SITC 2019

Gaylord National Hotel
& Convention Center

Nov. 6-10

NATIONAL HARBOR, MARYLAND

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Society for Immunotherapy of Cancer

SITC 2019
Gaylord National Hotel & Convention Center Nov. 6-10
NATIONAL HARBOR, MARYLAND

Cancer vaccines

personalized versus antigen-agnostic approaches

VUmc Medical Oncology
IMMUNOTHERAPY LAB

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Amsterdam UMC
University Medical Centers

SITC 2019
Gaylord National Hotel & Convention Center Nov. 6-10
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Disclosures

I have received consultancy fees from
DCPrime
TILT Biotherapeutics
Macrophage Pharma

I have received research funding from
Idera Pharmaceuticals
Macrophage Pharma

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Amsterdam UMC
University Medical Centers

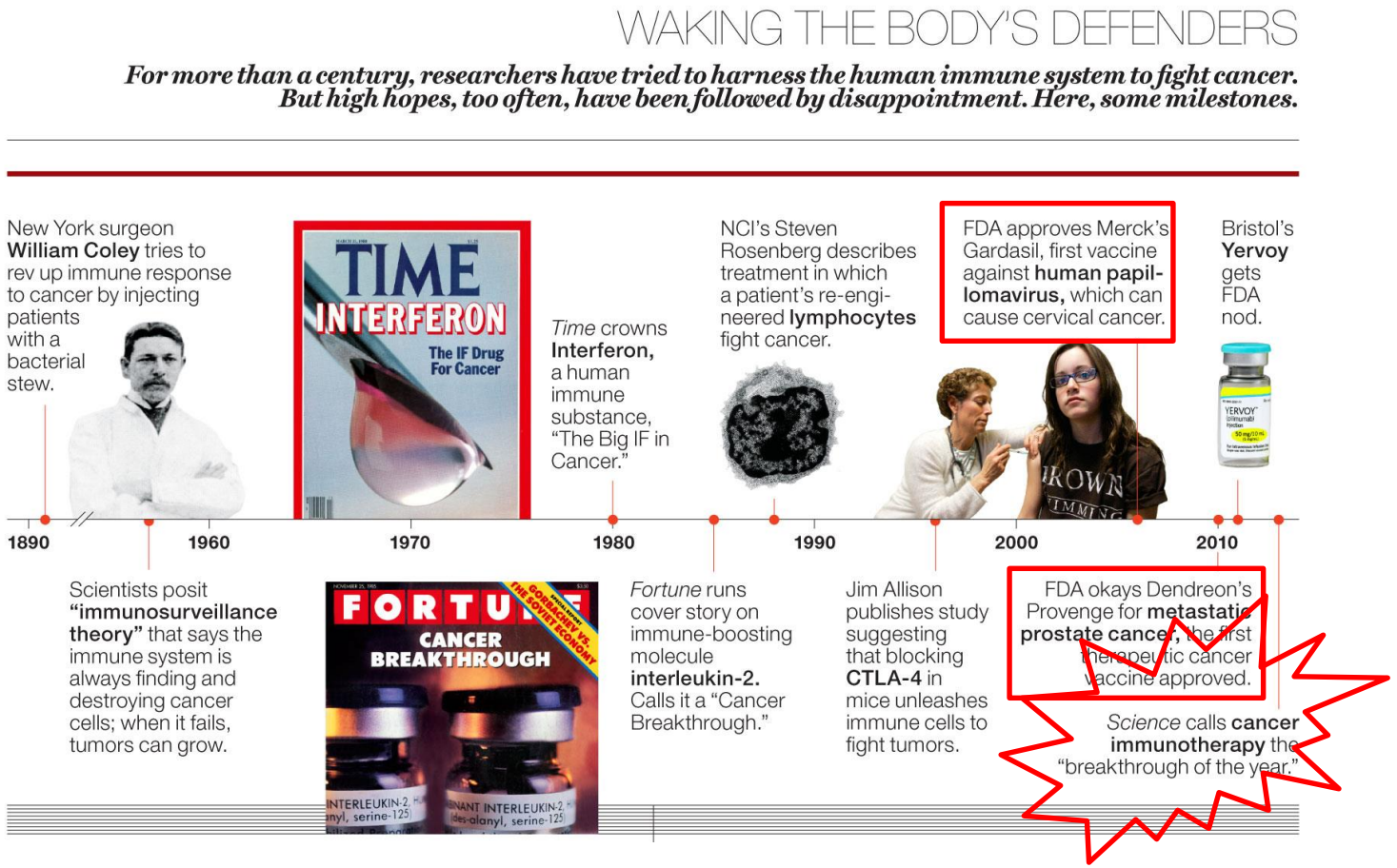
Learning goals

1. **Understanding the stumbling blocks and requirements for the design of successful therapeutic vaccines: choice of antigens and adjuvants**

2. **Becoming familiar with some of the current approaches to vaccination against cancer: broader definition includes *in vivo* vaccination**

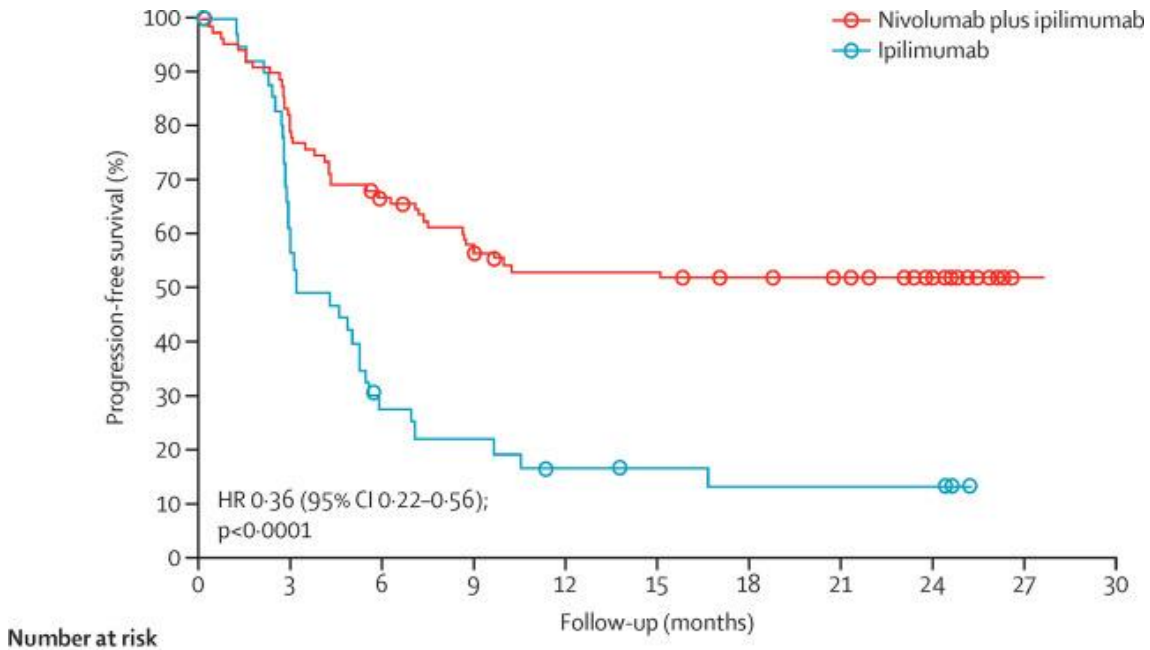
3. **Acquiring an understanding of the positioning of cancer vaccines in the developing field of cancer immunotherapy**

Cancer Immunotherapy: a bit of history



http://fortune.com/2014/06/02/fortune-500-bristol-myers/

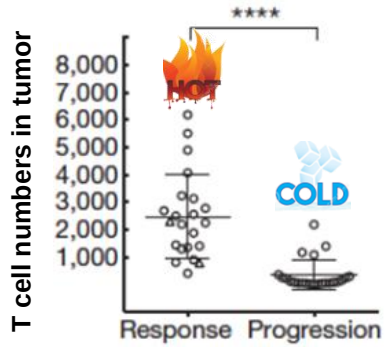
The promise of cancer immunotherapy: durable responses



Number at risk (censored)											
Nivolumab plus ipilimumab	95 (0)	69 (5)	58 (7)	47 (9)	43 (10)	43 (10)	40 (12)	38 (14)	24 (28)	2 (50)	0 (52)
Ipilimumab	47 (0)	22 (6)	10 (7)	8 (7)	5 (8)	4 (9)	3 (9)	3 (9)	3 (9)	0 (12)	0 (12)

Still…not everyone responds.

How come?



T cell infiltration: role for vaccination!

Hodi et al. Lancet Oncol 2016
Tumeh et al Nature 2014

Cancer vaccination: the basics

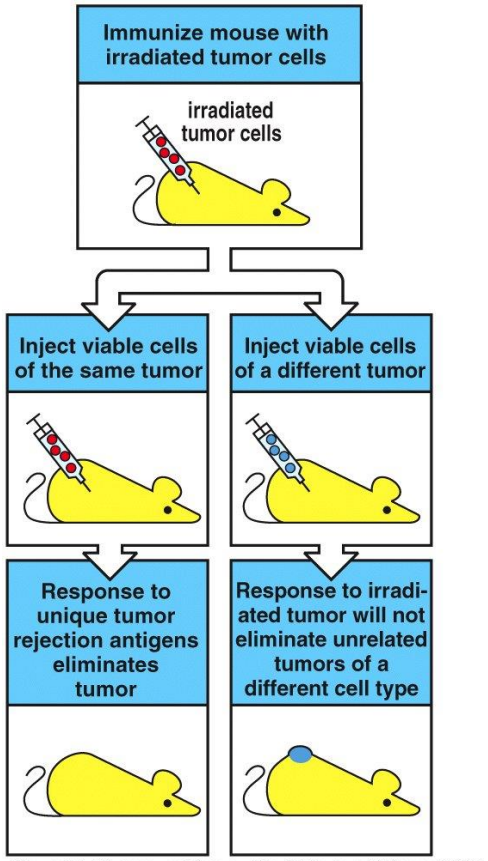


Figure 14-10 Immunobiology, 6/e. (© Garland Science 2005)

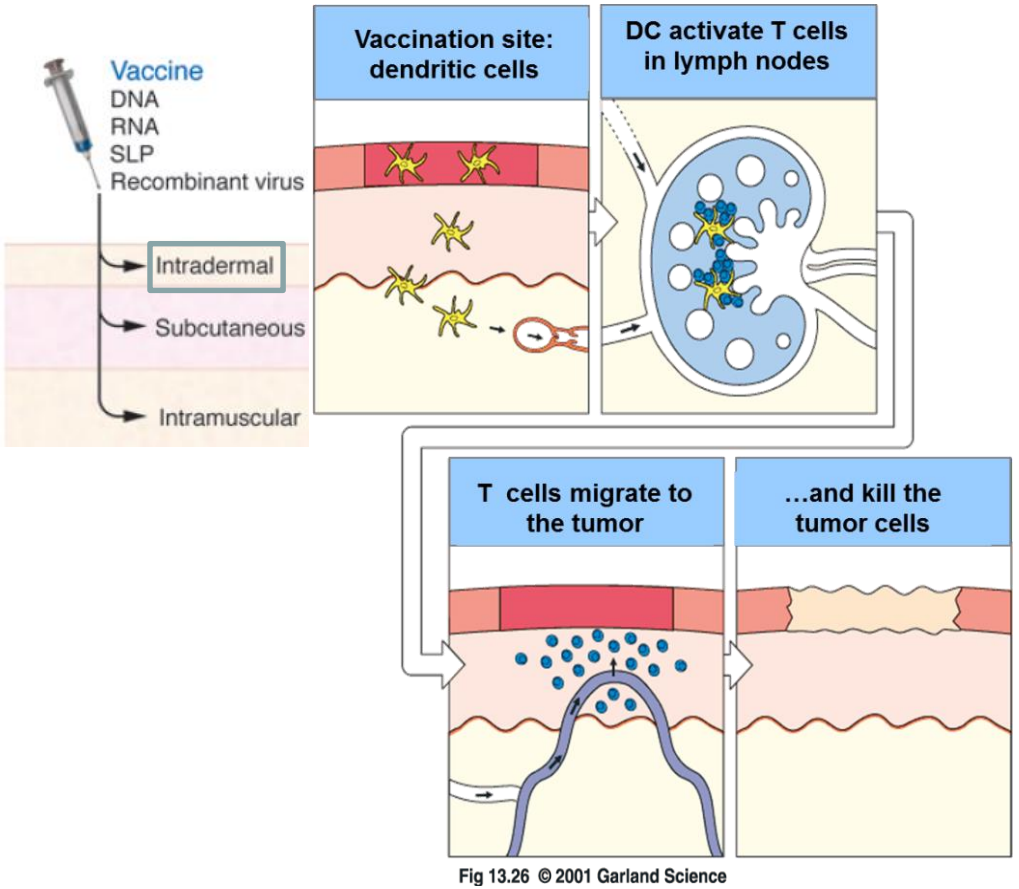
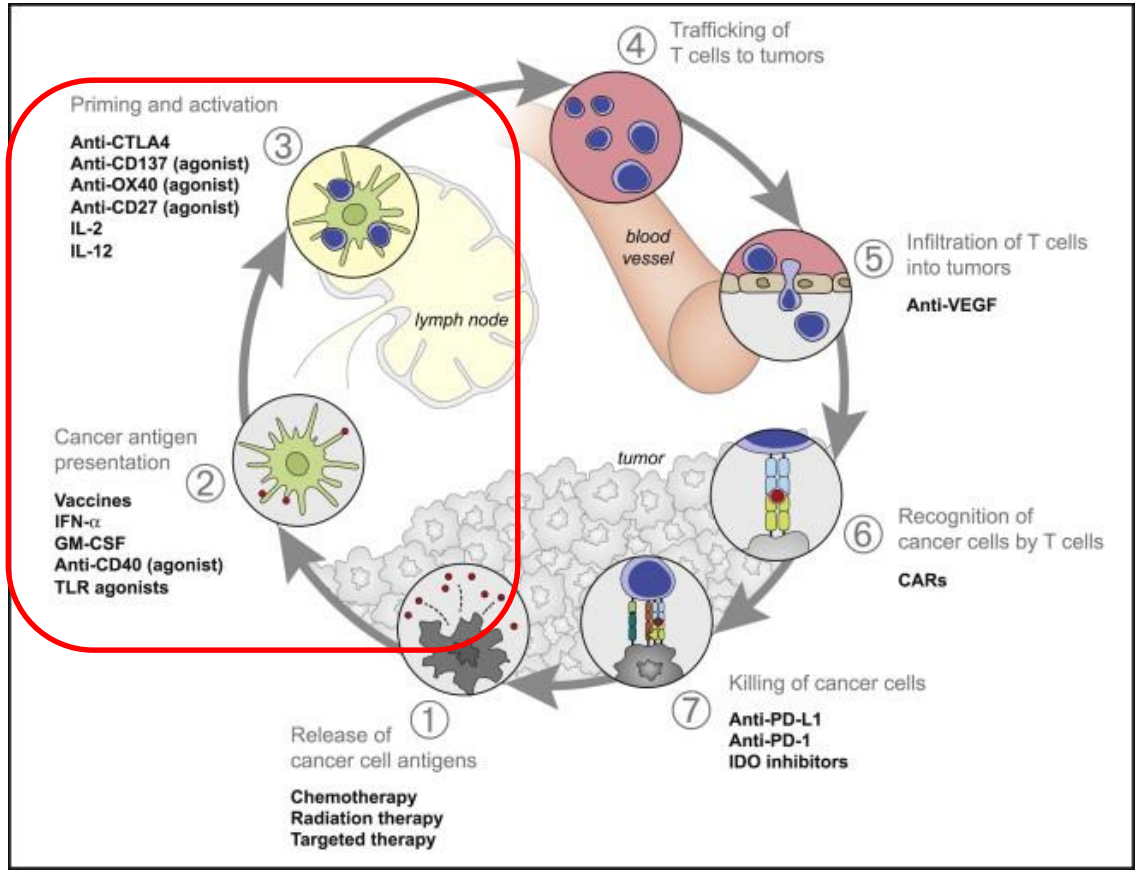


Fig 13.26 © 2001 Garland Science

Cancer Immunotherapy: therapeutic windows

vaccination



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

Vaccine=Antigen+Adjuvant

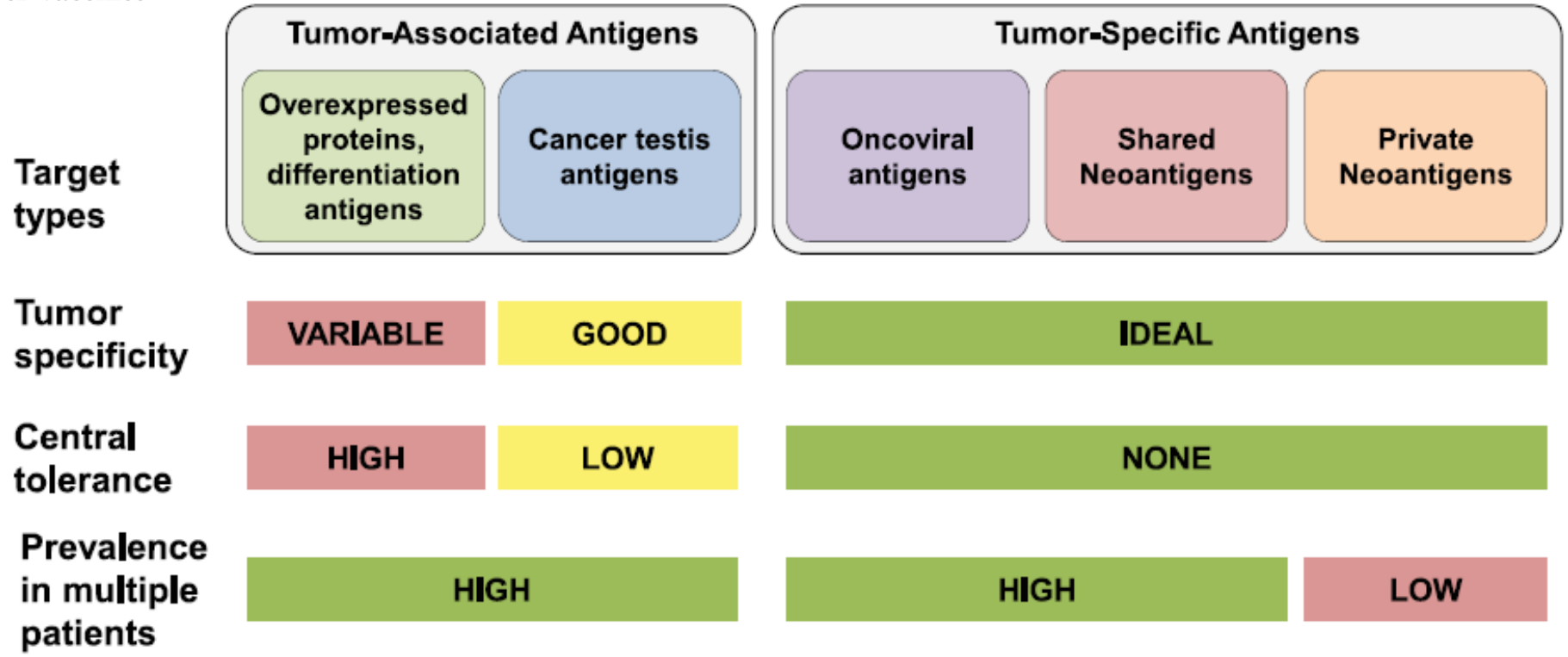
REVIEW ARTICLE OPEN

Turning the corner on therapeutic cancer vaccines

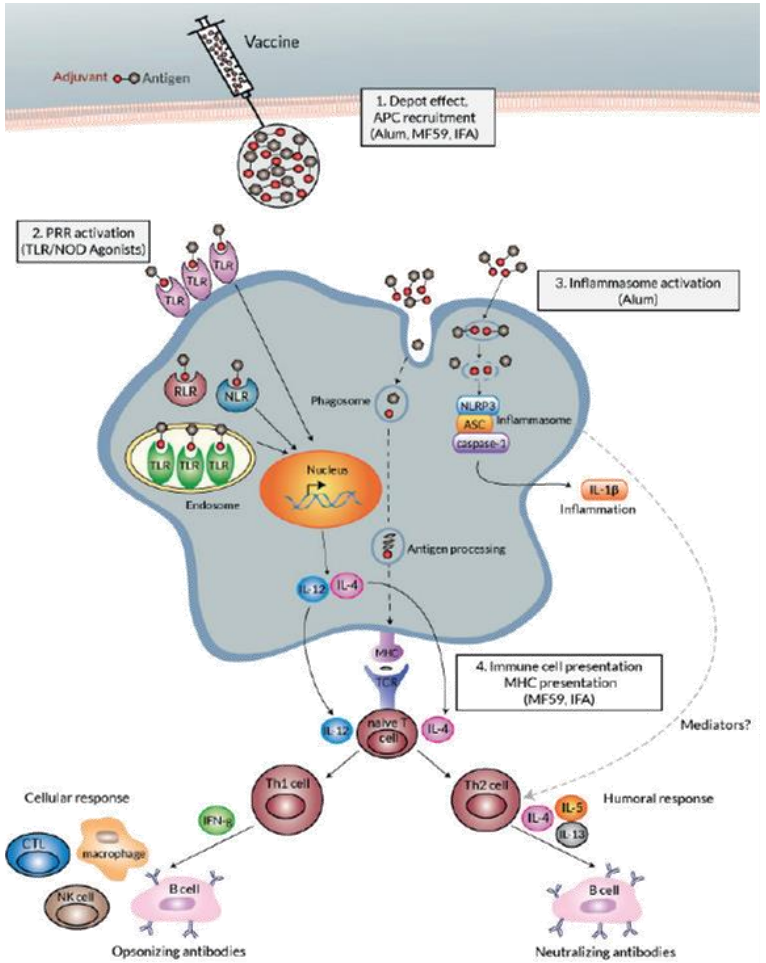
Robert E. Hollingsworth[1] and Kathrin Jansen[2]

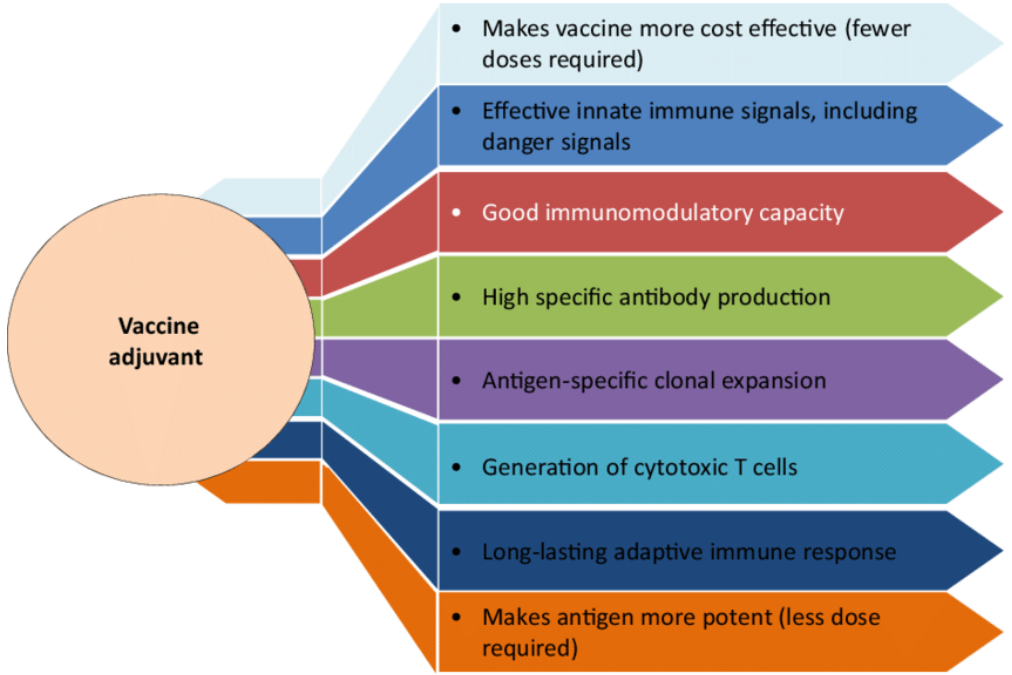
npj | Vaccines

npj Vaccines (2019)4:7



Vaccine=Antigen+Adjuvant



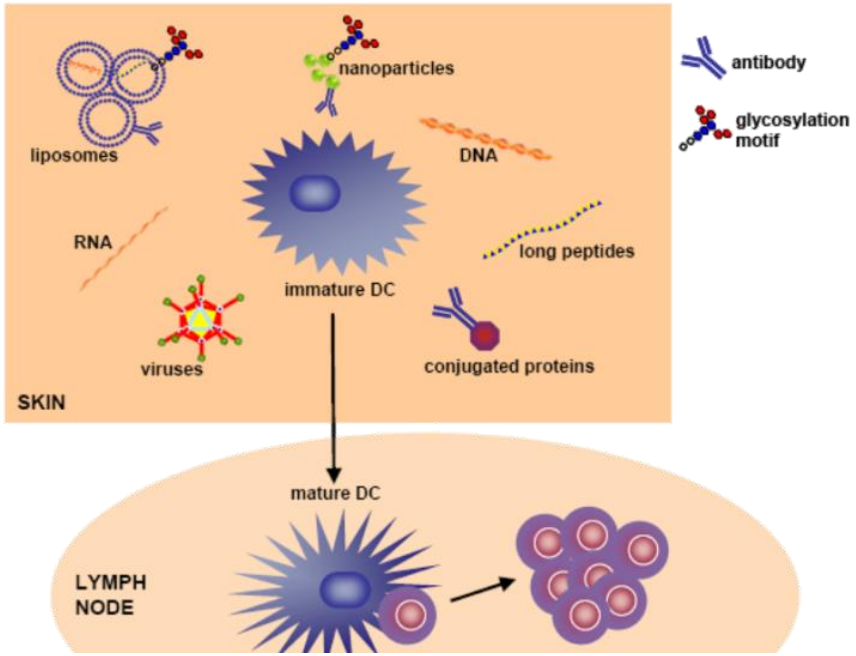


Trends in Pharmacological Sciences

Bonam et al. 2017

Review
InvivoGen

Cancer vaccine formulations and choice of adjuvant



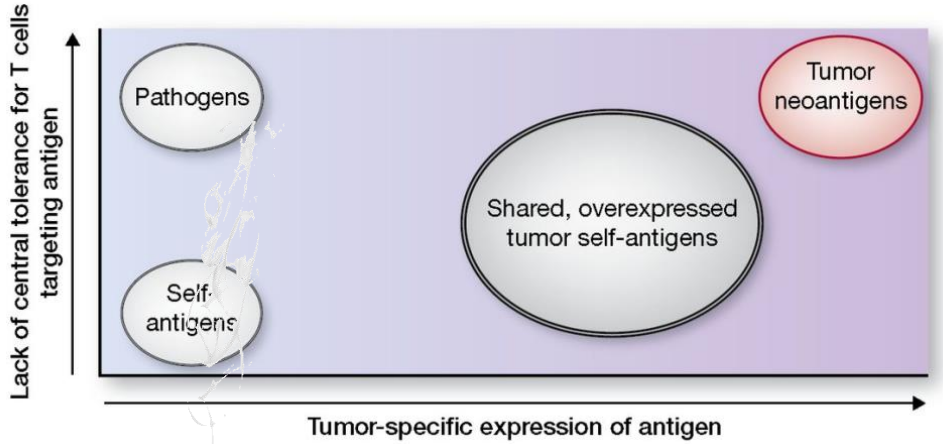
Oosterhoff et al. in: T.J. Curiel (ed.), Cancer Immunotherapy, 2013

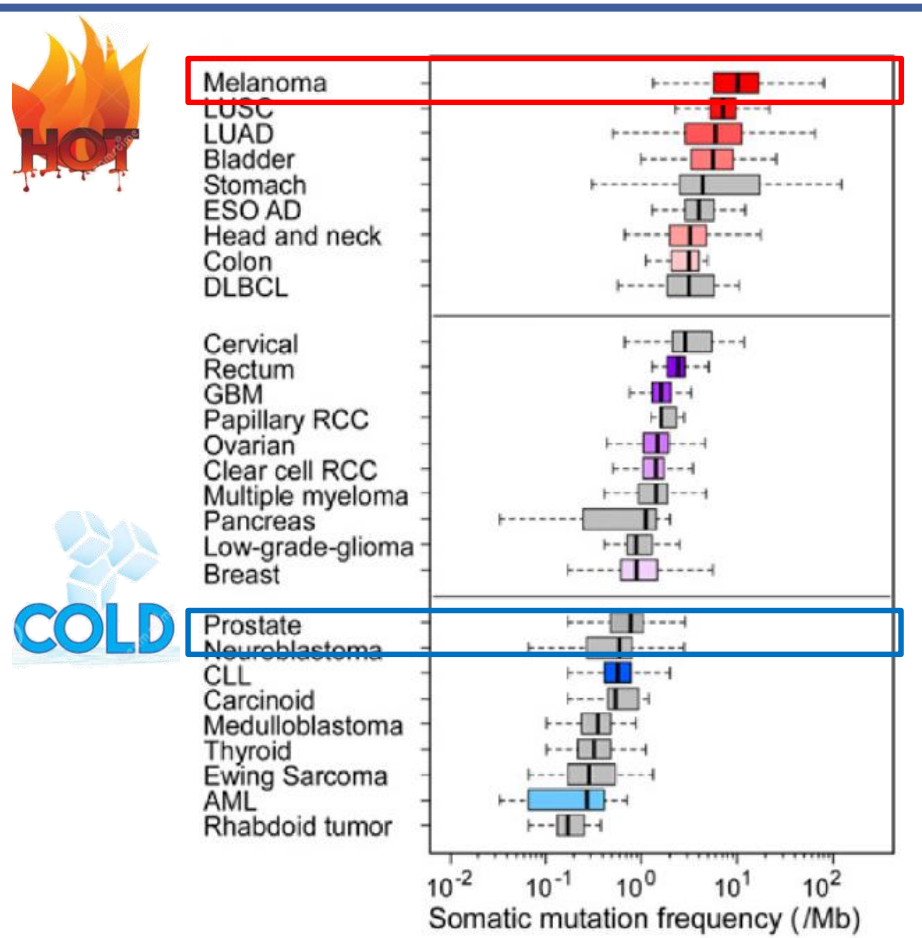
Science
Personalized vaccines for cancer immunotherapy
Ugur Sahin and Özlem Türeci
Science **359** (6382), 1355-1360.

Vaccine format	Advantages	Challenges
Synthetic peptides (*45*)	Cell-free manufacturing Automated synthesis established Proven clinical activity of long peptides Compatible with a wide range of formulations to improve delivery Transient activity and complete degradation	Lack of clinical-grade manufacturability of a substantial portion of sequences High variability in the physicochemical properties of individual peptides, complicating manufacturing Irrelevant immune responses against artificial epitopes created by peptide degradation in the extracellular space
Messenger RNA (*46*)	Cell-free manufacturing Inherent adjuvant function via TLR7, TLR8, and TLR3 signaling Proven clinical activity Highly efficient systemic delivery into DCs established Transient activity and complete degradation All types of epitopes can be encoded	Fast extracellular degradation of mRNA if not protected by appropriate formulation Interpatient variability of TLR7-driven adjuvant activity
DNA plasmids (*47*)	Cell-free manufacturing Inherent adjuvant activity driven by TLR9 Cost-effective and straightforward manufacturing All types of epitopes can be encoded	Potential safety risks by insertional mutagenesis Successful transfection requires entry into nucleus, thereby limiting effective delivery of vaccines into DCs
Viral vectors (*48*) (adenoviral and vaccinia)	Strong immunostimulatory activity Extensive clinical experience with vector formats in the infectious disease field All types of epitopes can be encoded	Complex manufacturing Immune responses against components of the viral vector backbone, limiting successful in vivo vaccine delivery and efficacy
Engineered attenuated bacterial vectors (*49*) (*Salmonella*, *Listeria*)	Strong immunostimulatory activity Could be combined with plasmid DNA All types of epitopes can be encoded	Complex manufacturing and "sterility" testing Immune responses against bacterial components, limiting vaccine delivery and vaccine immunogenicity Potential safety risks due to delivery of live, replication-competent bacteria
Ex vivo antigen-loaded DCs (*50*)	Strong immunostimulatory activity Proven clinical efficacy of DC vaccines Can be loaded with various antigen formats	Higher costs and resources required for adoptive cell therapy approaches

Choice of antigens: what do T cells react to in tumors?

Hacohen et al. CIR 2013





Rajasagi et al Blood 2014

Personalized neoantigen vaccines

LETTER

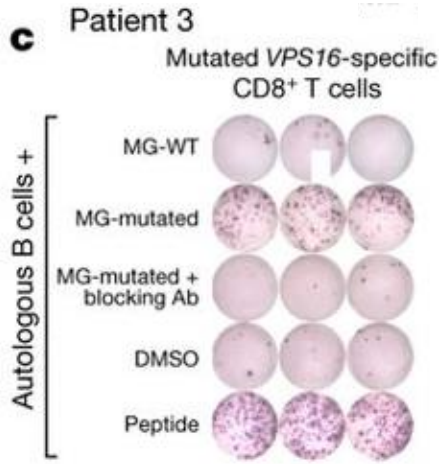
doi:10.1038/nature22991

An immunogenic personal neoantigen vaccine for patients with melanoma

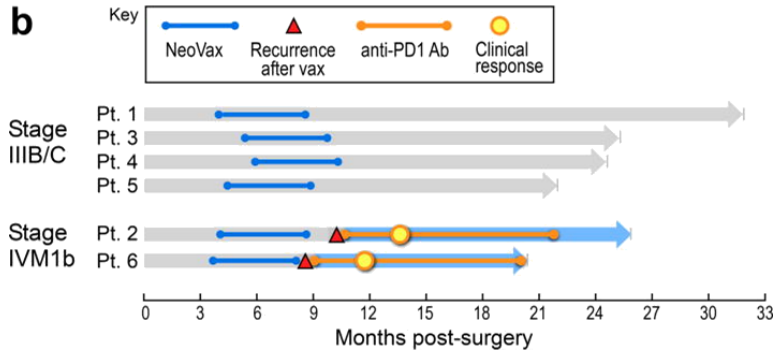
Patrick A. Ott[1,2,3]*, Zhuting Hu[1]*, Derin B. Keskin[1,3,4], Sachet A. Shukla[1,4], Jing Sun[1], David J. Bozym[1], Wandi Zhang[1], Adrienne Luoma[5], Anita Giobbie-Hurder[6], Lauren Peter[7,8], Christina Chen[1], Oriol Olive[1], Todd A. Carter[4], Shuqiang Li[4], David J. Lieb[4], Thomas Eisenhaure[4], Evisa Gjini[9], Jonathan Stevens[10], William J. Lane[10], Indu Javeri[11], Kaliappanadar Nellaiappan[11], Andres M. Salazar[12], Heather Daley[1], Michael Seaman[7], Elizabeth I. Buchbinder[1,2,3], Charles H. Yoon[3,13], Maegan Harden[4], Niall Lennon[4], Stacey Gabriel[4], Scott J. Rodig[9,10], Dan H. Barouch[3,7,8], Jon C. Aster[3,10], Gad Getz[3,4,14], Kai Wucherpfennig[3,5], Donna Neuberg[6], Jerome Ritz[1,2,3], Eric S. Lander[3,4], Edward F. Fritsch[1,4]†, Nir Hacohen[3,4,15] & Catherine J. Wu[1,2,3,4]

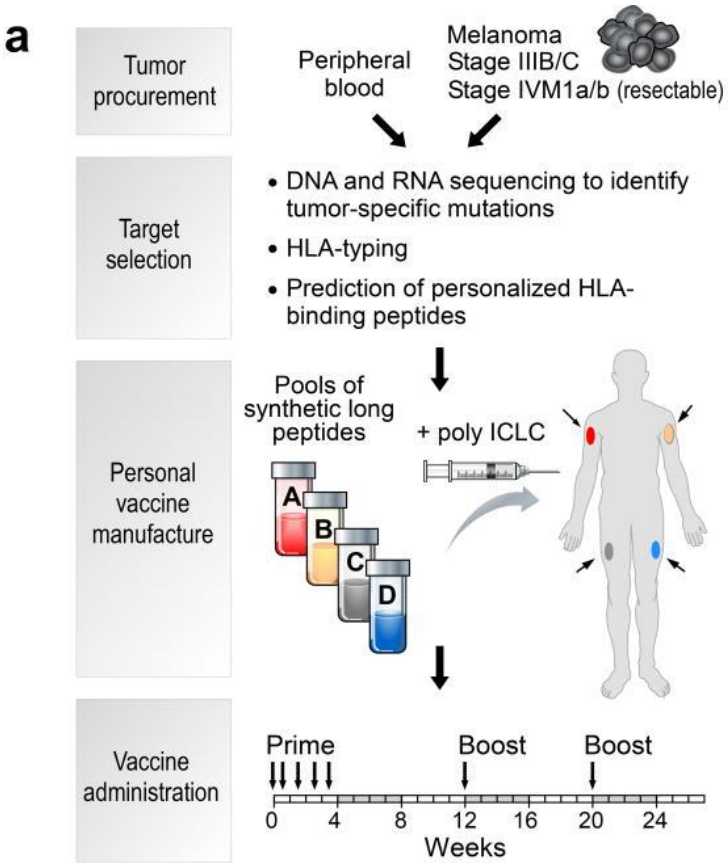
13 JULY 2017 | VOL 547 | NATURE | 217

Immune response:



Tumor control:





Personalized neoantigen vaccines

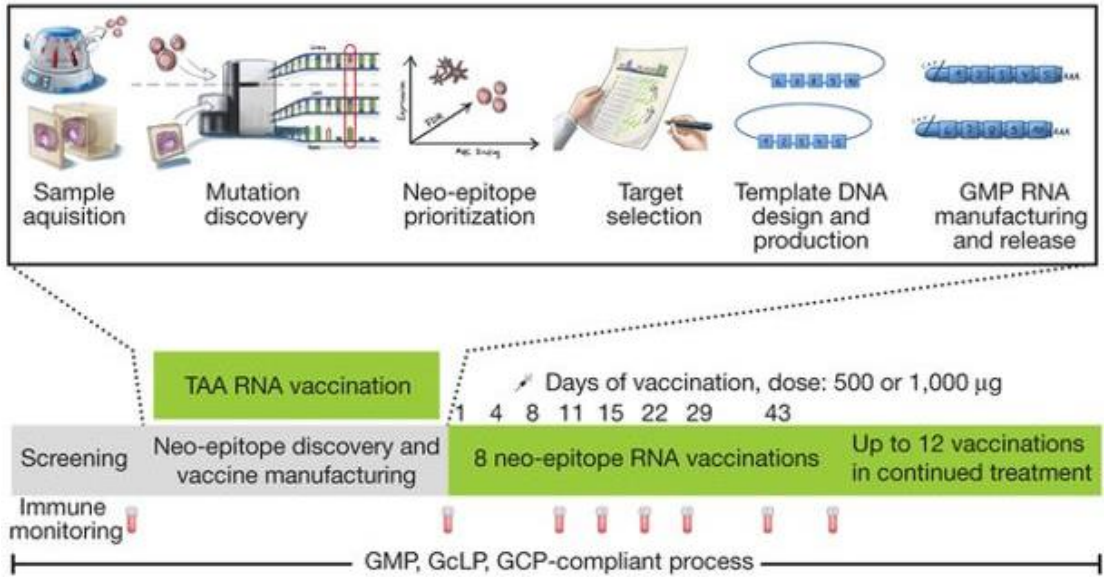
LETTER

doi:10.1038/nature23003

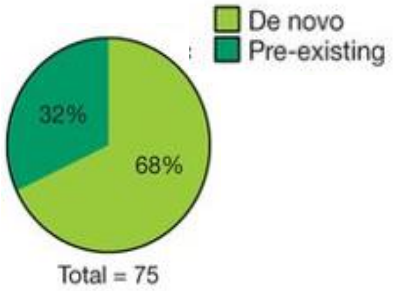
Personalized RNA mutanome vaccines mobilize poly-specific therapeutic immunity against cancer

Ugur Sahin[1,2,3], Evelyna Derhovanessian[1], Matthias Miller[1], Björn-Philipp Kloke[1], Petra Simon[1], Martin Löwer[2], Valesca Bukur[1,2], Arbel D. Tadmor[2], Ulrich Luxemburger[1], Barbara Schrörs[2], Tana Omokoko[1], Mathias Vormehr[1,3], Christian Albrecht[2], Anna Paruzynski[1], Andreas N. Kuhn[1], Janina Buck[1], Sandra Heesch[1], Katharina H. Schreeb[1], Felicitas Müller[1], Inga Ortseifer[1], Isabel Vogler[1], Eva Godehardt[1], Sebastian Attig[2,3], Richard Rae[2], Andrea Breitkreuz[1], Claudia Tolliver[1], Martin Suchan[2], Goran Martic[2], Alexander Hohberger[3], Patrick Sorn[2], Jan Diekmann[1], Janko Ciesla[4], Olga Waksmann[4], Alexandra-Kemmer Brück[1], Meike Witt[1], Martina Zillgen[1], Andree Rothermel[2], Barbara Kasemann[2], David Langer[1], Stefanie Bolte[1], Mustafa Diken[1,2], Sebastian Kreiter[1,2], Romina Nemecek[5], Christoffer Gebhardt[6,7], Stephan Grabbe[3], Christoph Höller[3], Jochen Utikal[6,7], Christoph Huber[1,2,3], Carmen Loquai[3]* & Özlem Türeci[8]*

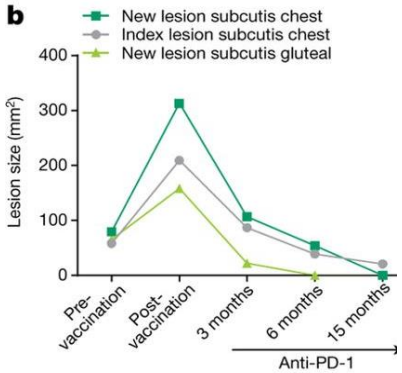
| NATURE | VOL 547 | 13 JULY 2017



Immune response:

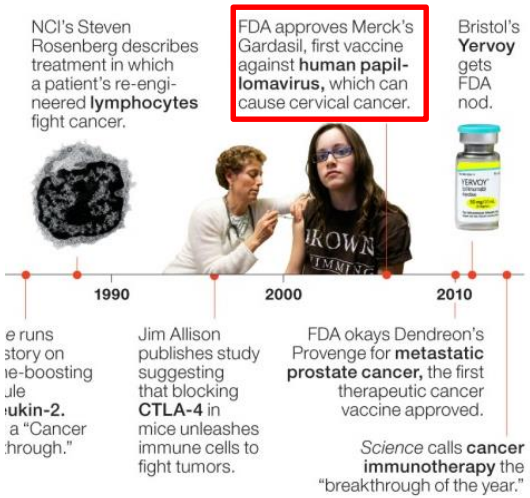


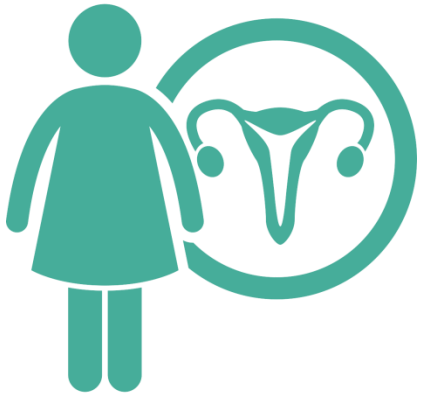
Tumor control:



Successful (cancer) vaccines: prophylactic and antibody based

https://library.nshealth.ca/Cancer/Screening





Doug Lowy & John Schiller

Prophylactic and active:

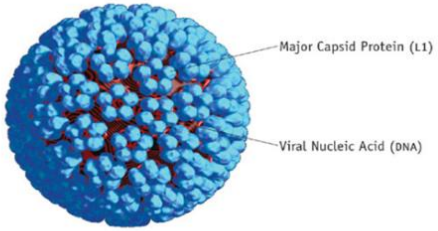
BBC NEWS UK EDITION

Cervical cancer jab 'in a year'

A vaccine shown to be 100% effective against two virus strains that cause most cervical cancer could be available within a year, say manufacturers.

Gardasil worked against the sexually transmitted human papillomavirus (HPV).
Some 12,167 women aged 16 to 23 from 13 countries, including the UK, took part in the drug company study.

Researchers believe a vaccine could work best if given before adolescence, but critics fear this could encourage under-age sex.



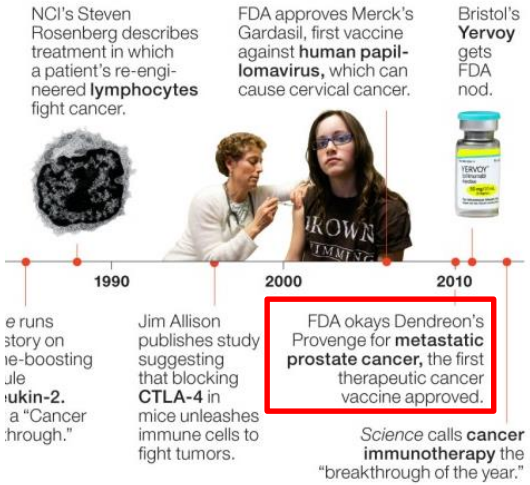
Merck's vaccine is in head-to-head competition with a rival from UK-based GlaxoSmithKline called Cervarix.

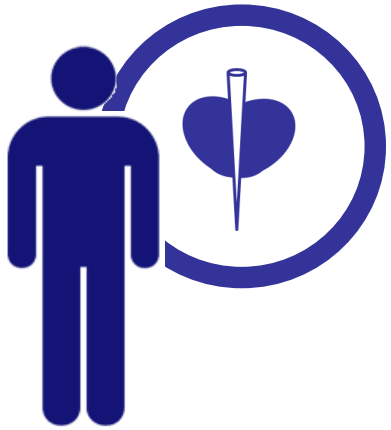
The two-year Future II trial found Gardasil was *100% effective at preventing early stage cancers and pre-cancerous abnormalities* caused by the two key strains of HPV - the 16 and 18 strains - which cause 70% of cervical cancers.

Friday, 7 October 2005, 04:31 GMT 05:31 UK

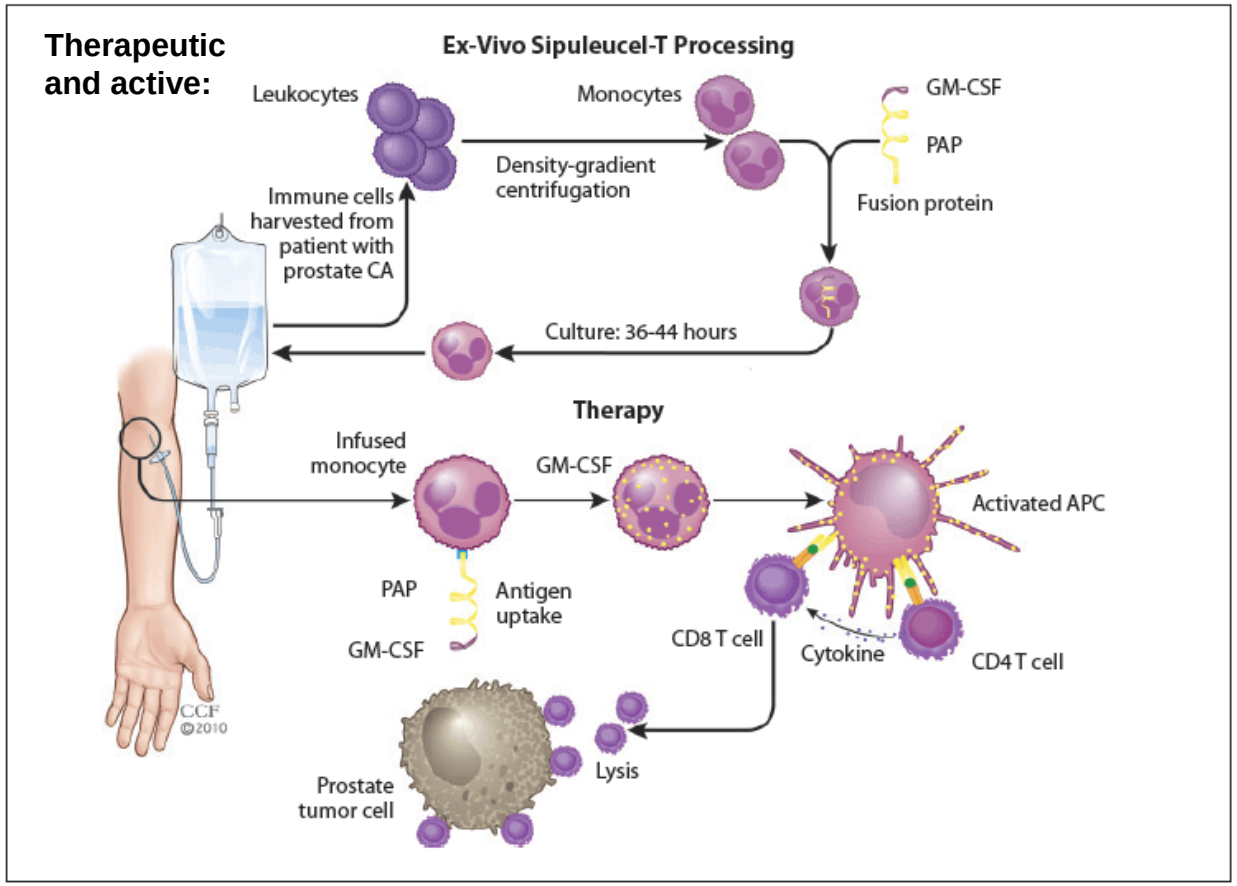
http://fortune.com/2014/06/02/fortune-500-bristol-myers/

More challenging cancer vaccines: therapeutic and T cell based





Therapeutic and active:



http://fortune.com/2014/06/02/fortune-500-bristol-myers/

http://www.cancernetwork.com/prostate-cancer/immunotherapy-castration-resistant-prostate-cancer-integrating-sipuleucel-t-our-current-treatment

The trouble with therapeutic cancer vaccines…

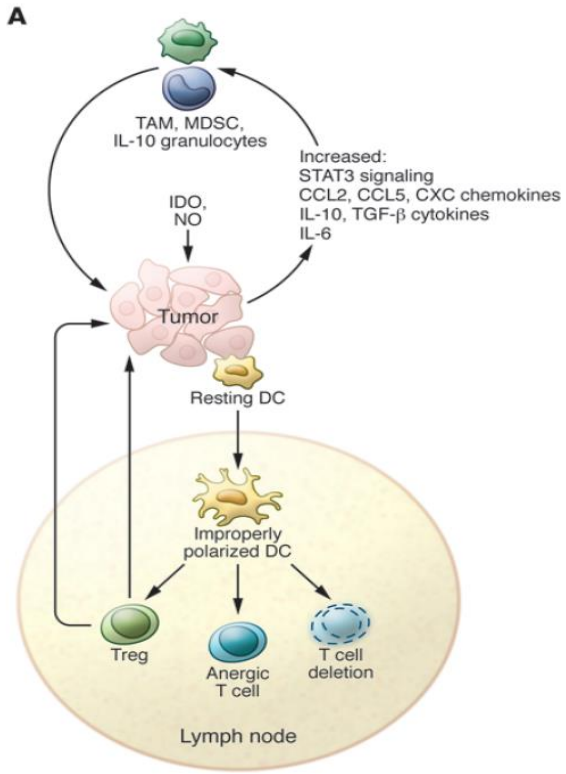
Melief et al J Clin Invest 2015

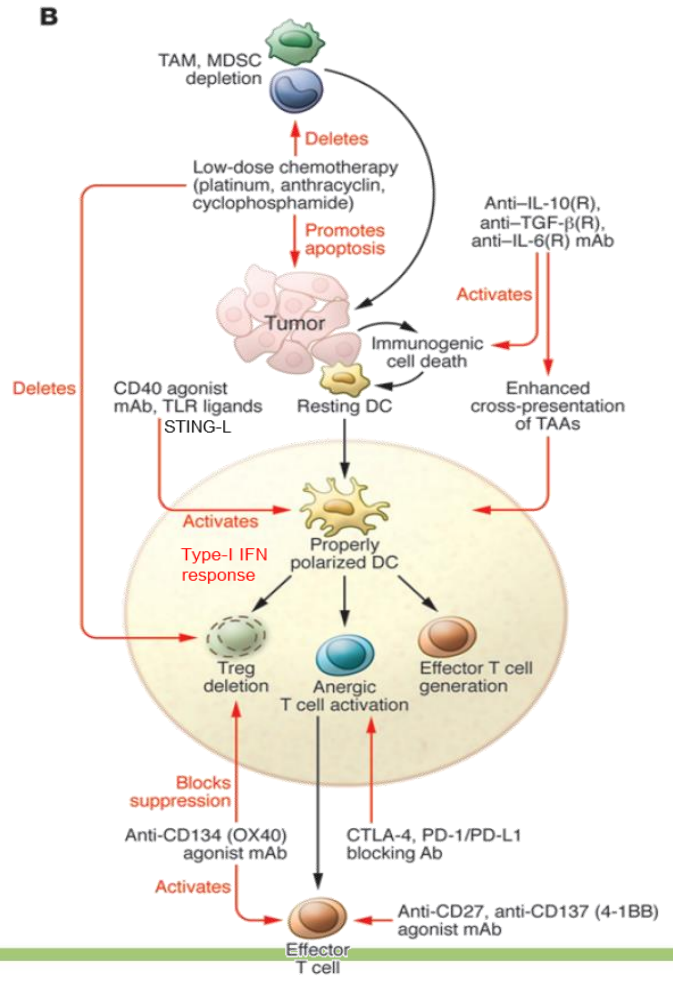
JCI The Journal of Clinical Investigation

Therapeutic cancer vaccines

Cornelis J.M. Melief, … , Ferry Ossendorp, Sjoerd H. van der Burg

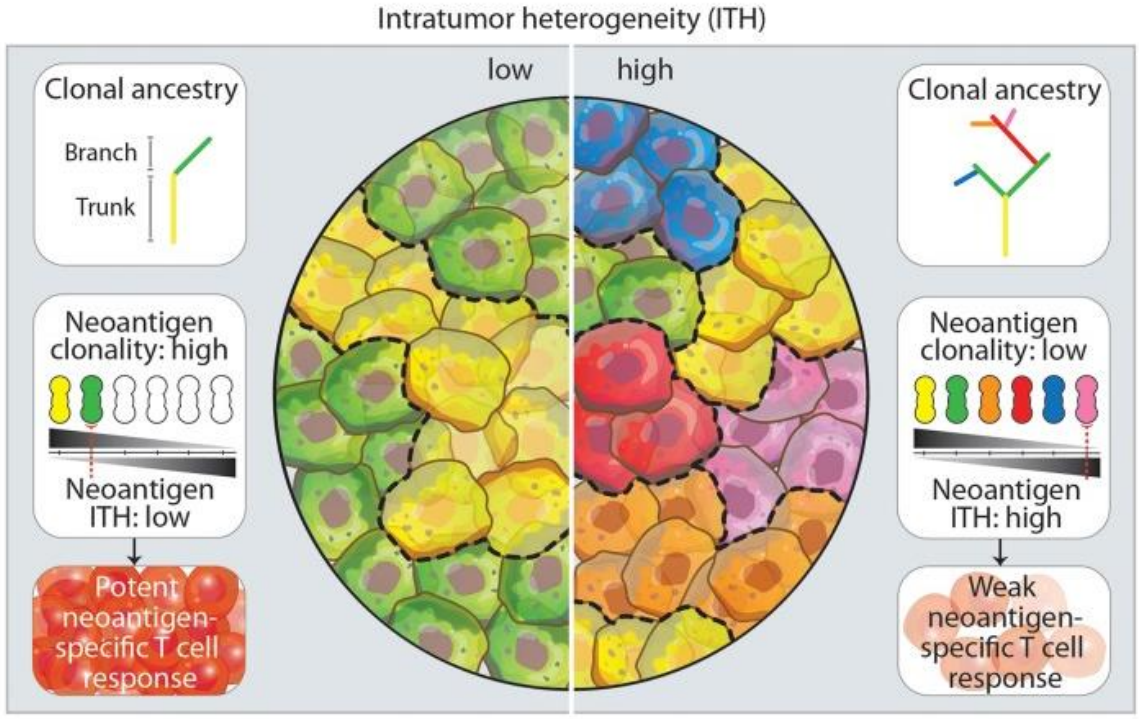
J Clin Invest. 2015;125(9):3401-3412. https://doi.org/10.1172/JCI80009.

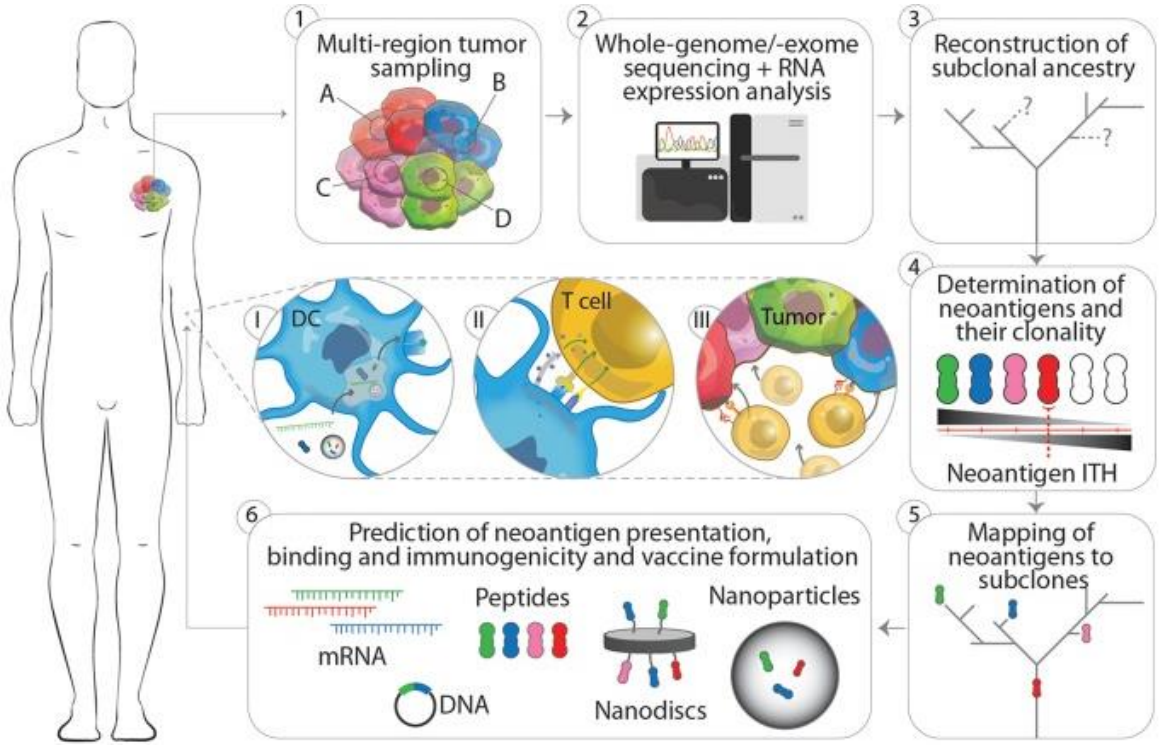




The trouble with therapeutic cancer vaccines…

Fennemann et al. Front. Immunol. 10:824, 2019





One solution: go early

HPV16 SLP vaccine in VIN: 16/20 PR/CR

Vaccination against HPV-16 Oncoproteins for Vulvar Intraepithelial Neoplasia

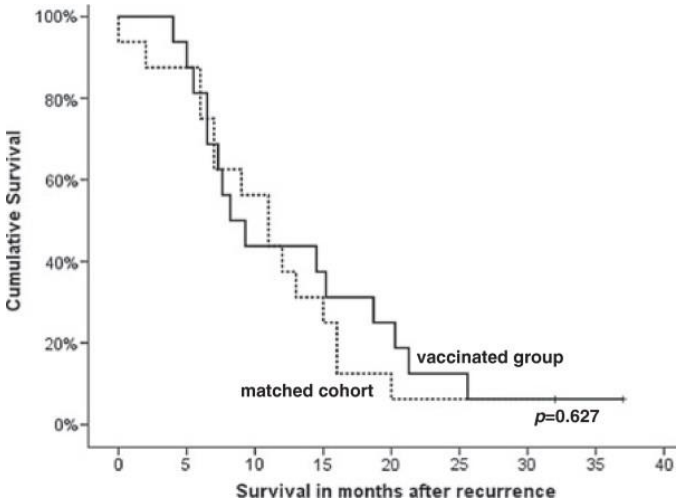
Gemma G. Kenter, M.D., Ph.D., Marij J.P. Welters, Ph.D., A. Rob P.M. Valentijn, Ph.D., Margriet J.G. Lowik, Dorien M.A. Berends-van der Meer, Annelies P.G. Vloon, Farah Essahsah, Lorraine M. Fathers, Rienk Offringa, Ph.D., Jan Wouter Drijfhout, Ph.D., Amon R. Wafelman, Ph.D., Jaap Oostendorp, Ph.D., Gert Jan Fleuren, M.D., Ph.D., Sjoerd H. van der Burg, Ph.D., and Cornelis J.M. Melief, M.D., Ph.D.

N Engl J Med 2009;361:1838-47.

Table 3. Clinical Results at 3, 12, and 24 Months after the Last Vaccination.*

Patient No.	No. of Vaccinations	At 3 Months				At 12 Mo		At 24 Mo
		Symptoms	Lesion Response	Histologic Findings	Type of HPV Infection	Symptoms	Lesion Response	Lesion Response
1	4	Mild to moderate	Partial	VIN 2	16	Mild to moderate	Partial	Partial†
2	4	Severe	None	VIN 3	16		Carcinoma	
3	4	Severe	None	VIN 3	16	None	Partial	Partial‡
6	4	None	Complete	Normal	16	None	Complete	Complete
7	4	None	Complete	Normal	None	None	Complete	Complete
8	4	Mild to moderate	Complete	Normal	6b	None	Complete§	Complete
9	3	None	Complete	Normal	None	None	Complete	Complete
10	4	None	Partial	VIN 3	16	Lost to follow-up¶		
11	4	None	None	VIN 3	16	None	Complete	Complete
12	4	Mild to moderate	None	VIN 3	16	Mild to moderate	Partial	None‖
13	4	Mild to moderate	Partial	VIN 3	16	Mild to moderate	Partial	Partial
16	4	Mild to moderate	Partial	VIN 1	16	Mild to moderate	Complete	Complete
18	4	Severe	None	VIN 3	16	Severe	None	None
22	4	Mild to moderate	None	VIN 3	16	Severe	Partial	Partial
23	4	Mild to moderate	Partial	VIN 2	16	None	Partial	Microinvasive carcinoma**
26	4	None	None	VIN 3	16	None	None	None
27	3	None	Partial	VIN 3	16	None	Complete	Complete
28	4	None	None	VIN 3	16	None	None	None
29	4	None	Complete	Normal	None	None	Complete	Complete
30	4	Mild to moderate	Partial	VIN 2	16	None	Complete	Complete

…but in cancer: none!



van Poelgeest *et al. Journal of Translational Medicine* 2013, 11:88
http://www.translational-medicine.com/content/11/1/88

JOURNAL OF TRANSLATIONAL MEDICINE

RESEARCH Open Access

HPV16 synthetic long peptide (HPV16-SLP) vaccination therapy of patients with advanced or recurrent HPV16-induced gynecological carcinoma, a phase II trial

Mariette I E van Poelgeest[1†], Marij J P Welters[2†], Edith M G van Esch[1], Linda F M Stynenbosch[2], Gijs Kerpershoek[1], Els L van Persijn van Meerten[3], Muriel van den Hende[1], Margriet J G Löwik[1], Dorien M A Berends-van der Meer[1], Lorraine M Fathers[4], A Rob P M Valentijn[4], Jaap Oostendorp[4], Gert Jan Fleuren[5], Cornelis J M Melief[6,7], Gemma G Kenter[1,8†] and Sjoerd H van der Burg[2*†]

Another solution: optimizing vaccines and combination therapies

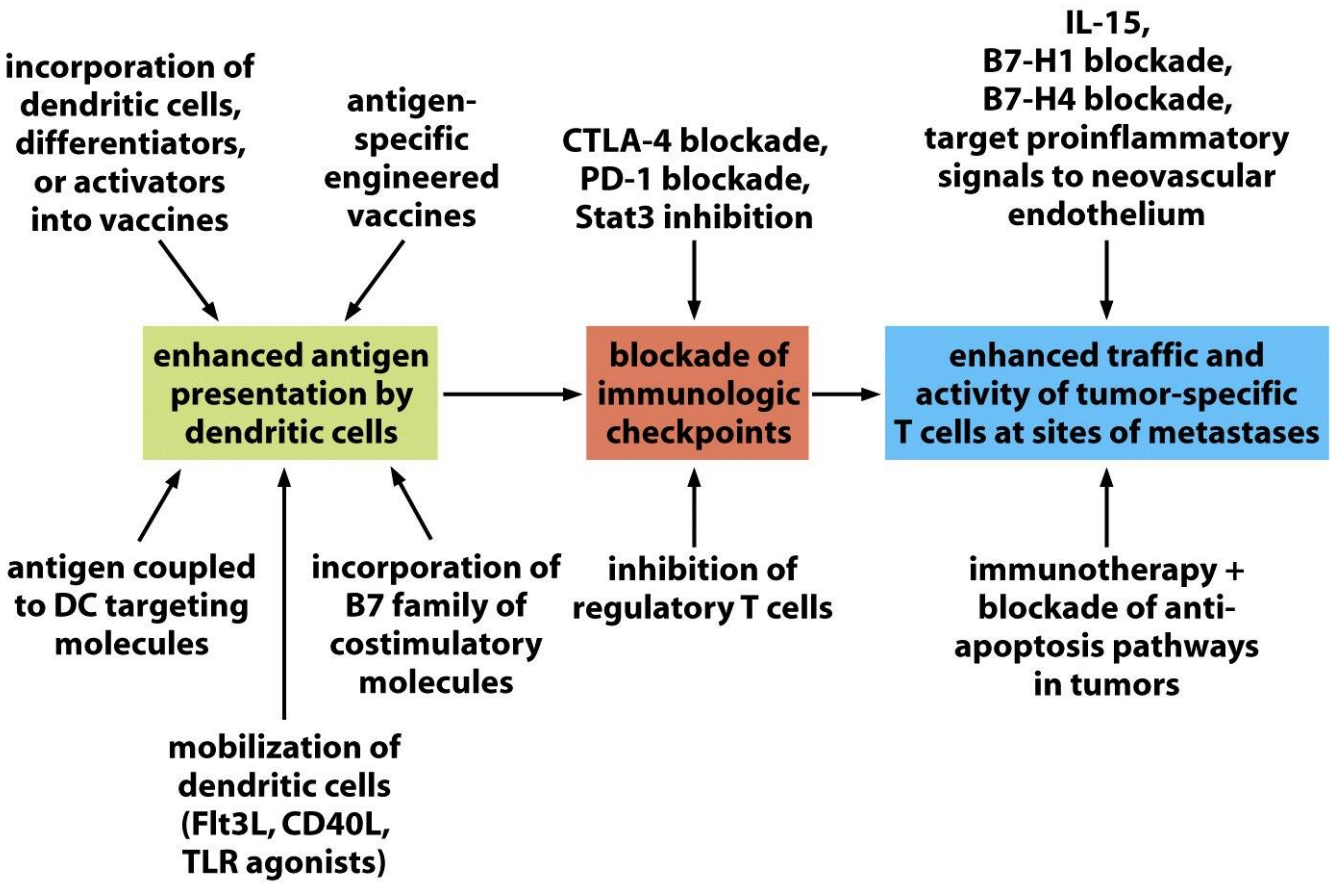


Figure 15.45 The Biology of Cancer (© Garland Science 2007)

Another solution: optimizing vaccines and combination therapies

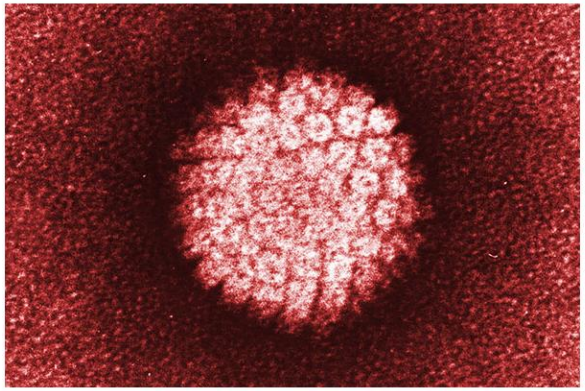
MEDPAGE TODAY

A One-Two Punch for HPV-16–positive Cancers?

—Individually, vaccines and immune checkpoint inhibitors have been no match for HPV-related cancers, but what happens when the 2 therapies are combined?

By Kristin Bundy
Reviewed by Michael Leapman, MD

Independent of one another, therapeutic vaccines and immune checkpoint inhibition with anti-programmed cell death 1 (PD-1) antibodies have proven largely ineffective in treating recurrent HPV-16–positive malignant neoplasms.



But could they overcome a tumor-induced immunosuppressive environment when used together?

More On This Topic

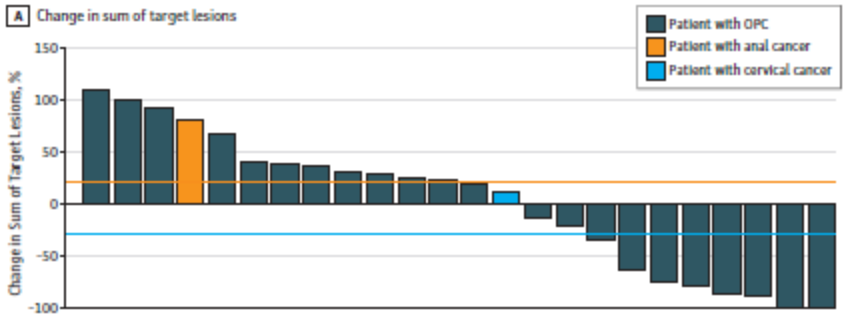
- Tumor Mutational Burden: A Biomarker for anti-PD-1 and anti-PD-L1 Tx?
- Obese Patients Do Better on Immune Checkpoint Blockade—But Why?
- Flu Vaccine in Patients Receiving Immune Checkpoint Inhibitors—Is It Safe?
- Quiz Yourself: Immunotherapy
- Interactive Case: 6 Months of Hematuria and a Complex History
- Do Immune Checkpoint Inhibitors Make Sense in Patients with HIV and Advanced Cancer?
- Metastatic NSCLC: Exploring New Therapeutic Combinations
- What Role for a Chemo-free Initial Approach to Indolent Lymphoma?

JAMA Oncology | Original Investigation

Combining Immune Checkpoint Blockade and Tumor-Specific Vaccine for Patients With Incurable Human Papillomavirus 16–Related Cancer
A Phase 2 Clinical Trial

Erminia Massarelli, MD; William William, MD; Faye Johnson, MD, PhD; Merrill Kies, MD; Renata Ferrarotto, MD; Ming Guo, MD; Lei Feng, MS; J. Jack Lee, PhD; Hai Tran, PharmD; Young Uk Kim, PhD; Cara Haymaker, PhD; Chantale Bernatchez, PhD; Michael Curran, PhD; Tomas Zecchini Barrese, MD; Jaime Rodriguez Canales, MD; Ignacio Wistuba, MD; Lerong Li, MS; Jing Wang, PhD; Sjoerd H. van der Burg, PhD; Cornelis J. Melief, PhD; Bonnie Glisson, MD

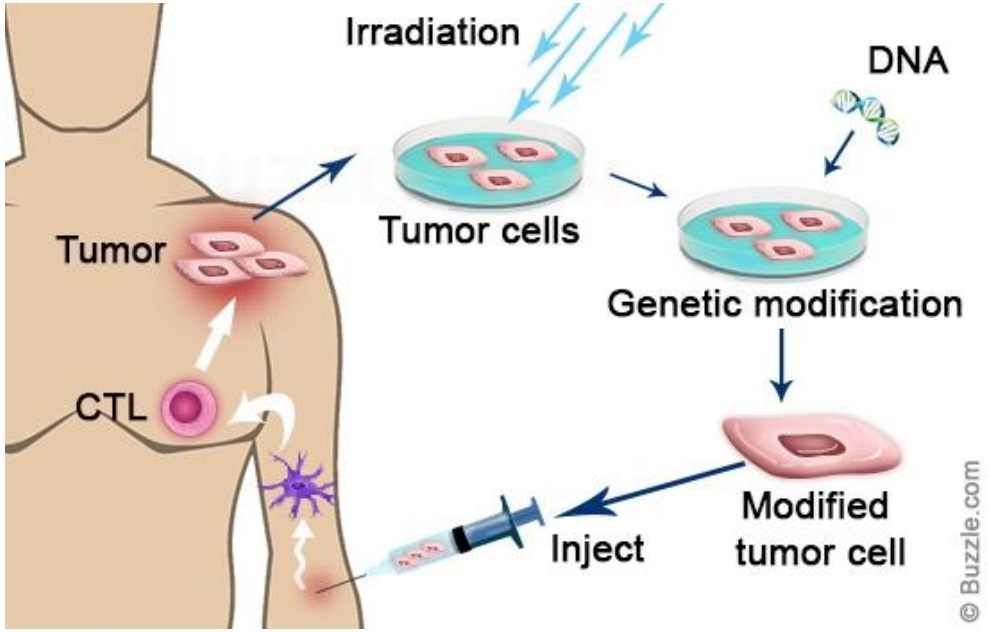
Figure 2. Efficacy of ISA101 and Nivolumab



CONCLUSIONS AND RELEVANCE The overall response rate of 33% and median overall survival of 17.5 months is promising compared with PD-1 inhibition alone in similar patients. A randomized clinical trial to confirm the contribution of HPV-16 vaccination to tumoricidal effects of PD-1 inhibition is warranted for further study.

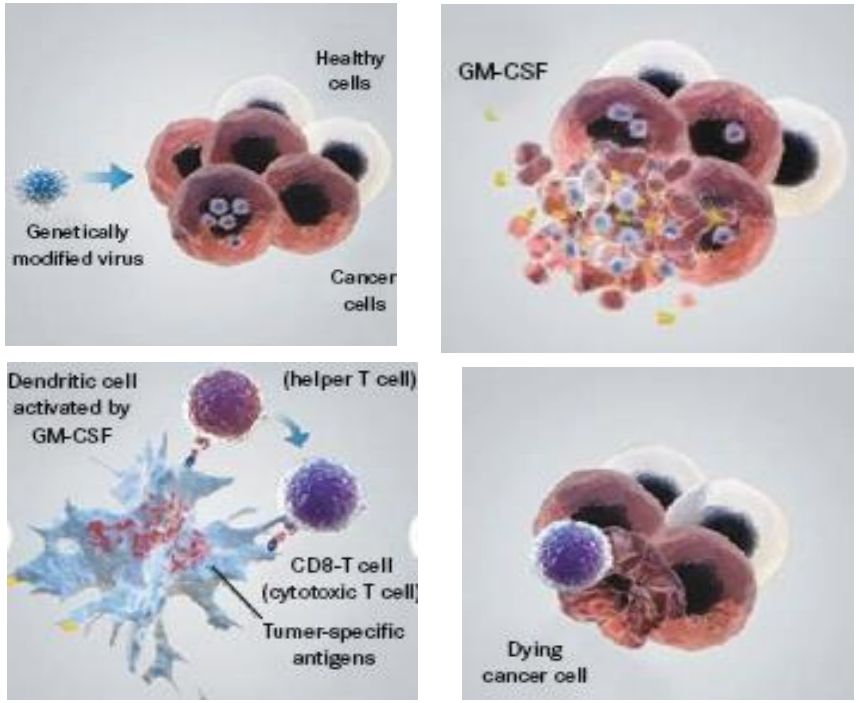
Antigen agnostic cancer vaccination approaches

1) Whole cancer cell vaccines



https://healthhearty.com/strategies-for-cancer-vaccine-development

2) Oncolytic virotherapy



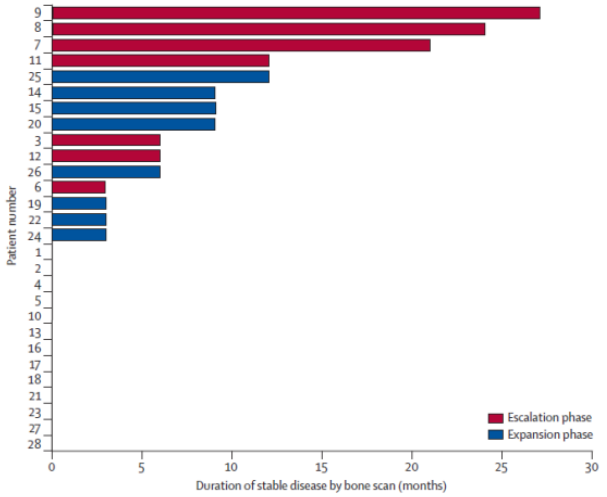
https://www.gotoper.com/publications/ajho/2016/2016apr/an-update-on-talimogene-laherparepvec

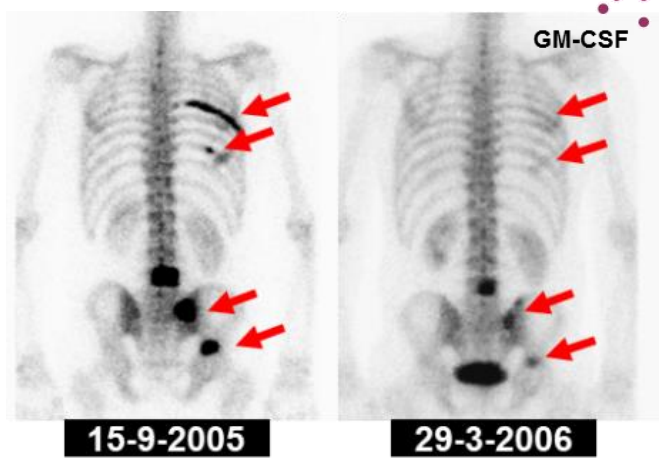
Whole cancer cell vaccines: GVAX with checkpoint blockade - turning up the heat

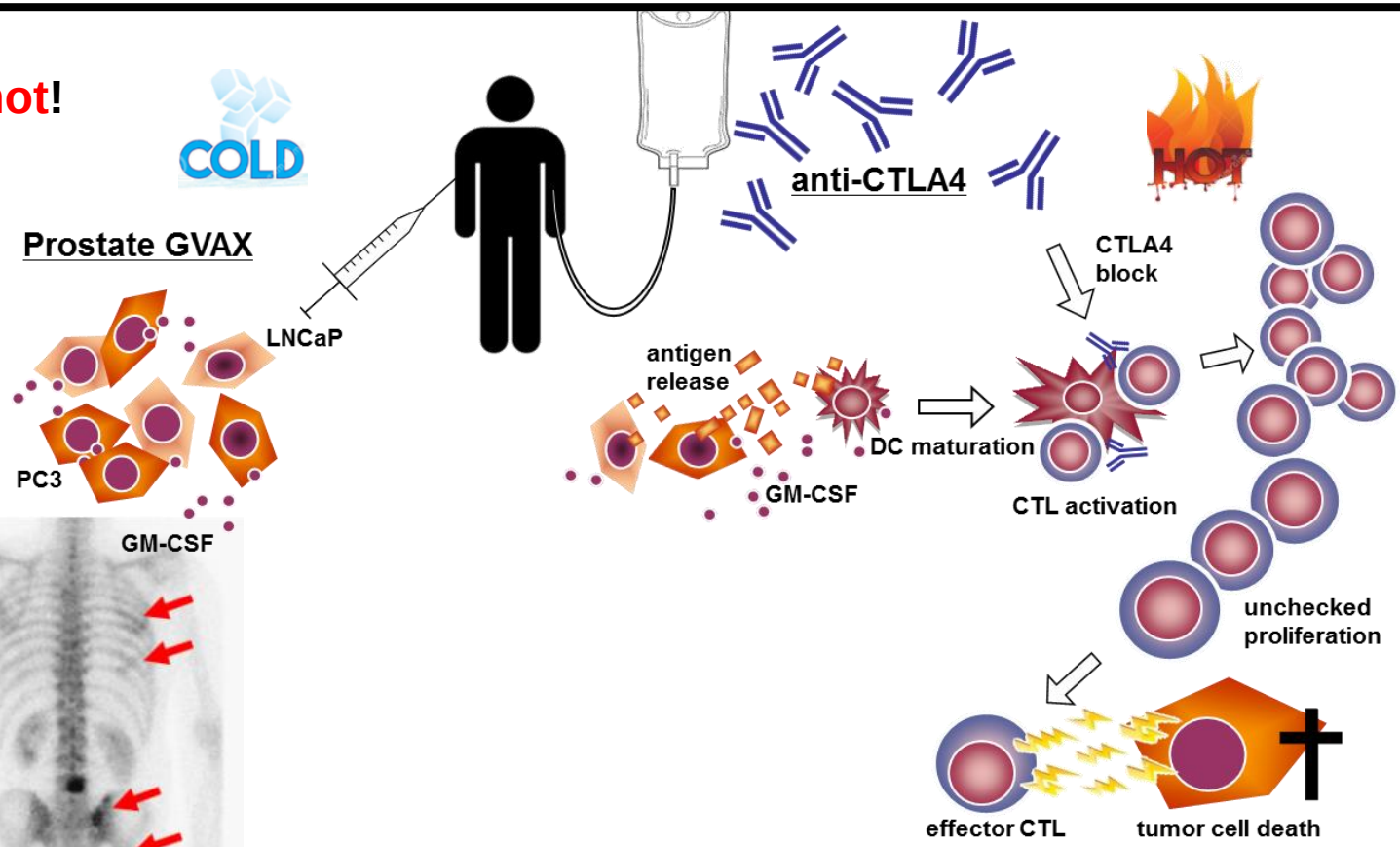
Turning a cold tumor hot!

Lancet Oncol 2012; 13: 509–17

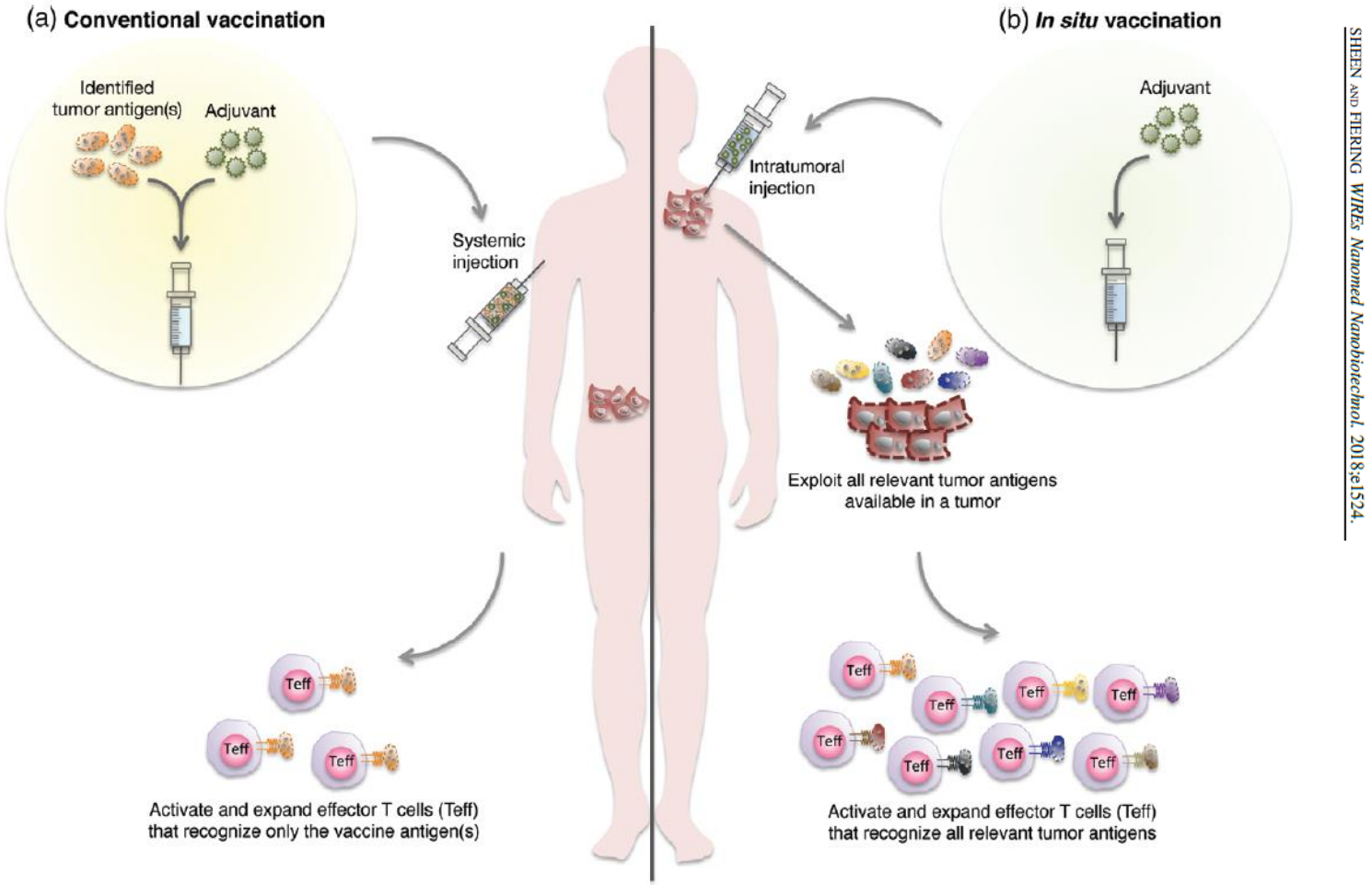
Category:	Number of patients
PSA Partial Response (PR)	5 / 28
PSA Stable Disease (SD)	12 / 28
PSA Progressive Disease (PD)	11 / 28





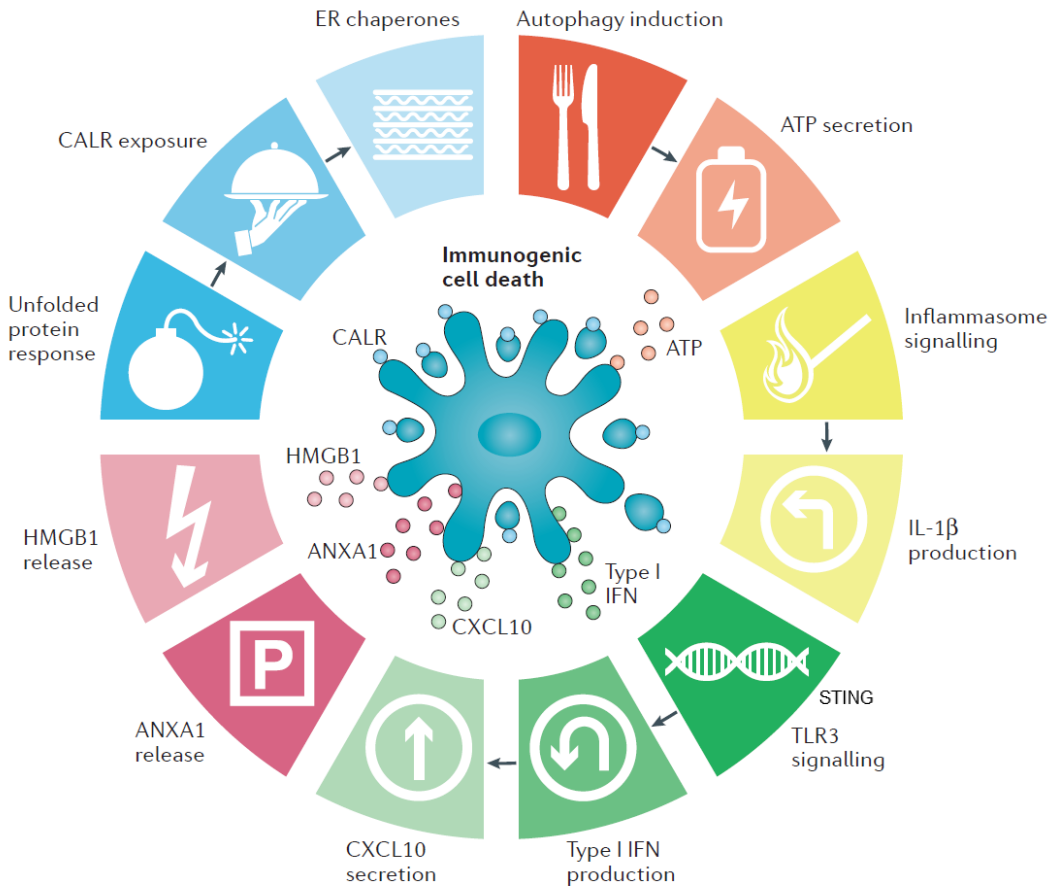


Conventional versus *in vivo* vaccination

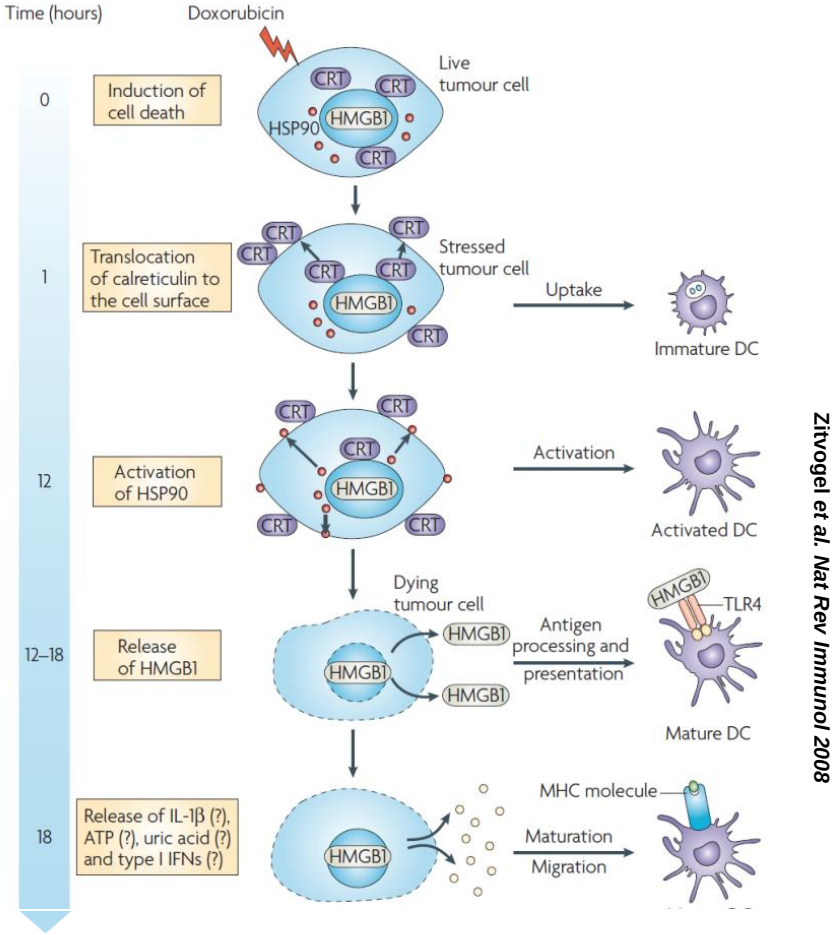


SHEEN AND FIERING *WIREs Nanomed Nanobiotechnol.* 2018;e1524.

In vivo vaccination: requirements for an effective antitumor T cell response

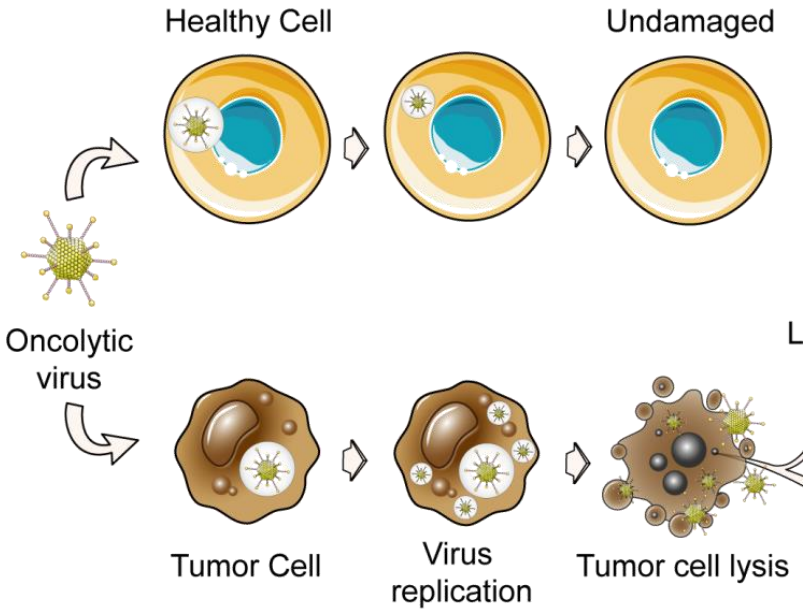


Galluzi *et al. Nat Rev Immunol 2017*

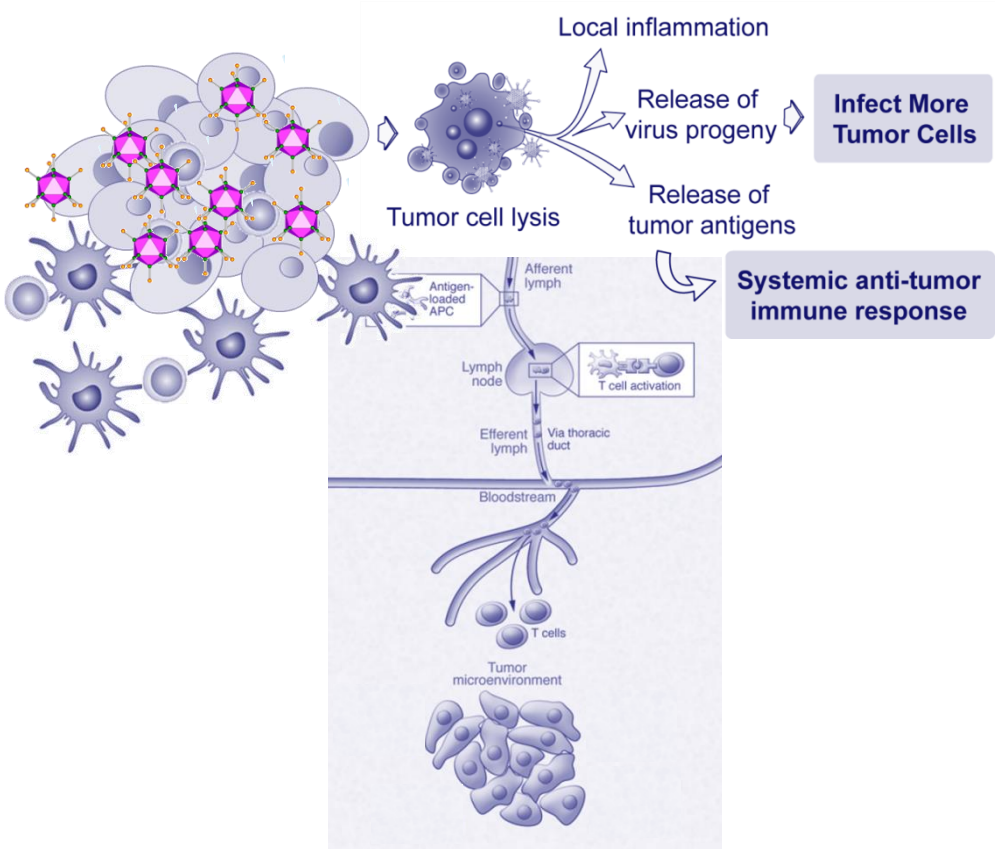


Zitvogel *et al. Nat Rev Immunol 2008*

Oncolytic virotherapy: *in vivo* vaccination



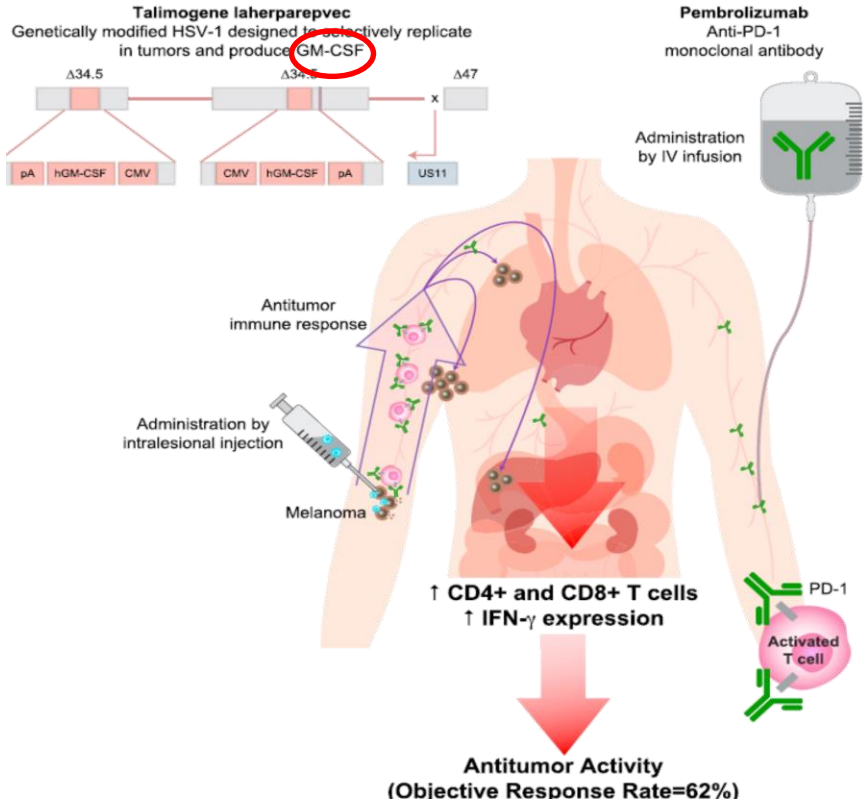
https://www.creative-biolabs.com/car-t/oncolytic-virus-therapy-development.htm

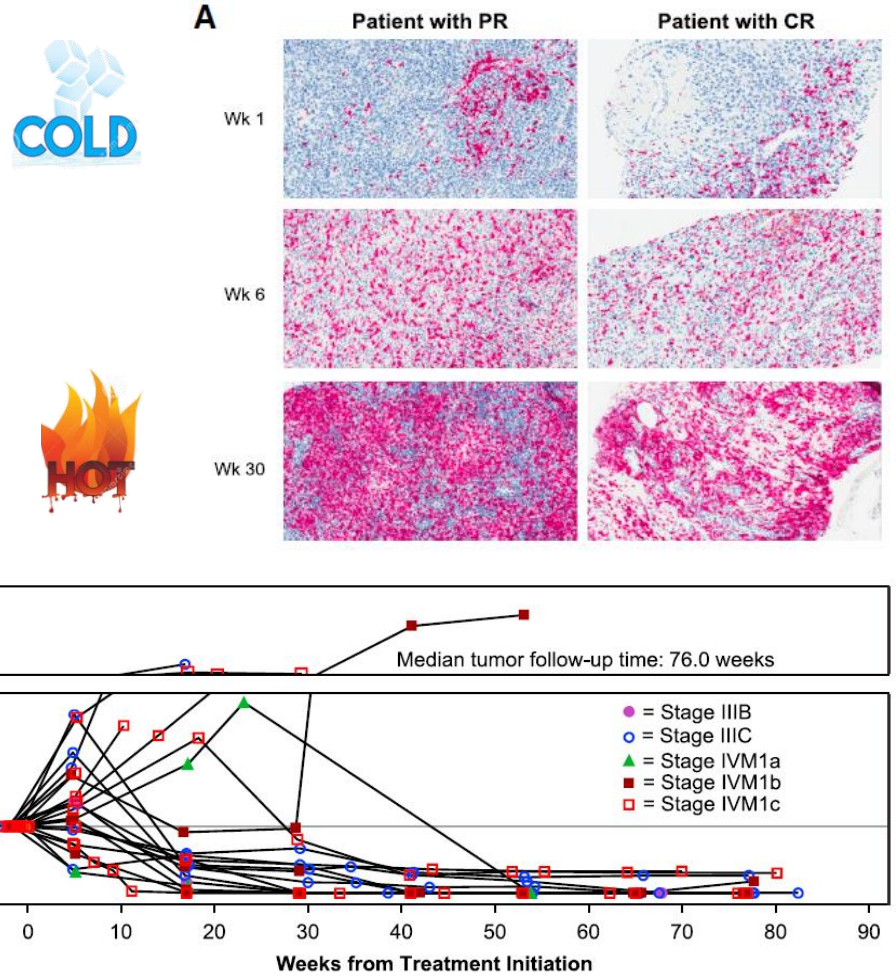


Melief et al JCI 2015

Oncolytic viruses (T-vec) and immune checkpoint blockade

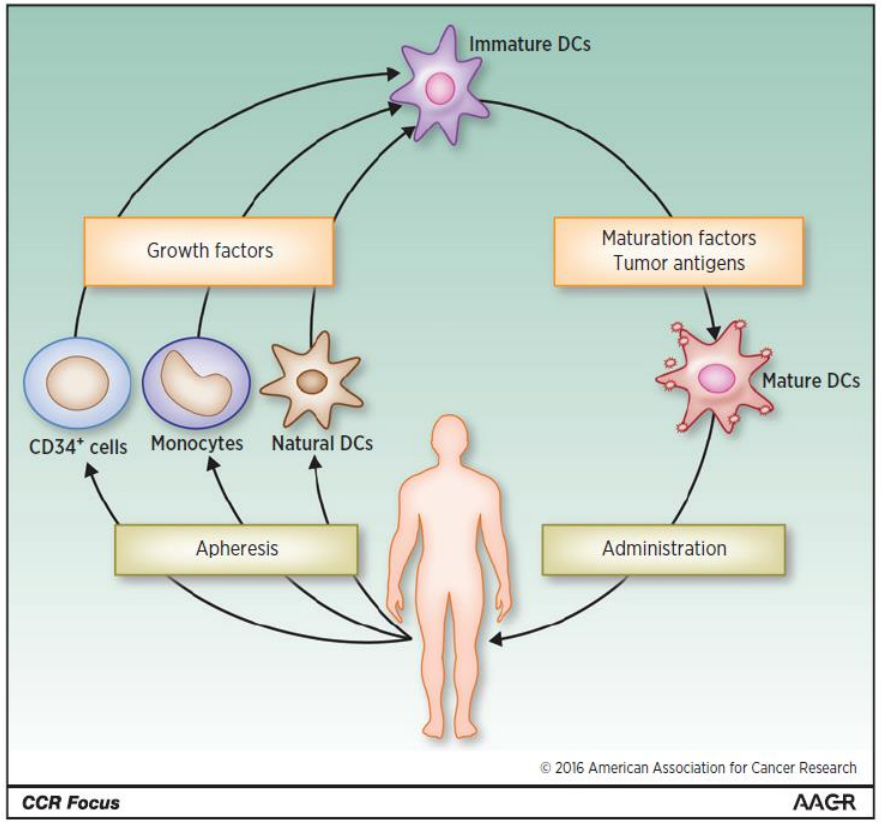
Role for dendritic cells!





Ribas et al. Cell 2017

Dendritic cell vaccines: classic approach

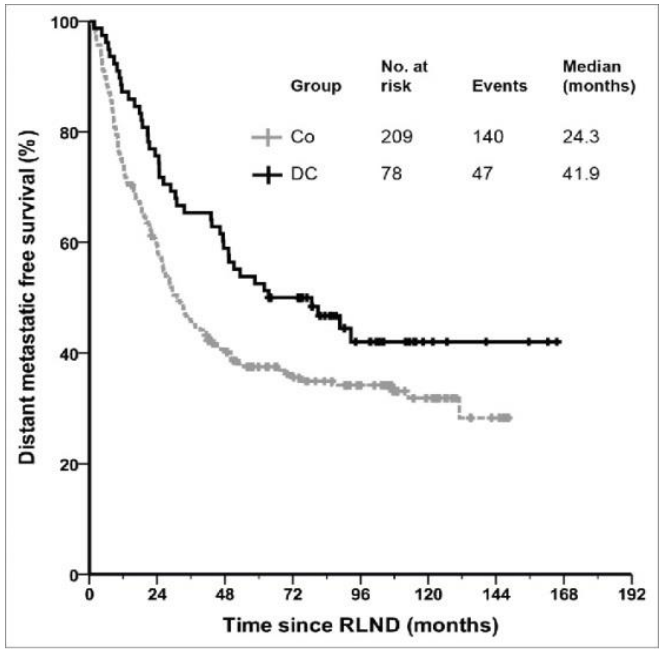


CCR FOCUS

Dendritic Cell–Based Immunotherapy: State of the Art and Beyond

Kalijn F. Bol[1,2], Gerty Schreibelt[1], Winald R. Gerritsen[2], I. Jolanda M. de Vries[1,2], and Carl G. Figdor[1]

Clin Cancer Res; 22(8) April 15, 2016



ORIGINAL RESEARCH
Oncoimmunology 5:1, e1057673; January 2016; © 2016 Taylor & Francis Group, LLC

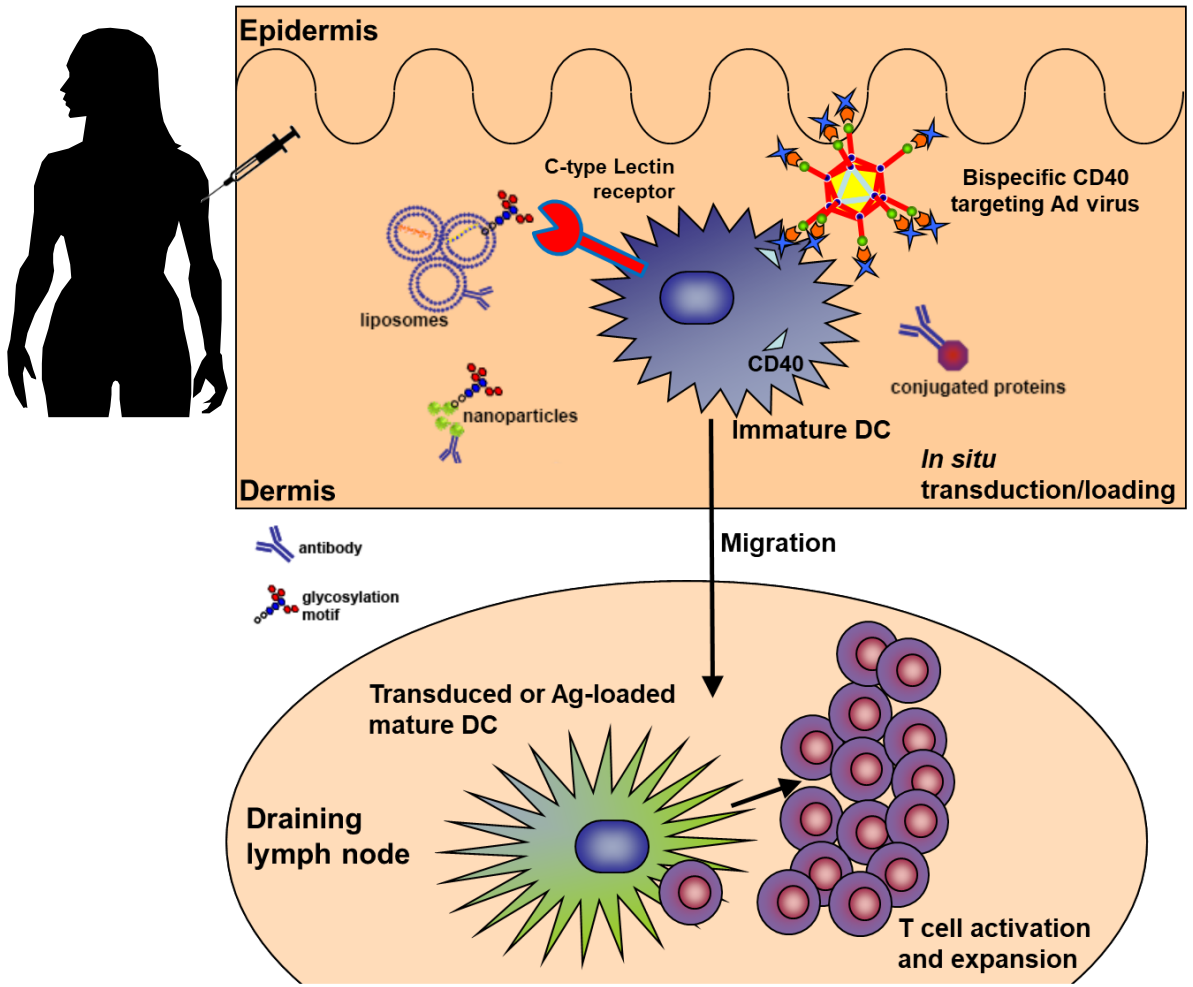
Favorable overall survival in stage III melanoma patients after adjuvant dendritic cell vaccination

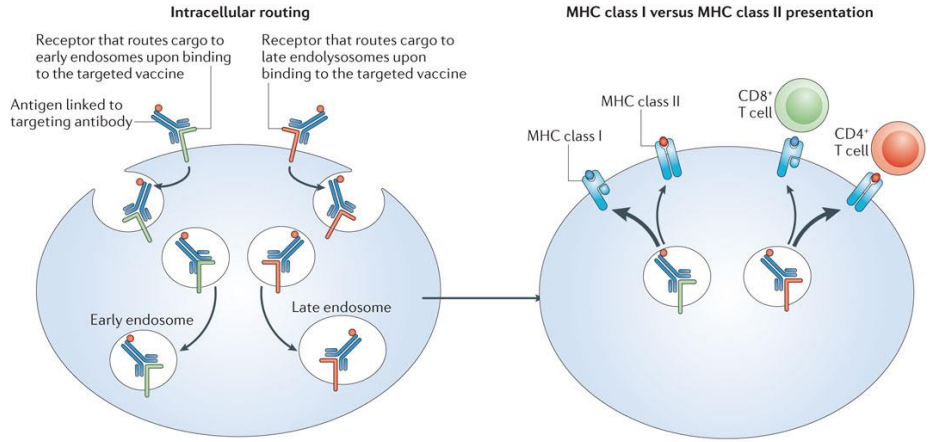
Kalijn F Bol[1,2], Erik H J G Aarntzen[1,2,3], Florentien E M in 't Hout[1,4], Gerty Schreibelt[1], Jeroen H A Creemers[1], W Joost Lesterhuis[1,5], Winald R Gerritsen[3], Dirk J Grunhagen[6], Cornelis Verhoef[6], Cornelis J A Punt[7], Johannes J Bonenkamp[4], Johannes H W de Wilt[4], Carl G Figdor[1], and I Jolanda M de Vries[1,2,*]

[1]Department of Tumor Immunology; Radboud Institute for Molecular Life Sciences; Radboud University Medical Center; Nijmegen, The Netherlands; [2]Department of Medical Oncology; Radboud University Medical Center; Nijmegen, The Netherlands; [3]Department of Radiology and Nuclear Medicine; Radboud University Medical Center; Nijmegen, The Netherlands; [4]Department of Surgical Oncology; Radboud University Medical Center; Nijmegen, The Netherlands; [5]Department of Medicine and Pharmacology; University of Western Australia; Crawley, Australia; [6]Department Surgical Oncology; Erasmus MC Cancer Institute; Rotterdam, The Netherlands; [7]Department of Medical Oncology; Academic Medical Center; Amsterdam, The Netherlands

Alternative DC vaccines: *in vivo* targeting

Hangalapura *et al. Cancer Res 2011, J Gene Med 2012*



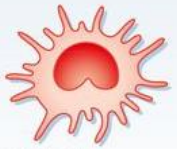
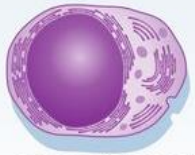


Receptor	Early endosomal compartment	Late endosomal compartment	Stimulates CD4+ T cells		Stimulates CD8+ T cells	
			In vitro	*In vivo*	*In vitro*	*In vivo*
CD205	No	Yes	+	+	+	++ +/– (human)
CD207	Yes	No	+	+	+	++
Mannose receptor 1	Yes	No	+	+	+	+
DC-SIGN	Yes (ligand dependent)	Yes (ligand dependent)	+	+	+	+
CLEC9A	Yes	No	+	+	+	++
DCIR2	No	Yes	+	++	+	+
CLEC12A	Not investigated	Not investigated	+	++	+	+/–
DC-ASGPR	No	Yes	+	++	+	+/–
Dectin 1	No	Yes	+	++	+	+
CD11c	Not investigated	Not investigated	+	+	+	++
CD11b	Not investigated	Not investigated	+	++	+	+
MHC class II	No	Yes	+	+	+	+/–
CD40	Yes	No	++ (human)	+	++ (human)	+
FcγR	No	Yes	+	+	+	+
XCR1 or XCL1	Not investigated	Not investigated	+	+	+	++

Kastenmüller *et al.* Nat Rev Immunol 2014

Nature Reviews | Immunology

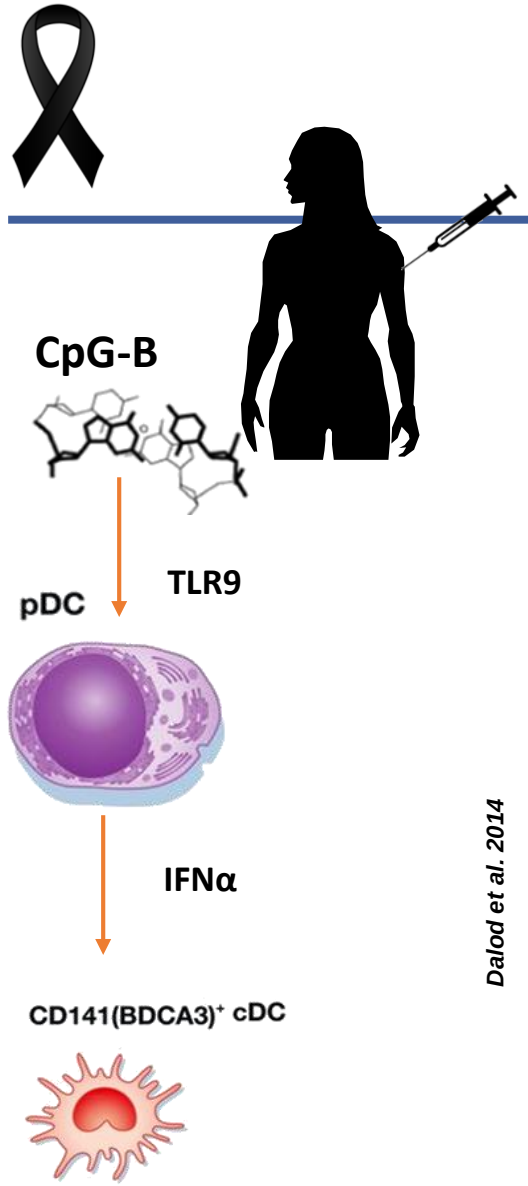
DC vaccines: what subset to target?

Blood	Pre-cDC		pDC	Classical monocyte
Lymphoid and non-lymphoid tissues				
HUMAN	**CD141(BDCA3)$^+$ cDC**	**CD11c(BDCA1)$^+$ cDC**	**pDC**	**moDC**
				
Other markers	XCR1$^+$ CLEC9A$^+$ FLT3$^+$	CD172a$^+$ CD11b$^+$ FLT3$^+$	CD303(BDCA2)$^+$ CD85g(ILT7)$^+$ FLT3$^+$	CD14$^+$ CD206$^+$ FLT3$^{-/low}$
Proposed conserved functional specification	TLR3-induced IFN-III production High efficiency for CD8$^+$ T cell activation? Cross-presentation of cell-associated antigens	Presentation of exogenous antigens to CD4$^+$ T cells Th2 or Th17 induction?	TLR7/9-induced IFN-I/III production Innate defenses against viruses?	Innate defenses against infections through TNF, ROI, NOI production? Humoral immunity to extracellular pathogens? Th17 induction?

cDC1

Dalod et al. 2014

Early cDC1 suppression in TDLN: immune escape



Dalod et al. 2014

CD141(BDCA3)⁺ cDC

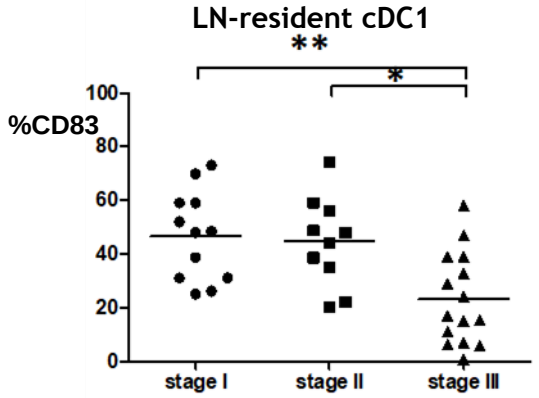
XCR1⁺
CLEC9A⁺
FLT3⁺

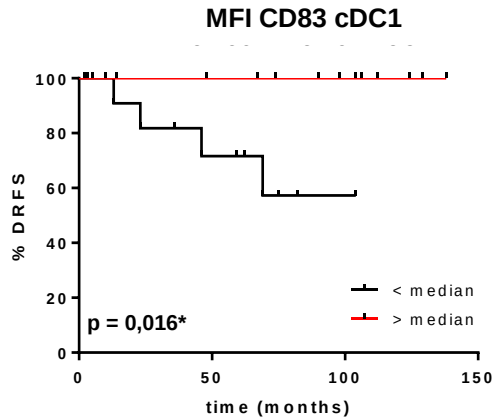
TLR3-induced
IFN-III production

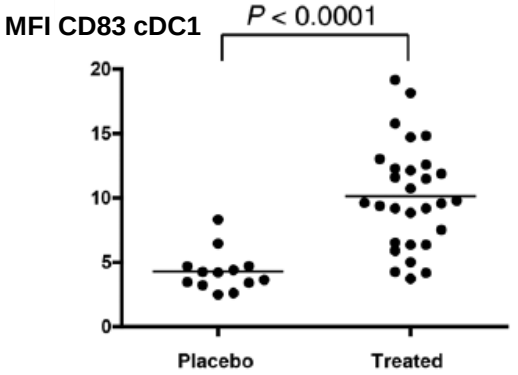
High efficiency for
CD8⁺ T cell activation?

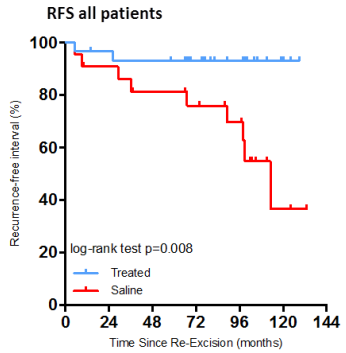
Cross-presentation of
cell-associated antigens

cDC1



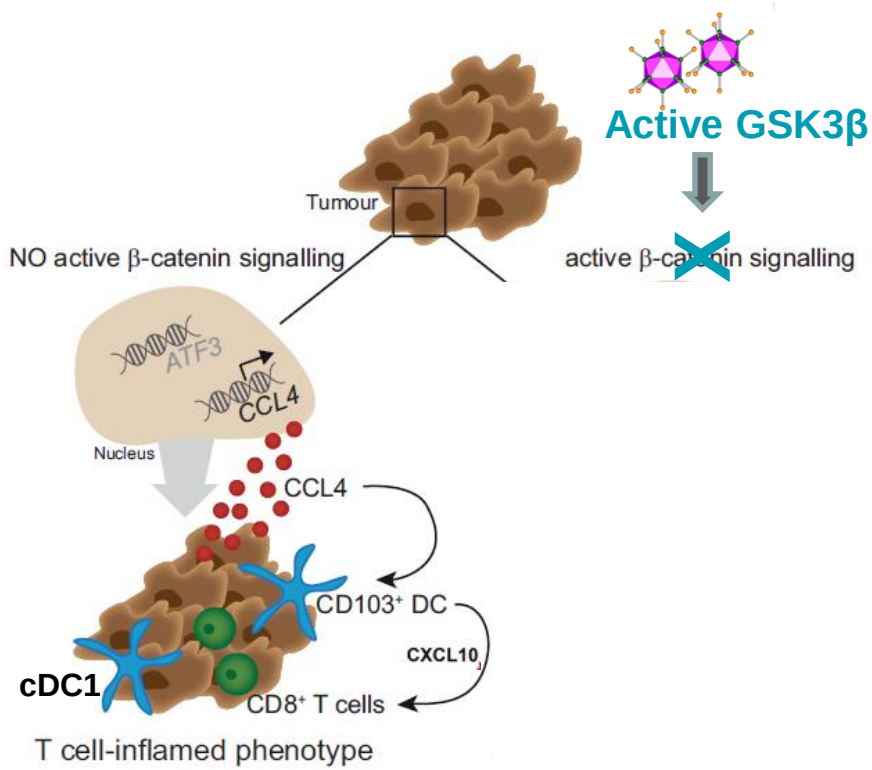


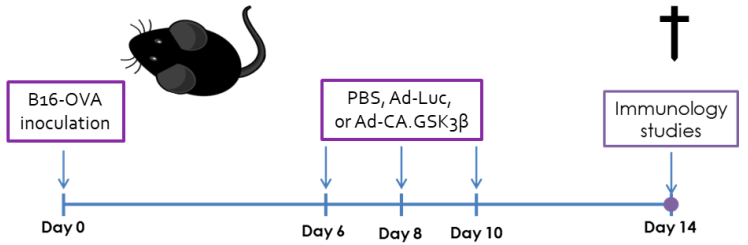


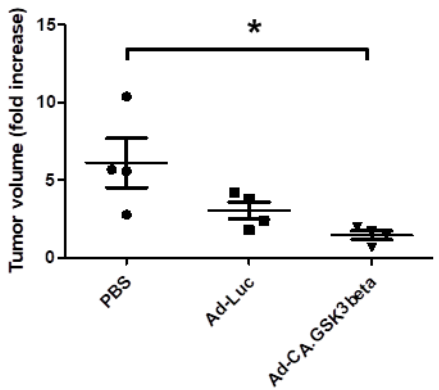


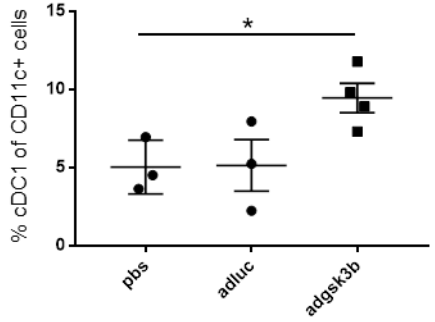
Van den Hout et al. Cancer Immunol Res 2017
Koster et al. Clin Cancer Res 2017

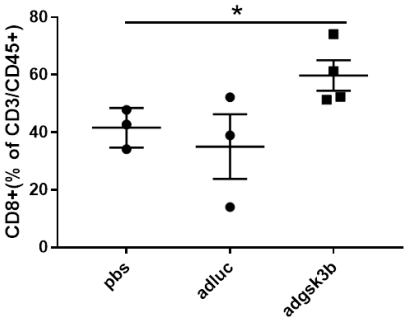
Melanoma T cell infiltration depends on DC: role for Wnt











Spranger et al. Nature 2015

Lopez-Gonzalez OncoImmunol 2019

Options and advantages of *in vivo* vaccination

High-intensity focused ultrasound

Stereotactic body radiation therapy (SBRT)

Microwave ablation (MW)

Oncolytic viruses

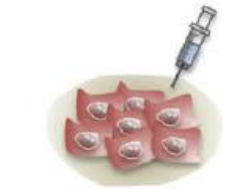
Chemotherapy

Radiofrequency ablation (RFA)

Cryoablation

Irreversible electroporation (IRE)

Immunogenic cell death: antigen and damage-associated molecular pattern (DAMP) release
Type-I IFN response
Ensure DC and T cell recruitment



In situ vaccination (ISV) into a recognized tumor

- ISV exploits all relevant antigens in the tumor, avoiding the need to identify tumor antigens or consider the HLA type
- ISV is simple and cost effective because it utilizes standard reagents and does not require patient-specific vaccines
- ISV takes advantage of the entire antigenic repertoire of a tumor to minimize immune escape
- ISV utilizes feasible local delivery with minimal systemic side effects
- ISV has the potential for synergy when combined with other therapies
- ISV can be effectively performed prior to surgery as neoadjuvant therapy

SHEEN AND FIERING *WIREs Nanomed Nanobiotechnol.* 2018;e1524.

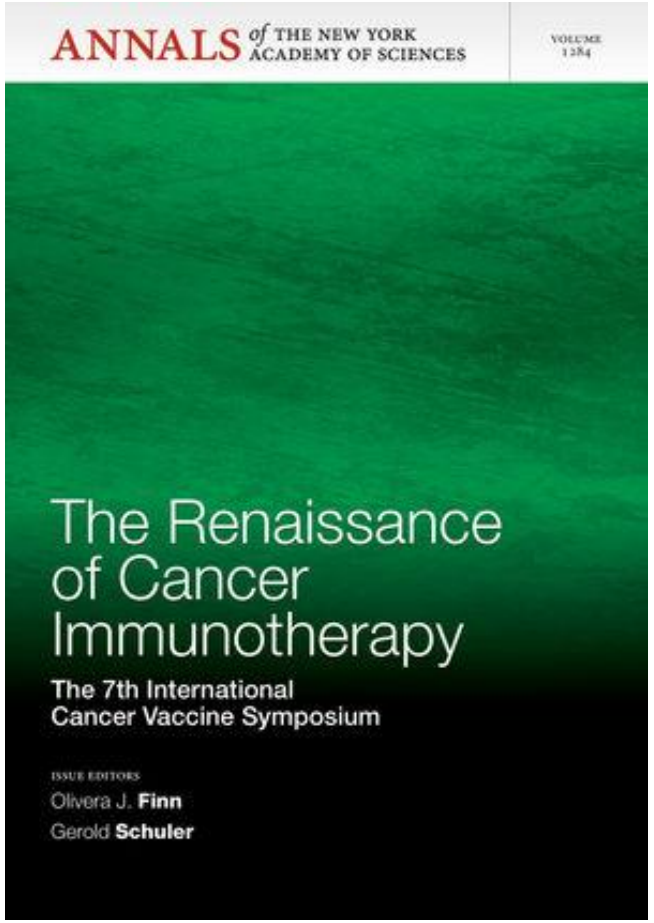
Learning goals

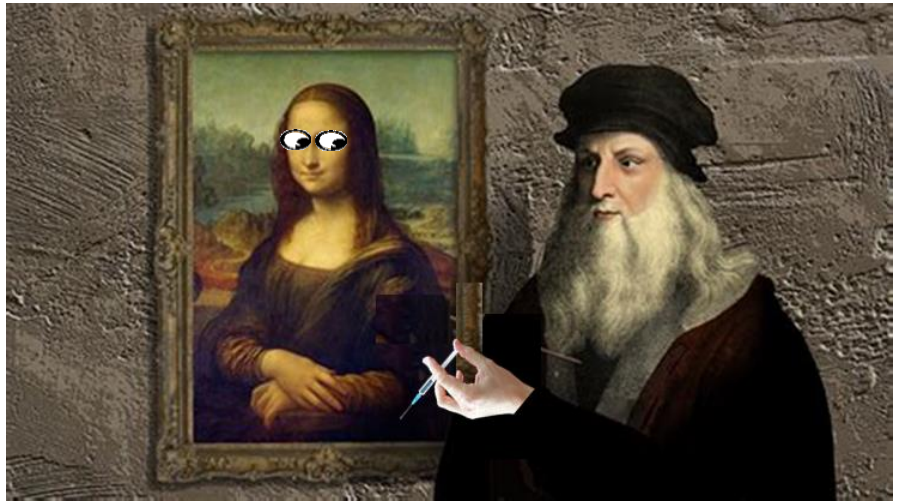
1. **Understanding the stumbling blocks and requirements for the design of successful therapeutic vaccines: choice of antigens and adjuvants**

2. **Becoming familiar with some of the current approaches to vaccination against cancer: broader definition includes *in vivo* vaccination**

3. **Acquiring an understanding of the positioning of cancer vaccines in the developing field of cancer immunotherapy**

Cancer vaccines: a renaissance in the golden age of immunotherapy?





https://owlcation.com/humanities/