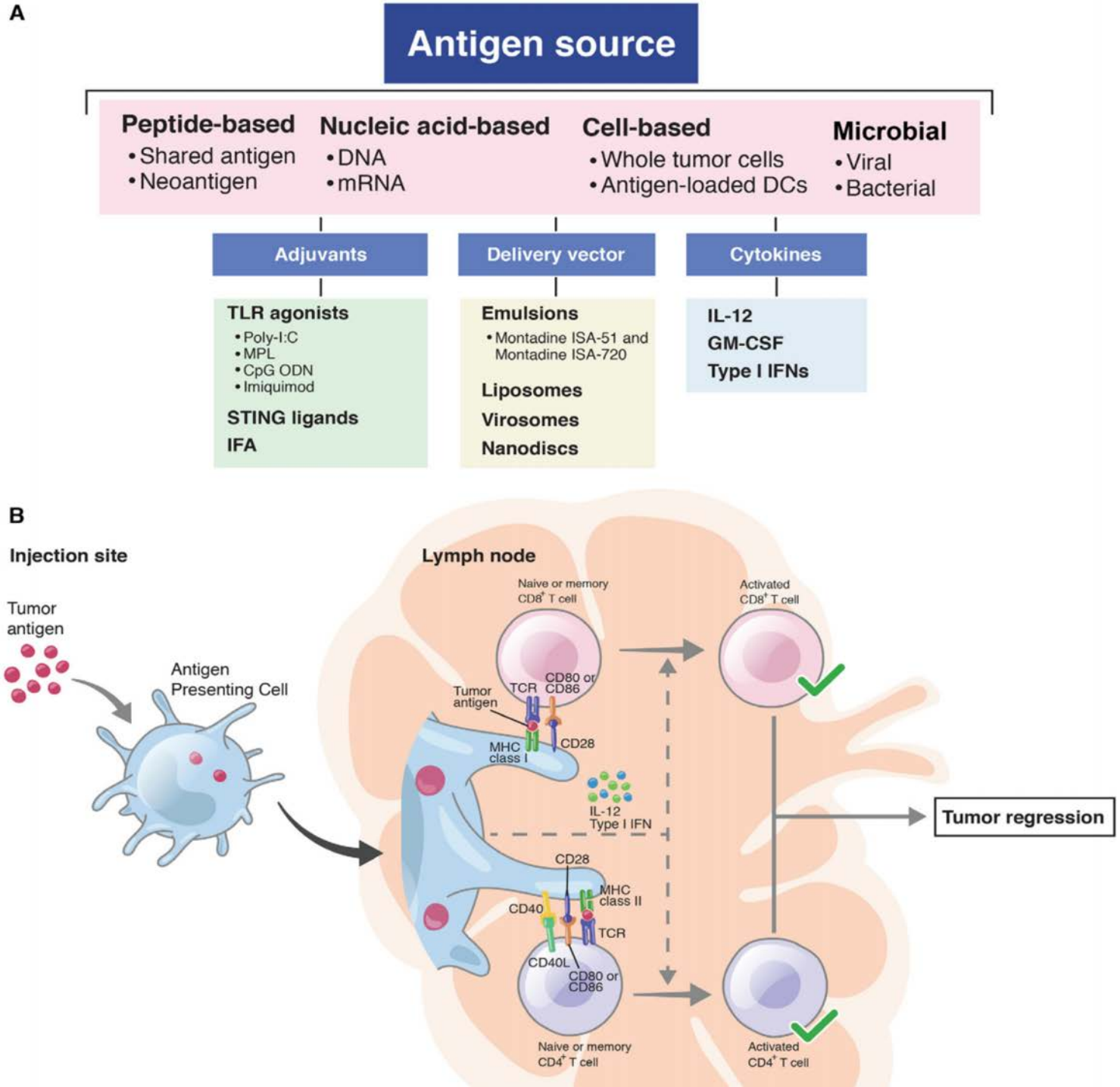


FIGURE 1 A timeline of vaccine development

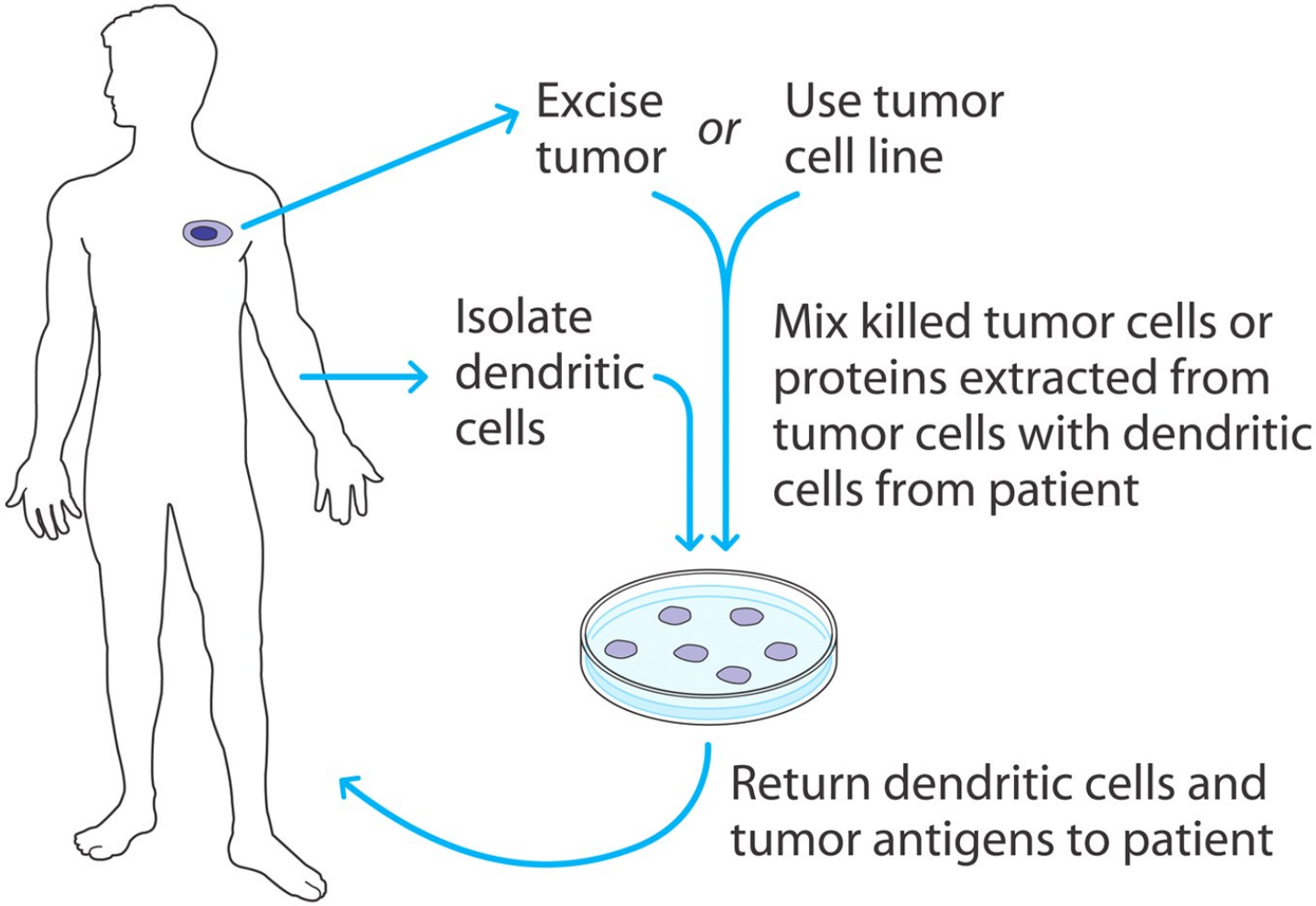

a
Injection site
Tumour antigen
APC
Lymph node
Tumour antigen
MHC class I
CD80 or CD86
CD70
TCR
CD28
CD27
Naive or memory CD8+ T cell
IL-12
Type I IFN
MHC class II
CD80 or CD86
CD70
CD40
TCR
CD28
CD27
CD40L
Naive or memory CD4+ T cell
Activated CD8+ T cell
Activated CD4+ T cell
Tumour site
IL-2
IFNγ
TNF
Tumour cell lysis
Released tumour antigens
Epitope spreading

Therapeutic Vaccines with Dendritic Cells

- Dendritic cells orchestrate type of immune response (relatively more or less antibodies vs T cells vs responses against parasites, etc)


A
Antigen source
Peptide-based
• Shared antigen
• Neoantigen
Nucleic acid-based
• DNA
• mRNA
Cell-based
• Whole tumor cells
• Antigen-loaded DCs
Microbial
• Viral
• Bacterial
Adjuvants
Delivery vector
Cytokines
TLR agonists
• Poly-I:C
• MPL
• CpG ODN
• Imiquimod
STING ligands
IFA
Emulsions
• Montadine ISA-51 and Montadine ISA-720
Liposomes
Virosomes
Nanodiscs
IL-12
GM-CSF
Type I IFNs
B
Injection site
Lymph node
Tumor antigen
Antigen Presenting Cell
Naive or memory CD8+ T cell
Activated CD8+ T cell
TCR
CD80 or CD86
Tumor antigen
MHC class I
CD28
IL-12
Type I IFN
Tumor regression
CD28
MHC class II
CD40
TCR
CD40L
CD80 or CD86
Naive or memory CD4+ T cell
Activated CD4+ T cell

Ex vivo dendritic cell therapy for cancer.



Clinical Trials completed in last 5 years

- About 60 trials of cancer vaccines; not impressive results
- 18 trials with combination of vaccine and checkpoint inhibitor; improved over checkpoint inhibitor alone
- Ongoing 11 trials with personalized vaccine against neoantigens, together with checkpoint inhibitor
  - Neoantigens isolated by RNA or DNA analysis or Mass Spectrometry of MHC-bound peptides

Learning Objectives

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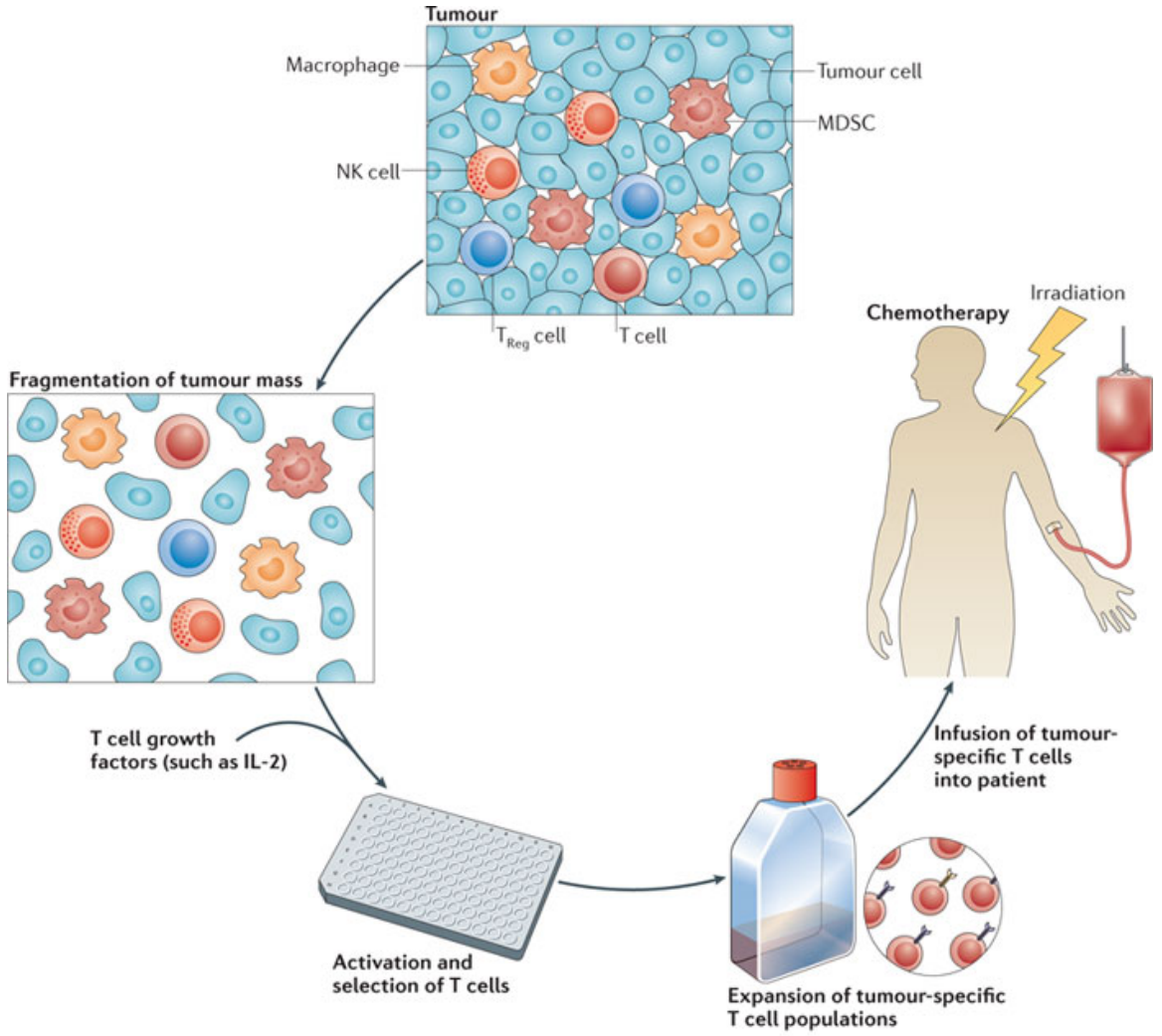
Hear some predictions for future directions

Adoptive T cell Therapies

- Tumor Infiltrating Lymphocytes (TILs)
- Engineered T cells
  - TCRs
  - CARs

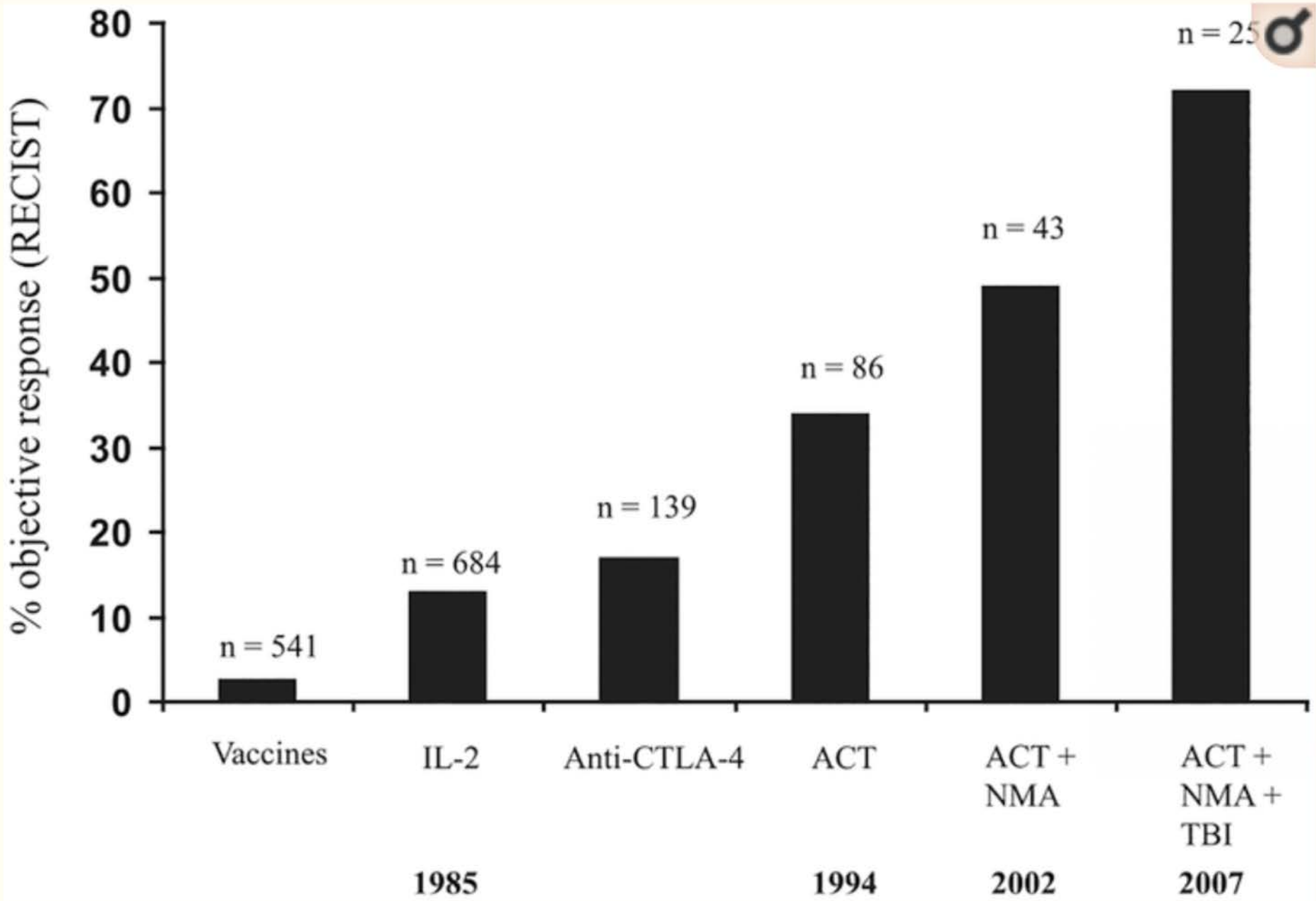
Adoptive T Cell Transfer (ACT) of Tumor Infiltrating Lymphocytes (TILs)



Nature Reviews | Immunology Restifo *et al.*, 2012

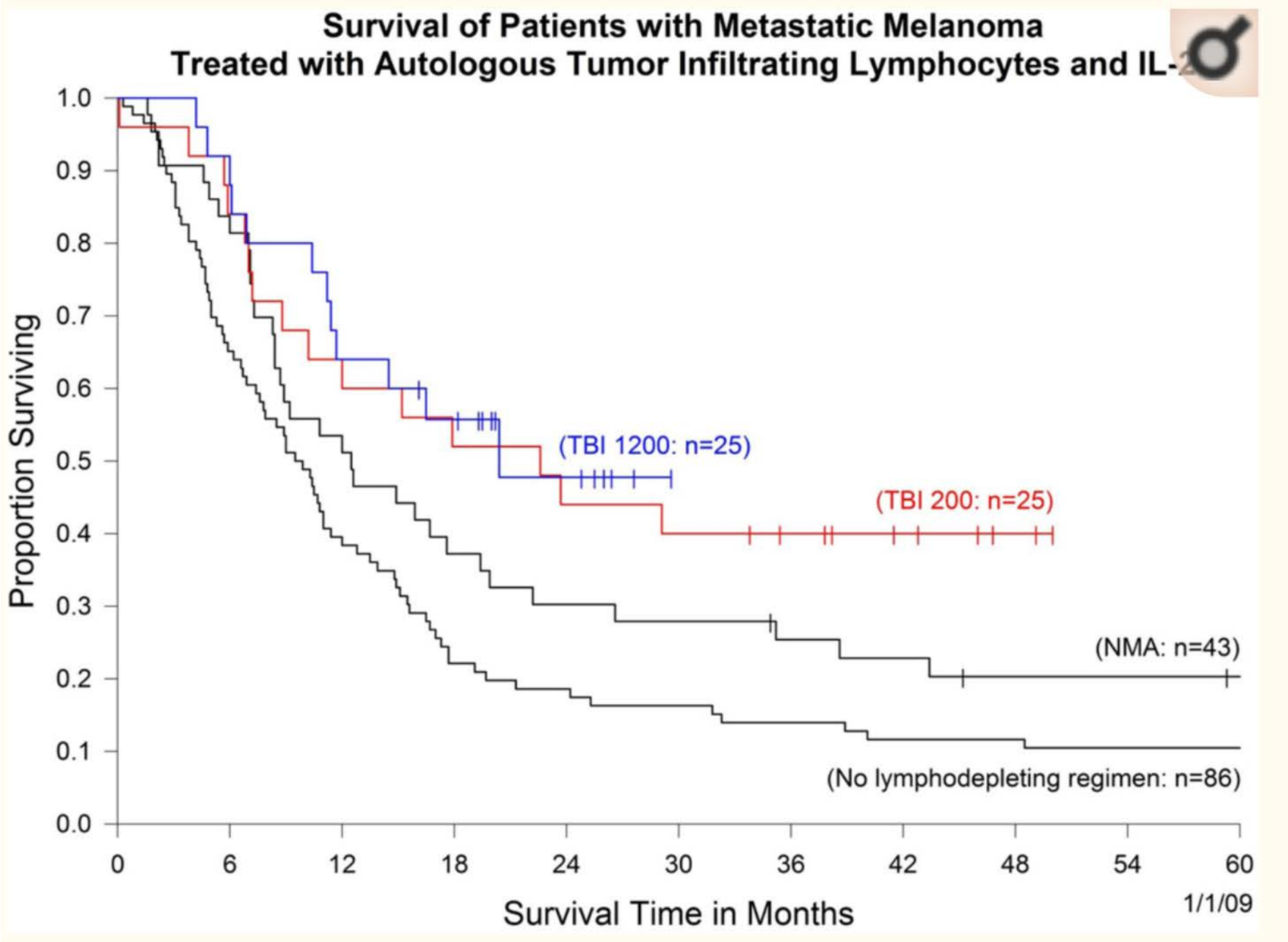
Lymphodepletion before Adoptive Cell Transfer: single dose chemotherapy or radiation

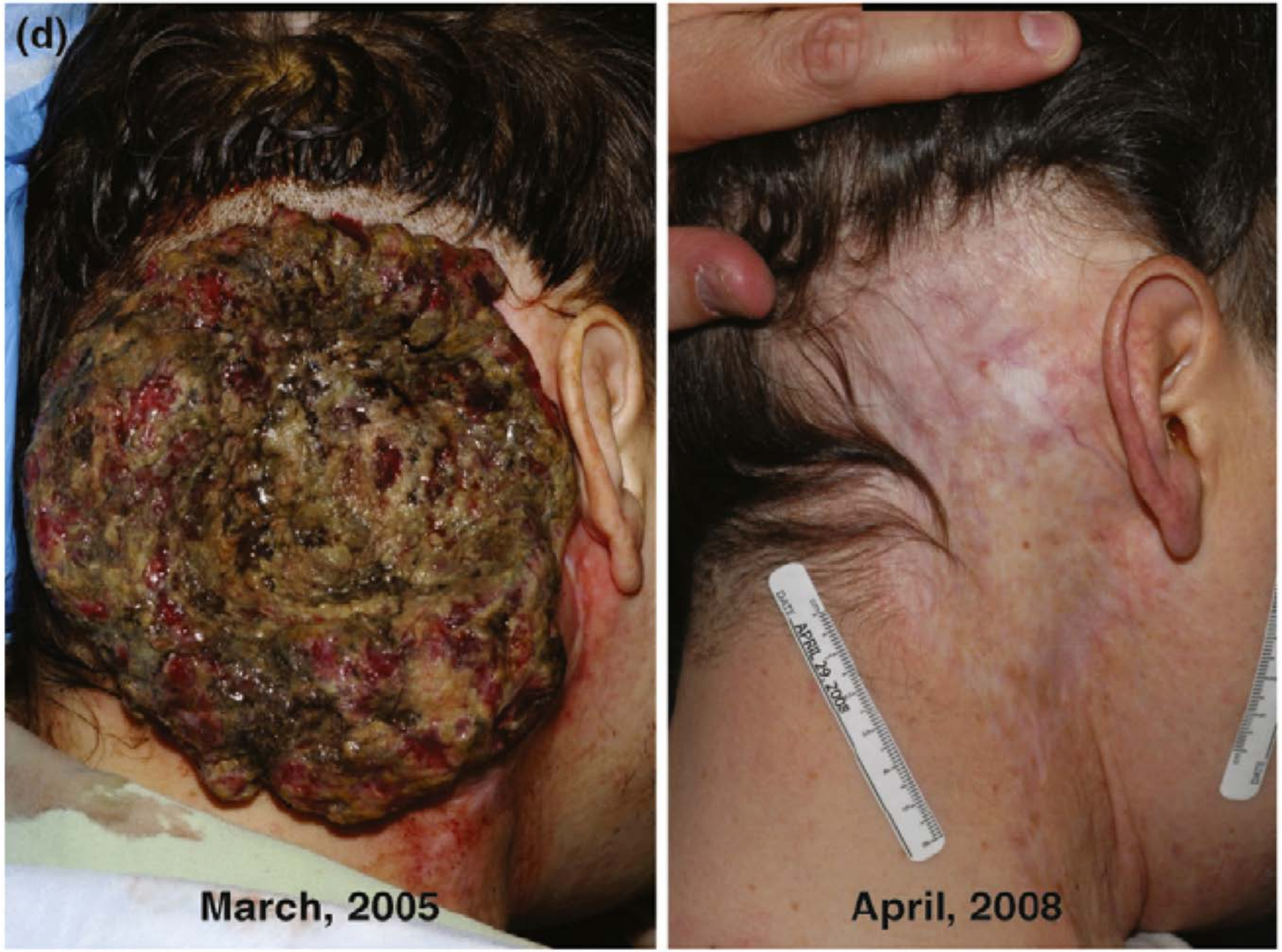
- Creates “room” for new T cells (limited amount of supportive cytokines)
- Removes Tregs and Myeloid Derived Suppressor Cells from Tumor Microenvironment
- Creates damage to tumor and shedding of antigens
- Dose that does not destroy bone marrow stem cells (“non-myeloablative”)


% objective response (RECIST)
80
70
60
50
40
30
20
10
0
n = 541
n = 684
n = 139
n = 86
n = 43
n = 25
Vaccines
IL-2
Anti-CTLA-4
ACT
ACT + NMA
ACT + NMA + TBI
1985
1994
2002
2007

Objective response rates (using Response Evaluation Criteria in Solid Tumors criteria) using various forms of cancer immunotherapy of patients with metastatic melanoma treated in the Surgery Branch at the National Cancer Institute. Only anecdotal responses have been seen utilizing cancer vaccine approaches. A response rate of 2.6% was seen using 541 different vaccines in 440 patients with metastatic cancer (84). Using an anti-CTLA Ab, a response rate of ~15% was seen but varied with the dose and schedule of administration (85). Utilizing IL-2 response rates of ~15% were seen that increased to 34% when IL-2 was given following ACT. The response rates increased to 49% when cell transfer was preceded by a nonmyeloablative chemotherapy (NMA) consisting of cyclophosphamide (60 mg/kg 2×) and fludarabine (25 mg/kg 5×) and was increased to 72% when cells were transferred following NMA plus 12 Gy TBI. The years of these reports are shown on the bottom line of the figure.

Rosenberg, 2014


Survival of Patients with Metastatic Melanoma
Treated with Autologous Tumor Infiltrating Lymphocytes and IL-2
Proportion Surviving
1.0
0.9
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0.0
(TBI 1200: n=25)
(TBI 200: n=25)
(NMA: n=43)
(No lymphodepleting regimen: n=86)
0
6
12
18
24
30
36
42
48
54
60
Survival Time in Months
1/1/09

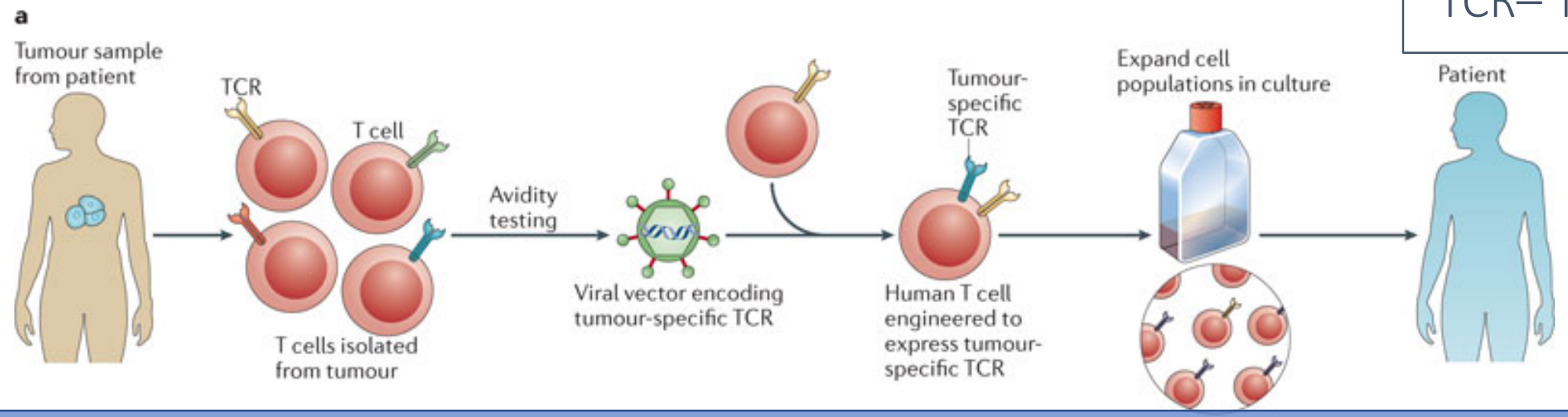


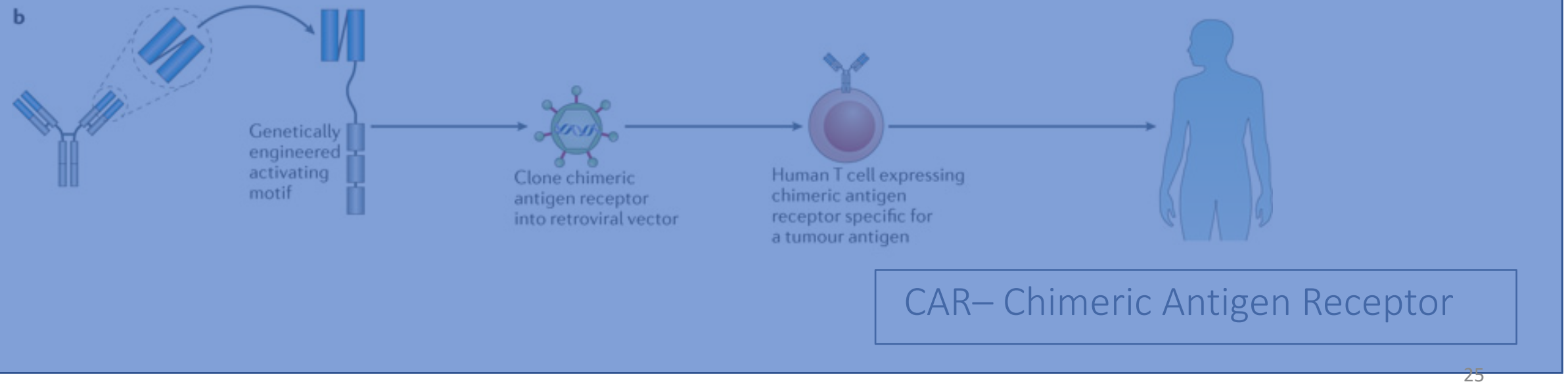
Rosenberg and Dudley 2009

Current Opinion in Immunology

Adoptive Cell Transfer (ACT) of Engineered TCR T cells

TCR– T Cell Receptor





CAR– Chimeric Antigen Receptor

Restifo *et al.*, *Nat Rev Immunol* 2012

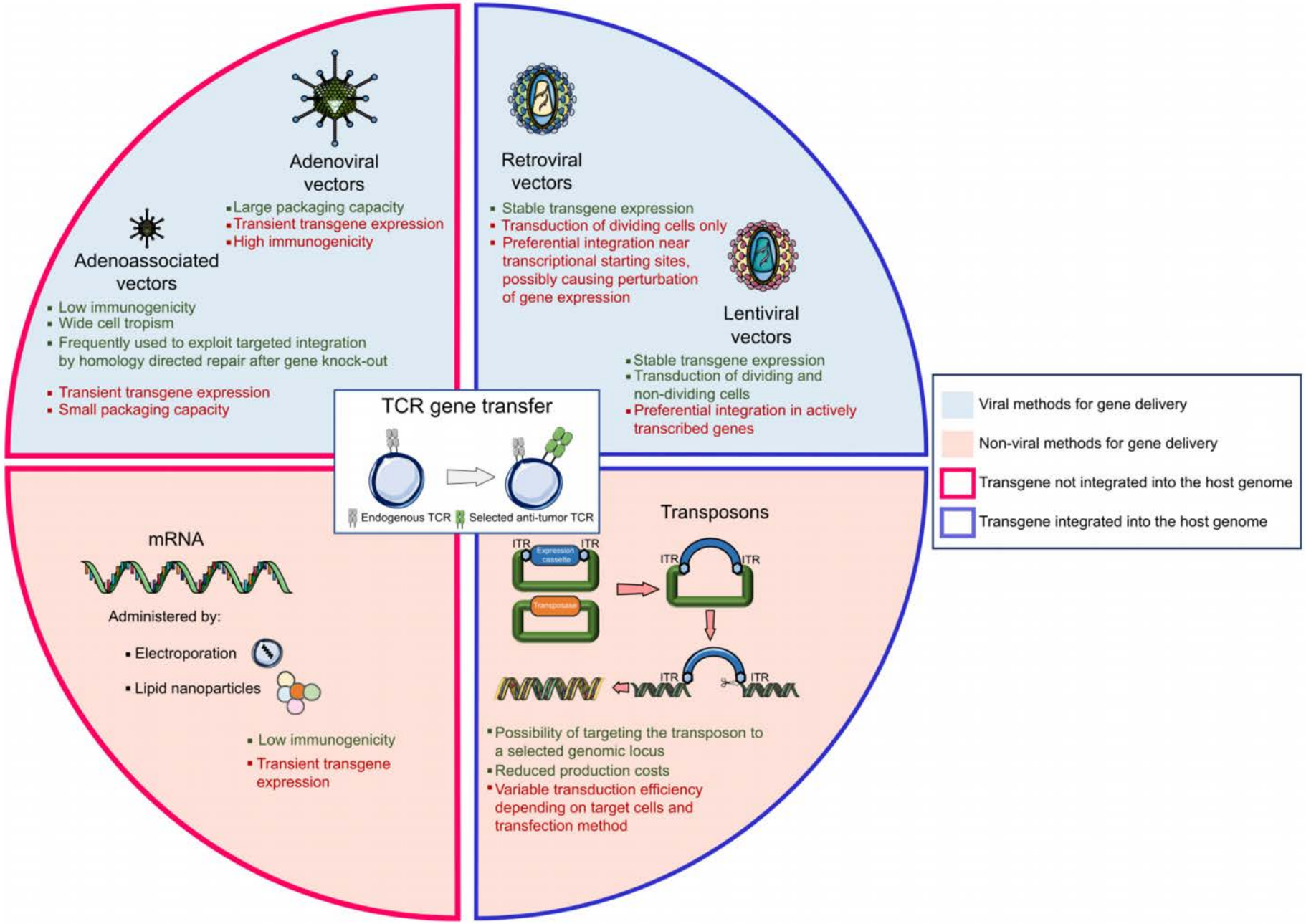
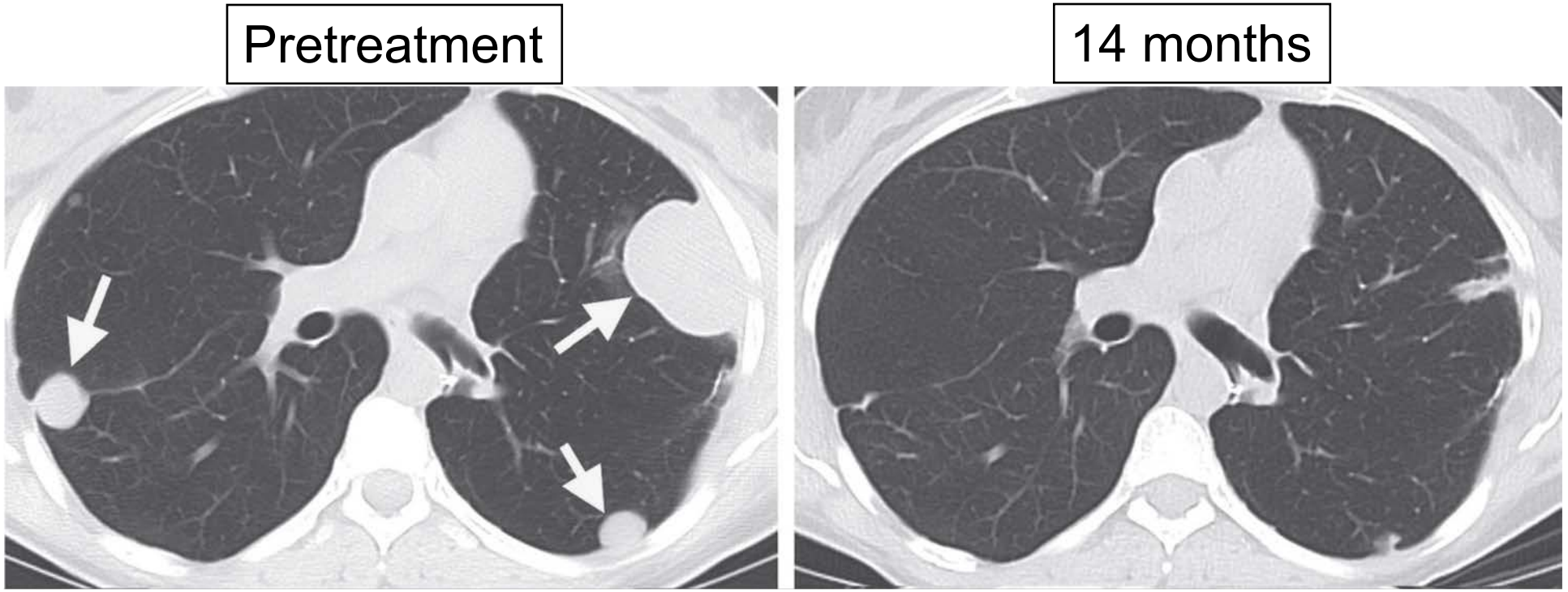


FIGURE 2 | The landscape of gene delivery methods. The genetic transfer of an exogeneous T cell receptor (TCR) into a donor T cell can be obtained with different vectors, the most widely used being viral vectors, mRNA, and transposons systems. Strengths and weaknesses are listed for each technology.

T Cells Against Solid Cancers (e.g. sarcoma)

Rosenberg's group, NCI; *J Clin Oncology*, 2011



Lung metastases in patient with sarcoma

Treated with T cells transduced with TCR against NY-ESO-1

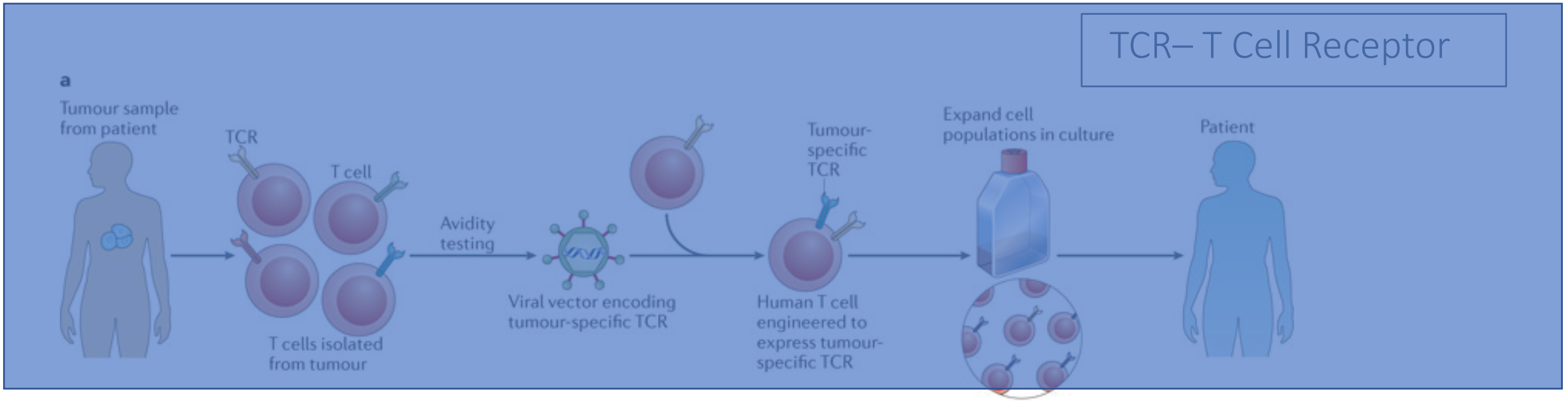
Table 1. Overview of T Cell-based Immunotherapies for Treatment of Solid Cancers

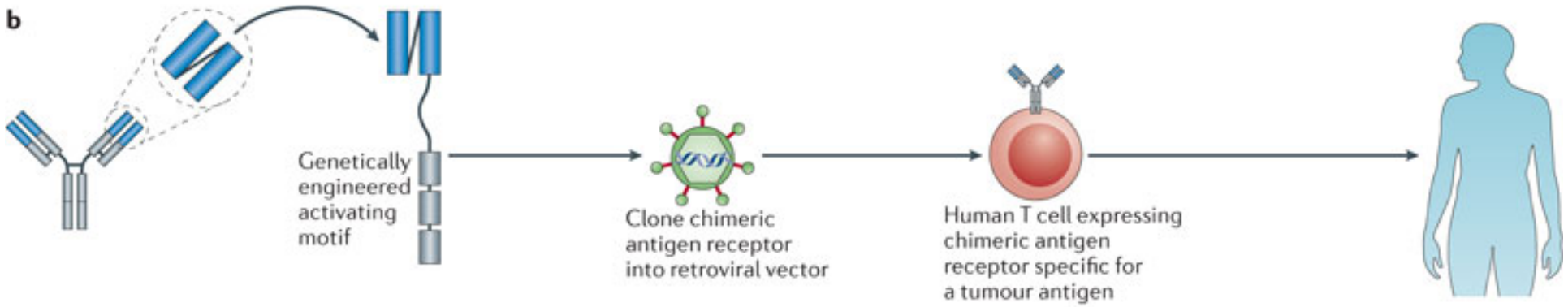
Therapy Type			Formulation	Administration	Mechanism of Action
Antigen-nonspecific	IL-2		human recombinant IL-2 (main T lymphocyte growth factor)	intravenous	stimulating endogenous T cells that may recognize cancer (unspecified tumor antigens)
	ICIs		monoclonal antibodies targeting molecules that inhibit T cell function (i.e., CTLA-4, PD-1, PD-L1)	intravenous	disinhibiting endogenous T cells that may recognize cancer (unspecified tumor antigens)
	oncolytic viruses		attenuated, native or genetically modified viral particles that selectively infect cancer cells	intratumoral, intravenous	inducing immunogenic cell death and potential release of new tumor antigens
Antigen specific	cancer vaccines[a]		selected tumor antigens that can be loaded onto the APCs, embedded in a viral vector, or represented as peptides or nucleic acids; usually in combination with an adjuvant	cutaneous, subcutaneous, intramuscular, intravenous	generating/stimulating endogenous T cell responses to selected tumor antigens
	ACT	TILs	unmodified T cells expanded from a patient's tumor (or PBL), selected for recognition of cancer cells or specific tumor antigens	intravenous (following preparative lymphodepleting chemotherapy)	transferred T cells seek and destroy cancer cells that present the targeted antigens on specific MHC molecules
		TCR-transduced T cells	autologous lymphocytes obtained by leukapheresis and transduced to express a TCR directed against a specific tumor antigen	intravenous (following preparative lymphodepleting chemotherapy)	transferred T cells seek and destroy cancer cells that present the targeted antigens on specific MHC molecules
		CAR-transduced T cells	autologous lymphocytes obtained by leukapheresis and transduced to express a CAR directed against a specific membrane-bound antigen	intravenous (with or without preparative lymphodepleting chemotherapy)	transferred CAR T cells seek and destroy cancer cells that express the targeted antigen on the cell surface, independently of MHC molecules

[a]Some cancer vaccines entail administration of attenuated or lysed tumor cells. These can be classified as antigen nonspecific.

Adoptive Cell Transfer (ACT) of CAR-T Cells

TCR– T Cell Receptor





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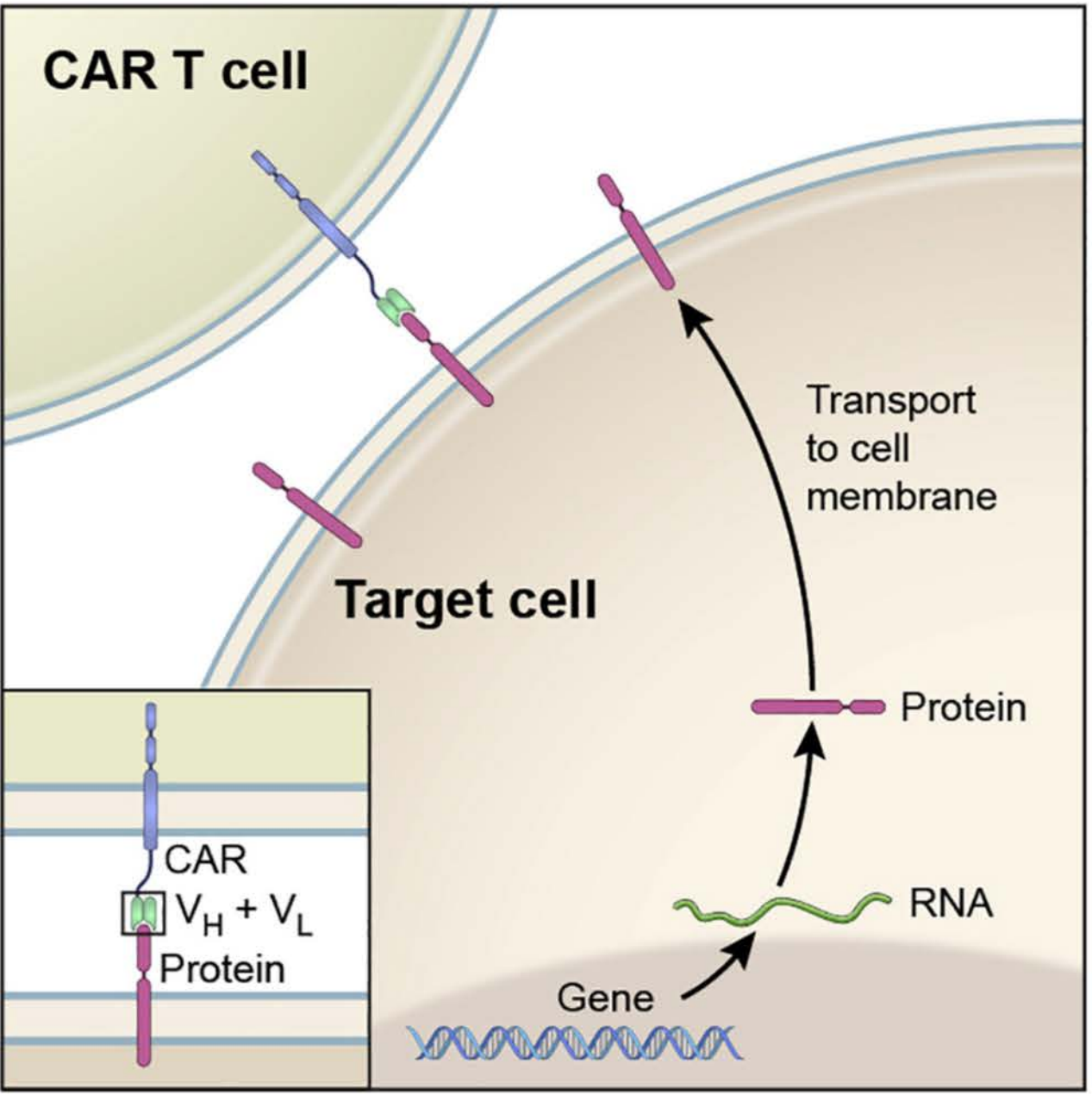
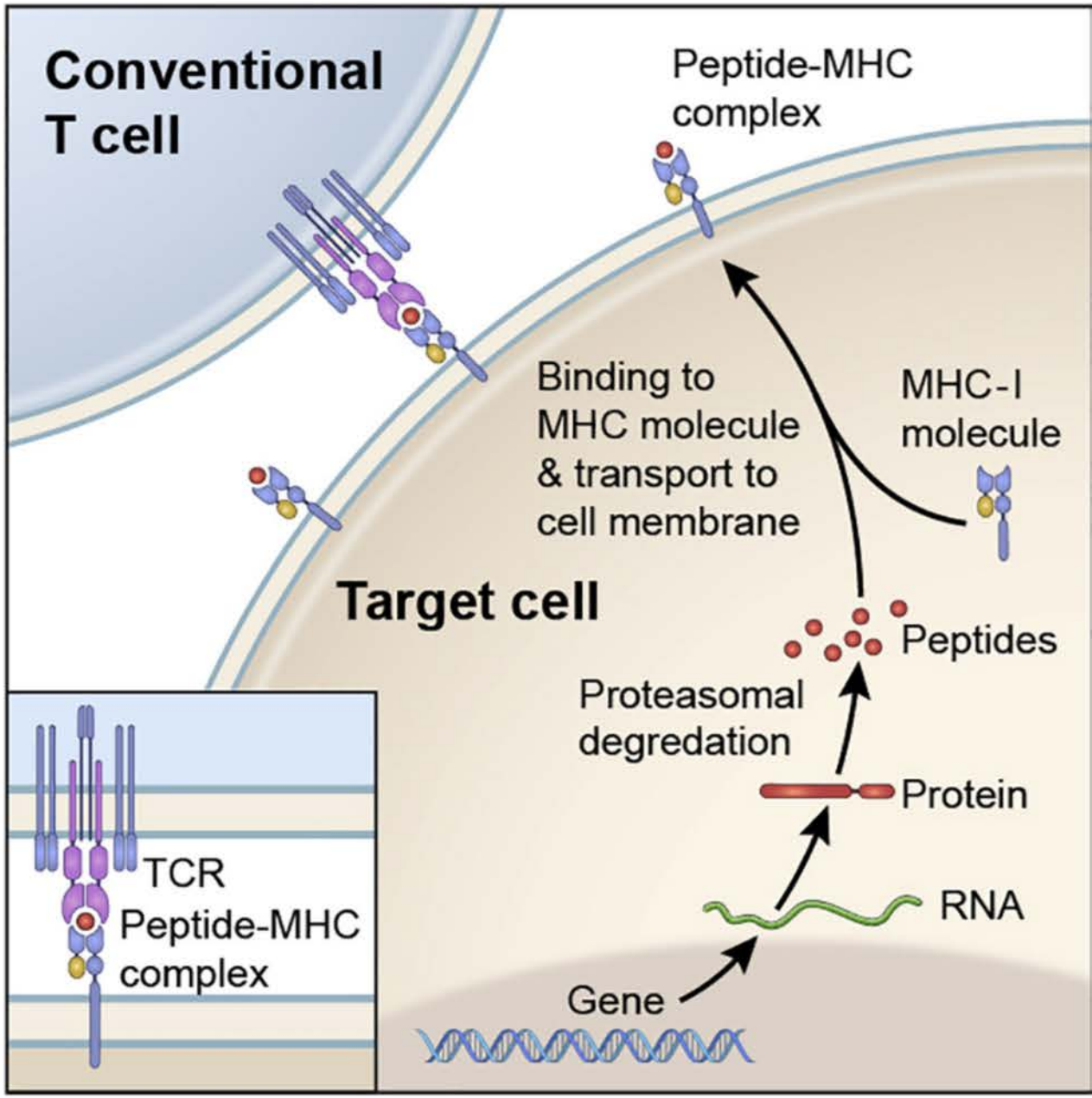




Leko and Rosenberg, 2020

Kymriah

- In August 2017, it became the first FDA-approved treatment that included a gene therapy step in the United States.[2]
- Targeting CD19 (similar strategy to CD20 targeting of rituximab monoclonal antibody)
- CD19 used instead of CD20 because of intellectual property issues (Genentech has CD20)

Clinical responses to CAR T cell therapies in hematopoietic cancers have been remarkable

The results of a study in children with relapsed acute lymphoblastic lymphoma resulted in FDA approval. Kymriah induced remission in 81% of those patients (compared to 20% with another chemotherapy).

‘A new frontier:’ US FDA approves Novartis’ $475,000 CAR-T cell cancer therapy

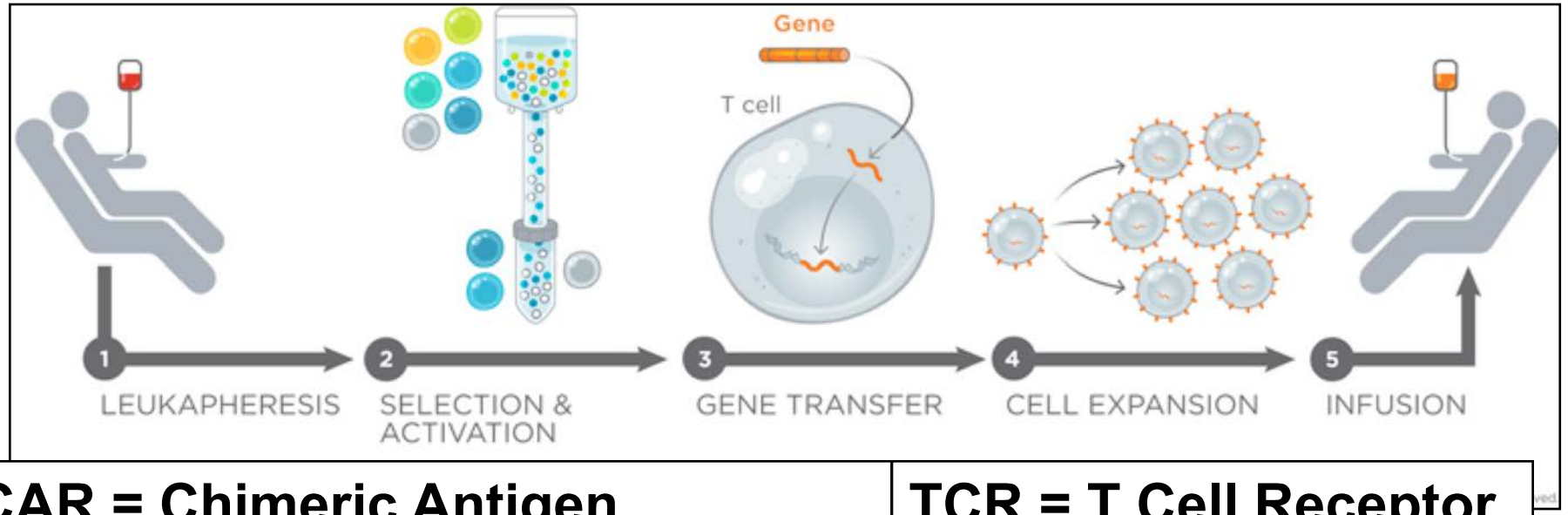
By Dan Stanton+

31-Aug-2017

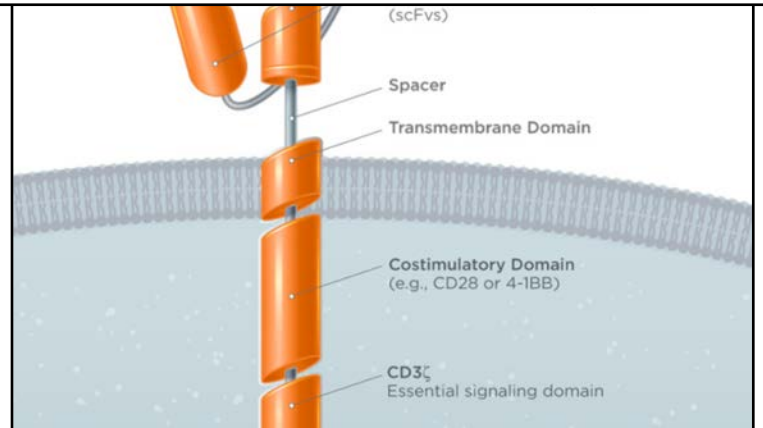
Last updated on 31-Aug-2017 at 14:13 GMT

Cellular Immunotherapies
Example: Juno Therapeutics

(Founded in 2013; Acquired by Celgene for $9B in 2018: Celgene acquired for 95B by BMS)



CAR = Chimeric Antigen Receptor



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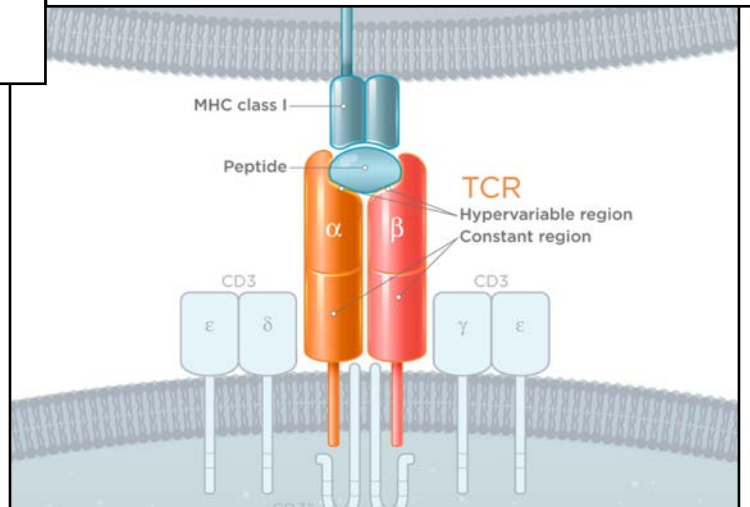

Pause to Consolidate Your Memories

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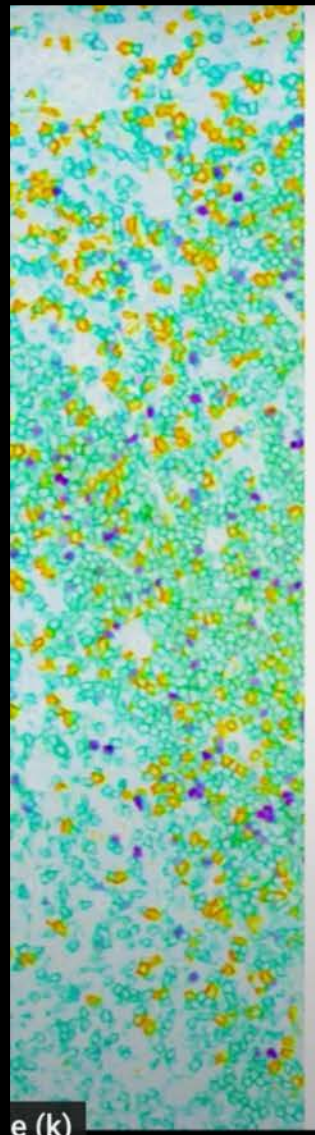
More Complicated than we thought

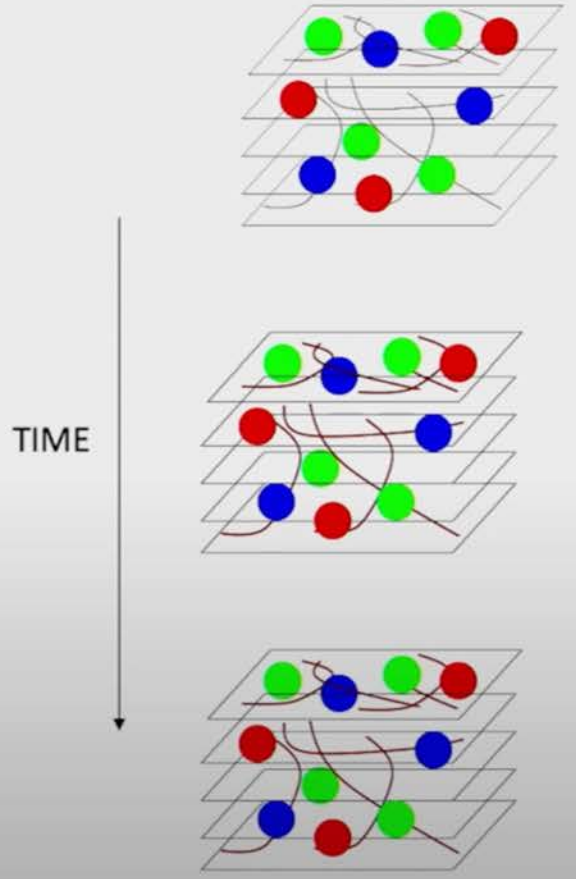
- Tumors co-op normal feedback mechanisms to produce an “immunosuppressive microenvironment”
- Immune response shifts to wound-healing
- Negative feedback on further inflammatory and T cell-mediated responses

Immunosuppressive Microenvironment

- Induced by inflammation (IFNg, PGE2)
- Cytokines (TGF and IL-10)
- Suppressive Cells (Tregs, MDSC, Tumor Associated Macrophages,)
- Hypoxia
- Nutrient loss (IDO and Arginase)
- Cell intrinsic changes (CTLA-4, PD1)

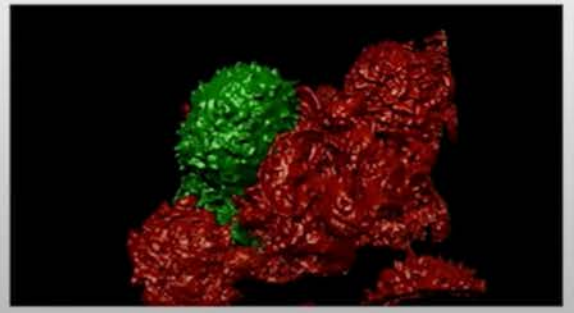


Making Movies



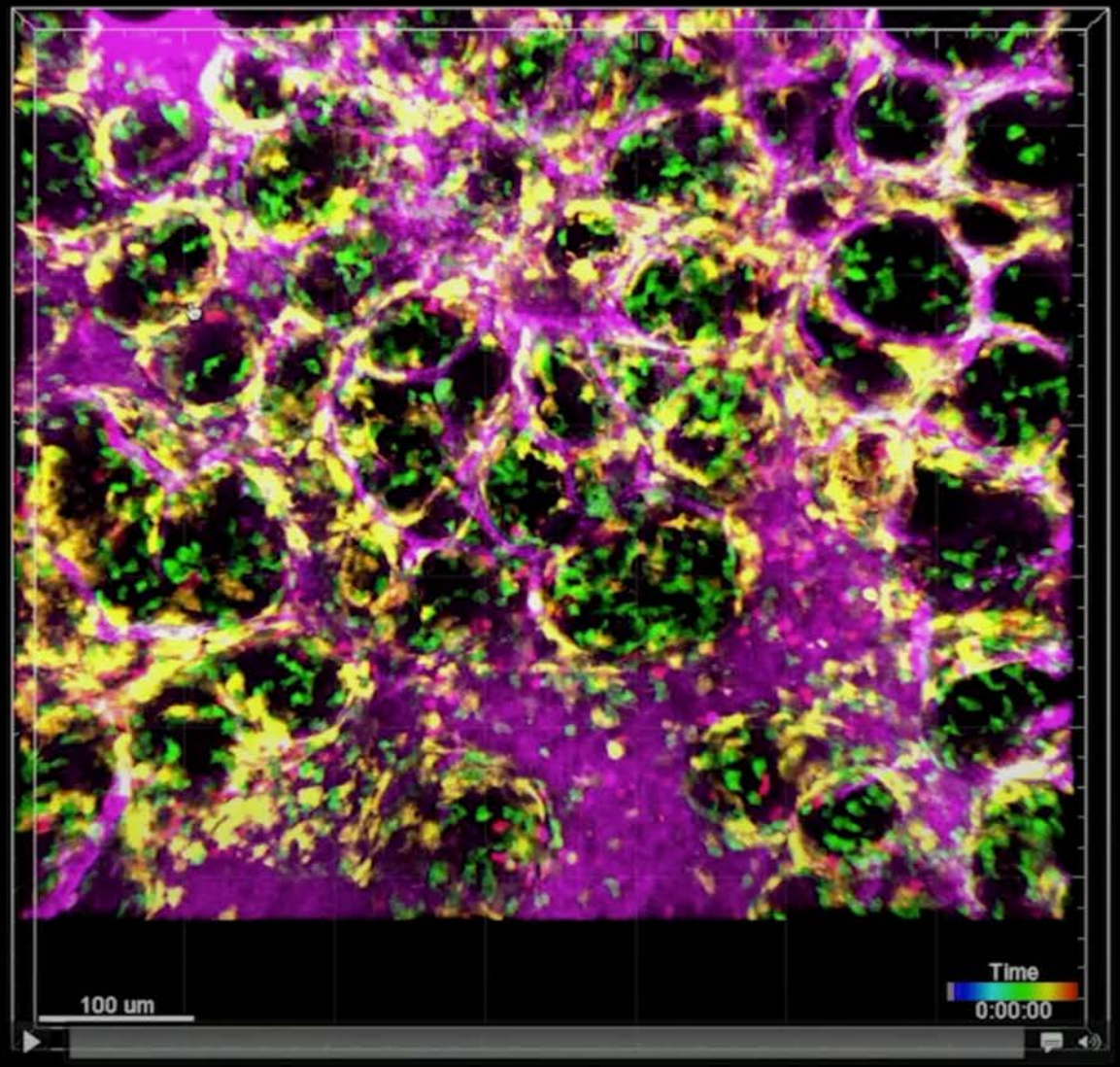
"…like the billowing dancing figures in a brightly lit ballroom that you gaze into from outside in the dark—and from a distance so great that you can no longer hear the music… the turning and twisting movement of the couples seems senseless."

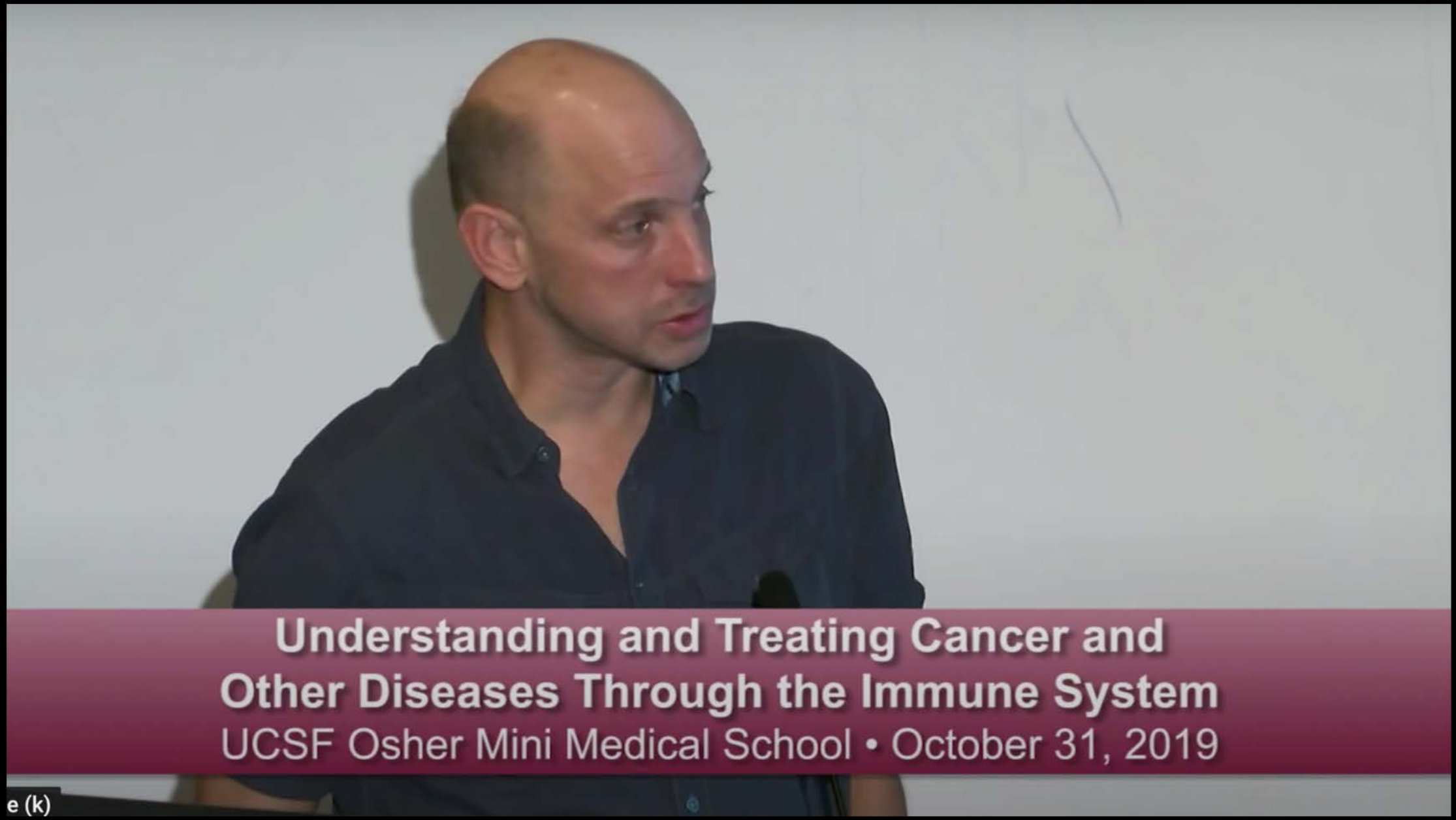
Gustav Mahler, on the third movement of his second symphony



UCSF

Immune Systems Within Actively Growing Tumors

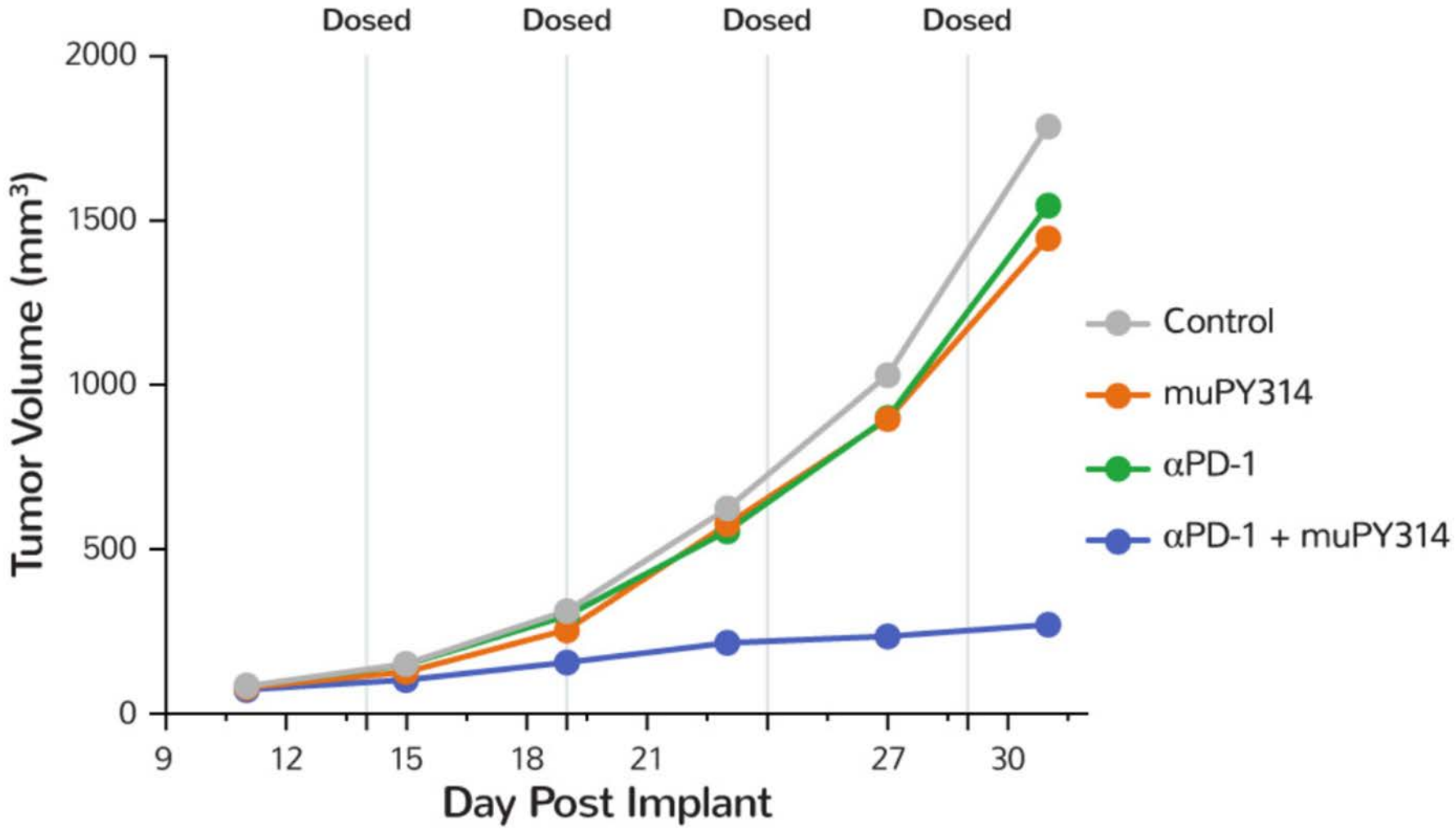



Understanding and Treating Cancer and
Other Diseases Through the Immune System
UCSF Osher Mini Medical School • October 31, 2019
e (k)

- https://www.youtube.com/watch?v=j9WMfbcWwE4&t=3101s

“Pionyr's Myeloid Tuning™ technology is based on the discovery that altering the tumor microenvironment to favor immune-activating cells over immune-suppressing cells enhances the body’s ability to combat cancer, particularly in combination with checkpoint inhibitors.”

Leading drug candidate is monoclonal antibody against TREM-2, a surface protein on Tumor Associated Macrophages, which are immunosuppressive.



Pionyr's muPY314 in Combination with Anti-PD-1 Treatment Controls Tumor Growth in the Anti-PD-1-Resistant Mouse CT26 Tumor Model

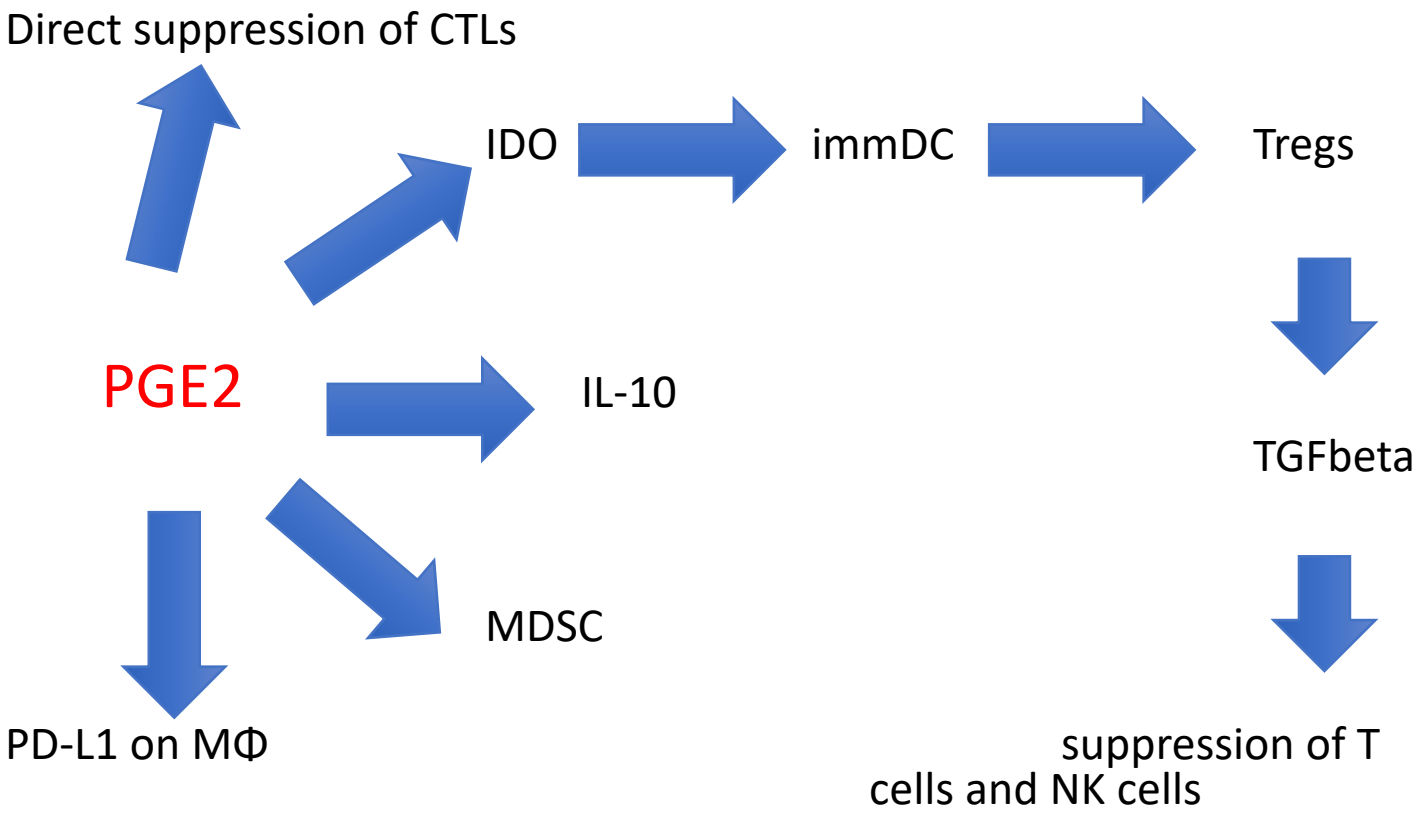
Pionyr deal with Gilead

- Gilead bought 49% interest for $275 million, with option to buy remainder for about $1 billion

Immunosuppression Factors in Tumor Microenvironment

- TGFbeta
- IDO
- IL-10
- Arginase
- Treg
- MDSC
- Potassium
- M2 Macrophage
- Adenosine
- Prostaglandin E2 (PGE2)
- PD-1, CTLA-4, LAG-3, TIM-3
- Immunosuppressive DC

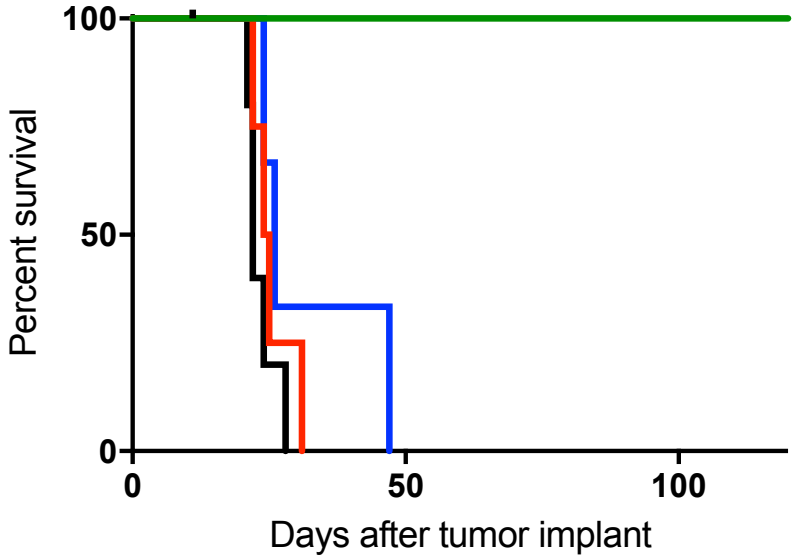
PGE2 may be pivotal



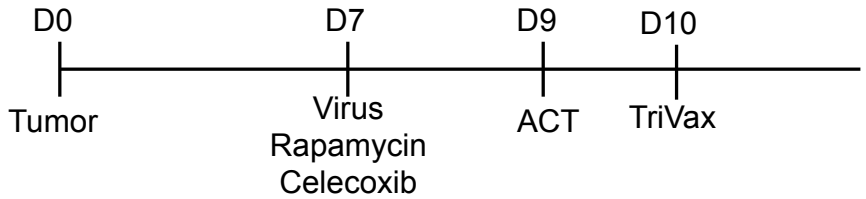
Roy Lab Combination Treatment for Brain Tumors (in mice)

1. Source of Tumor-Specific T cells
2. Oncolytic Virus to Kill some tumor cells
3. Virus provides locally expressed IL-15-IL15R∝ to attract T cells and NK cells
4. Prostaglandin Synthesis Inhibitor (Celecoxib) to reduce Immunosuppression in Tumor Microenvironment

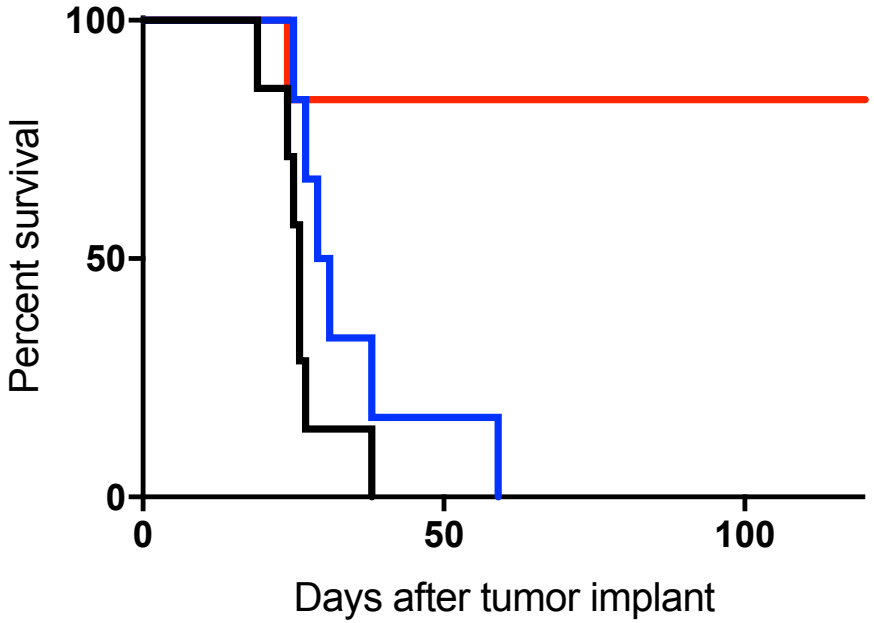
Adoptive T cell transfer is essential with vvDD-IL15-Rα



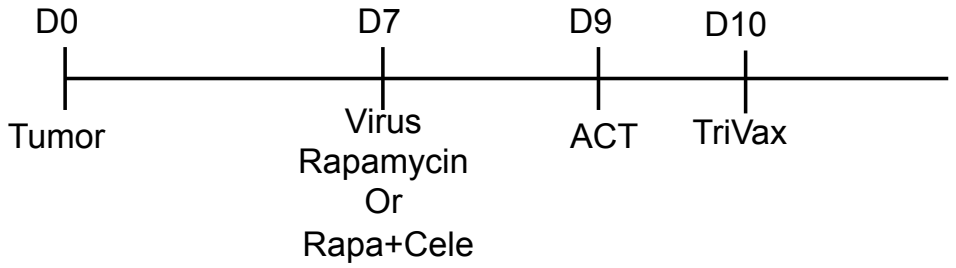
	Virus Treatment	Rapa+Cele	ACT (TriVax)	n
—	PBS	✓	—	5
—	vvDD-IL15-Rα	✓	—	3
—	vvDD-RFP	✓	✓	4
—	vvDD-IL15-Rα	✓	✓	4



Myxoma Virus IL15/IL15Rα



	Virus Treatment	Rapa	Cele	ACT (TriVax)	n
—	PBS	✓	✓	—	7
—	vMyx-IL15Rα-tdTr	✓	—	✓	6
—	vMyx-IL15Rα-tdTr	✓	✓	✓	6



Learning Objectives

Learn about vaccination as a strategy to promote a T cell response against tumors

Learn about adoptive cell therapies: tumor infiltrating lymphocytes, engineered T cells, chimeric antigen receptor T cells

Learn about the tumor microenvironment

Learn a little about the economics of immunotherapy

Hear some predictions for future directions

MEDICARE TO COVER COSTLY CAR T-CELL CANCER THERAPY NATIONWIDE

BY JOHN COMMINS | AUGUST 08, 2019

- **CAR-T therapy can cost as much as $375,000 for a one-time treatment. That estimate does not include hospital stays and other related expenses.**
- **In the final rule, CMS dropped a requirement that hospitals collect data on patient outcomes under the CAR-T therapies, which hospitals had complained was too burdensome.**
- **Instead, CMS said it will monitor medical data from the FDA's post-approval safety studies.**

Cost of Cancer

- Cancer is most expensive disease
- A 2015 National Bureau of Economic Research study found when calculating the average cost for one extra year of life, patients and insurers paid $54,100 in 1995. The price for one year of life increased to $139,100 in 2005 and $207,000 in 2013.
- https://www.drugwatch.com/news/2015/10/07/cost-of-cancer/#:~:text=Cost%20of%20Cancer%20on%20the,Cancer%20costs%20%24895%20billion%20annually.

Costs to the Individual

- Hospital and clinic visits
- Medicine and prescription drugs
- Lab tests
- Treatments
- Surgeries
- Home health services

Range of costs

- Surgery: $15k - $60k
- Chemotherapy $13k - $100k
- Radiation: $11k - $35k

Orphan Drug Act of 1983

- An orphan disease is a rare disease or condition that affects fewer than 200,000 people in the United States
- Over 40 per cent of orphan drugs are indicated to treat various cancers
- Some of the top grossing oncology drugs – 'household' brand names like Rituxan, Herceptin, Avastin - have orphan status
- Due to “personalized” medicines: e.g. only 25% of breast cancers are positive for the Herceptin target, which brings it into the “orphan” category

Orphan Drug Act of 1983

The intervention by government on behalf of orphan drug development can take a variety of forms (Wikipedia):

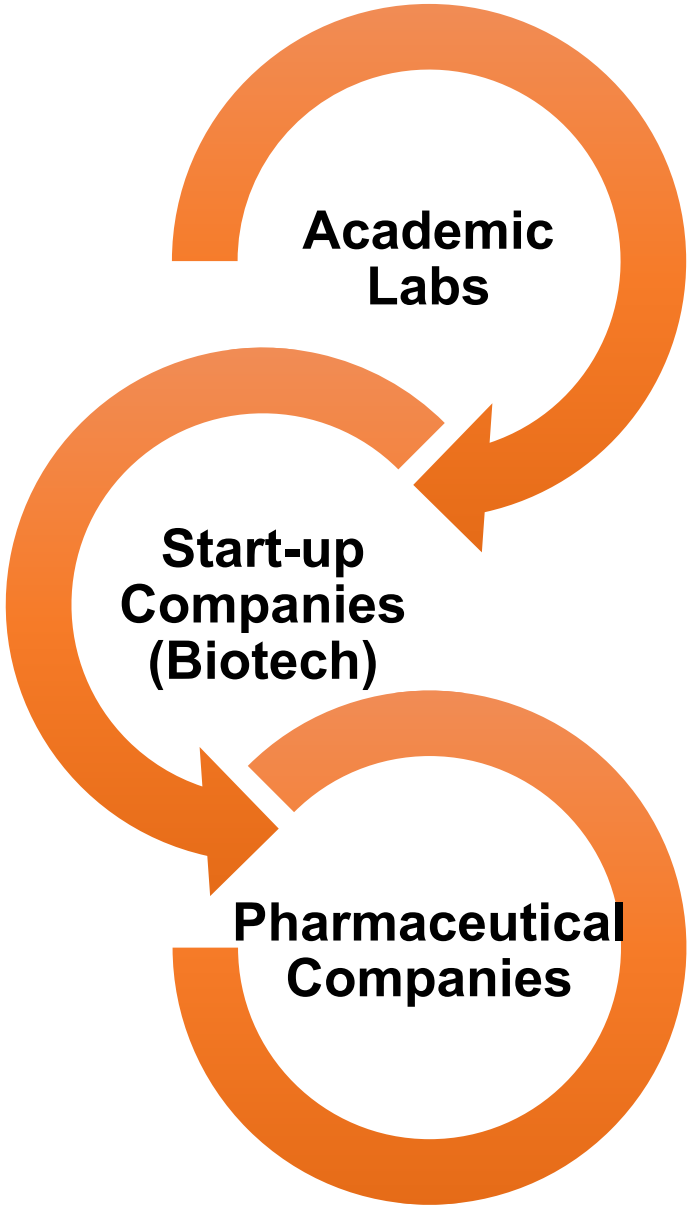
- Tax incentives
- Enhanced patent protection and marketing rights
  (7 additional years of exclusivity)
- Clinical research subsidies
- Creating a government-run enterprise to engage in research and development

What does Insurance Reimburse?

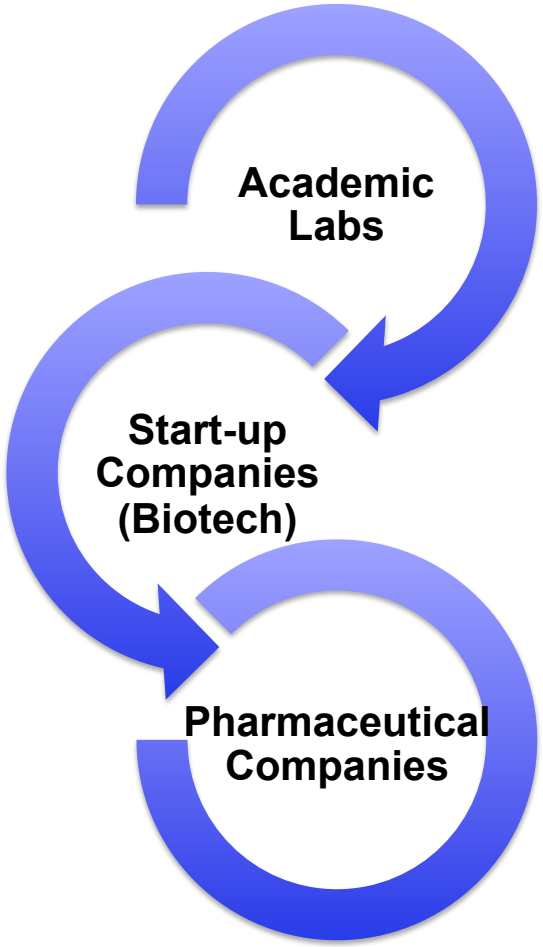
- With Physicians approval, insurance will cover most FDA-approved treatments
- Problem might be individual insurance policies, with most having co-pays of 10 to 20% and different maxima*
- If patient exhausts all FDA-approved options, might be too costly for other options

*Co-pay of 20% on ant-PD1/anti-CTLA-4 treatment costs $60,000. This does not include many other costs involving hospital visits, doctor costs, etc

Typical Path for Cancer Product Development



Typical Path for Cancer Product Development



~ Amount of $$$ at Stage of a Single Therapeutic Product and Lifetime to Market:

- **$1,000,000** — **5 years**
- **$100,000,000** — **5 years**
- **$2,000,000,000** — **5 years**

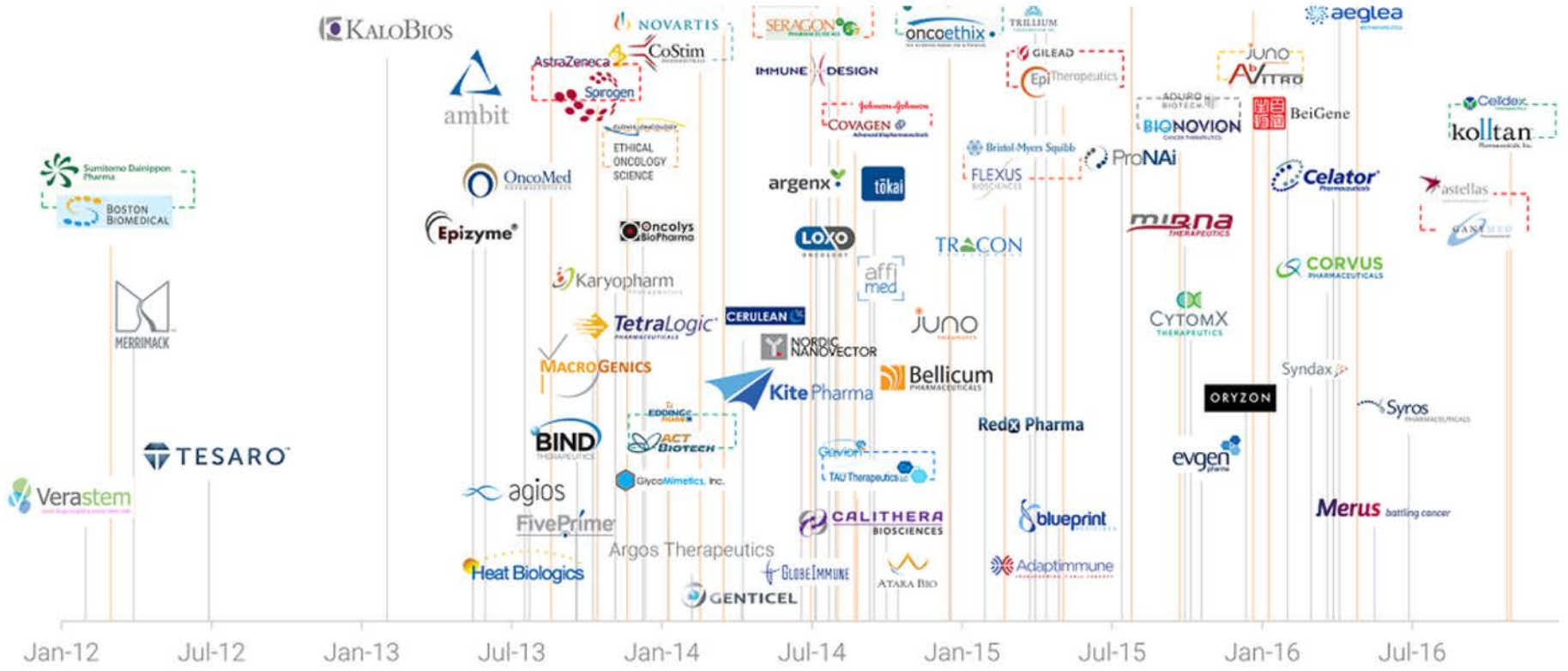
>$2B total, 15 years

Startup Companies in the Field of Cancer (2016 posting)

Startups working on cancer therapies have received over $12B across 680+ deals in the last 5 years. The potential in the market was highlighted by Stemcentrx's acquisition this quarter by biopharma company AbbVie for $10.2B.
This year also saw 9 IPOs (Initial Public Offerings)

https://www.cbinsights.com/blog/cancer-startups-exit-timeline/

Timeline: The Rise Of Cancer Startup Exits In One Infographic



Cancer therapy startups have seen over 100 exits since 2012. 60% of the exited companies were venture-backed
Note: "Exits" refer to Acquisitions or Initial Public Offerings

Every Major Pharmaceutical Company Now has an Immuno-Oncology Division

Many companies have hired academic leaders in this area to head their immuno-oncology divisions

For example, Glenn Dranoff recently moved from Harvard to head Novartis' program

Estimated that 95% of biotech startups fail

Learning Objectives

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Future Directions

- Combinations of multiple treatment modalities
  - Provide ample number of tumor-specific T cells
  - Prevent the exhaustion of the T cells
  - Reverse immunosuppression in local environment of tumor
- More development of gene sequencing for identification of multiple neoantigens (part of broad trend toward personalized treatments)
- Engineering of CARs and TCRs, including using CRISPR

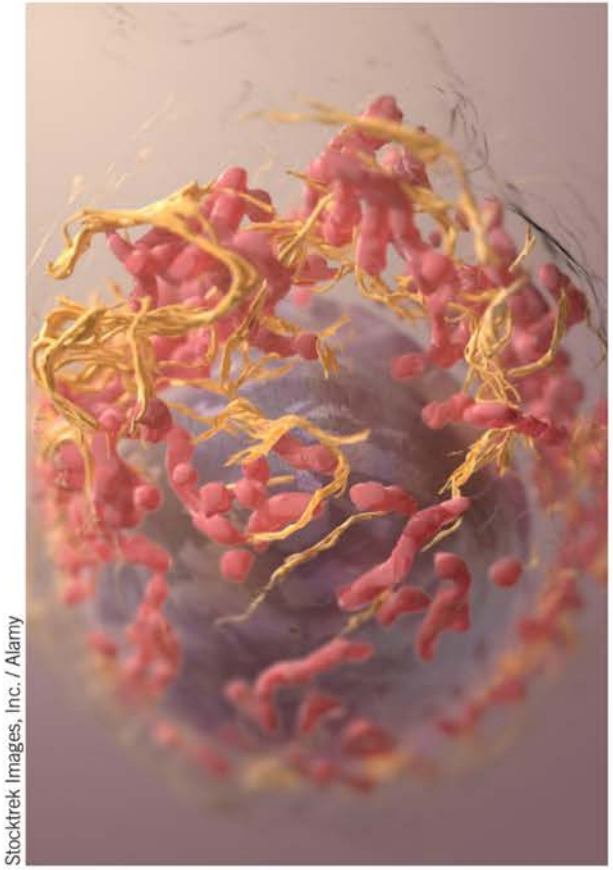
Approval may embolden industry to combine cancer therapies

In the fight against cancer, researchers agree that it is a good idea to combine targeted drugs with each other or with immunotherapies: tumor cells mutate and can become resistant to treatment that works via one route, so an additional therapy makes effective treatment more likely. But for drug companies, deciding to test promising combinations has not been easy.

In some cases, pharmaceutical developers simply view it as against their interests to collaborate. "Drug companies too often are reluctant to work together, because they think it won't be to their advantage," observes Carlos Moreno of the Winship Cancer Institute of Emory University in Atlanta.

For example, one company might have a candidate therapy that would make sense to test with a drug from a different firm. But because the two firms hold the patents to each separately, both parties might worry about future liabilities, intellectual property (IP) rights, and secondary IP (that is, IP issues that might arise from unexpected new therapeutic benefits from combining the drugs).

Fears such as this might make working



Stocktrek Images, Inc. / Alamy

It takes two: Combo treats melanoma.

cobimetinib, a mitogen-activated protein kinase (MEK1) inhibitor co-developed by the Roche subsidiary Genentech and the South San Francisco–based Exelixis, with

NCI Almanac. The information it provides will go some way in helping to figure out which drugs might work better when given together than when given individually.

The database will pool results from an ambitious project the NCI began a few years ago that helps rationalize drug combination approaches. Every combination of FDA-approved oncology drugs was tested against cancer cell lines the NCI has characterized, to create a matrix that plots the efficacy of each combination. These data will become available as a web tool for drug developers to see which drug pairs are active against which cell lines, and which might potentially be toxic.

Avoiding toxicity

"Drug companies are developing targeted cancer agents faster than they're able to develop appropriate models for figuring out how to combine them," says James Doroshow, deputy director for clinical and translational research at the NCI and one of the developers of the database. "There are simply too many possibilities, and they don't have the resources to screen them."

Putting drugs together can introduce unexpected problems not seen when

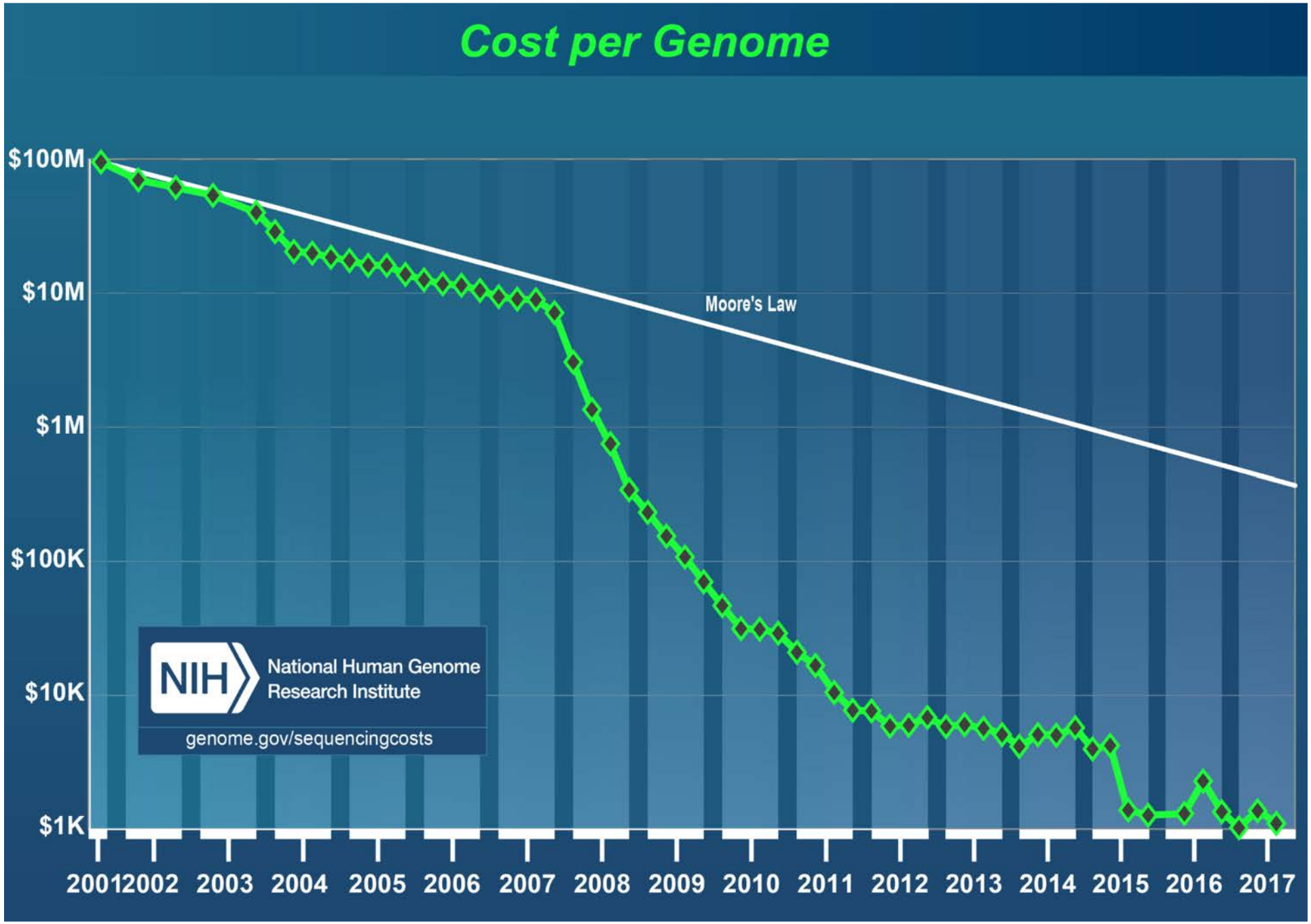
Nature Medicine, 2015

Towards personalized, tumour-specific, therapeutic vaccines for cancer

Zhuting Hu[1], Patrick A. Ott[1–3] and Catherine J. Wu[1–4]

Abstract | Cancer vaccines, which are designed to amplify tumour-specific T cell responses through active immunization, have long been envisioned as a key tool of effective cancer immunotherapy. Despite a clear rationale for such vaccines, extensive past efforts were unsuccessful in mediating clinically relevant antitumour activity in humans. Recently, however, next-generation sequencing and novel bioinformatics tools have enabled the systematic discovery of tumour neoantigens, which are highly desirable immunogens because they arise from somatic mutations of the tumour and are therefore tumour specific. As a result of the diversity of tumour neoepitopes between individuals, the development of personalized cancer vaccines is warranted. Here, we review the emerging field of personalized cancer vaccination and discuss recent developments and future directions for this promising treatment strategy.

Nature Reviews Immunology, 2018


Cost per Genome
$100M
$10M
$1M
$100K
$10K
$1K
Moore's Law
NIH
National Human Genome Research Institute
genome.gov/sequencingcosts
2001
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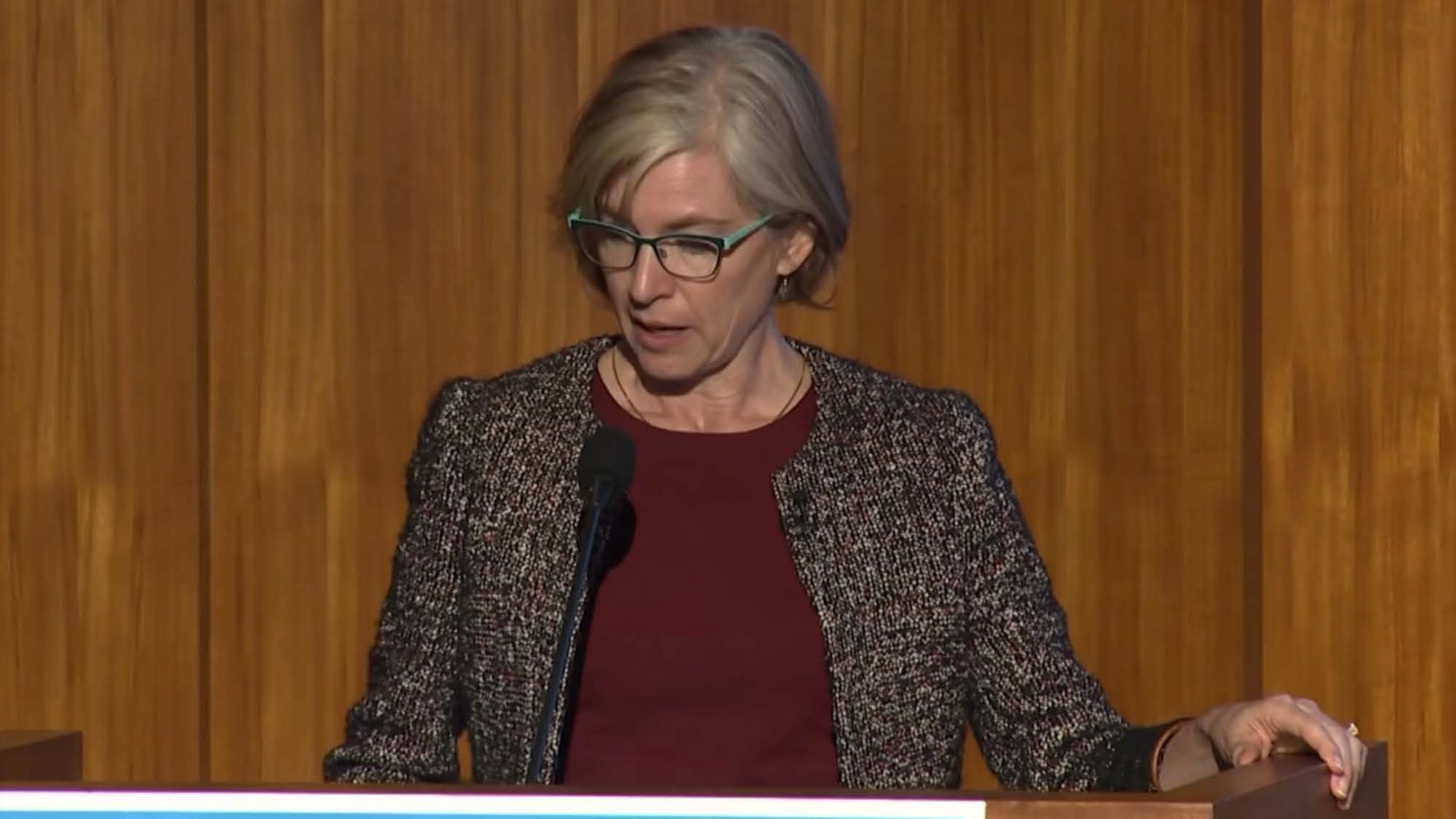
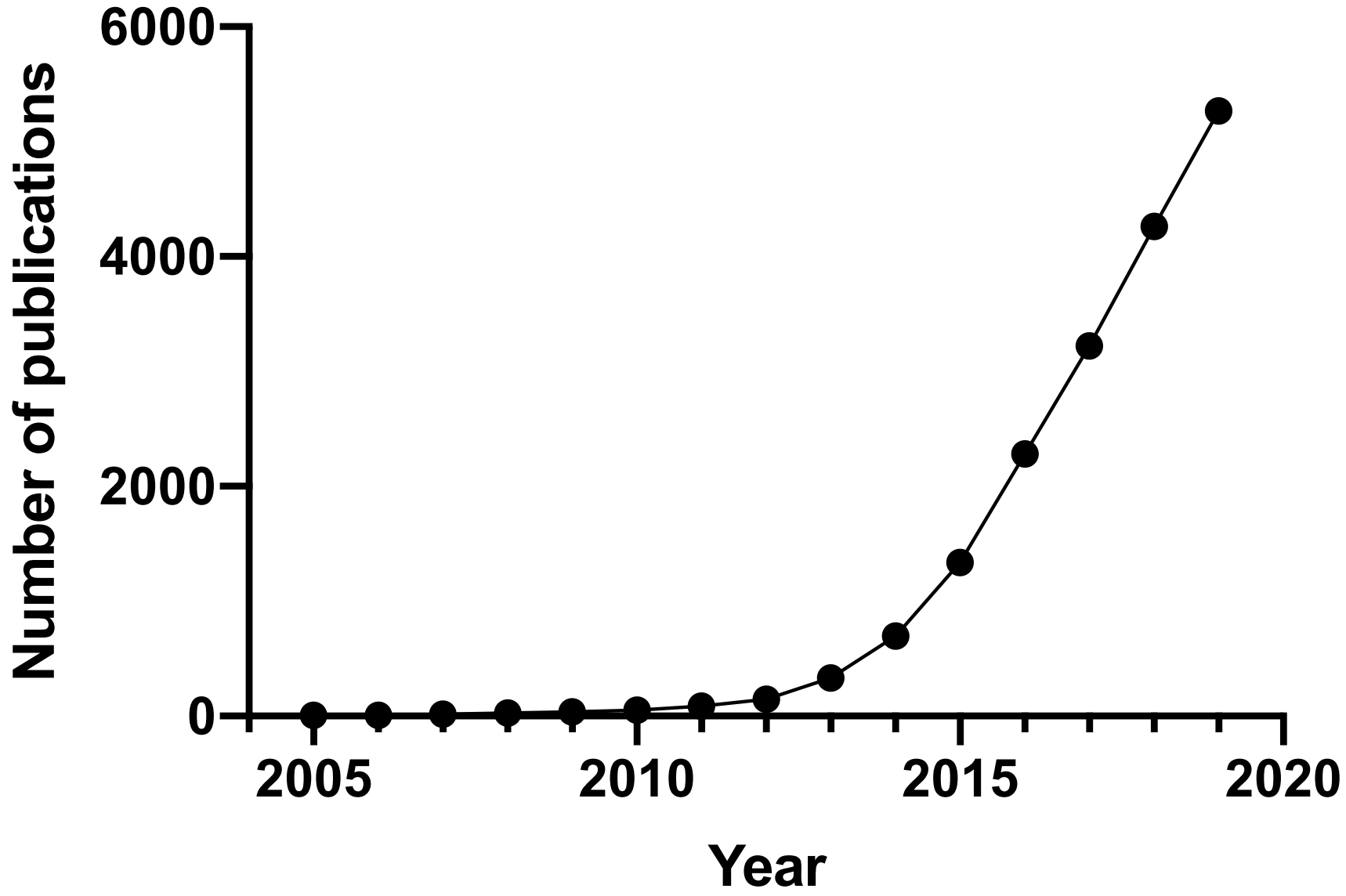
CRISPR-Cas9

- Emmanuelle Charpentier and Jennifer Doudna won 2020 Nobel Prize in Chemistry for CRISPR-Cas9
- Clustered Regularly Interspaced Short Palindromic Repeats-CRISPR Associated Protein 9
- Published in 2012



- https://www.youtube.com/watch?v=bkLvZwDaQLo

Publications on CRISPR in PubMed



Clinical Trial > Nat Med. 2020 May;26(5):732-740. doi: 10.1038/s41591-020-0840-5.
Epub 2020 Apr 27.

Safety and feasibility of CRISPR-edited T cells in patients with refractory non-small-cell lung cancer

You Lu [1], Jianxin Xue [2], Tao Deng [3], Xiaojuan Zhou [2], Kun Yu [3], Lei Deng [4], Meijuan Huang [2], Xin Yi [5], Maozhi Liang [6], Yu Wang [7], Haige Shen [7], Ruizhan Tong [2], Wenbo Wang [8], Li Li [2], Jin Song [5], Jing Li [5], Xiaoxing Su [9], Zhenyu Ding [2], Youling Gong [2], Jiang Zhu [2], Yongsheng Wang [2 6], Bingwen Zou [2], Yan Zhang [2], Yanying Li [2], Lin Zhou [2], Yongmei Liu [2], Min Yu [2], Yuqi Wang [5], Xuanwei Zhang [2], Limei Yin [2], Xuefeng Xia [5], Yong Zeng [3], Qiao Zhou [10], Binwu Ying [11], Chong Chen [12], Yuquan Wei [12], Weimin Li [13], Tony Mok [14]

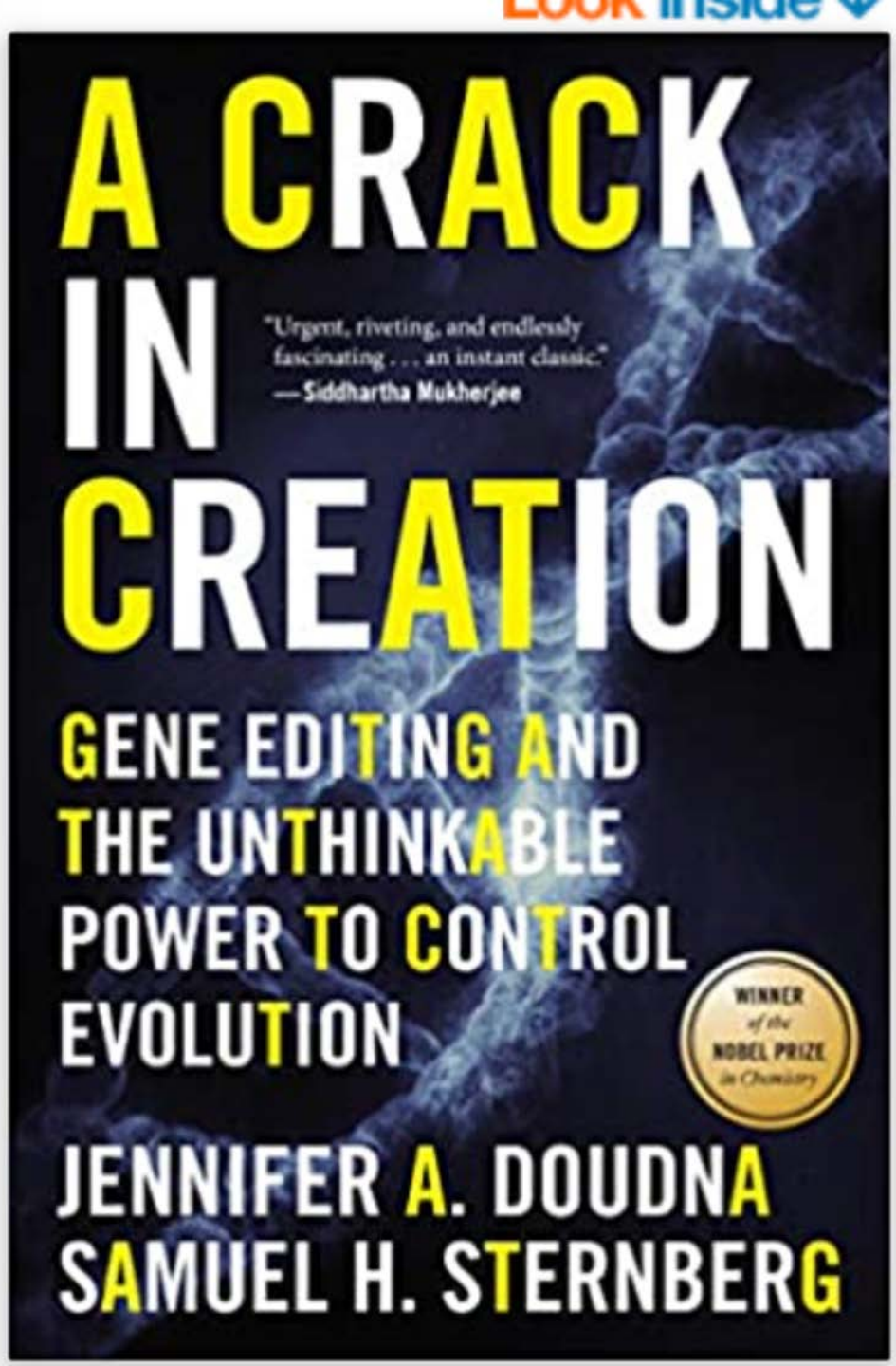
Affiliations ... expand

Generation of glucocorticoid resistant SARS-CoV-2 **T-cells** for adoptive cell therapy.

Basar R, Uprety N, Ensley E, Daher M, Klein K, Martinez F, Aung F, Shanley M, Hu B, Gokdemir E, Mendt M, Silva FR, Acharya S, Laskowski T, Muniz-Feliciano L, Banerjee P, Li Y, Li S, Garcia LM, Lin P, Shaim H, Yates SG, Marin D, Kaur I, Rao S, Mak D, Lin A, Miao Q, Dou J, Chen K, Champlin R, Shpall EJ, Rezvani K.

bioRxiv. 2020 Sep 15:2020.09.15.298547. doi: 10.1101/2020.09.15.298547. Preprint.
PMID: 32995792 **Free PMC article.**

We observed that the choice of cytokines modulates the expansion, phenotype and hierarchy of antigenic recognition by SARS-CoV-2 **T-cells**. ...SARS-CoV-2 **T-cells** could not be efficiently


Look inside
A CRACK IN CREATION
"Urgent, riveting, and endlessly fascinating . . . an instant classic."
—Siddhartha Mukherjee
GENE EDITING AND THE UNTHINKABLE POWER TO CONTROL EVOLUTION
WINNER of the NOBEL PRIZE in Chemistry
JENNIFER A. DOUDNA
SAMUEL H. STERNBERG

Finally, What Drives Pioneers?

- William Coley and Steven Rosenberg were clinicians who saw a nearly miraculous cure early in their careers and had faith that it was due to the immune system.
- Jim Allison was driven by the memory of family members who died of cancer and had the passion to keep advocating for his treatment discovery.
- Jennifer Doudna was interested in basic biochemistry and recognized both the power of her serendipitous discovery and great responsibility to use it wisely.

Thanks for Staying to the End!

- Questions?