1980-2021 Four Decades in the Life of Immunotherapy: Looking Back and Looking Forward to Immunotherapy of Cancer Coming of Age

Vol. 7, 759s–760s, March 2001 (Suppl.) Clinical Cancer Research

A Decade in the Life of Tumor Immunology

Olivera J. Finn[1] and Michael T. Lotze
University of Pittsburgh Cancer Institute, University of Pittsburgh School of Medicine, Pittsburgh, Pennsylvania 15261 [O. J. F.], GlaxoSmithKline Pharmaceuticals, King of Prussia, Pennsylvania 19406

The role of the immune system in the recognition and prevention or therapy of cancer remains a fascinating and important topic of research. The first in the series of Keystone Symposia on Cellular Immunity and Immunotherapy of Cancer was held in 1990 in Park City, Utah (1). Progress in tumor immunology and new developments in immunology that could impact on this field have been featured and appraised in these meetings at 3- or 4-year intervals (2, 3). The fourth meeting in this series was held in January 2000 in Santa Fe, NM. This special issue of Clinical Cancer Research is devoted to the major topics discussed at the meeting. It features original articles by the meeting particip... search in cancer im...

cytokine-activated T cells that were not antigen specific but could kill tumor cells, the identification of tumor antigens focused the field on specificity. Years of experiments with tumors in mice taught two important lessons: antitumor immune responses can be tumor specific, and tumor growth can be prevented by immunization. Identification of tumor antigens in human tumors foreshadowed the future of tumor-specific immunization in people. This goal was very appealing and every newly identified tumor peptide brought that goal closer to reality. Already by the time of the second Symposium, Phase I clinical trials in peptide-based cancer vaccines occupied a large portion of the meeting agenda. Progress in identification of new tumor antigens and their use in cancer immunotherapy continues to generate excitement in the field, and papers by Kao *et al.*, Geiger, *et al.*, Beatty *et al.*, Santin *et al.*, Rudolf *et al.*, Gajewski *et al.*, Meaker *et al.*, Zier *et al.*, Pittet *et al.*, and Romero *et al.* featured in this

...odels where

KEYSTONE SYMPOSIA

Cancer vaccine tested

PITTSBURGH (AP) — Doctors are testing a vaccine that could trigger immunity to three forms of cancer and eventually prevent the disease.

A 56-year-old man with colon cancer was injected with the vaccine yesterday at the Pittsburgh Cancer Institute. He was the second of 30 patients to undergo treatment for cases of colon, breast or pancreatic cancer now considered incurable.

"We want to know if we can induce immunity," said Dr. Olivera J. Finn, director of the center's immunology program. "If this is eventually successful, clearly I see it as the first therapy that a patient would receive following surgery or following diagnosis."

The patients will continue to receive shots for six weeks and doctors will be able to evaluate the success of the treatment after a year, Finn said.

The vaccine is developed from an abnormal form of a complex of protein and sugars called mucin, a molecule found on the surface of cells in the breast, colon and pancreas. Other cancer vaccines are made from whole proteins and from tumor cells.

"We're shining a light, a beacon, on this abnormal mucin," said Dr. Michael T. Lotze. "We're identifying a target for the vaccine."

If the vaccine produces immunity, it could be administered to patients after surgery to help prevent a recurrence of cancer, he said.

"That's the ideal time to consider a vaccine," said Dr. Philip Livingston of Memorial Sloan-Kettering Cancer Center in New York. "If that proves to be effective in that setting, then you can of course consider using it in patients with high-risk factors."

Lotze said Pittsburgh researchers hope someday to inject people at risk for developing cancer as a preventative.

The vaccine can cause slight side effects such as fever, chills and swelling, Lotze said.

The Pittsburgh Cancer Institute received U.S. Food and Drug Administration approval for vaccine testing on Dec. 17, Finn said.

AP Photo

While in her lab at the University of Pittsburgh Medical Center yesterday, Olivera J. Finn tells how the cancer vaccine she helped develop works.

DECEMBER 29, 1993

387,144
2.18.21

Michael T. Lotze, MD
Chief Cellular Therapy Officer (CCO); Nurix Therapeutics
Email: mlotze@nurixtx.com
Cell: 412-478-3316

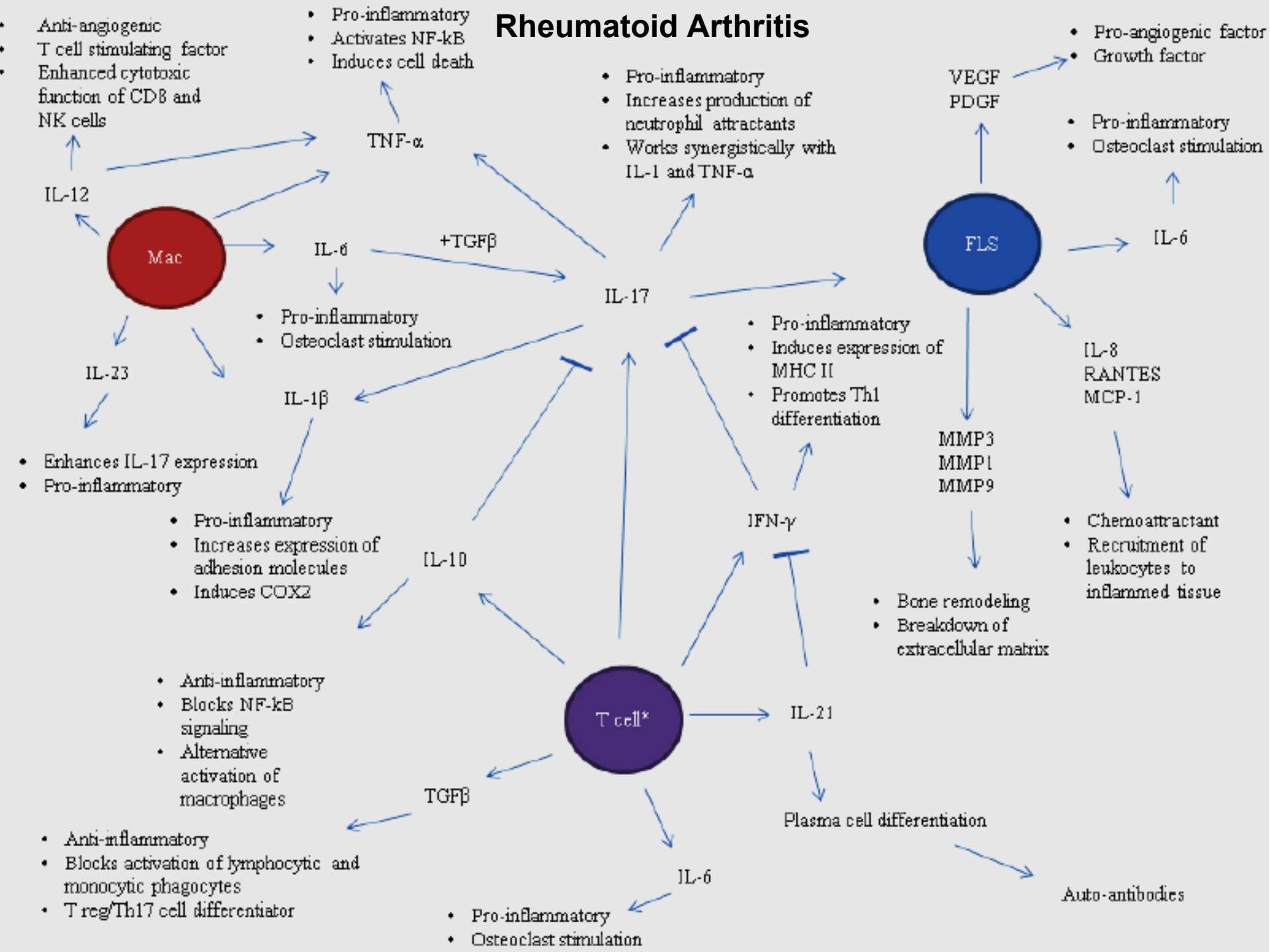
Disclosures-Company & Consultant

- **Clinigen (IL-2)**
- **Nurix (NextACT) Chief Cellular Therapy Officer**
- **Checkmate, Inc. (TLR9/Checkpoints)**
- **iRepertoire, Inc. (Hudson Alpha Institute)**

Before we begin, I would like to remind you that my comments and responses to questions reflect my views only and are not necessarily those of Nurix, Nurix's management team or Nurix's board of directors.

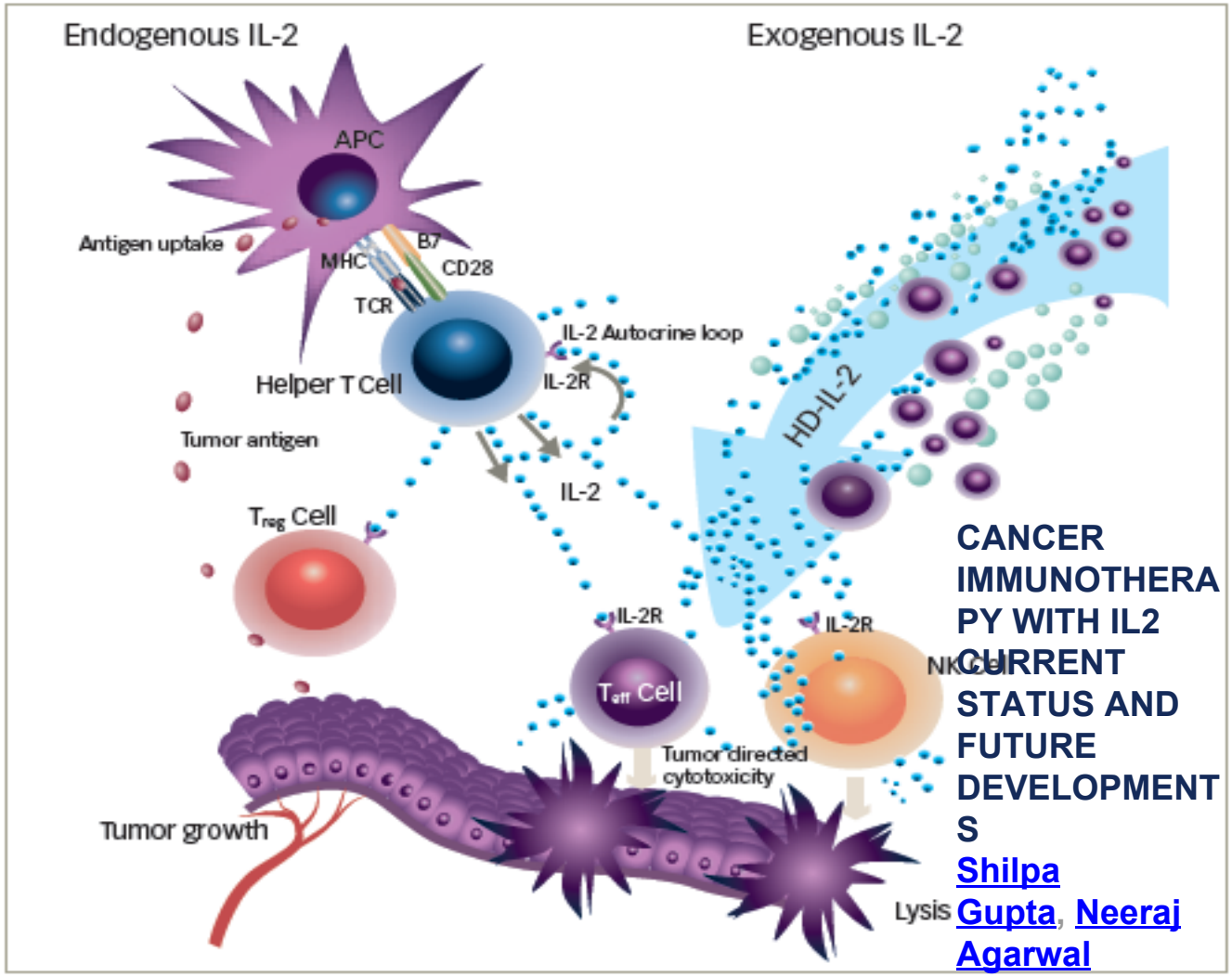
Moreover, my comments and responses are made only as of today, and may include statements related to Nurix, Nurix's product candidates and Nurix's business that are forward-looking statements under the federal securities laws. Actual results may differ materially from those contained in or implied by these forward-looking statements due to risks and uncertainties associated with Nurix's business. For a discussion of the material risks and other important factors that could impact Nurix's actual results, please refer to Nurix's SEC filings, which can be found on the Nurix website.

Finally, any statements I may make about Nurix, Nurix's product candidates and Nurix's business are not intended to contradict or modify Nurix's existing public disclosures.


Rheumatoid Arthritis
Anti-angiogenic
T cell stimulating factor
Enhanced cytotoxic function of CD8 and NK cells
Pro-inflammatory
Activates NF-kB
Induces cell death
TNF-α
IL-12
Mac
IL-6
+TGFβ
Pro-inflammatory
Increases production of neutrophil attractants
Works synergistically with IL-1 and TNF-α
IL-17
VEGF
PDGF
Pro-angiogenic factor
Growth factor
Pro-inflammatory
Osteoclast stimulation
FLS
IL-6
Pro-inflammatory
Osteoclast stimulation
IL-23
IL-1β
Pro-inflammatory
Induces expression of MHC II
Promotes Th1 differentiation
IL-8
RANTES
MCP-1
MMP3
MMP1
MMP9
Enhances IL-17 expression
Pro-inflammatory
Pro-inflammatory
Increases expression of adhesion molecules
Induces COX2
IL-10
IFN-γ
Chemoattractant
Recruitment of leukocytes to inflammed tissue
Bone remodeling
Breakdown of extracellular matrix
Anti-inflammatory
Blocks NF-kB signaling
Alternative activation of macrophages
T cell*
IL-21
TGFβ
Plasma cell differentiation
Anti-inflammatory
Blocks activation of lymphocytic and monocytic phagocytes
T reg/Th17 cell differentiator
IL-6
Auto-antibodies
Pro-inflammatory
Osteoclast stimulation

Cancer Immunotherapy

Figure 1: Dual mechanism of action of interleukin-2



APC = antigen-presenting cell; HD-IL-2 = high-dose interleukin; NK = natural killer; MHC = major histocompatibility complex. TCR = T cell receptor. Source: Prescott Group.

Nature Reviews Cancer 2004DOI:10.1038/nrc1252

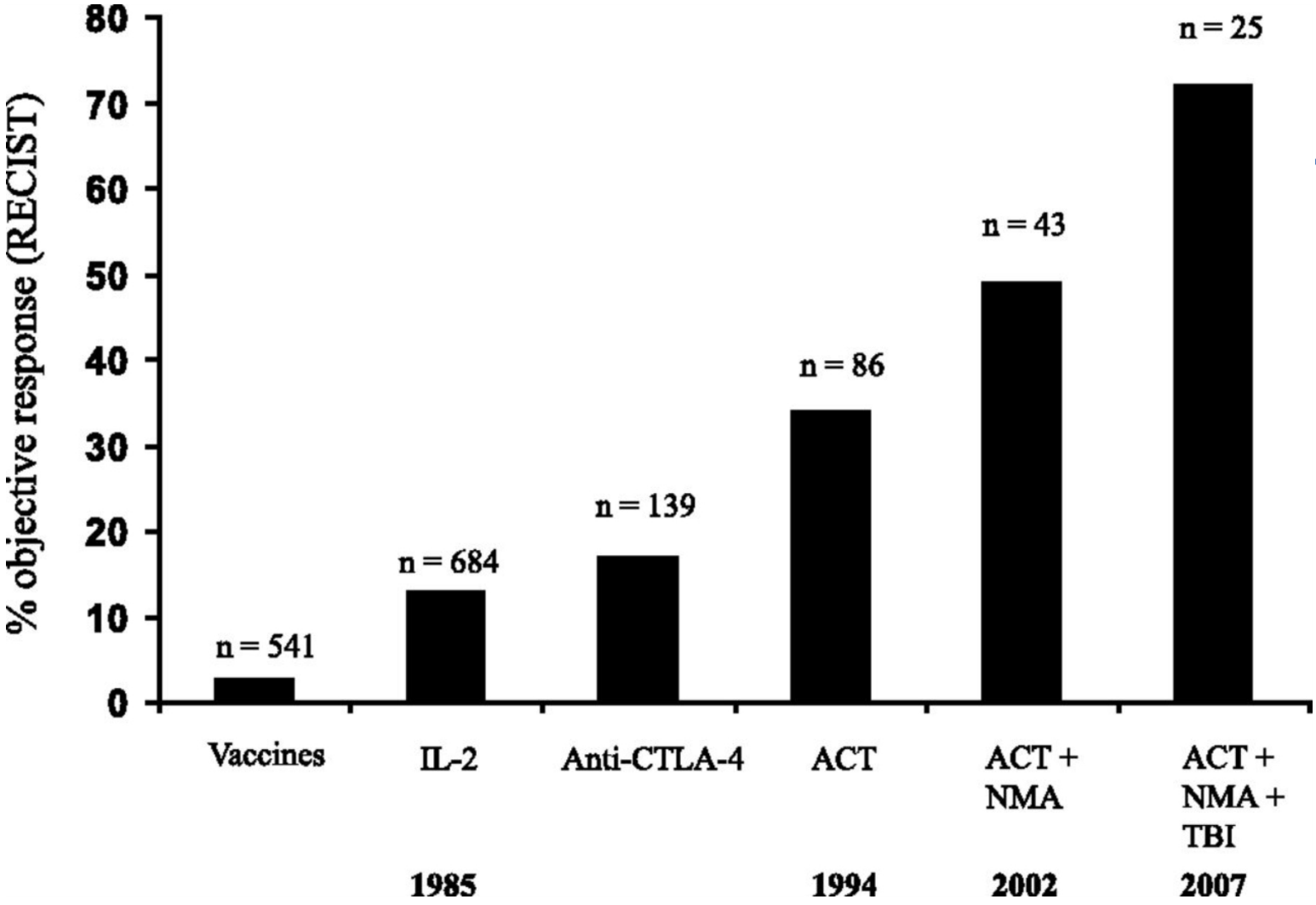
Cytokines in cancer pathogenesis and cancer therapy

•Glenn Dranoff

CANCER IMMUNOTHERAPY WITH IL2 CURRENT STATUS AND FUTURE DEVELOPMENTS

Shilpa Gupta, Neeraj Agarwal

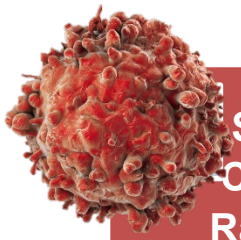
Oncology & Hematology Review, 2016;12



IL-2: The First Effective ImmunoRx for Human Cancer

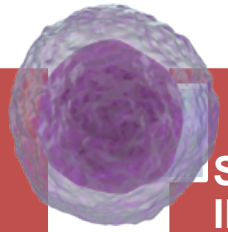
Steven A. Rosenberg JImmunol June 15, 2014, 192: 54515458 DOI: https://doi.org/10.4049/jimmunol.1490019

Foundations of Cancer Therapy



Surgery
ChemoRx
Radiation

- Other Targets:
- Signal Transduction
- Autophagy
- Oncogenes
- Tumor Suppressor Genes



T Cells

Immune Stimulants
IL2-1st ICI

- Checkpt Inhibition- CTLA4, PD1, PDL1
- Adoptive Cell Therapy (CARTs, TIL)
- DC, Other Vaccines

Anti-VEGF

- Chloroquine
- Platelet Derived Growth Factor (PDGF)
- Fibroblast Growth Factor (FGF)
- Tie 2 Kinase stabilization
- β-phosphatase inhibitors

Disturbance of function (***functio laesa***): the legendary 5th cardinal sign of inflammation, added by Galen to the four cardinal signs of Celsus=Autophagy.

Rather LJ. Bull N Y Acad Med. 1971.

Calor (warmth), *dolor* (pain), *tumor* (swelling) and *rubor* (redness), and (later) loss of function Celsus, *De Medicina*

Cancer is the endstage of chronic inflammation in adults

Evolution of Cancer Treatments: Surgery (ACS)

Ancient physicians and surgeons knew that cancer would usually come back after it was surgically removed. The Roman physician Celsus wrote, “After excision, even when a scar has formed, none the less the disease has returned.”

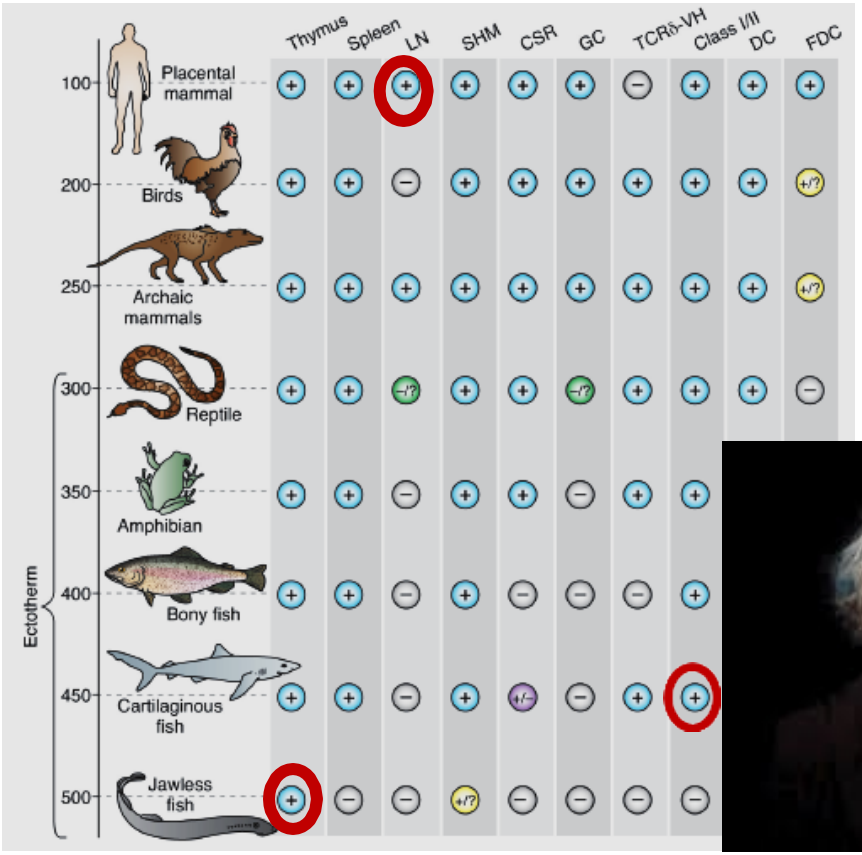
Successful Surgical Excision is Immunotherapy
Successful Radiation Therapy is Immunotherapy
Successful Hormonal Therapy is Immunotherapy
Successful Chemotherapy is Immunotherapy

A cold-blooded view of adaptive immunity
Nature Review Immunology (2018)

Martin F. Flajnik Department of Microbiology and Immunology
University of Maryland Baltimore

Innate immunity in single cell organisms (4byrs) evolved:
0) TLRs, NLRs, ALRs, RLRs, STING (STRANGER-Janeway)

and jasmonic acid) that limit pathogens;
4) SIRPα/CD47
5) PIR's

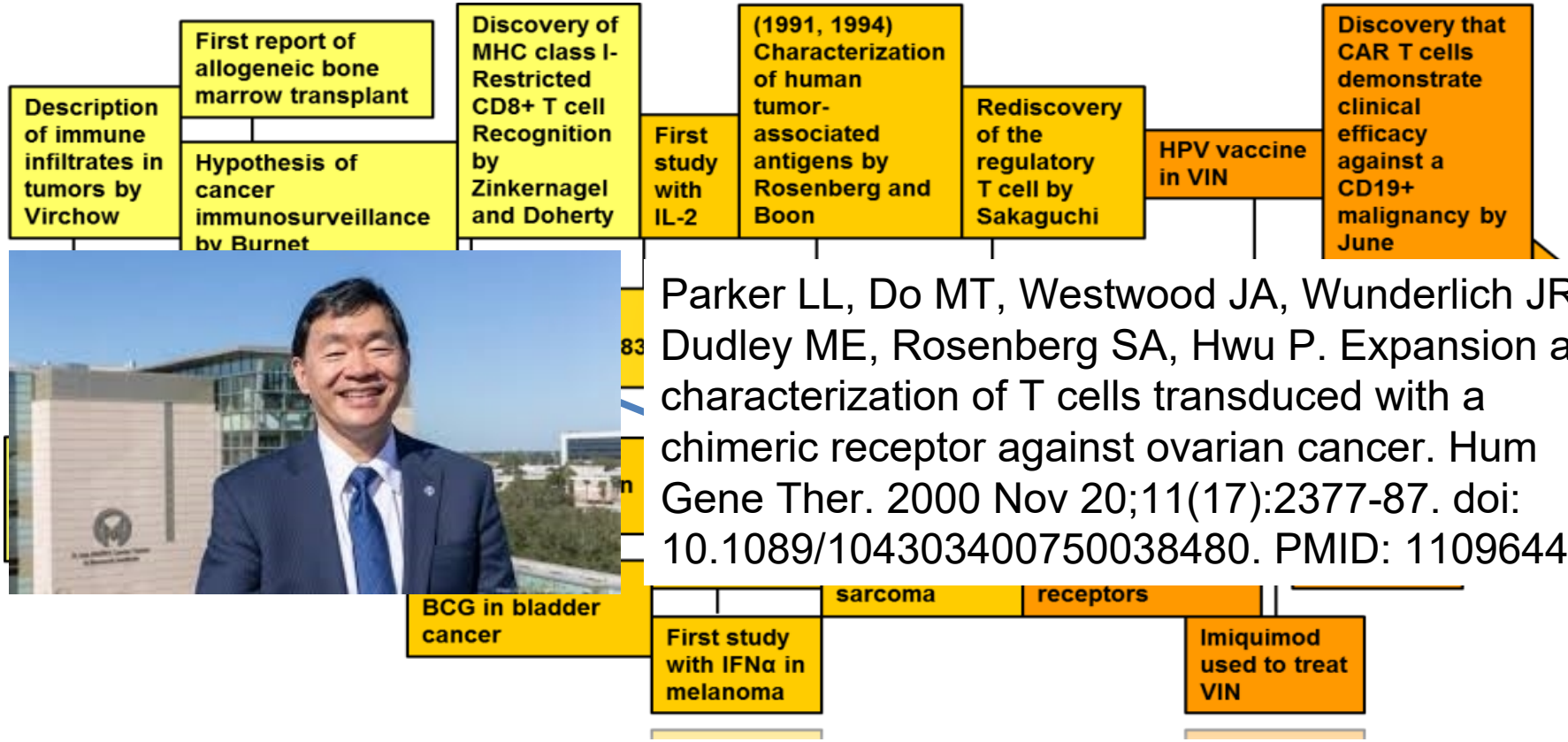


NK cells and MHC-like molecules (Maternal/Fetal interface): *Botryllus schlosseri* is a colonial

DANGER-Matzinger

History of Immunotherapy

Porter DL, Levine BL, Kalos M, Bagg A, June CH. **Chimeric antigen receptor-modified T cells in chronic lymphoid leukemia.** N Engl J Med. 2011;365:725–733.



Parker LL, Do MT, Westwood JA, Wunderlich JR, Dudley ME, Rosenberg SA, Hwu P. Expansion and characterization of T cells transduced with a chimeric receptor against ovarian cancer. Hum Gene Ther. 2000 Nov 20;11(17):2377-87. doi: 10.1089/10430340750038480. PMID: 11096442.

Kochenderfer JN, Wilson WH, Janik JE, Dudley ME, Stetler-Stevenson M, Feldman SA, Maric I, Raffeld M, Nathan DA, Lanier BJ, Morgan RA, Rosenberg SA. **Eradication of B-lineage cells and regression of lymphoma in a patient treated with autologous T cells genetically engineered to recognize CD19.** Blood. 2010 Nov 18;116(20):4099-102.

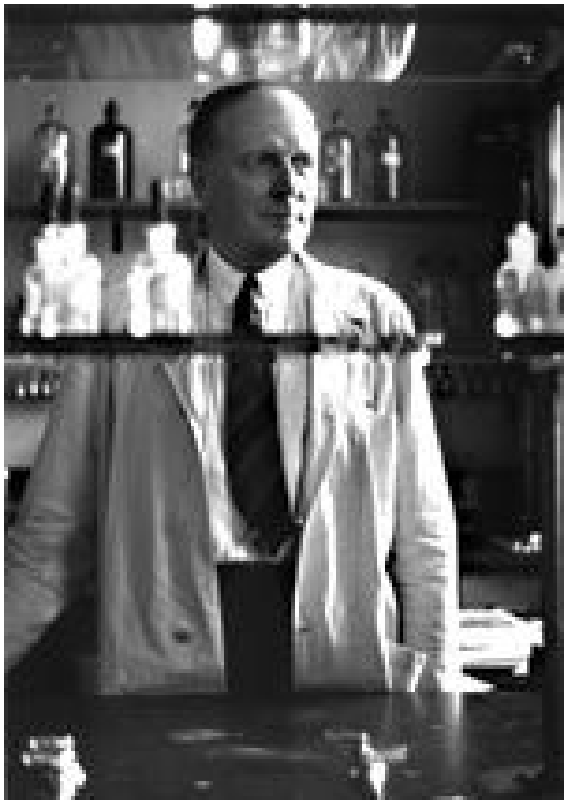
Fraietta, Joseph A <jfrai@upenn.edu>

The lymphocyte as a factor in natural and induced resistance to transplanted cancer. Proc Natl Acad Sci U S A 1:435–437; 1915

Hence, it would seem fair to conclude that

the lymphocyte is a necessary factor in cancer

immunity – James B. Murphy and John J. Morton (Murphy and Morton 1915)



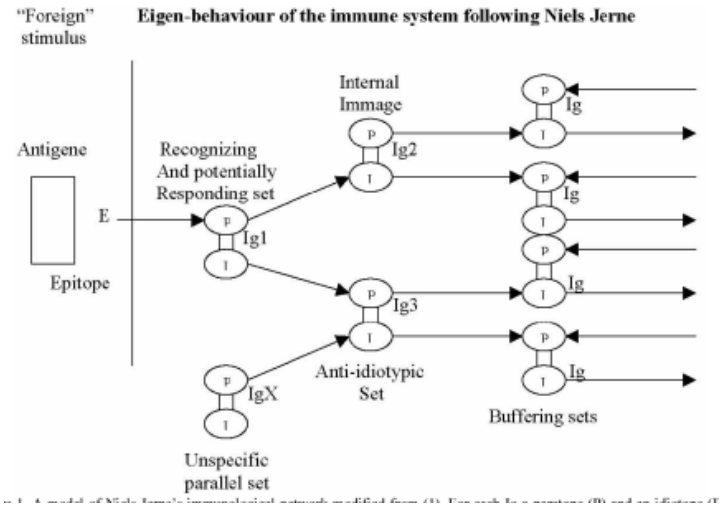
NIELS K. JERNE, M.D.

Professor and Chairman, Department of Microbiology, 1962-1966

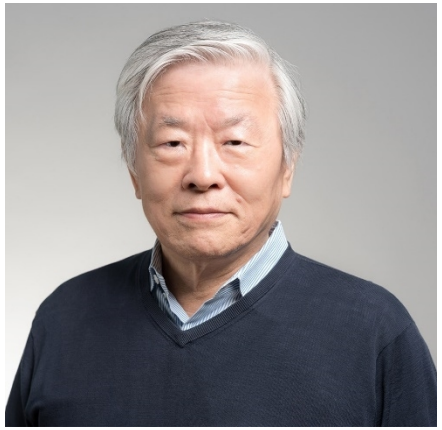
Winner of the

1984 Nobel Prize in Physiology or Medicine

ributions to the understanding of the immune



Rearranged Receptors in B and T Cells



Susumu Tonegawa Professor, Nobel Laureate
(1987 Nobel Prize In Physiology or Medicine)
Massachusetts Institute of Technology
Massachusetts, US

Davis MM, Chien YH, Gascoigne NR, Hedrick SM. A murine T cell receptor gene complex: isolation, structure and rearrangement. Immunol Rev 1984;81:235-58.

Kavaler J, Davis MM, Chien Y. Localization of a T-cell receptor diversity -region element. Nature 1984;310:421-3.

Robertson M. Receptor gene rearrangement and ontogeny of T lymphocytes. Nature 1984;311:305-6.

Royer HD, Acuto O, Fabbi M, et al. Genes encoding the Ti beta subunit of the antigen/MHC receptor undergo rearrangement during intrathymic ontogeny prior to surface T3-Ti expression. Cell 1984;39:261-6.

Siu G, Kronenberg M, Strauss E, Haars R, Mak TW, Hood L. The structure, rearrangement and expression of D beta gene segments of the murine T-cell antigen receptor. Nature 1984;311:344-50.

Hayday AC, Saito H, Gillies SD, et al. Structure, organization, and somatic rearrangement of T cell gamma genes. Cell 1985;40:259-69.

Lefranc MP, Rabbitts TH. Two tandemly organized human genes encoding the T-cell gamma constant-region sequences show multiple rearrangement in different T-cell types. Nature 1985;316:464-6.

The Immunologic Big Bang

Pillars of Immunology

The Journal of Immunology

A Convergent Immunological Holy Trinity of Adaptive Immunity in Lampreys: Discovery of the Variable Lymphocyte Receptors

Martin F. Flajnik

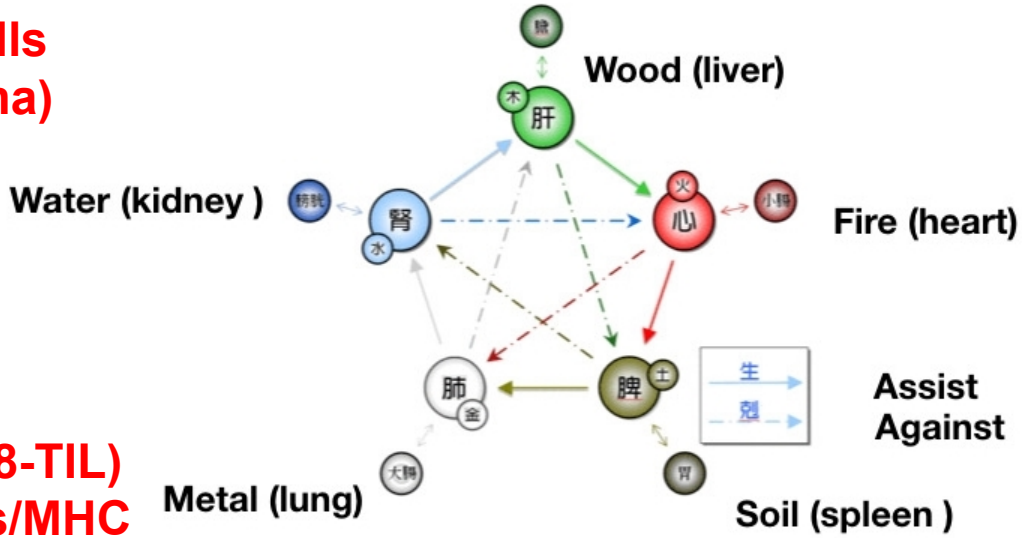
doi: 10.4049/jimmunol.1800965
J Immunol 2018; 201:1331-1335

Zeev Pancer and Max Cooper With a Larval Lamprey at UAB

>500 Million Years of Adaptive Immunity-Wu Xing
The Immunologic Big Bang

NK Cells (1980-LAK)-Stress Ligands/MHC$^{-/-}$

Antibody-B cells
(1986-Melanoma)
Shape/FcR



NKT Cells (2009)
Lipids/CD1

αβ T cells (1988-TIL)
Linear Peptides/MHC

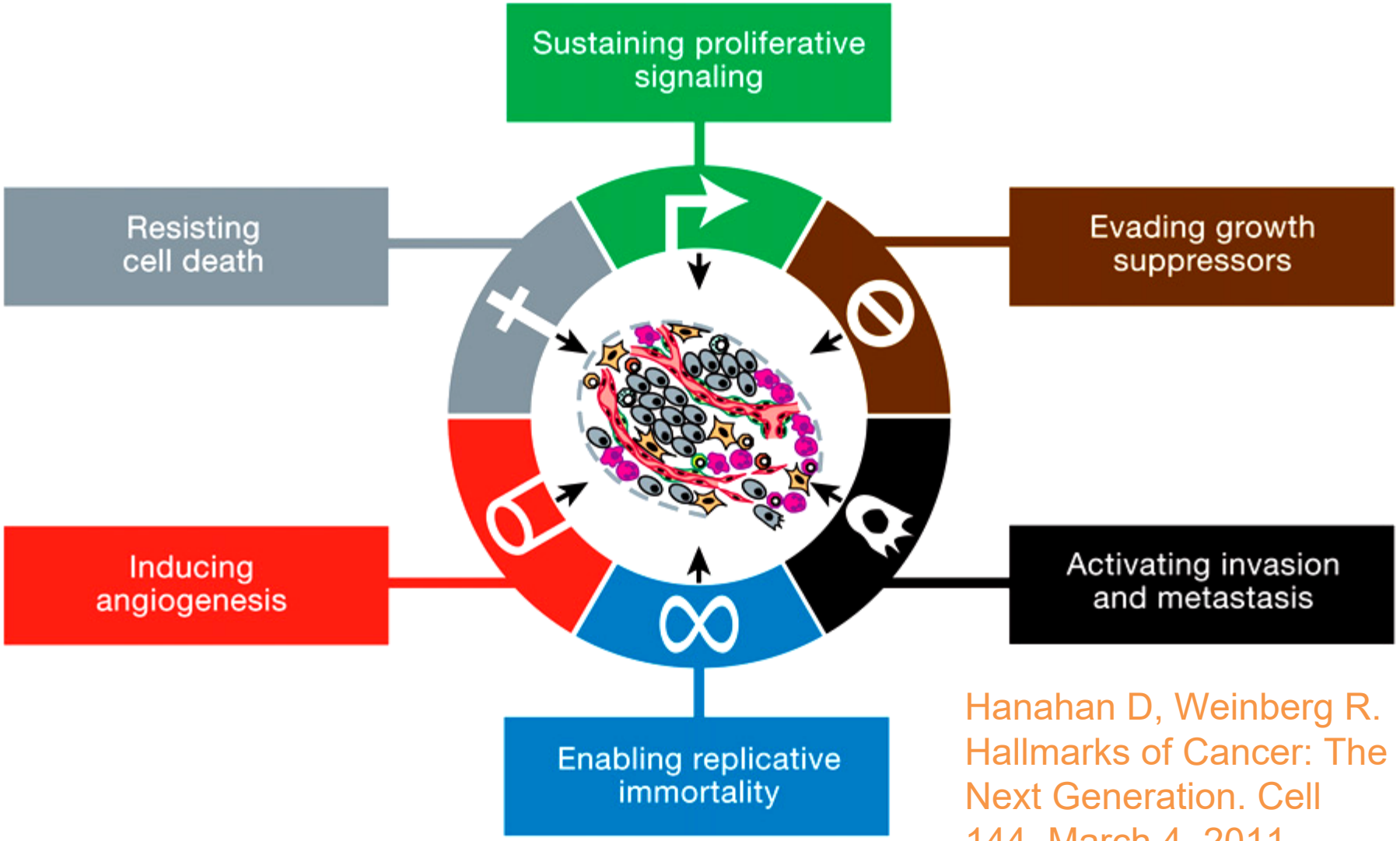
γδ T cells (2007)
Metabolites

"Wǔ zhǒng liúxíng zhī qì" (五種流行之氣) or "the five types of chi dominating at different times".

The Hellström Paradox

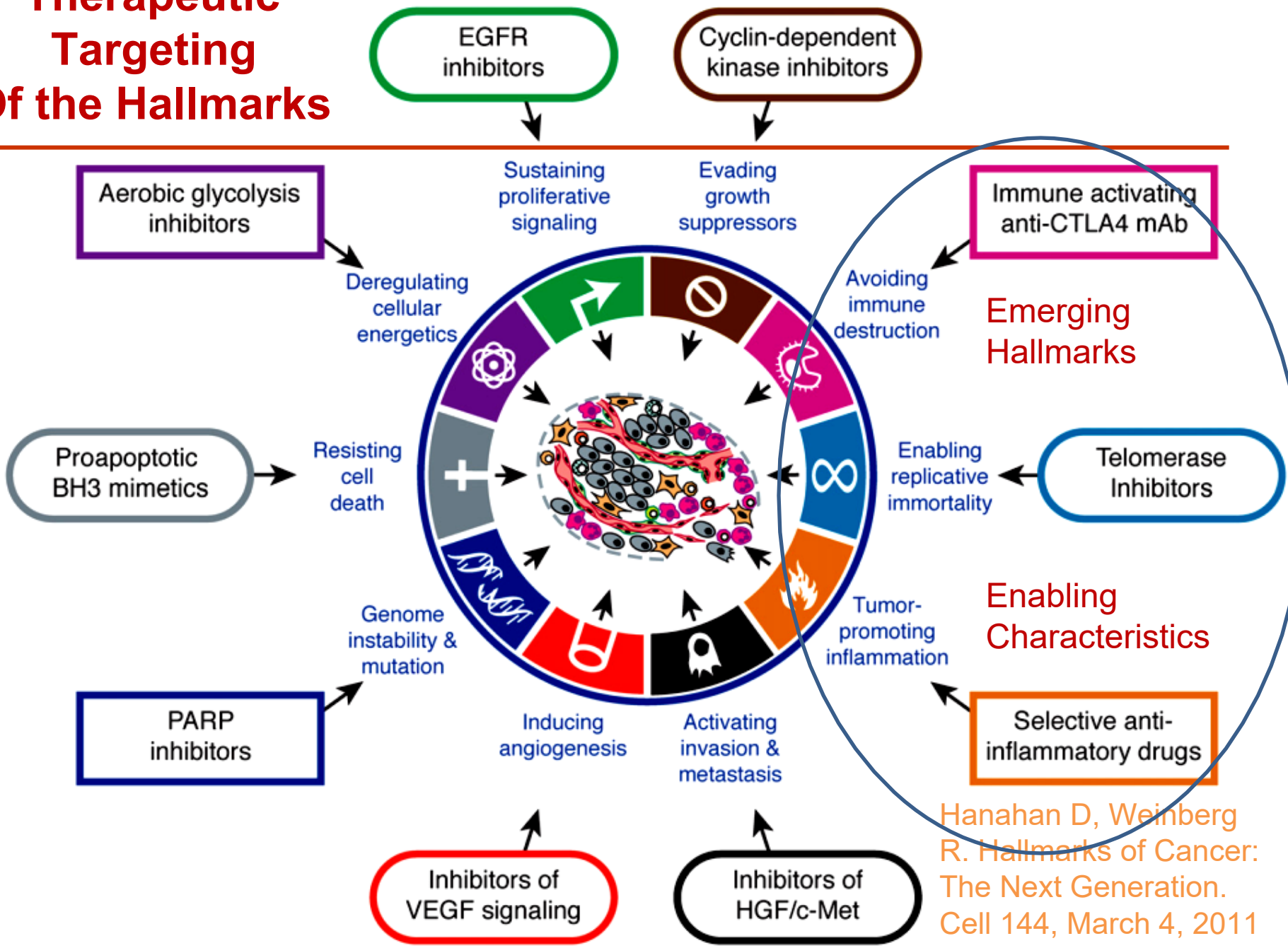
- A paradox lies at the heart of cancer.
- Coursing through many tumors are legions of immune cells, including the T cells that should be fighting the cancer.
- Yet these T cells are typically dysfunctional — they stop working and let the tumor grow with abandon.
- Scientists have a name for this conundrum: the Hellström paradox, after Ingegerd and Karl Hellström, the immunologists who first drew attention to it more than 50 years ago.
- Selective Localization of Radiolabeled Immune Lymphocytes into Syngeneic Tumors. J. J. Mulé, F. R. Jones, I. Hellström, K. E. Hellström. The Journal of Immunology August 1, 1979, 123 (2) 600-

Original Hallmarks of Cancer



Hanahan D, Weinberg R. Hallmarks of Cancer: The Next Generation. Cell 144, March 4, 2011

Therapeutic Targeting Of the Hallmarks



Hanahan D, Weinberg R. Hallmarks of Cancer: The Next Generation. Cell 144, March 4, 2011

The Beginning of Molecular Therapeutics - 1978

PEOPLE.COM • ARCHIVE

Will Interferon Kill Cancer? Finnish Dr. Kari Cantell Is Helping the World Find Out

But Cantell and the Finnish Red Cross, now producing 250 billion units (5,285 quarts) a year, have provided the great bulk of pure interferon used for clinical studies on humans, including a $2 million batch bought last year by the American Cancer Society. “Production is the bottleneck,” says Cantell, who finds it “stupid and irritating” that until recently nobody else has tried to produce the substance in large-scale volume.

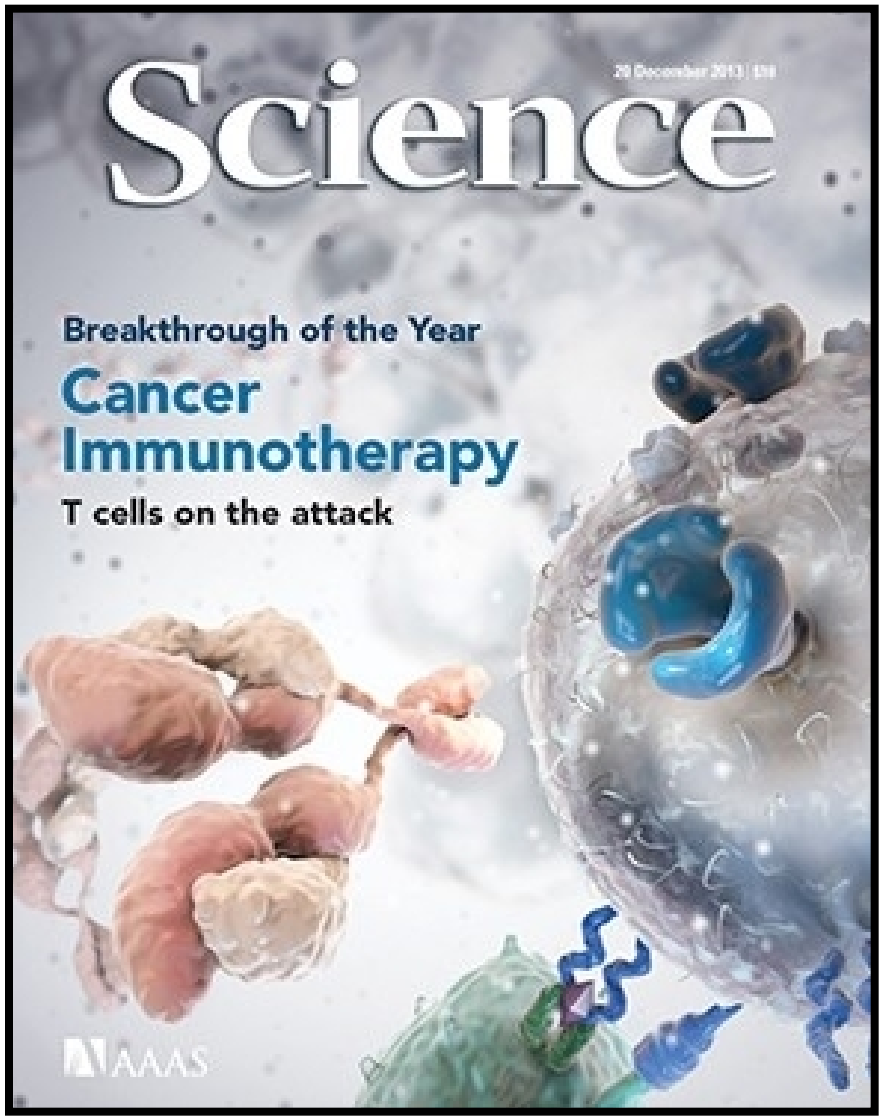
History of SITC

- 1980-1984 NCI Frederick Biologic Response Modifiers (nonspecific immunotherapies) - Journal of Biologic Response Modifiers (1982); Society for Biologic Therapy (1984) - SBT
- 1985 Cytokine Therapeutics – 1st Annual Meeting of SBT (1986) in Williamsburg
- 1990's Antibody (Her2, CD20, VEGF, etc.) Therapeutics – First Primer on Tumor Immunology (1998, Pittsburgh)
- 2000's Cancer Vaccines - iSBTc (2002); SITC (2010)
- 2010's Cell Therapies (TIL, CART, DC, NK/NKT, etc.) - Journal for ImmunoTherapy of Cancer (2013)
- 2015 Checkpoint Inhibitors; Oncolytic Viruses/Cytokines
- 2021+ The Future Just Ain't What it Used to be (Yogi Berra) – 1st Cancer Immunotherapy Winter School (2019); 1st SCION Workshop (2022)

The First Winter Course SITC 2019 Mesa AZ

The First SCION 2022

Cancer Immunotherapy



2013

2014

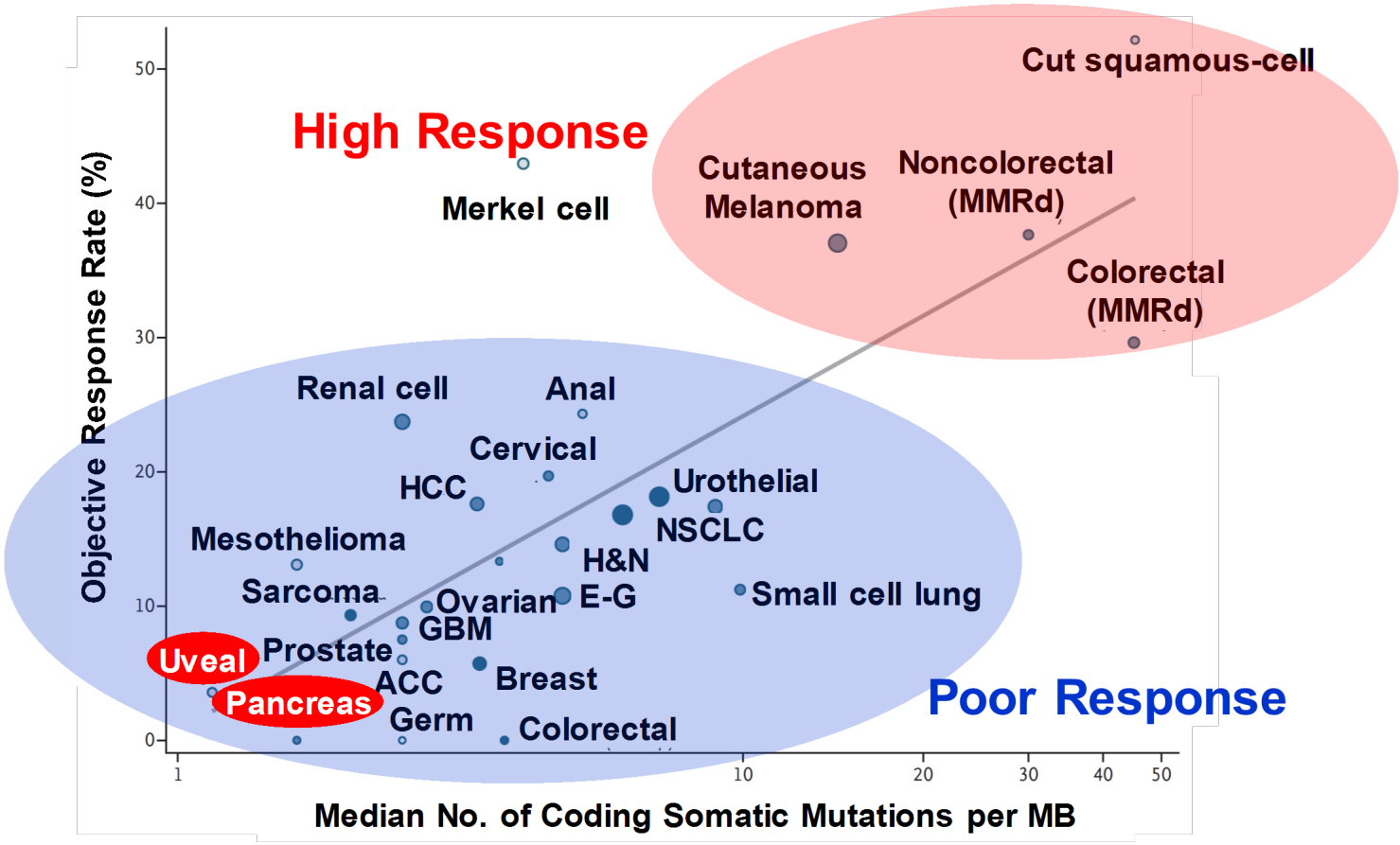
James Allison
Immunotherapy
Nobel Prize 2018

Yoshinori Ohsumi
Autophagy
Nobel Prize 2016

Tasuku Honjo
Immunotherapy
Nobel Prize 2018

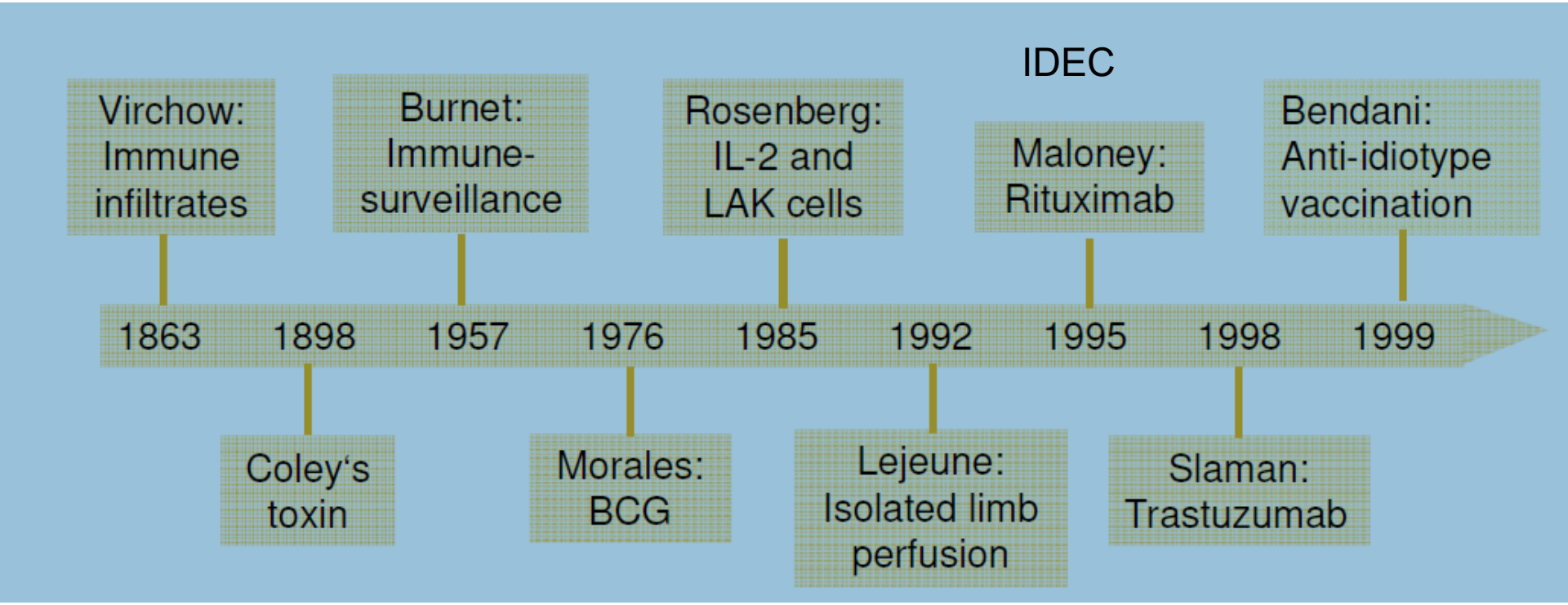
Dana-Farber scores legal win on immunotherapy patents likely worth billions: 6 things to know Alia Paavola, **May 20th, 2019**
In a major win for Boston-based Dana-Farber Cancer Institute, a federal court ruled that one of its researchers should be listed as an inventor on six patents that are believed to be worth billions of dollars.

The Critical Need for More Effective Immunotherapies for Solid Tumors



Adapted from NEJM Dec 21 2017

Before There were Checkpoints



https://oncologypro.esmo.org/content/download/85243/1583430/file/ESMO-Preceptorship-Immuno-Oncology-Siena-July-2016-STAHEL.pdf

Coley's Toxins, 1893

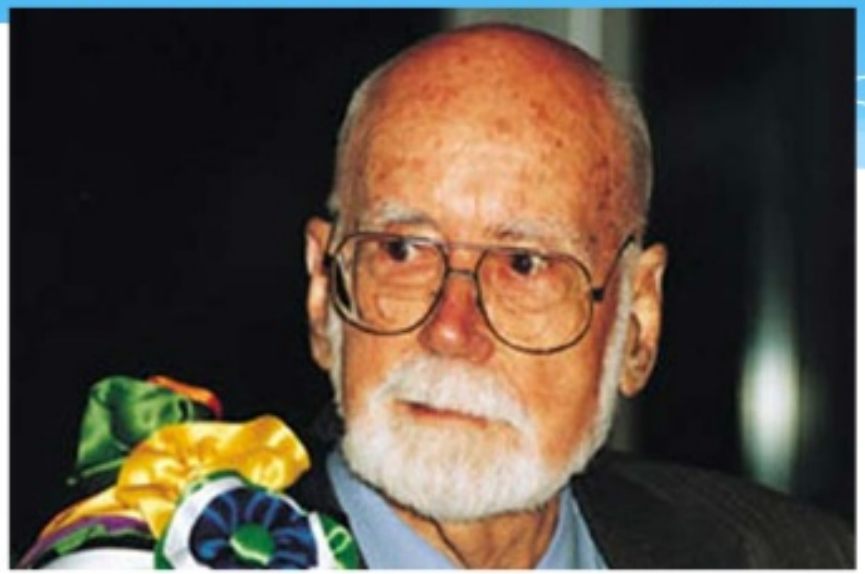
Fig. 2. Patient as he first appeared to Coley in 1891, 7 years after the accidental erysipelas-induced regression of inoperable sarcoma (Coley, 1893a).

W. Busch. Einfluß von Erysipel. Berliner Klin Wschr 1866. 3: 245–246.

Complete remission of a sarcoma in a patient after 2 episodes of erysipelas caused by streptococcus pyogenes

William Coley, 1893

E. Donnall Thomas
The Nobel Prize, 1990



first succsessful HSCT in treatment of acute leukemias

Thomas ED, Lochte HL, Lu WC, Ferrebee JW. Intravenous infusion of bone marrow in patients receiving radiation and chemotherapy. N. Engl. J. Med. 1957; 257: 491

Cooperstown, NY Mary Imogene Bassett Hospital

First 40 Yrs of Cancer Immunotherapy

Steven A. Rosenberg

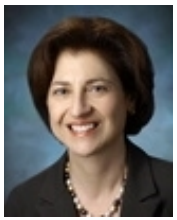
IL-2 Activate NK/LAK Cells Infused

1980

Michael T. Lotze

IL-2 Given to Patients- The First Checkpoint Inhibitor

1985



Suzanne Topalian

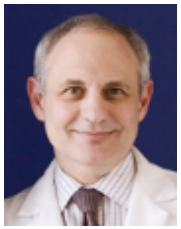
Tumor Infiltrating Lymphocytes (TILs) And gene therapy (PD-1/PD-L1)

1987

Yutaka Kawakami

IL-4 given to patients; MART-1/Melan A

1989



Michael Atkins

IL-12 given to patients

1995

Hideaki Tahara

IL-12 Gene Therapy

1996

Olja Finn

Dendritic Cells Given To Patients

1997

Daolin Tang

HMGB1 as the Ur-Cytokine; regulates autophagy and apoptosis

2017

T-cells & TCGF

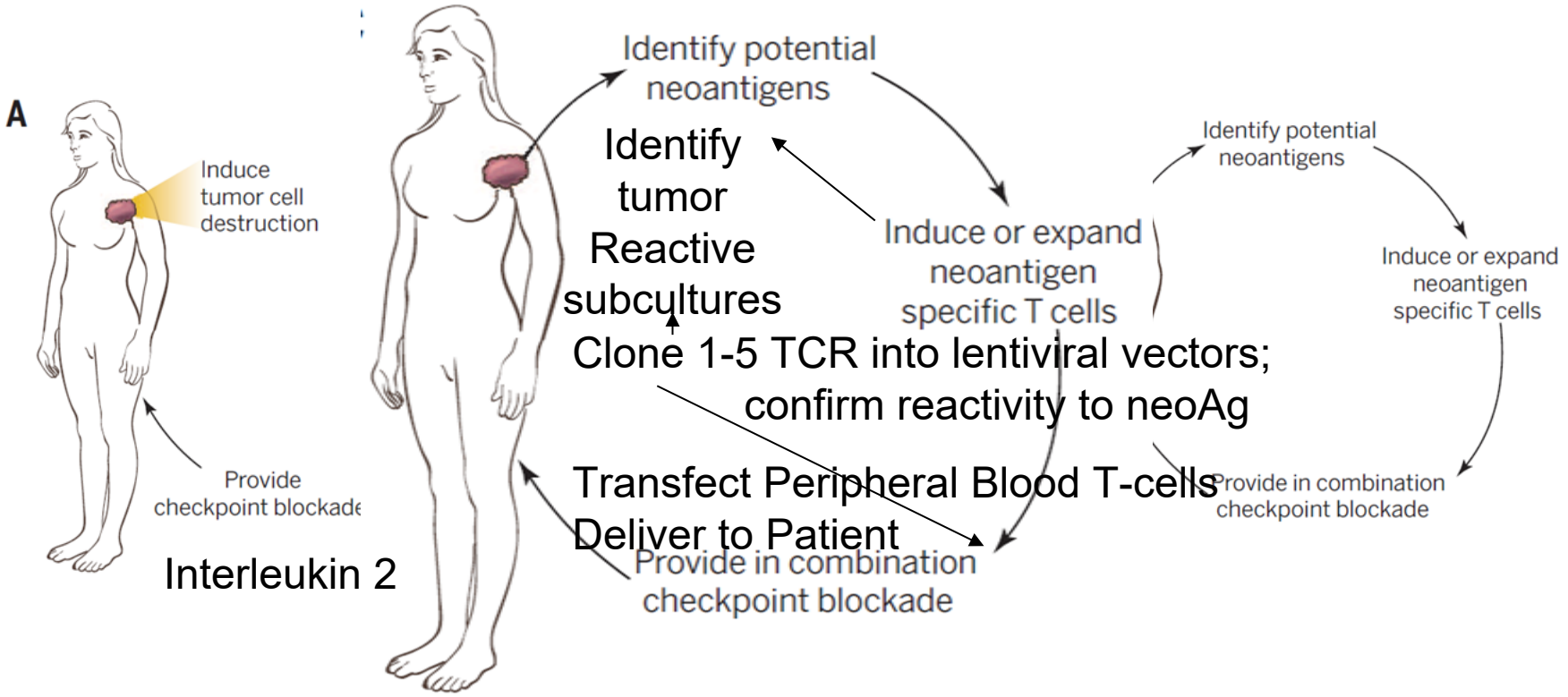
Tumor Vaccines

Innate Immunity Checkpoints

Pubmed: > 387,294 articles - Tumor Immunology 2.19.21

2014 PD-1

Unpacking Current Immunotherapies to Drive T-cell Responses



SCIENCE sciencemag.org 3 APRIL 20, 2015• VOL 348 ISSUE 623

Cytokines are medically relevant endogenous small (~15kDa) proteins

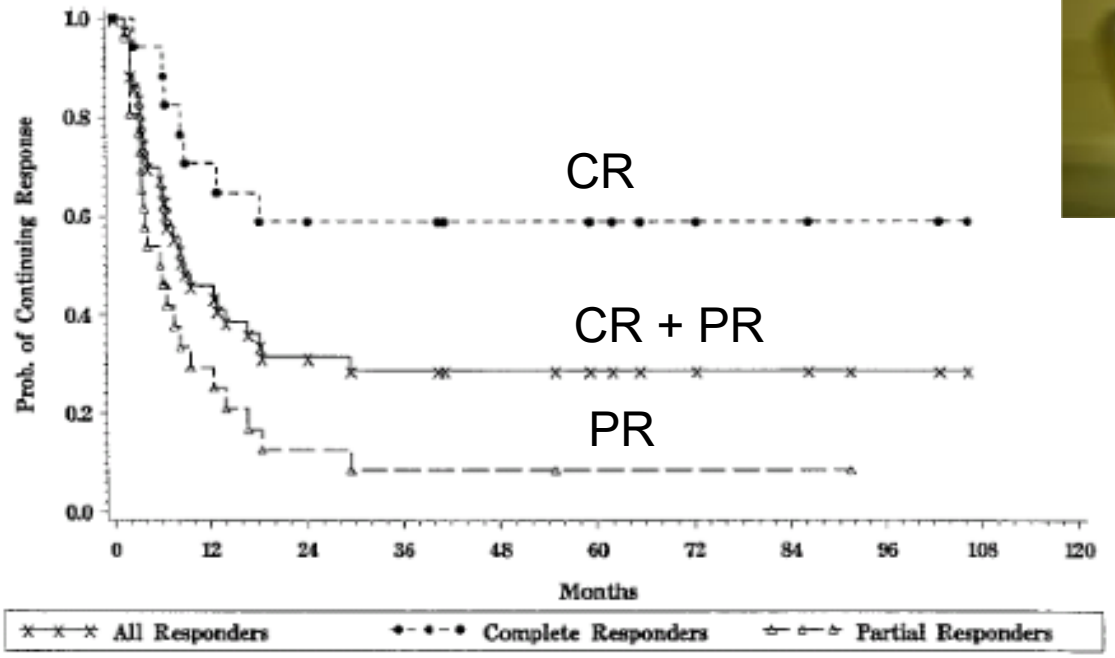
Cytokine-based therapies in human disease

Cytokine	Brand name	Status	Indication	Year of 1st FDA Approval
IL-2	Proleukin	Approved	Cancer	1992
IL-11	Neumega	Approved	Thrombocytopenia	1994
EPO	Epogen	Approved	Anemia	1989
GCSF	Neupogen	Approved	Myelosuppression from chemo	1991
GM-CSF	Leukine	Approved	Myelosuppression from chemo	1991
IFN-α	Intron-A	Approved	Hepatitis, Cancer	1991
IFN-β	Betaseron	Approved	Multiple sclerosis	1993
IFN-γ	Actimmune	Approved	Granulomatosis	1990
IL-7		Clin dev	Cancer, anti-viral	
IL-10		Clin Dev	Cancer, anti-inflammatory	
IL-12		Clin dev	Cancer, anti-viral	
IL-15		Clin dev	Cancer	
IL-21		Clin dev	Cancer	

Baldo, 2018
Drug Safety

Dupont 1983
Taniguchi, T 1983
Roche 9/84
Cetus-PEG
Chiron 1990
Novartis
Prometheus
Nestle
Clinigen

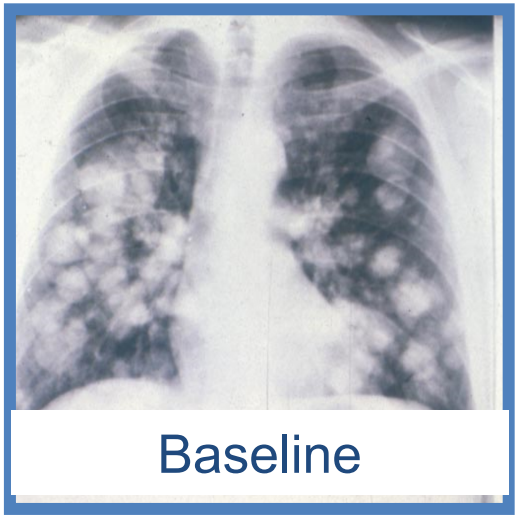
Proof of Principle:
Deep responses produce remissions



Atkins, Lotze et al. J Clin Oncol. 1999

High Dose IL-2 Immunotherapy

- Approved in patients with melanoma and kidney cancer.
- Significant ‘toxicity’.
- Associated with ‘cytokine storm’.
- iNOS blockers, sTNF-R or IL -1Ra have yielded limited reduction in side effects.
- IL-2 treatment is associated with a ‘systemic autophagic syndrome’ and temporally limited tissue dysfunction.


Baseline


After Treatment

AR. Chavez, X Liang, MT Lotze.
Ann. N.Y.Acad.Sci.1182:14-27 (2009)

Cytokine Working Group
CWG: The Abbreviated History (SITC 2018)

David McDermott, MD
Beth Israel Deaconess Medical Center
Dana Farber/Harvard Cancer Center
Harvard Medical School

Beth Israel Deaconess Medical Center

HARVARD MEDICAL SCHOOL TEACHING HOSPITAL

NCI Designated Comprehensive Cancer Center

A founding member of Dana-Farber/Harvard Cancer Center

Second Randomized Treatment with Interleukin 2 as Immunotherapy for Cancer

VOLUME 23 · N

JOURNAL OF

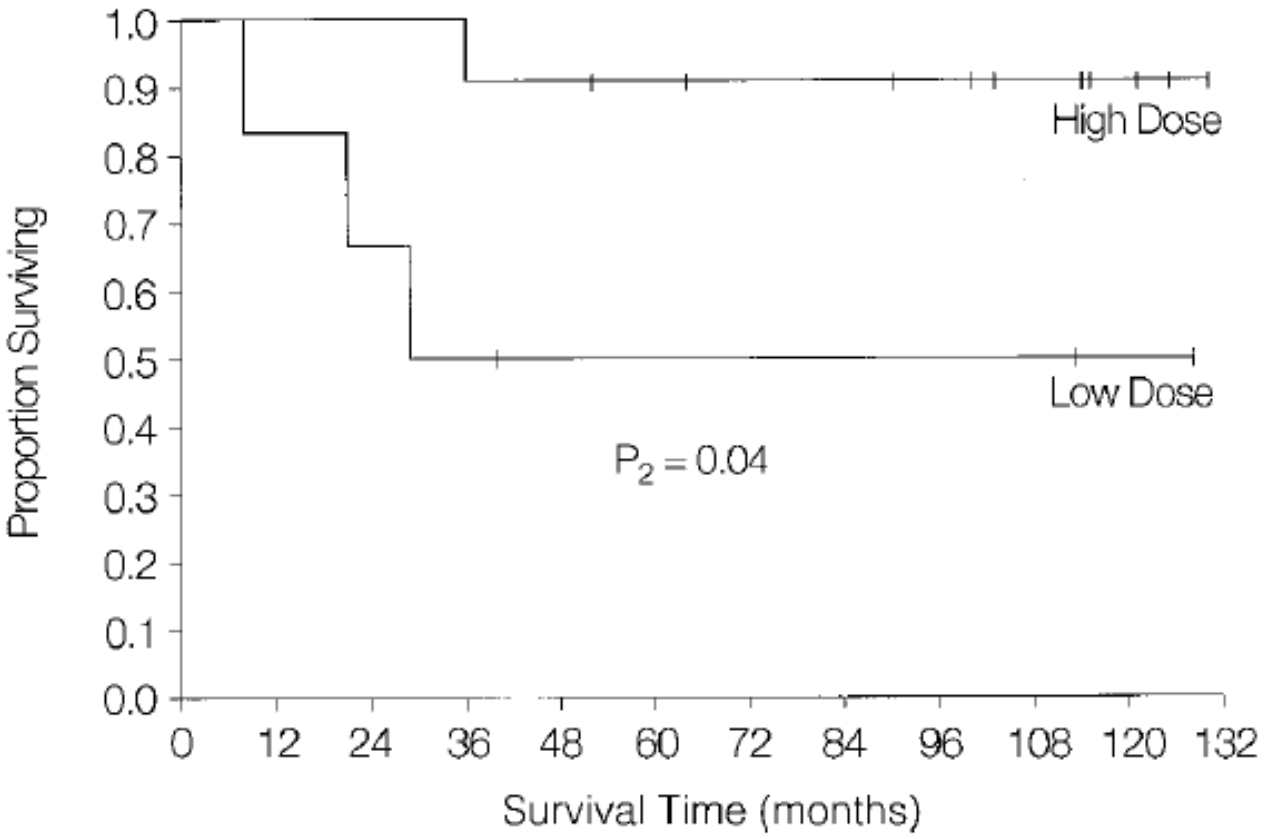


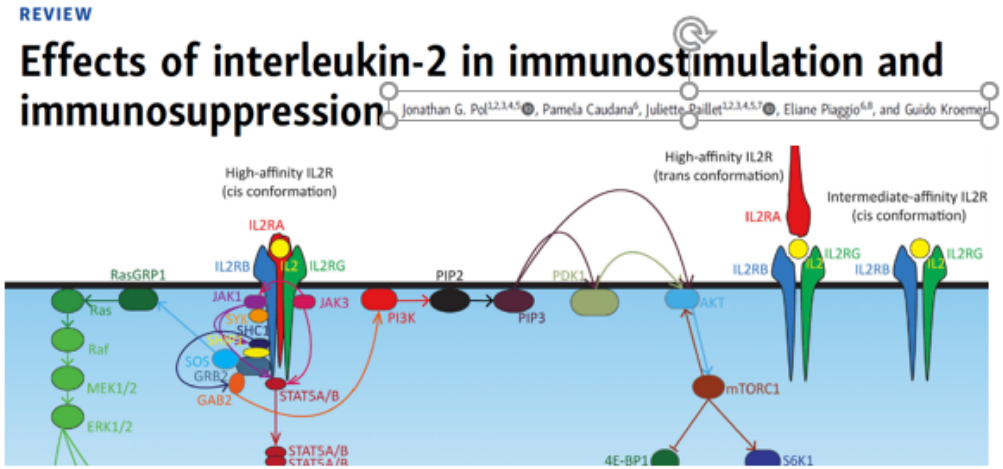
Fig 2. Survival of patients completely responding to high-dose versus low-dose intravenous interleukin-2.

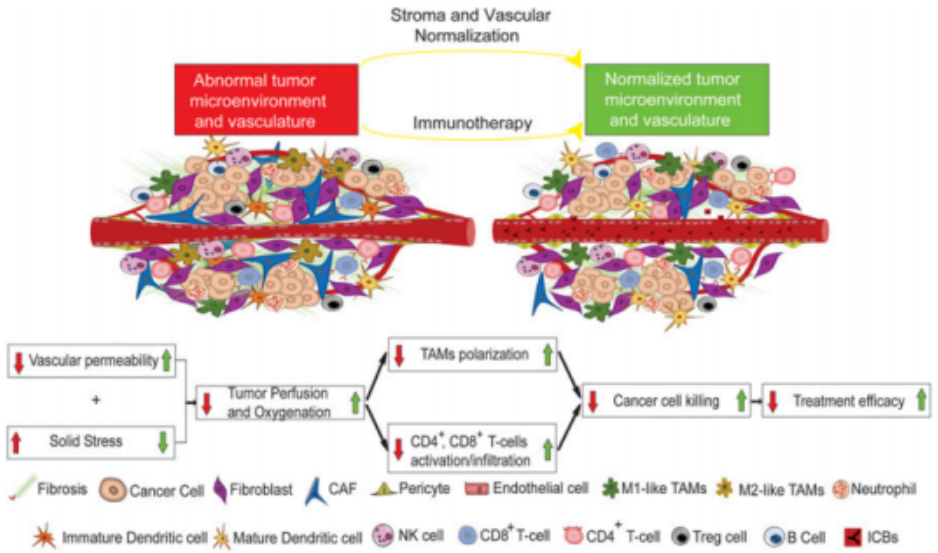
J Clin Oncol 2005; 23:133-

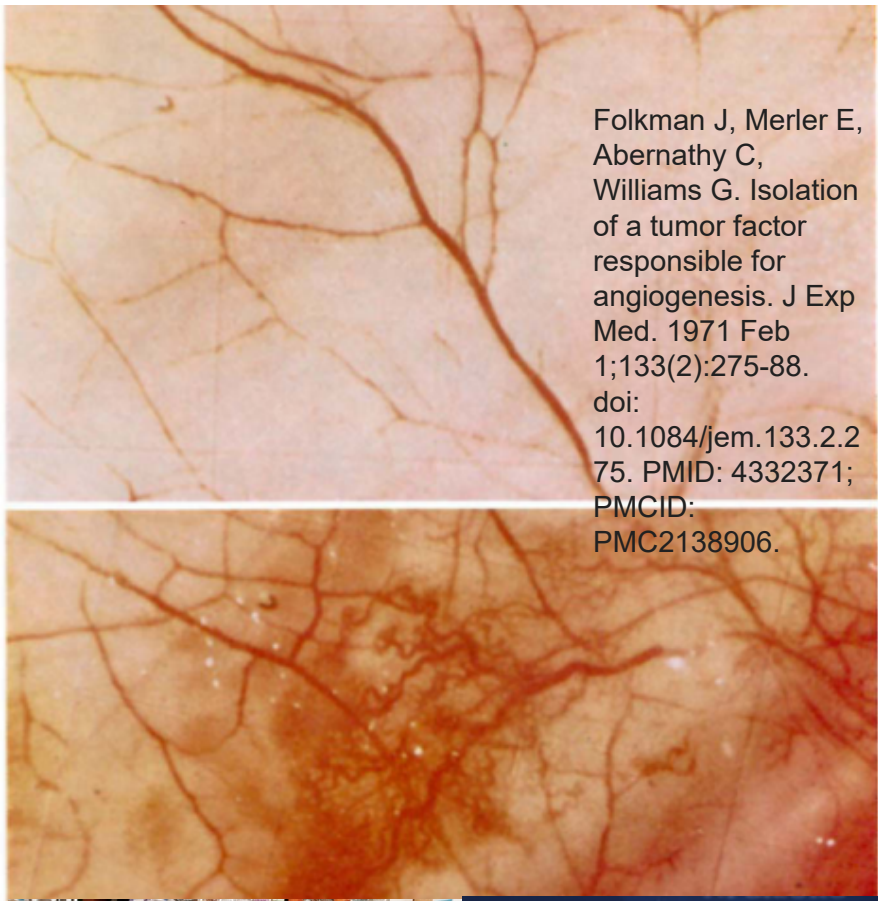
J Clin Oncol 21:3127-3132. © 2003 by American Society of Clinical Oncology.

Combining microenvironment normalization strategies to improve cancer immunotherapy – Rakesh Jain PNAS February 18, 2020 117:3728–3737 www.pnas.org/cgi/doi/10.1073/pnas.1919764117

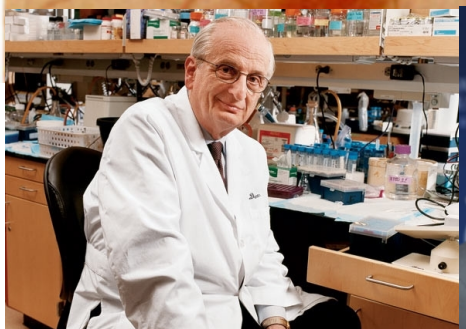
Pol JG, Caudana P, Paillet J, Piaggio E, Kroemer G. Effects of interleukin-2 in immunostimulation and immunosuppression. J Exp Med. 2020 Jan 6;217(1):e20191247. doi: 10.1084/jem.20191247. PMID: 31611250; PMCID: PMC7037245.







Folkman J, Merler E, Abernathy C, Williams G. Isolation of a tumor factor responsible for angiogenesis. J Exp Med. 1971 Feb 1;133(2):275-88. doi: 10.1084/jem.133.2.275. PMID: 4332371; PMCID: PMC2138906.

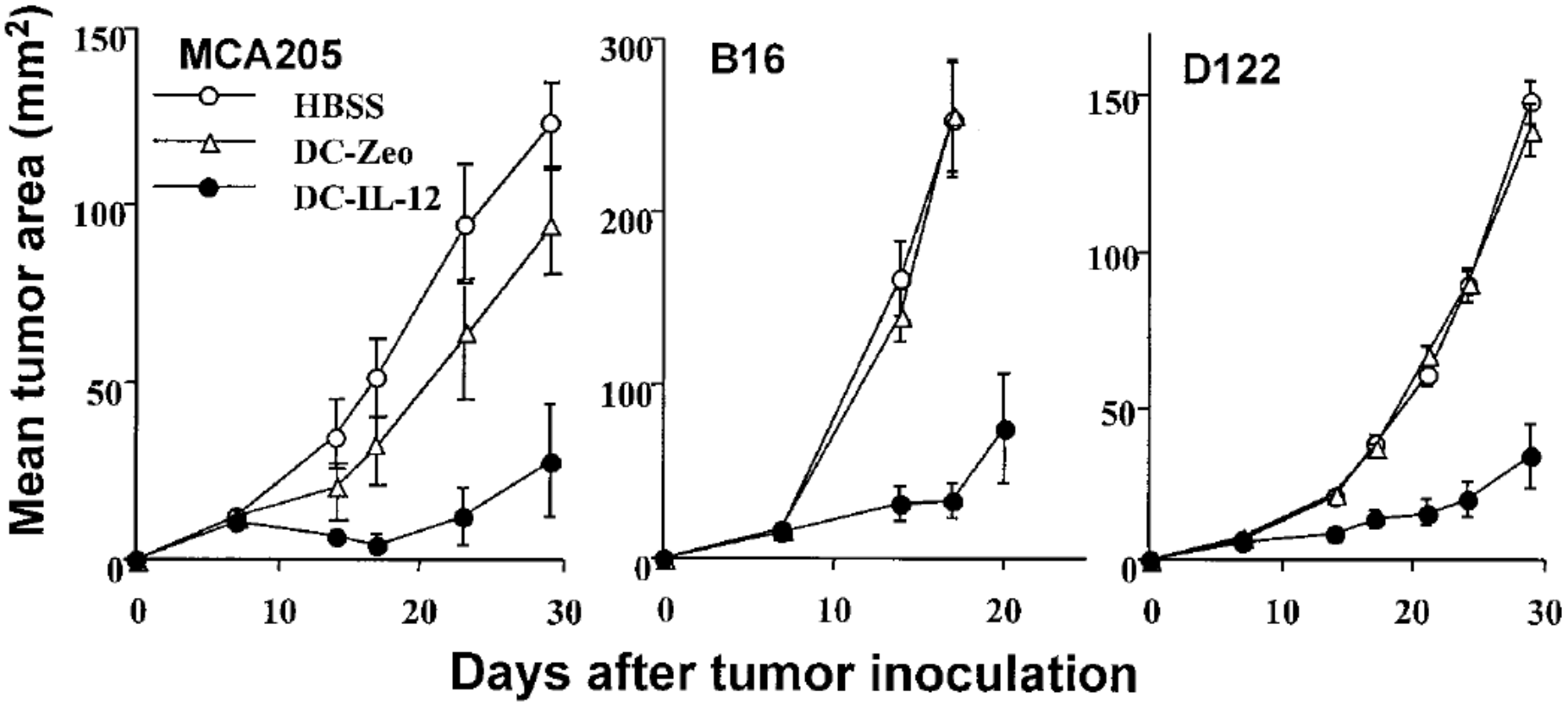


[CANCER RESEARCH 59, 4035–4041, August 15, 1999]

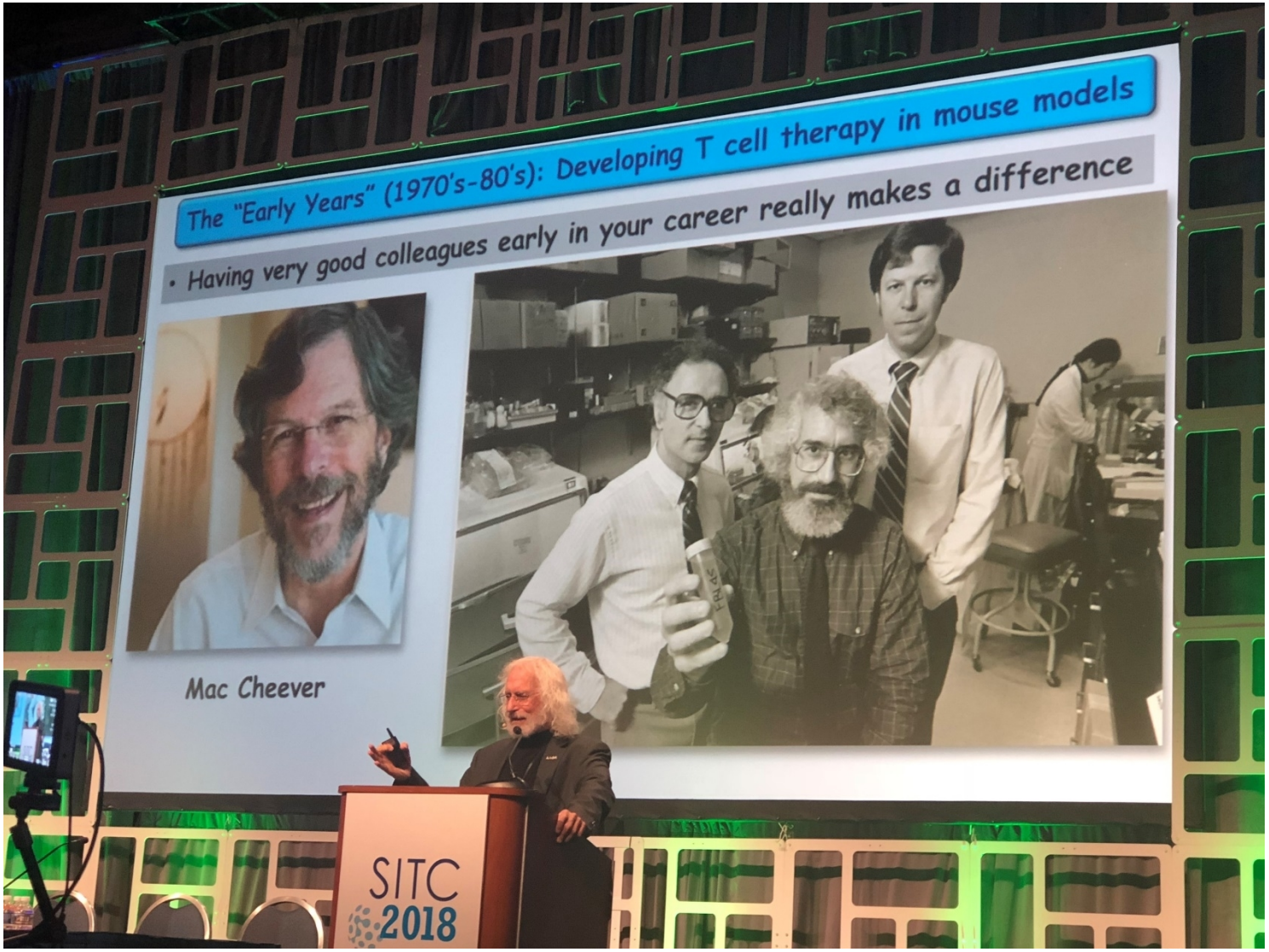
Induction of Systemic and Therapeutic Antitumor Immunity Using Intratumoral Injection of Dendritic Cells Genetically Modified to Express Interleukin 12[1]

Yasuhiko Nishioka, Motohiro Hirao, Paul D. Robbins, Michael T. Lotze, and Hideaki Tahara[2]

Departments of Surgery [Y. N., M. H., M. T. L., H. T.] and Molecular Genetics and Biochemistry [Y. N., M. H., P. D. R., M. T. L., H. T.], School of Medicine, University of Pittsburgh Cancer Institute, University of Pittsburgh, Pittsburgh, Pennsylvania 15213

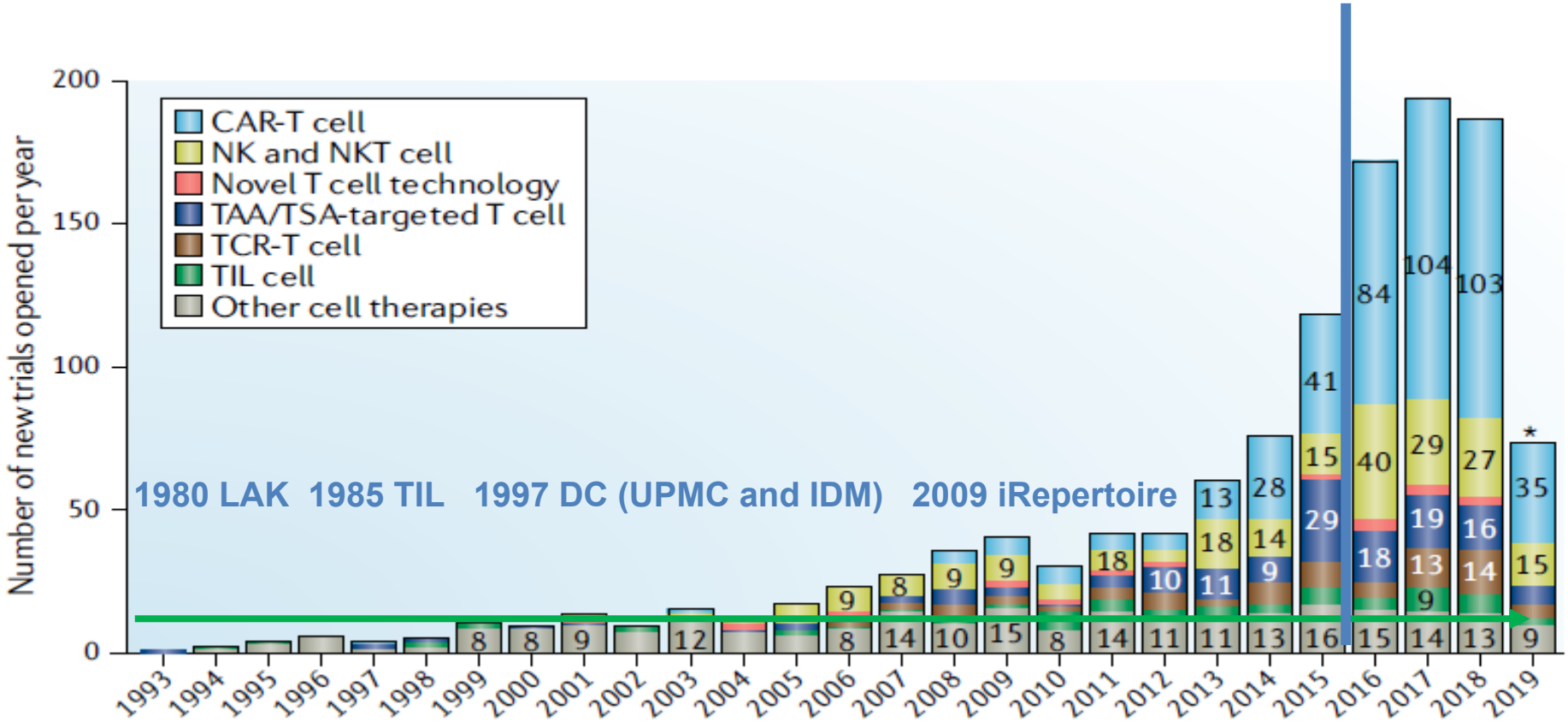


Cheever, Greenberg, Fefer



Growth of Cell Therapy Last 25 Years

IOVANCE
FPI – Reg
2020?




cm
DATE


cm
DATE

Survival of Patients with Metastatic Melanoma Treated with Autologous Tumor Infiltrating Lymphocytes and IL-2

(TBI 1200: n=25)

(TBI 200: n=25)

(NMA: n=43)

(No lymphodepleting regimen: n=86)

Proportion Surviving

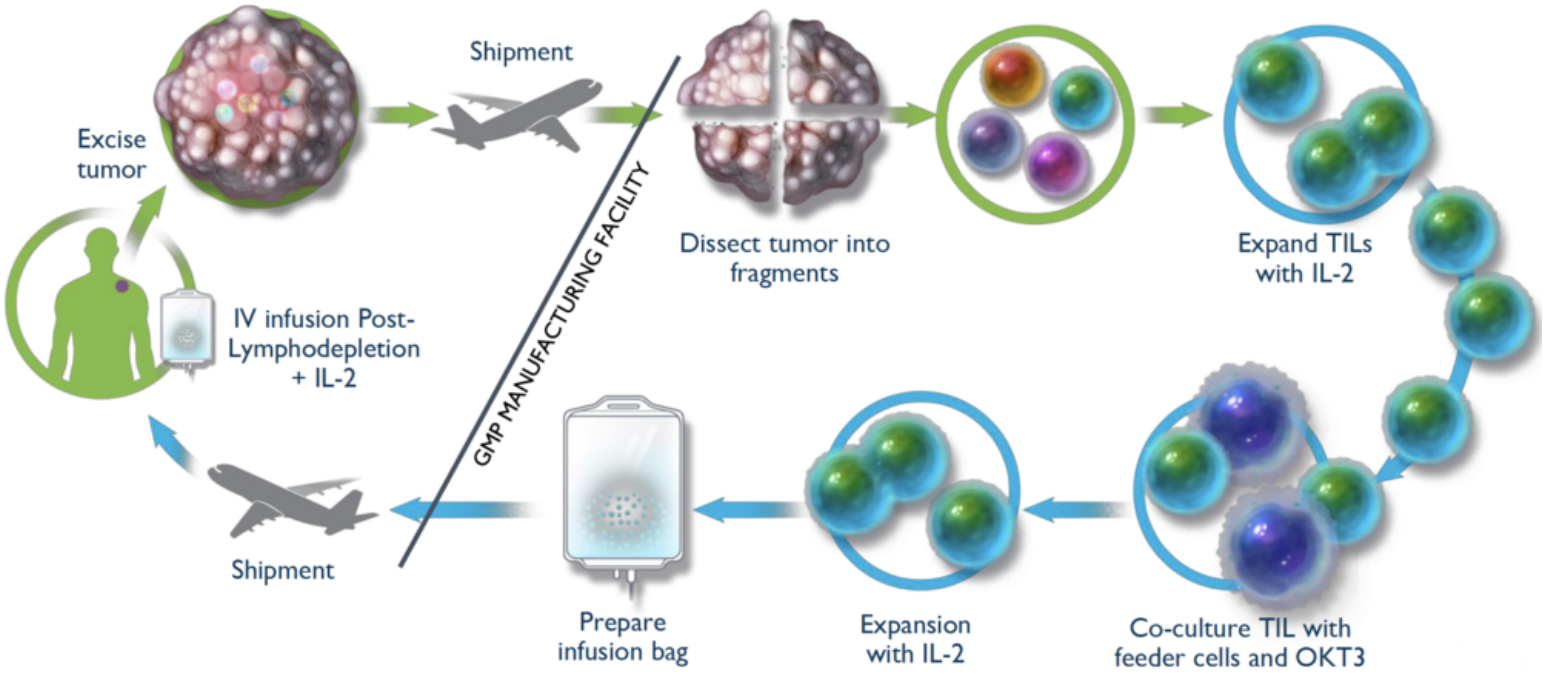
1.0
0.9
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0.0

0 6 12 18 24 30 36 42 48 54 60

Survival Time in Months

8/1/09

Tumor Infiltrating Lymphocyte (TIL) Therapy – Iovance (Instil, Myst, NxACT-Nurix, Achilles…)



Lotze, US Patent 20190083539 2018

FROM THE ANALYST'S COUCH

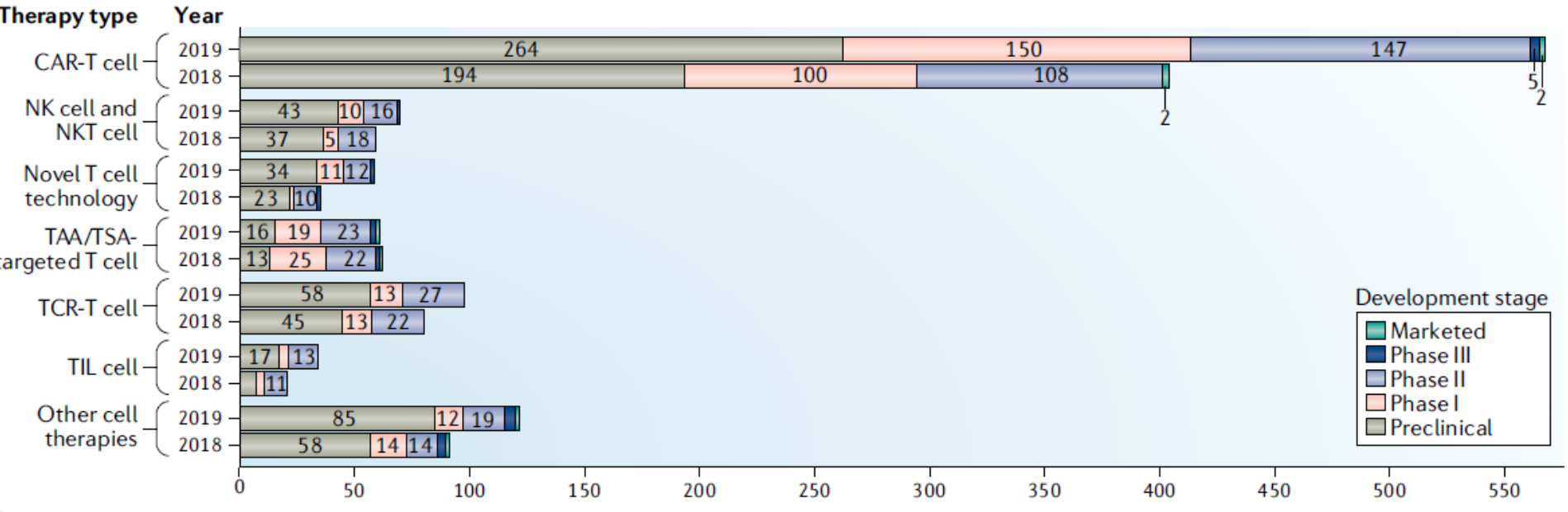
nature reviews drug discovery

The global pipeline of cell therapies for cancer

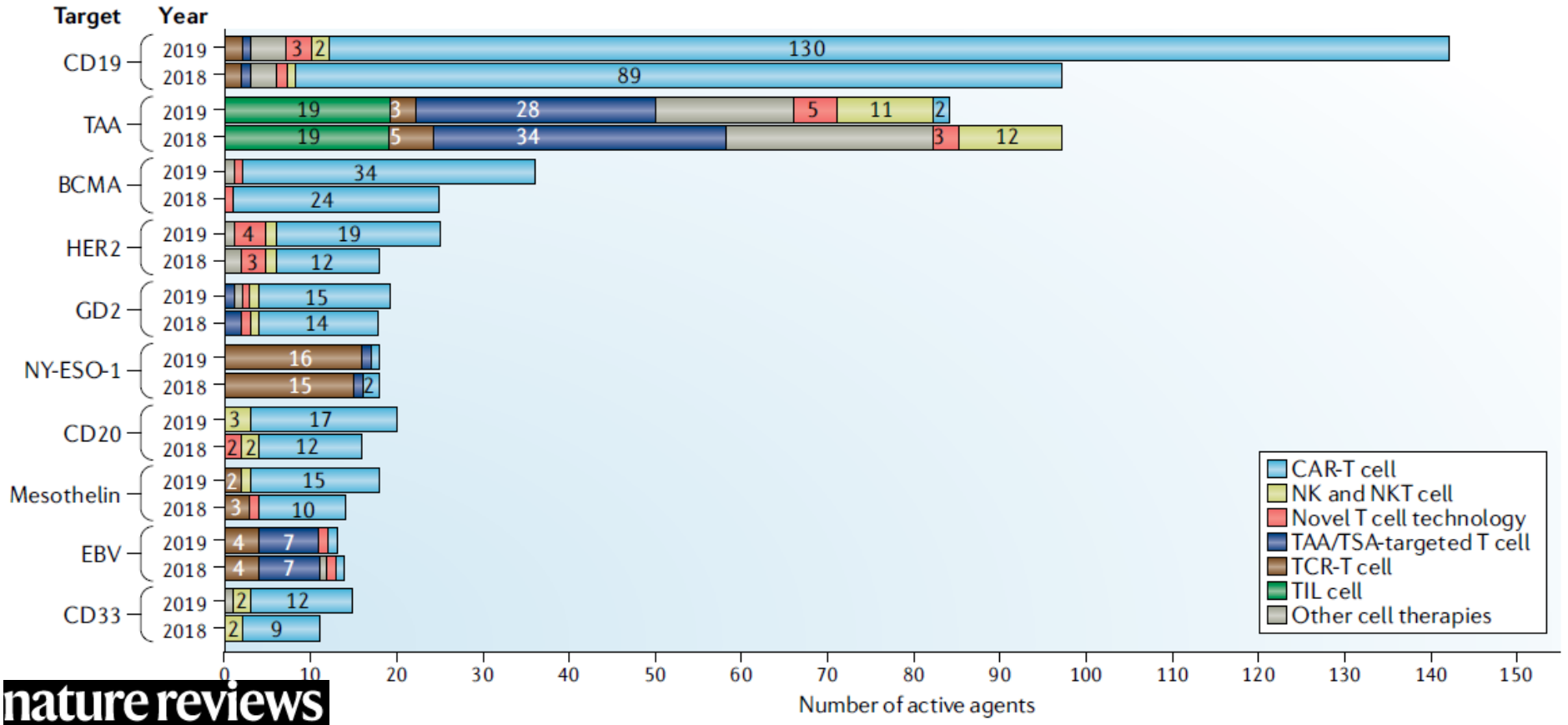
Credit: Natalya Erofeeva/Alamy Stock Photo

Jia Xin Yu, Vanessa M. Hubbard-Lucey and Jun Tang

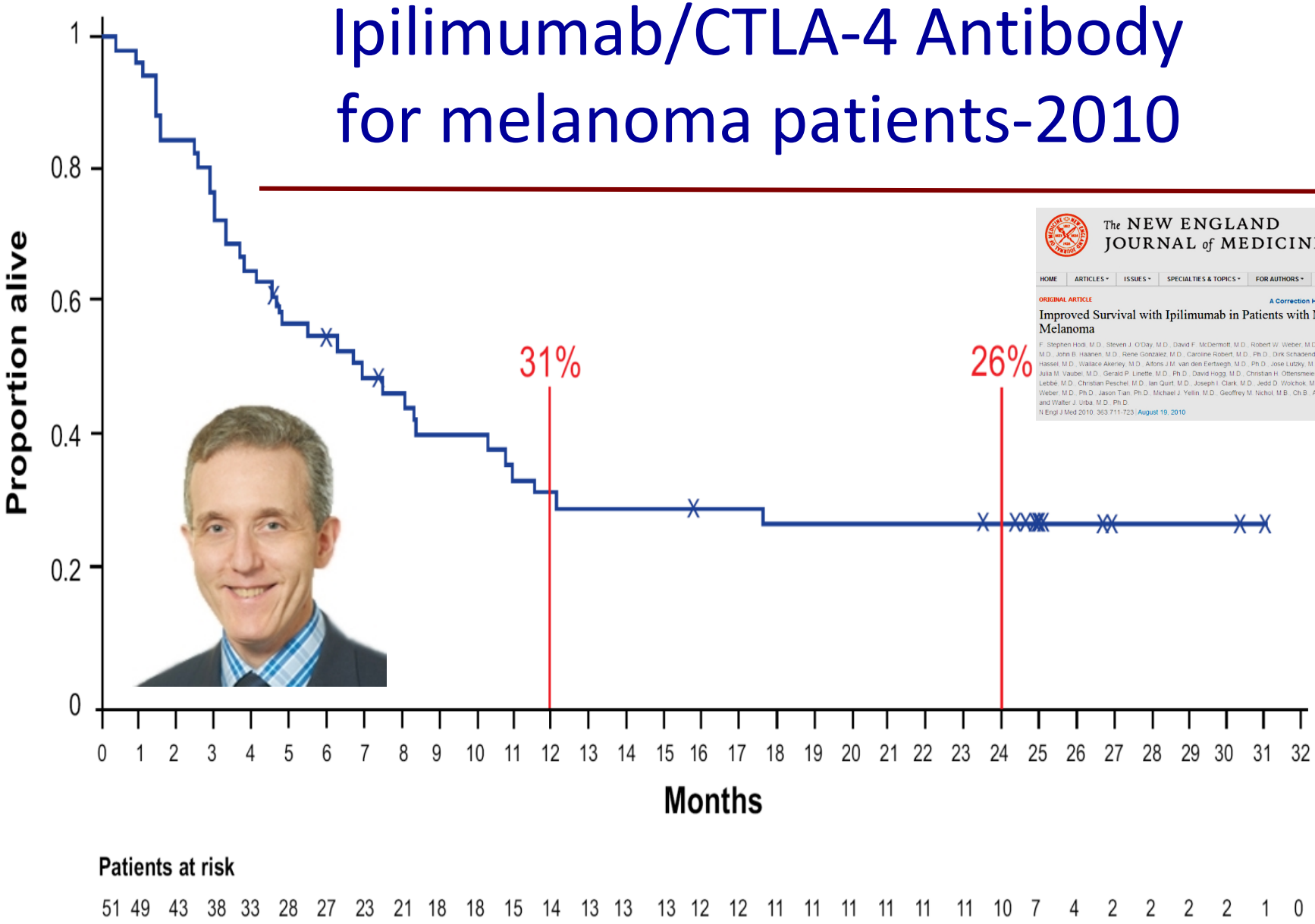
822 | NOVEMBER 2019 | volume 18
www.nature.com/nrd



Molecular Targets for Cell Therapy

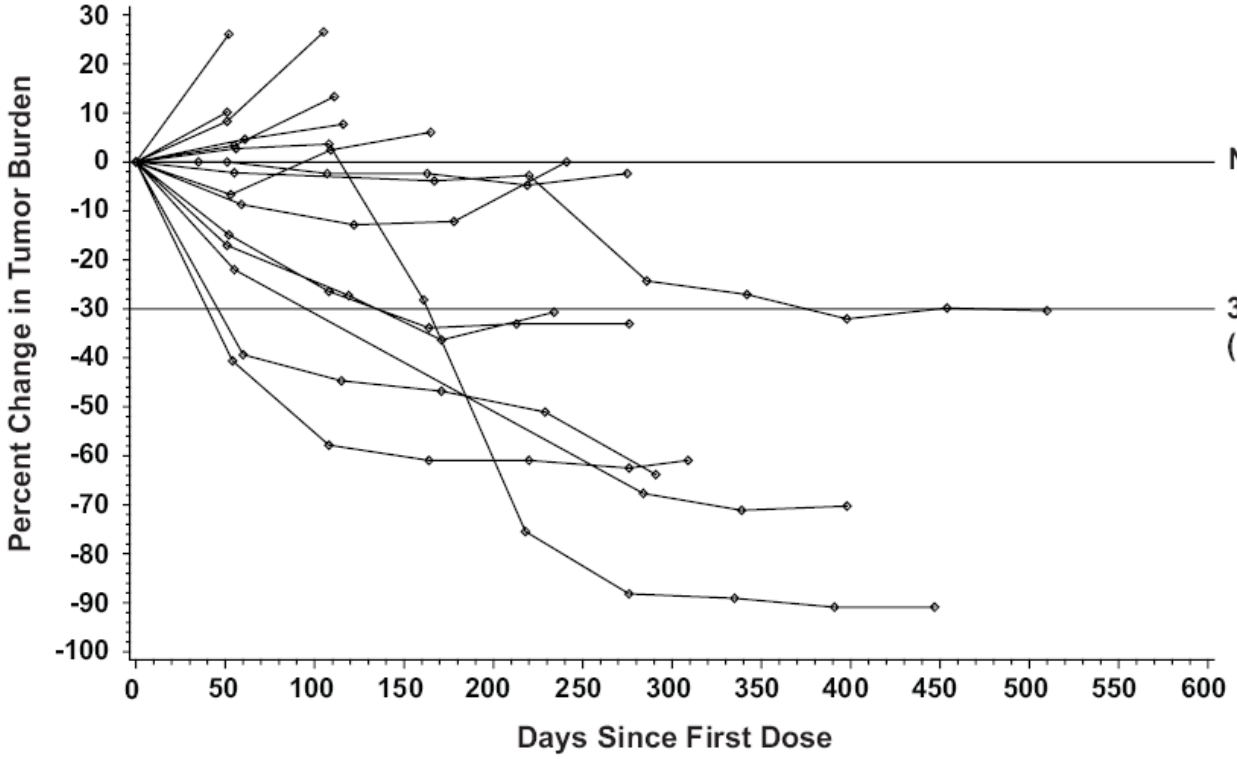


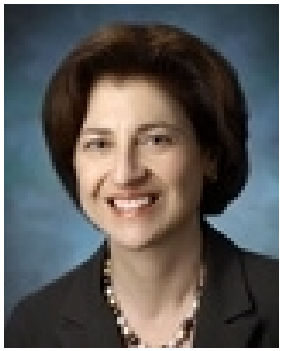
Ipilimumab/CTLA-4 Antibody for melanoma patients-2010



x = censored data

PD1 AB RESULTS: RCC PATIENTS



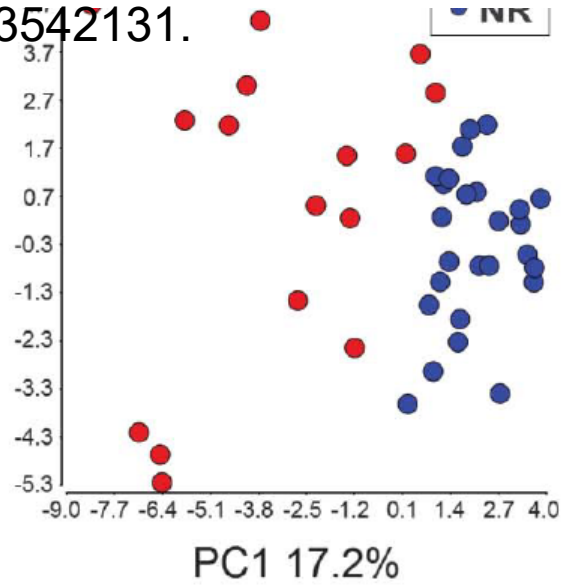


*Patients treated at the 10 mg/kg dose

Immunotherapy Drugs Slow Skin Cancer That Has Spread to the Brain

NYT August 22, 2018

Davar D, Dzutsev AK, McCulloch JA, Rodrigues RR, Chauvin JM, Morrison RM, Deblasio RN, Menna C, Ding Q, Pagliano O, Zidi B, Zhang S, Badger JH, Vetizou M, Cole AM, Fernandes MR, Prescott S, Costa RGF, Balaji AK, Morgun A, Vujkovic-Cvijin I, Wang H, Borhani AA, Schwartz MB, Dubner HM, Ernst SJ, Rose A, Najjar YG, Belkaid Y, Kirkwood JM, Trinchieri G, Zarour HM. Fecal microbiota transplant overcomes resistance to anti-PD-1 therapy in melanoma patients. Science. 2021 Feb 5;371(6529):595-602. doi: 10.1126/science.abf3363. PMID: 33542131.



Operational Taxonomic Units

Merck Pembro Anti-PD1 + *Bifidobacterium longum*