Cancer Vaccines

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Primer on Tumor Immunology and Biological Therapy of Cancer
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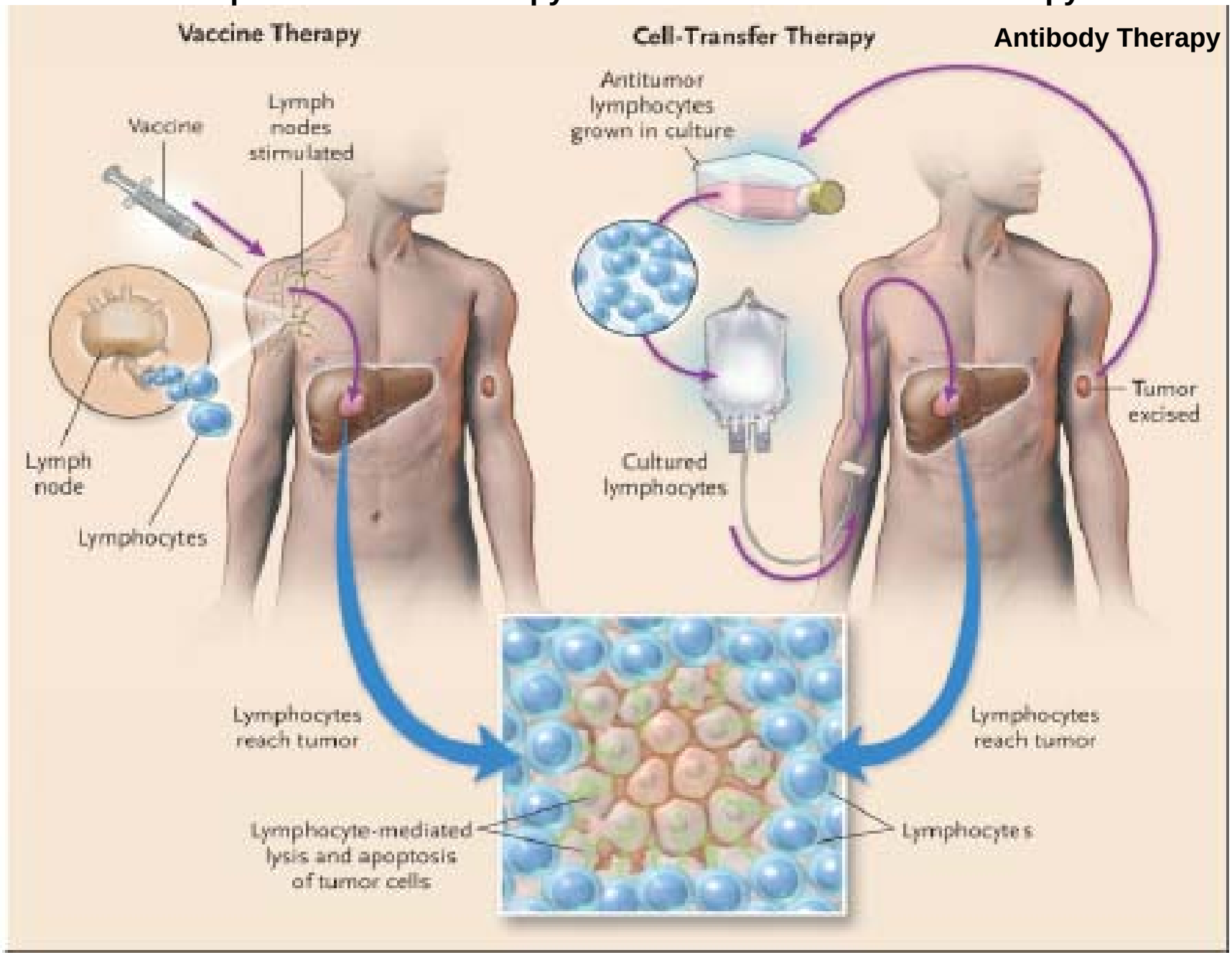
October 1, 2010

Walter J. Urba

The following relationships exist related to this presentation:

Bristol Myers Squibb: Honorarium, Speaker and Consultant

Active Specific Immunotherapy **Passive Immunotherapy**



Rosenberg SA ;NEJM 350:14 (2004)

Historical Perspective

- *1777* Nooth, surgeon to Duke of Kent, inoculated himself with cancer tissue from patient
- *1808* Alibert, physician to Louis XVIII, received an injection of breast cancer material
- Numerous trials since the turn of the century

Oettgen and Old. Biological Therapy of Cancer, 1991.

Homotransplantation of Human Cell Lines

(Abstract)

CHESTER M. SOUTHAM

Sloan-Kettering Institute for Cancer Research

- "Normal recipients have rejected implanted cells of all types".
- "In the cancer patients rejection was delayed or did not occur at all during the period of observation".
- In one of these individuals there was metastasis from the inoculation site on the forearm to the axillary lymph nodes".
- "….repeated implants formed smaller nodules and regressed more rapidly….".
- Acknowledged Ohio State penitentiary.

Bull. N.Y. Acad. Med. 1958

FATAL HOMOTRANSPLANTED MELANOMA

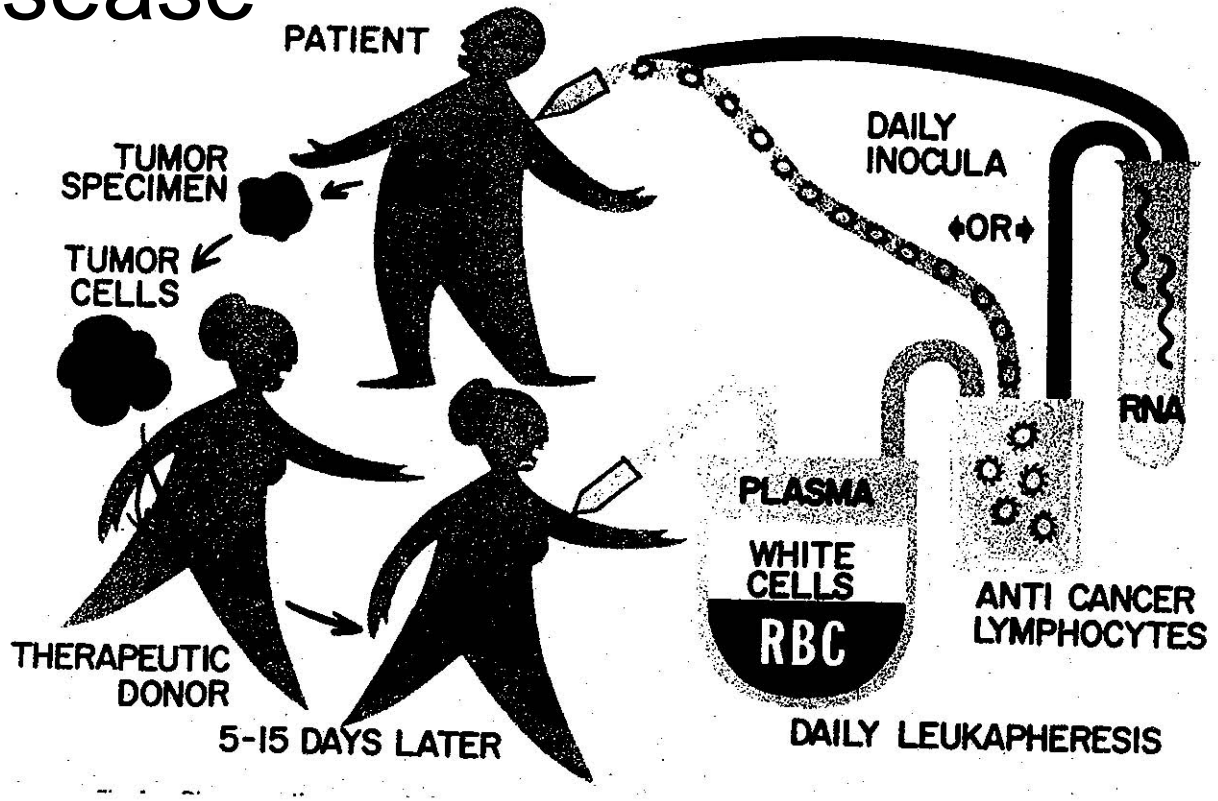
A Case Report

EDWARD F. SCANLON, M.D., ROGER A. HAWKINS, M.D.,*
WAYNE W. FOX, M.D., AND W. SCOTT SMITH, M.D.

- 50 yo WF Melanoma back (1958) – local excision
- Diffuse metastases (1961) – chemotherapy, transfusion from cured patient
- August 15, 1961 – healthy 80 yo mother inoculated with 0.5cm tumor
- August 16 – patient dies from peritonitis
- 24 days after inoculation mother has tumor (large excision rectus)
- Mother dies metastatic melanoma 14 months later

Cancer. 1965

Immunotherapy of Malignant Disease



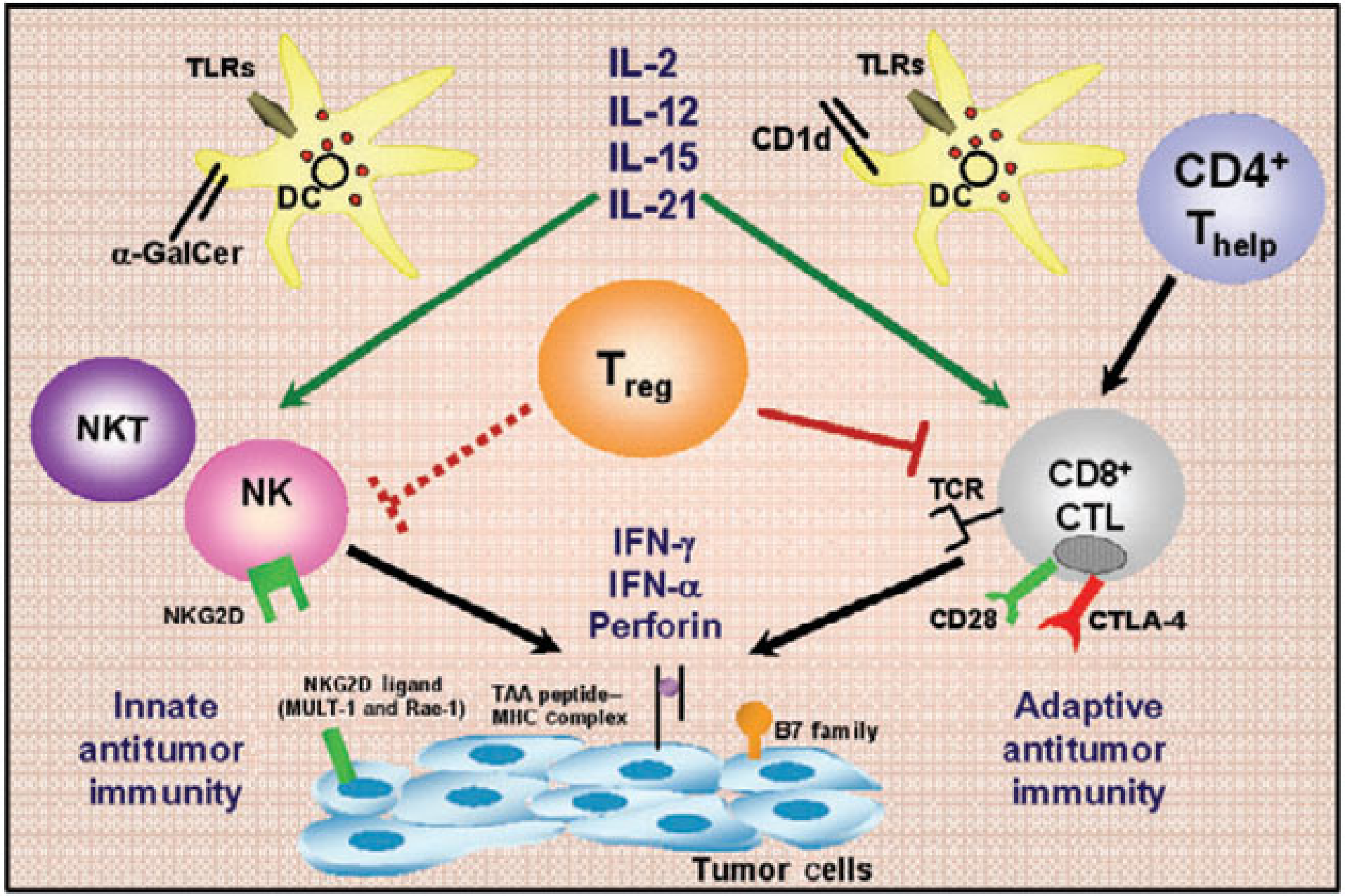
Nadler, SH, Moore, GE. Arch Surg/Vol 99, Sept 1969

Results of Treatment

Tumor Type	No. Responses
Malignant melanoma	18/86*
Breast	1/5
Colon	2/4
Soft tissue sarcoma	1/9
Osseous sarcoma	1/8†
Unknown primary, kidney, testicular	0/6
	23/188

* Complete-2
† Complete

Nadler, SH, Moore, GE. Arch Surg/Vol 99, Sept 1969



Pure, Allison & Schreiber Nature Immunol 6:1207 (2005)

Developing effective cancer vaccines

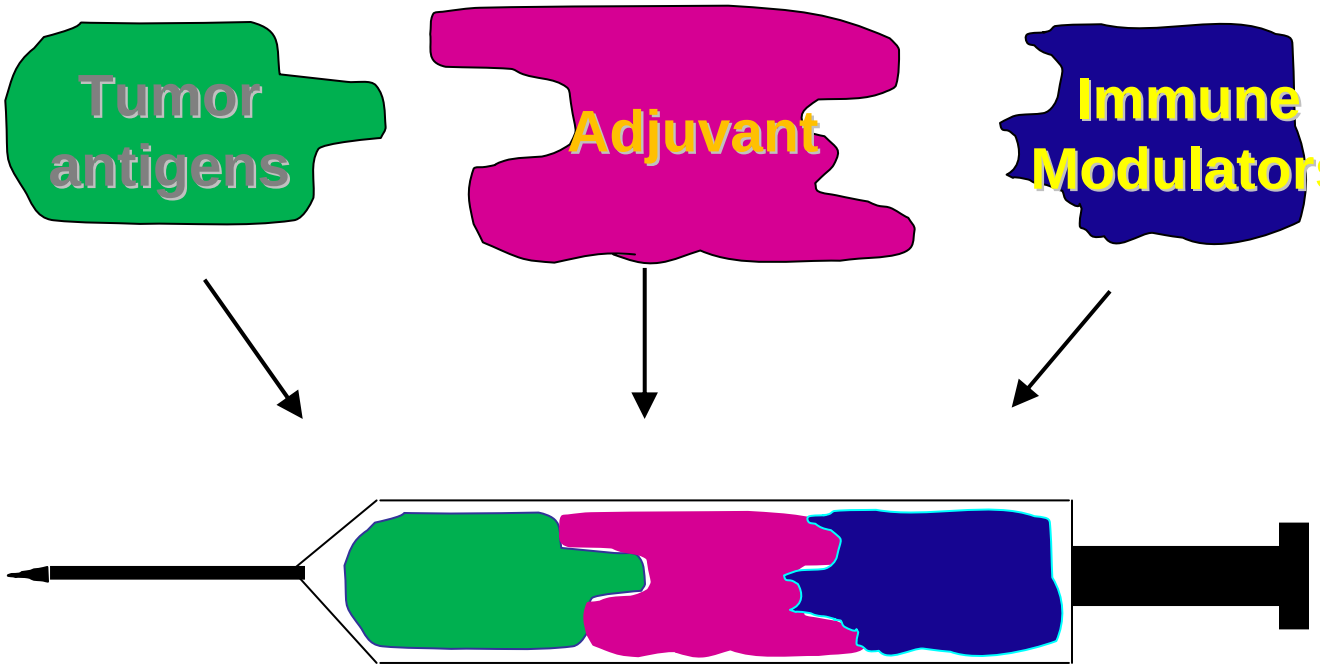
- Identify tumor-rejection antigen(s)
- Stimulate potent immune response
  - Choose the right adjuvant
  - Generate the right type of immune response
  - Elicit long-term memory
- Minimize risk of autoimmunity
- Prevent Immune evasion

Challenges facing development of effective cancer vaccines

- Tumor escape
  - Antigen/MHC loss; immunoediting
  - Immunosuppressive cytokines (TGF-B, IL-10…)
  - Tregs, MDSCs …
- T-cell trafficking
- Normal immune regulation (CTLA-4, PD-1…)
- Aging immune system

Vaccines: Teaching the immune system to recognize tumor cells

- Three components:



Human tumor antigens

- Shared tumor-specific antigens (Cancer – testis antigens)
  MAGE, BAGE, GAGE, GnTV, NY-ESO-1, RAGE, TRP2-INT2

- Antigens from new fusion proteins – bcr-abl, ETV6/AML

- Antigens resulting from mutations - BRAF, CDK4, β-catenin, CASP-8, K-ras, hsp70-2, EF2, TPI, Cdc27, p53

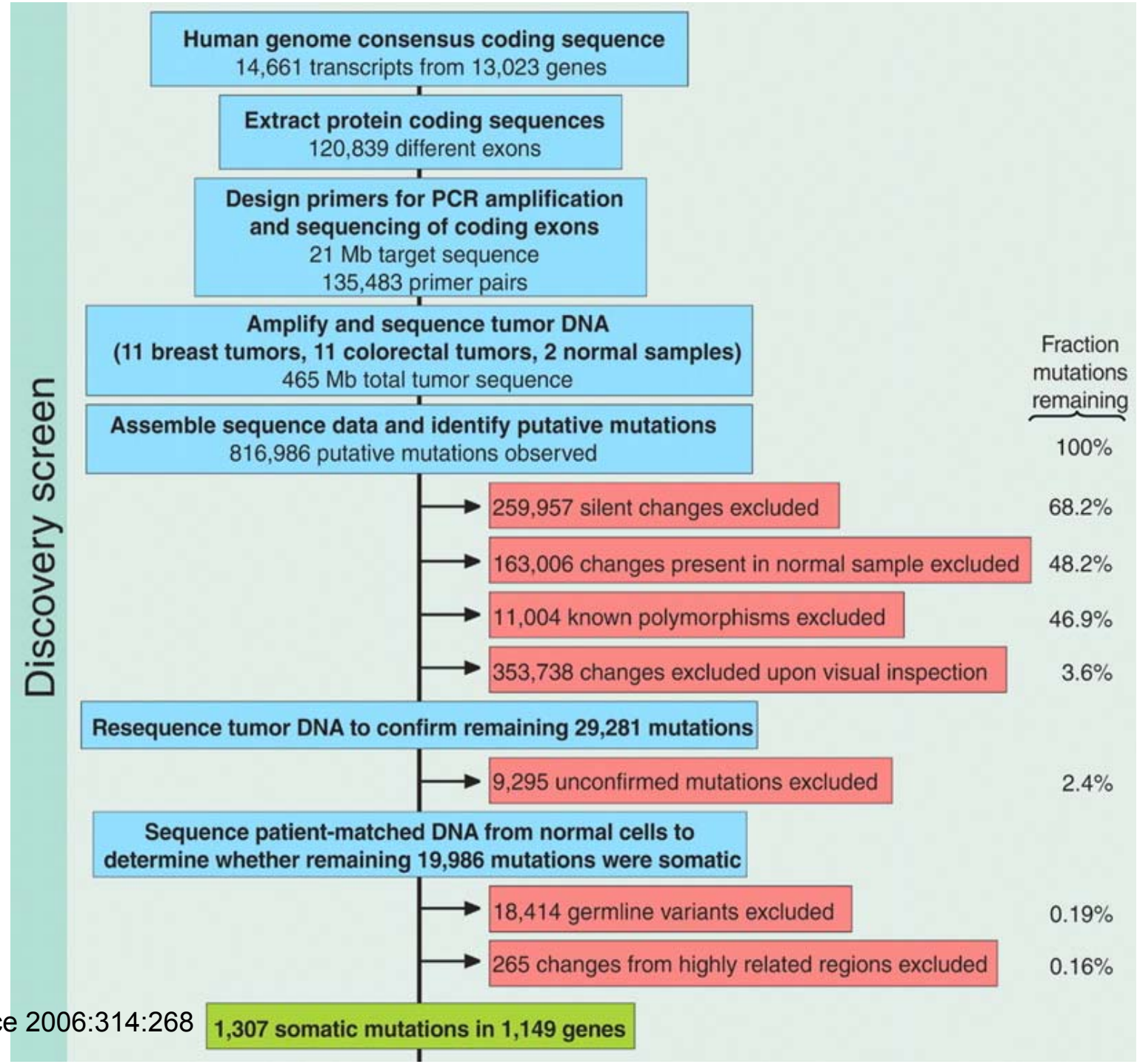
- Differentiation antigens - Tyrosinase, Melan-A ^{MART1,} gp100, gp75^{TRP1,} TRP2, CEA, PSA, PAP, PMSA

- Overexpressed antigens - P53, HER2-neu, PRAME, survivin, telomerase, WT-1,

- Viral antigens - HPV16 E7, EBV

- MUC-1
- Idiotype
- Hundreds of shared antigens are known but only about 20 have been tested clinically

Schematic of mutation discovery and validation screens



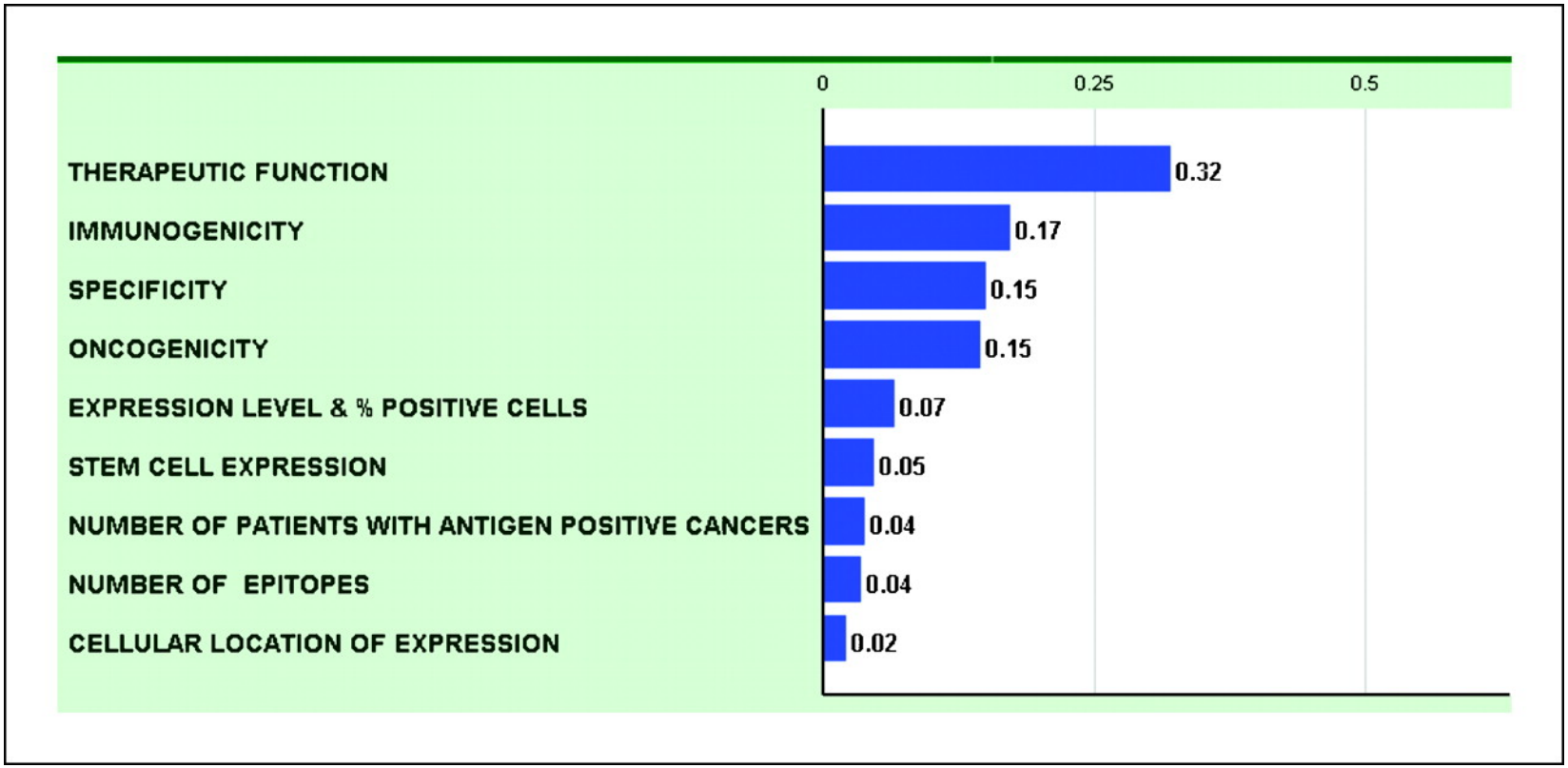
Sjoblom T et al Science 2006:314:268

Characteristics of an ideal cancer antigen

Criteria	Top subcriteria
Therapeutic function	Superb data controlled vaccine trial suggestive
Immunogenicity	T-cell and/or antibody responses elicited in clinical trials
Oncogenicity	Associated with oncogenic process (i.e., oncogenic “self” protein)
Specificity	Absolutely specific (e.g., mutated oncogene, idiotype protein, or viral protein
Expression level and % positive cells	Highly expressed on all cancer cells in patients designated for treatment
Stem cell expression	Evidence for expression on putative cancer stem cells
# patients with antigen-positive cancers	High level of expression in many patients with a particular tumor type
# epitopes	Longer antigen with multiple epitopes and the potential to bind to most MHC molecules
Cellular location of expression	Normally expressed on the cell surface with no or little circulating antigen

Cheever et al. Clin Cancer Res 2009; 15(17), 2009

Criteria for an ideal cancer antigen were weighted by pairwise comparison and the resulting relative weights are indicated.



Cheever M A et al. Clin Cancer Res 2009;15:5323-5337

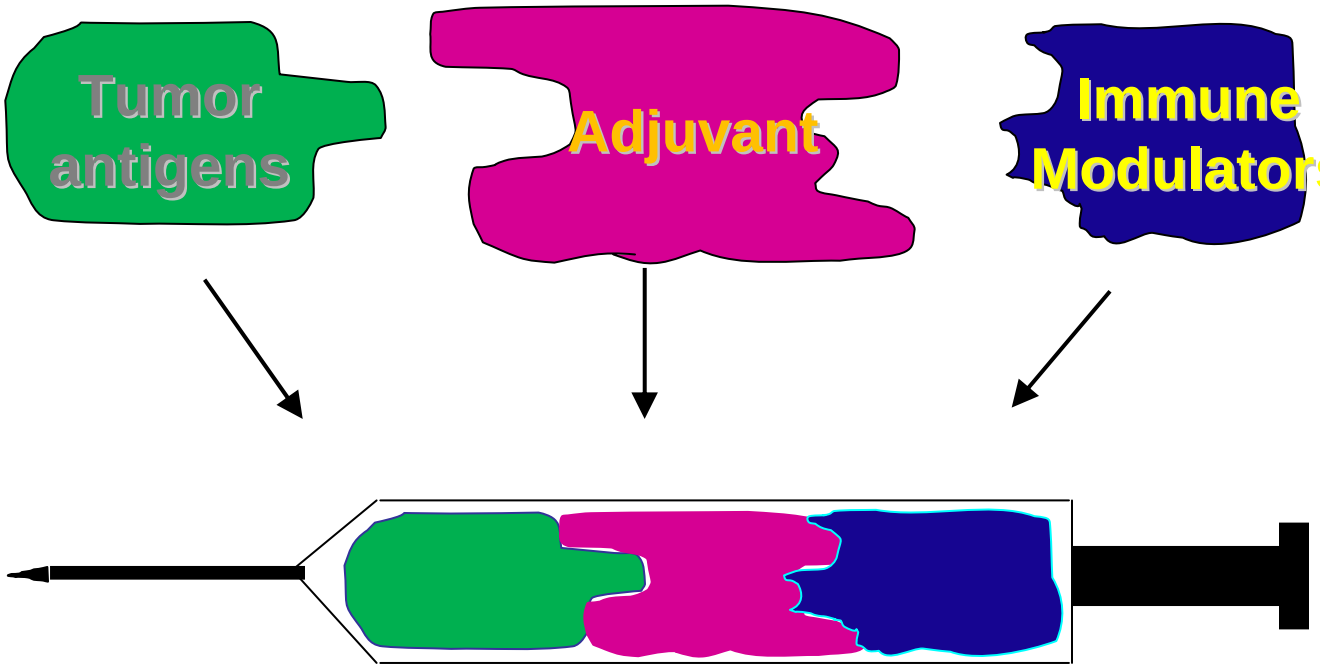
Cancer antigen pilot prioritization: ranking based on predefined and preweighted criteria

	Criteria				
Antigens (rank/reference number and name)	Cumulative score	Therapeutic function (0.32)	Immunogenicity (0.17)	Oncogenicity (0.15)	Specificity (0.15)
WT1	0.81	0.75 (fair)	1.0 (trials)	1.0 (oncogenic)	0.54 (oncofetal)
MUC1	0.79	0.75 (fair)	1.0 (trials)	1.0 (oncogenic)	0.23 (post-translational)
LMP2	0.78	0.75 (fair)	1.0 (trials)	0.34 (viral)	1.0 (absolute)
HPV E6 E7	0.77	0.89 (mixed)	1.0 (trials)	0.34 (viral)	1.0 (absolute)
EGFRvIII	0.76	0.76 (mixed)	1.0 (trials)	0.62 (mixed)	1.0 (absolute)
HER-2/neu	0.75	0.85 (adequate)	1.0 (trials)	1.0 (oncogenic)	0.35 (overexpressed)
Idiotype	0.75	0.76 (mixed)	1.0 (trials)	0.12 (differentation)	1.0 (absolute)
MAGE A3	0.71	0.79 (mixed)	1.0 (trials)	0.25 (mixed)	0.54 (oncofetal)
p53 nonmutant	0.67	0.42 (mixed)	1.0 (trials)	1.0 (oncogenic)	0.35 (overexpressed)
NY-ESO-1	0.66	0.75 (fair)	1.0 (trials)	0.25 (prognosis)	0.54 (oncofetal)

Cheever et al. Clin Cancer Res 2009; 15(17), 2009

Vaccines: Teaching the immune system to recognize tumor cells

- Three components:



Adjuvants

- Goals are to increase immunogenicity
- Mechanisms are very poorly understood; so choosing an optimal adjuvant is more art and religion than science.
- There are no standard approaches for defining optimal adjuvanticity other than measures of immune response or clinical response in a large trial (eg GSK AS15 vs AS01B)
- We need a better understanding of what makes an adjuvant work well, and that probably depends on the nature of antigen, the site of injection, and the goal (eg: humoral vs CTL response)

Adjuvants: potential roles

- Activation and recruitment of professional APC (eg dendritic cells) to present the antigen
  - Need immature DC for protein; mature DC OK for peptide
- Induction of a cytokine milieu to support a Th1 (or Th2, or Th17) response
  - At the vaccine site?
  - At the draining node?
- Activation of innate immunity
- Depot effect for antigen

Selection of Adjuvants

- Alum – prototypical adjuvant for humoral immunity
- BCG – long hx of use with cell-based vaccines, and used in bladder CA directly
  - Use limited by toxicity, but available
- Incomplete Freund's adjuvant (mineral oil with emulsifying agent) for use with aqueous Ag, as water-in-oil emulsion
  - based on Freund's work in 1938, for humoral imm
  - Adapted for use with peptides and other antigen formulations
- Cytokines: IL-12, GM-CSF, IFN-alpha, others (locally)
- Toll-like receptor agonists (TLR3, 4, 7, 8, 9)
- Saponins (eg: QS21)
- Combination adjuvants

Incomplete Freund's adjuvant

- Eg: Montanide ISA-51
  - Mineral oil
  - Emulsifying agent containing oleic acid (from beef tallow or olives)
  - Extensively used worldwide in veterinary applications for viral vaccines
- Preparation of stable emulsions critical per Freund, but not tested in humans
- Associated with homing of T cells to the vaccine site preferentially over homing to tumor, and assoc with T cell death at the vaccine site (sink) - *Willem Overwijk*
  - Could this contribute to transience or weak response?
  - Could it contribute to poor homing of T cells to tumor

Forms of Antigen for active immunization of cancer patients

- Antigenic peptides (short and long), whole proteins or virus-like particles (with adjuvants, combined with lipids or liposomes, with gp96, Hsp70, or Hsp90)
- Recombinant viruses containing tumor antigen genes (adenovirus, fowlpox virus, vaccinia virus)
- Naked DNA encoding tumor antigen genes (intramuscular or by “gene gun”)
- Recombinant bacteria containing tumor antigen genes (BCG, *Salmonella, Listeria*)
- Cells expressing tumor antigens (dendritic cells pulsed with antigen, modified or unmodified tumor cells)

Cancer Vaccines

Prophylactic

versus

Therapeutic

Oncogenic Infectious Agents

Agent	Tumor types	Annual cases worldwide (estimate)
Bacteria		
H. pylori	Stomach cancer, gastric lymphoma	603 000
Viruses		
HPV	Cervical, anal, vaginal, other cancers	561 000
HBV	Liver cancer	330 000
HCV	Liver cancer	195 000
EBV	Nasopharyngeal carcinoma, lymphomas (Hodgkin's, non-Hodgkin's, Burkitt's)	137 000[a)]
HHV-8	Kaposi's sarcoma	66 000[a)]
HTLV-1	Adult T cell leukemia	3000
Parasites		
Schistosomes	Bladder cancer	11 000
Liver flukes	Cholangiocarcinoma	2000

[a)] Adapted from [1]

Frazer, IH; Lowy, DR; Schiller, JT. Eur. J. Immunol. 2007. 37: S148-155

Cancers attributable to infection: estimate of worldwide distribution according to type (annual number of cases in thousands)[a)]

Tumor type	Developed countries	Developing countries	World	Percentage attributable to infection
Stomach cancer	192	400	592	63
Liver cancer	50	475	525	85
Cervical cancer	83	409	493	100
Nasopharyngeal cancer	6	72	78	97
Kaposi's sarcoma	4	62	66	100
Non-Hodgkin's	9	27	36	67
Hodgkin's disease	12	17	29	45
Anal cancer	13	14	27	90
Vulvar/vaginal cancer	7	9	16	40
Bladder cancer	0	11	11	3
Gastric lymphoma	6	6	12	77
Burkitt's lymphoma	0	7	7	83
Leukemias	1	2	3	
Cholangiocarcinoma	0	2	2	

Frazer, IH; Lowy, DR; Schiller, JT. Eur. J. Immunol. 2007. 37: S148-155

Vaccine status for cancer-associated infectious agents

Infectious agent	Oncogenic mechanism	Target antigen (prevention)	Status (prevention)	Target antigen (therapy)	Status (therapy)
HBV	Oncogene insertion, X protein	HBsAg VLP	Licensed	HBsAg, HBcAG, HBx	Preclinical
HPV	Oncogene insertion, E6 and E7	L1 capsid protein VLP	Licensed	E6 and E7 (+/- E2, E4)	Phase 2 x several
EBV	Oncogene insertion, EBNA-1 + EBER (oncogenic RNA)	Gp350	Phase 1	LMP-1	Phase 2
H. pylori	Oncoprotein injection, CagA Oncogene	CagA, Unrease	Phase 1	CagA	Preclinical
HCV	Uncertain	Gp120 VLP (Core +E1, E2)	Phase 1		
HHV-8	Immunomodulation	Membrane GP	Preclinical		
HTLV-1	Oncogene insertion, tax	Envelope protein	Preclinical		
Parasite (Schistosomes)	Irritation Immunomodulation	Outer membrane proteins	Phase 2		

Frazer, IH; Lowy, DR; Schiller, JT. Eur. J. Immunol. 2007. 37: S148-155

Therapeutic Exploitation

Cancer Vaccines – The Old Paradigm

- Sequential vaccination will overcome tolerance to “self” antigens and induce immune responses causing tumor regression with minimal or no toxicity

Rosenberg et al. *Nature Med* 2004;10:909-915

Results of clinical vaccine studies in patients with metastatic cancers

Vaccine type	Reference	Cancer type	Vaccine	Total patients	Patients responding
Peptide	43	Melanoma	Tyrosinase + GMCSF	16	0
	44	Melanoma	Peptides in IFA or on DC	26	3
	45	Melanoma	MART-1 + IL-12	28	2
	46	Prostate	Peptides	10	0
	47	Melanoma	Peptides on PBMC + IL-12	20	2
	48	Breast and prostate	Telomerase	7	0
	49	Cervix	HPV16 E7	17	0
	50	Colorectal	Peptides in IFA	10	0
	51	Multiple	NY-ESO-1	12	0
	52	Multiple	Ras in DETOX adjuvant	15	0
	53	Multiple	Peptides in IFA	14	0
Virus	29	Prostate	Vaccinia-PSA	33	0
	54	Prostate	Vaccinia-PSA	42	0
	55	Colorectal	Vaccinia-CEA	20	0
	56	Colorectal	Vaccinia-CEA and B7-1	18	0
	57	Multiple	Avipox-CEA (IGMCSF)	60	0
	58	Multiple	Avipox-CEA	15	0
	59	Multiple	Vaccinia + avipox-CEA	18	0
Tumor cells	60	Melanoma	Transduced with GM-CSF	26	1
	61	Melanoma	Membranes on silicone beads	17	1
	62	Lung	Transduced with GMCSF	26	1
	63	Lung	Transduced with GMCSF	43	3
	64	Breast	Transduced with B7-1	30	0
Dendritic cells	65	Melanoma	Pulsed with peptides	17	0
	66	Melanoma	Pulsed with peptides or lysates	33	3
	67	Melanoma	Pulsed with peptides or lysates	16	5
	68	Melanoma	Pulsed with peptides	24	1
	22	Melanoma	Pulsed with MAGE-3A1 peptide	11	0
	69	Childhood cancers	Pulsed with lysates	15	1
	70	Kidney	Transfected with RNA	15	0
	71	Colorectal	Pulsed with CEA peptides	12	1
	72	Kidney	Pulsed with tumor lysates	35	3
	23	Multiple	Pulsed with tumor lysates	20	0
Heat shock protein	73	Melanoma	Hsp-96	28	2
	74	Multiple	Hsp-96	16	0
			Total	765	29

Objective response rate = 3.8%.

N=765

29 responses

Objective response rate = 3.8%

Rosenberg SA et al. Nature Medicine 2004:10:909

Peptide Vaccines N=381; 2CR; 9PR

Peptide vaccine immunization of patients with metastatic cancer

Peptide	HLA restriction	Total patients	NR	PR	CR
MART-1_{27-35}	A2	23	22	1	0
MART-1_{27-35} + IL-12	A2	12	12	0	0
MART-1_{26-35}(27L)	A2	6	6	0	0
TRP-$2_{180-188}$	A2	20	19	1	0
$gp100_{209-217}$	A2	9	8	0	1
$gp100_{209-217}$(210M)[a]	A2	32	32	0	0
$gp100_{209-217}$(210M) + IL-12	A2	28	28	0	0
$gp100_{209-217}$(210M) + GM-CSF	A2	18	18	0	0
$gp100_{280-288}$	A2	9	9	0	0
$gp100_{280-288}$(2889V)[b]	A2	5	5	0	0
$gp100_{154-162}$	A2	10	0	0	0
gp100ES:$_{209-217}$(210)	A2	9	9	0	0
g209-2M + MART-27L	A2	23	23	0	0
g209-2M, g280-9V, MART-27L[c] + tyr3D[d]	A2	16	14	2	0
$gp100_{44-59}$	DR4	4	4	0	0
$gp100_{44-59}$ + g209-2M + MART-27L	A2/DR4	22	21	0	1
$Tyrosinase_{240-251}$	A1	16	15	1	0
$gp1001_{7-25}$	A3	12	12	0	0
$Tyrosinase_{206-214}$	A2	8	8	0	0
TRP-1 ORF1–9	A31	5	5	0	0
Combination peptides	Non-A2	15	15	0	0
MAGE-$12_{170-178}$	Cw7	9	8	1	0
NY-ESO-$1_{157-165}$(165V)	A2	19	19	0	0
NY-ESO-$1_{161-180}$	DP4	6	5	1	0
NY-ESO-$1_{161-180+157-165}$(165V)	A2/DP4	11	11	0	0
$Her2/neu_{369-378}$	A2	6	6	0	0
$Telomerase_{540-548}$	A2	13	13	0	0
Dendritic cells + g209-2M + MART-27L	A2	15	13	2	0
Total		381	370	9	2

Overall objective response rate = 2.9%. HLA, human leukocyte antigen; CR, patients showing complete response; PR, patients showing partial response; NR, patients showing no response.

Rosenberg SA et al. Nature Medicine 2004:10:909

Viral vaccine immunization of patients with metastatic cancer

Virus	HLA restriction	Total patients	NR	PR	CR
Fowlpox MART-1	Any	12	12	0	0
Fowlpox gp100	Any	20	20	0	0
Fowlpox gp100(210M, 288V)	A2	15	14	1	0
Fowlpox gp100($ES_{209-271}$(210M))	A2	46	46	0	0
Vaccinia MART-1	Any	5	5	0	0
Vaccinia gp100	Any	16	16	0	0
Adenovirus MART-1	Any	17	16	0	1
Adenovirus gp100	Any	7	7	0	0
DNA gp100(210M, 288V)	A2	22	21	1	0
Total		160	157	2	1

Overall objective response rate = 1.9%. HLA, human leukocyte antigen; CR, patients showing complete response; PR, patients showing partial response; NR, patients showing no response.

Viral vaccines N=160; 2PR; 1CR

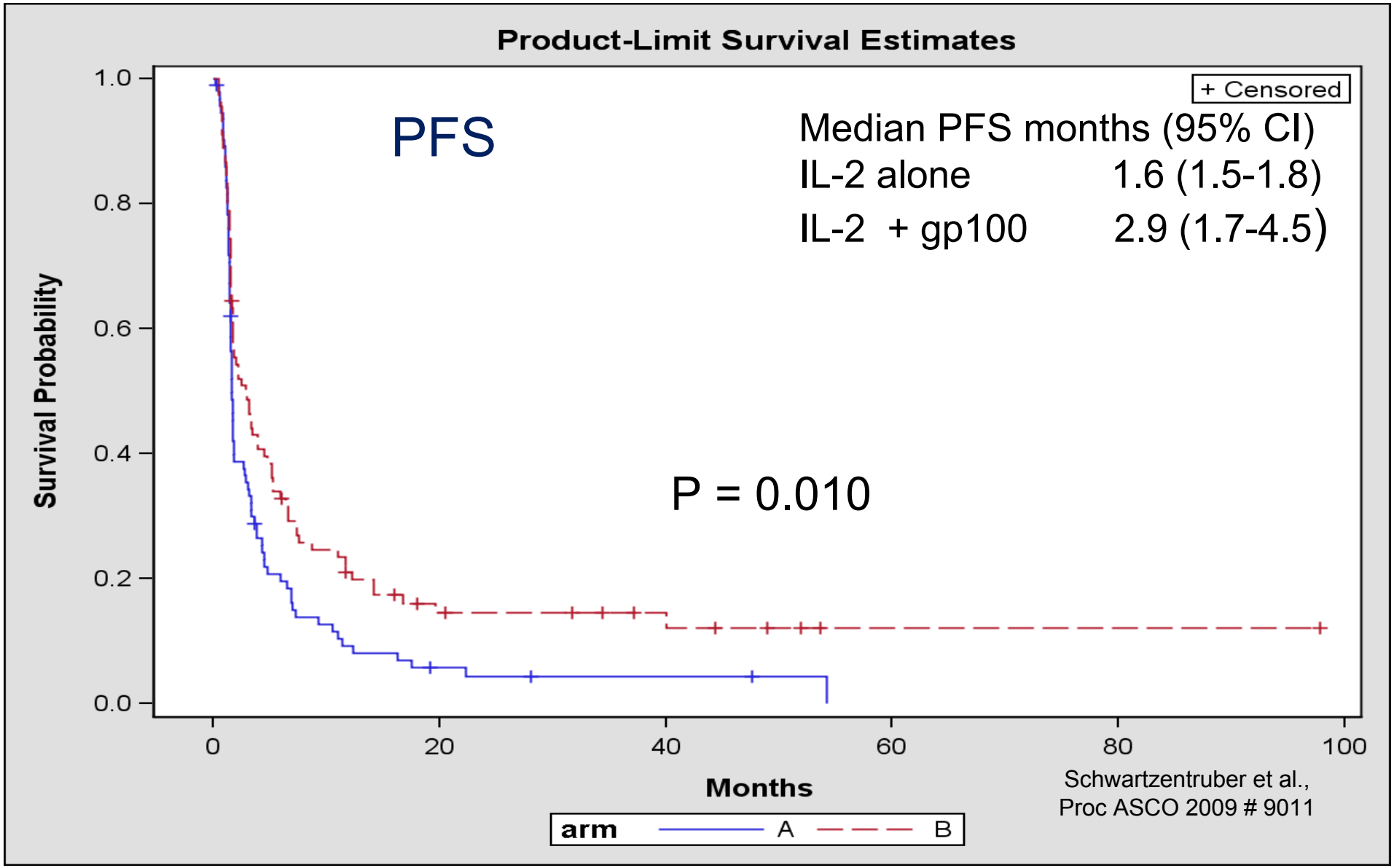
Rosenberg SA et al. Nature Medicine 2004:10:909

Recent studies suggest there is a clinical benefit of cancer vaccines using defined antigens

- Regression of cervical neoplasia with HPV vaccine.
  - Kenter et al. NEJM, 2009.
- Promising data for an idiotype lymphoma vaccine (phase III) Schuster et al, JCO (ASCO 2009)
- Peptide vaccine + HD IL-2 increases response rate and PFS in melanoma Schwartzentruber D et al. ASCO 2009
- PROSTVAC-VF improved survival in randomized phase II study Kantoff et al J Clin Oncol 28:2010
- Dendritic cell vaccine improves survival of metastatic hormone-refractory prostate CA
  - Provenge (Sipuleucel-T; Dendreon): DC + PAP
    - *Kantoff et al N Engl J Med 363:411, 2010*

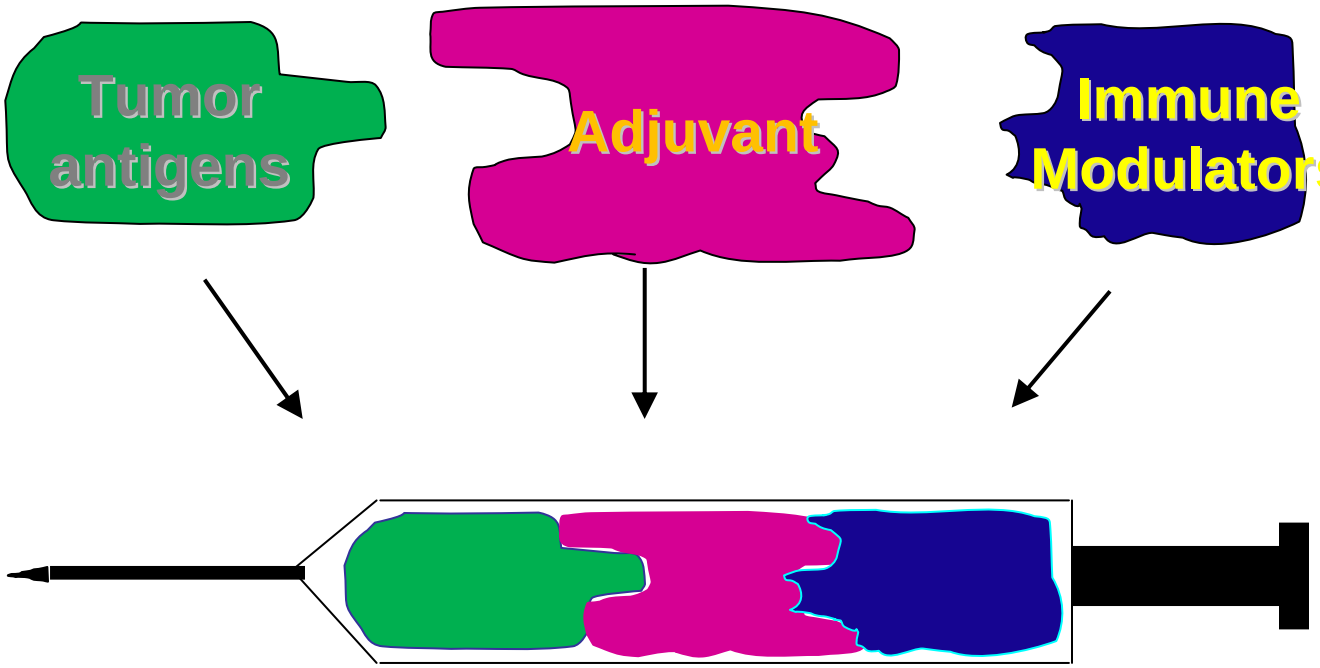
[*From Craig Slingluff*]

Vaccination with Gp100 peptide adds significantly to the benefit of HD IL-2



Vaccines: Teaching the immune system to recognize tumor cells

- Three components:



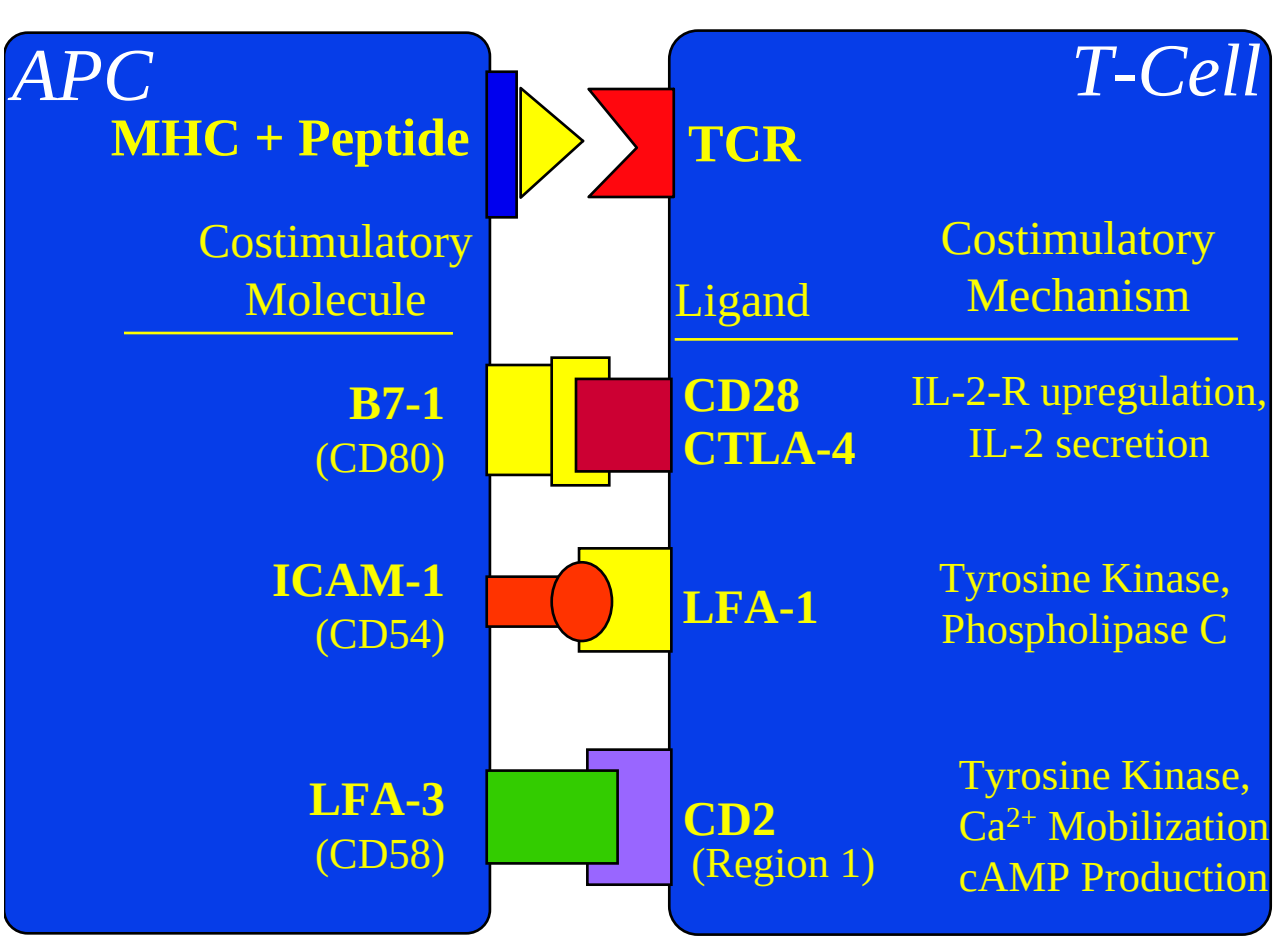
Recombinant Vaccine Vectors

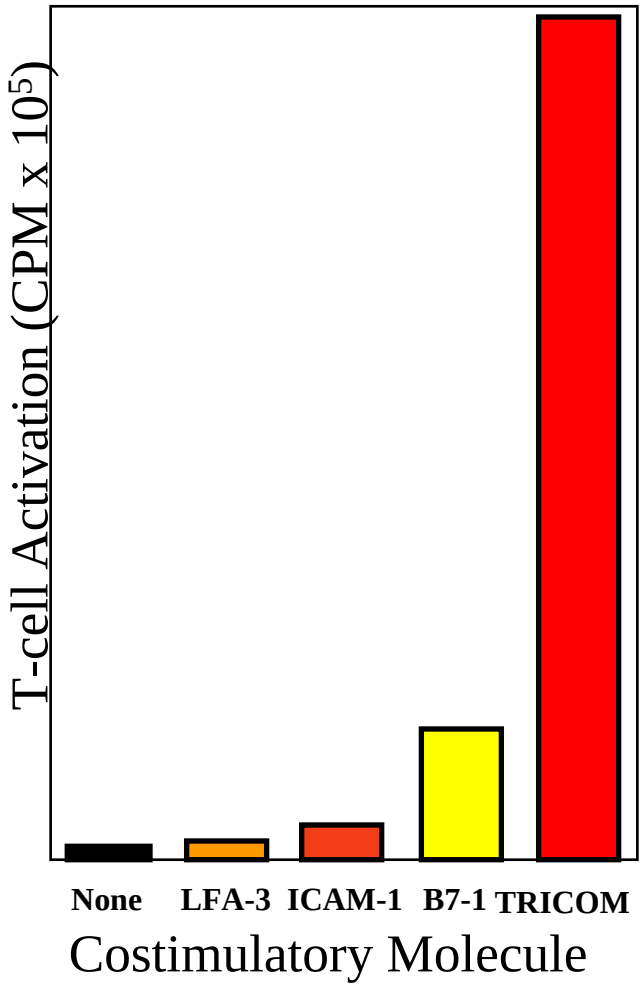
- Vaccinia (rV-) elicits a strong immune response
  - – host induced immunity limits its continuous use
  - – MVA (replication defective)

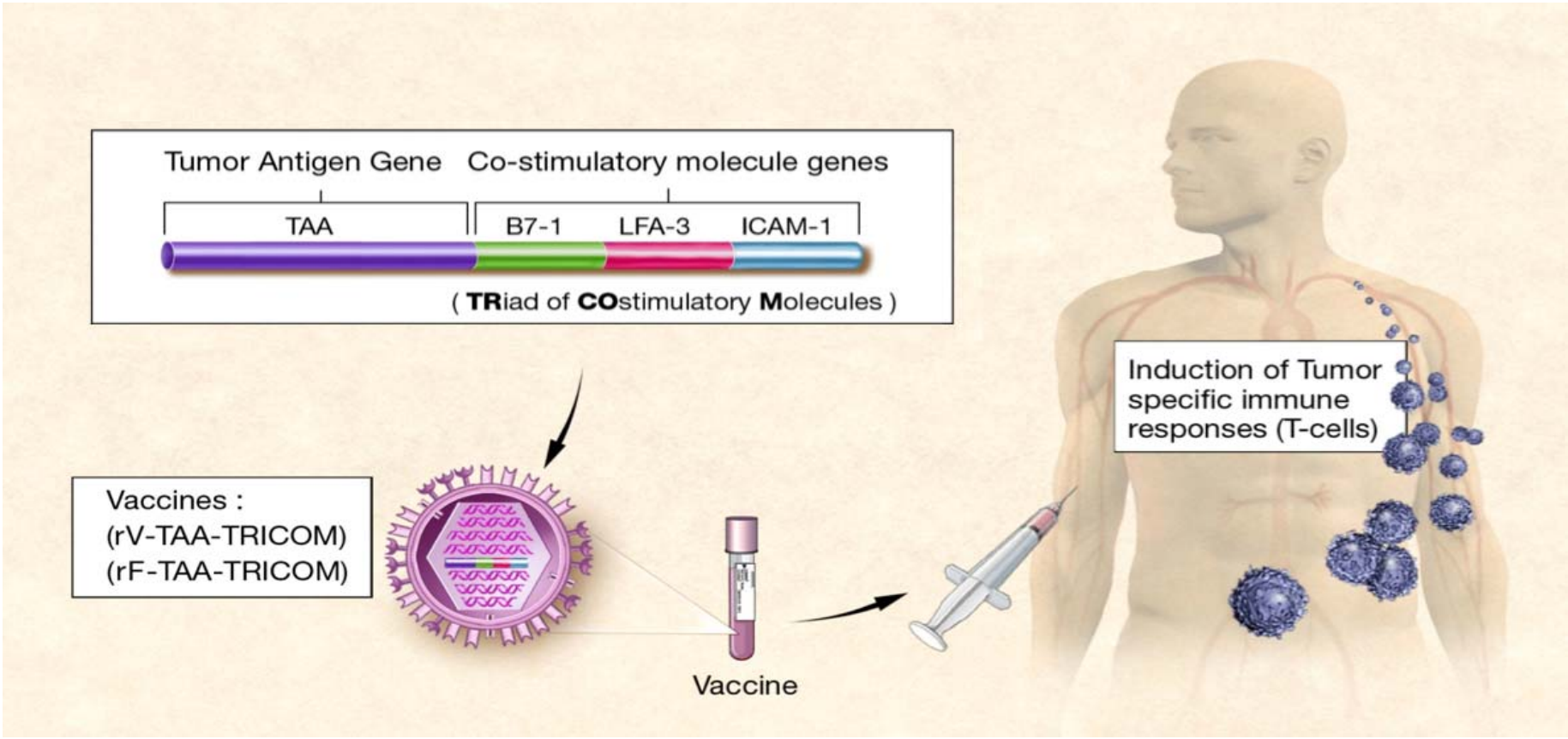
  Avipox (fowlpox rF-, ALVAC)
  - – derived from avian species
  - – safe; does not replicate
  - – can be used repeatedly with little if any host neutralizing immunity
- Can insert multiple transgenes
- Do not integrate into host DNA
- Efficiently infect antigen presenting cells including dendritic cells

Schlom et al

Costimulatory Molecule Candidates



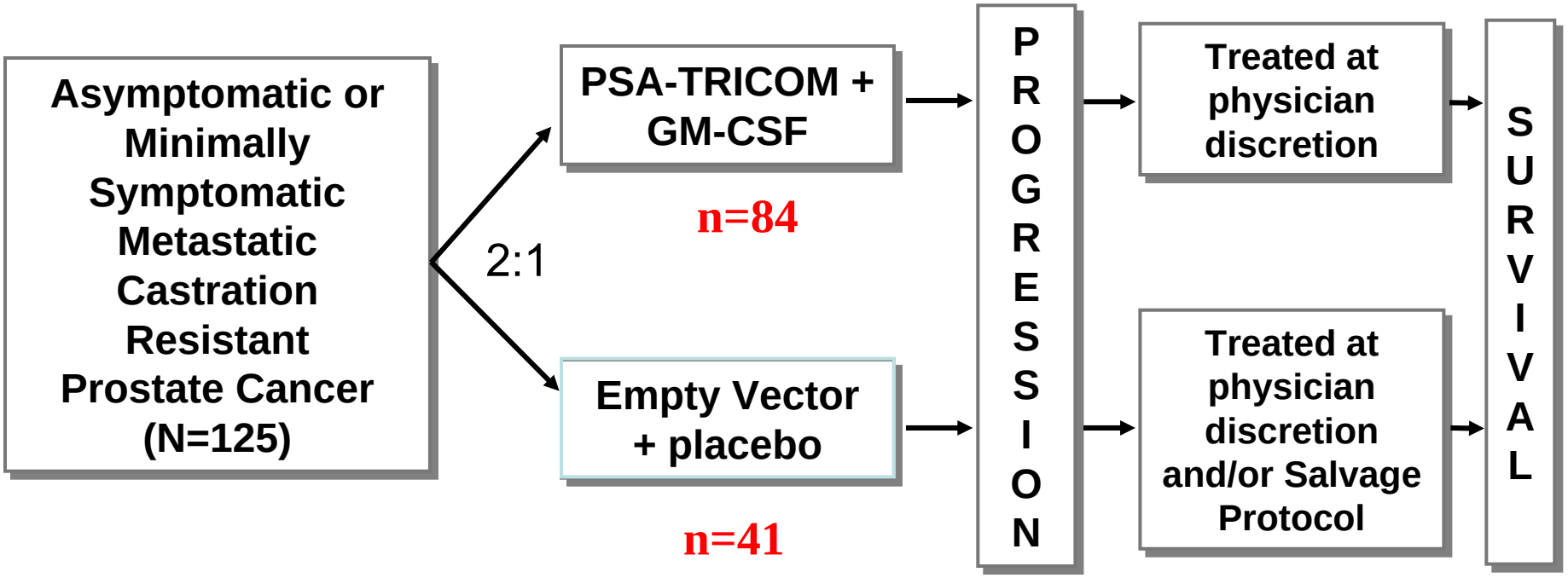




TAA - PSA, MUC-1 and CEA

Schlom et al

PSA-TRICOM: Randomized Controlled Double Blind Phase II Study

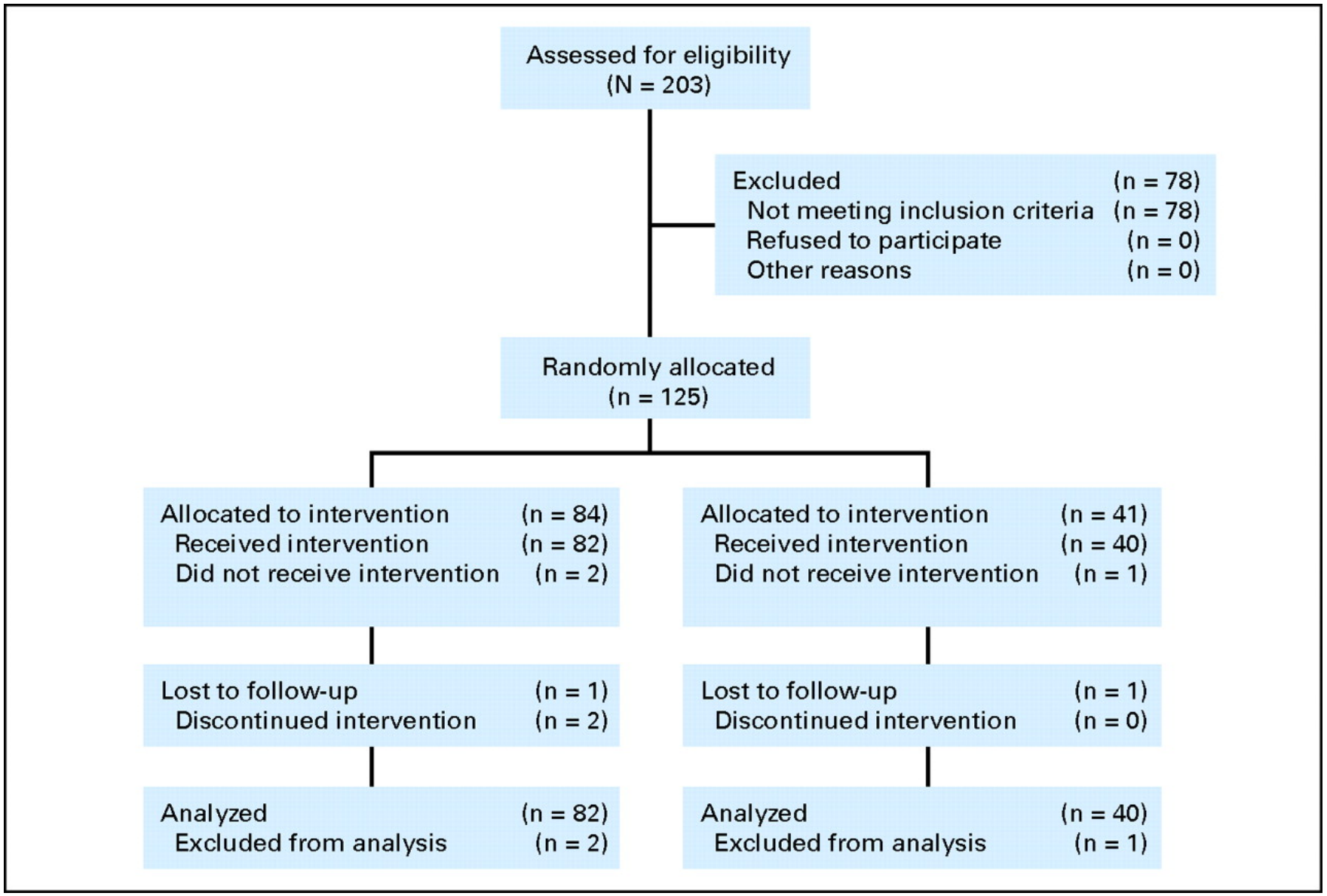


Primary endpoint: Progression Free Survival

Secondary endpoint: Overall Survival

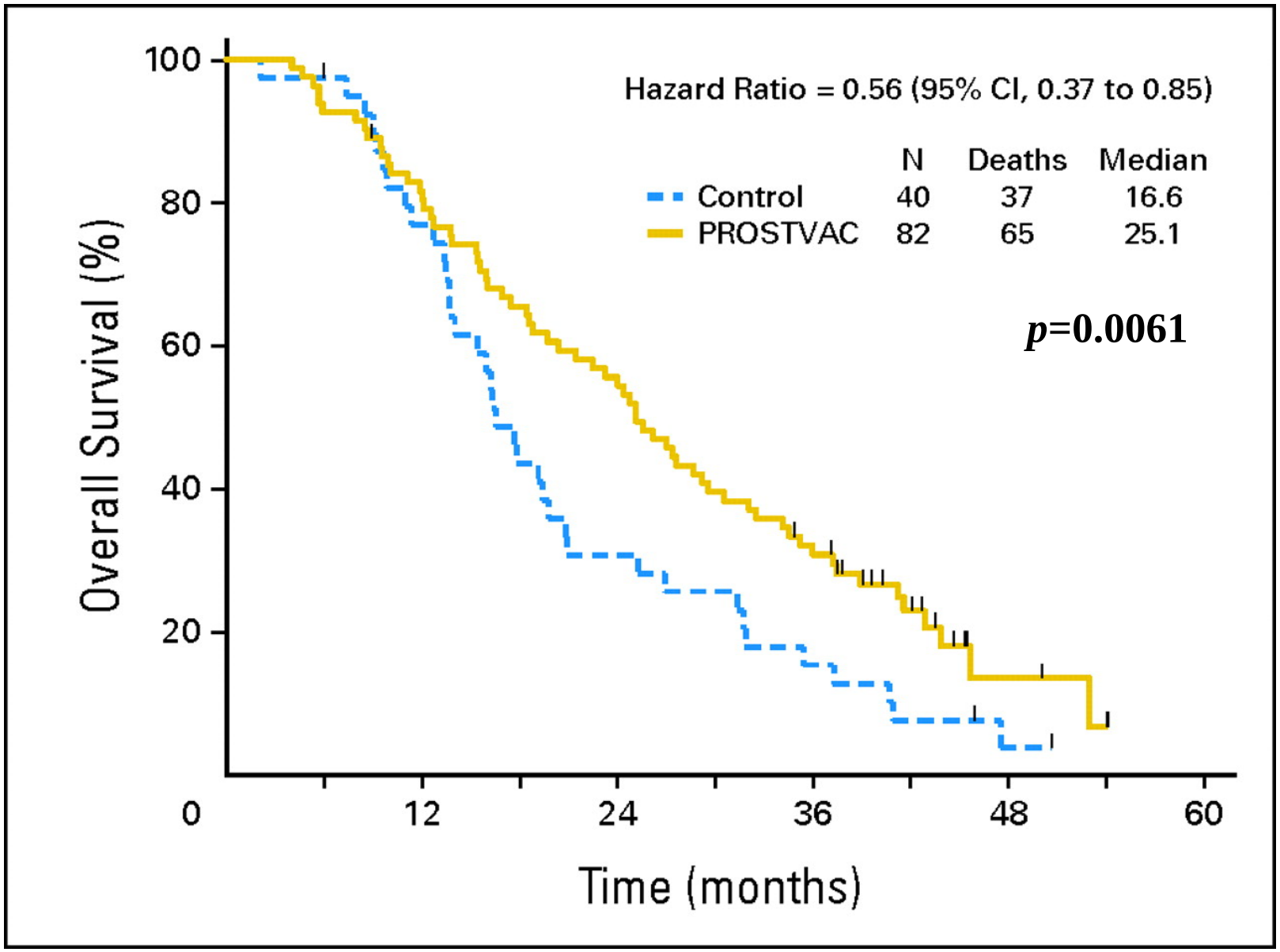
Kantoff (Schlom, Gulley) et al., JCO 2010

Disposition of patients: CONSORT diagram



Kantoff, P. W. et al. J Clin Oncol; 28:1099-1105 2010

Overall survival



Kantoff, P. W. et al. J Clin Oncol; 28:1099-1105 2010

Original Article

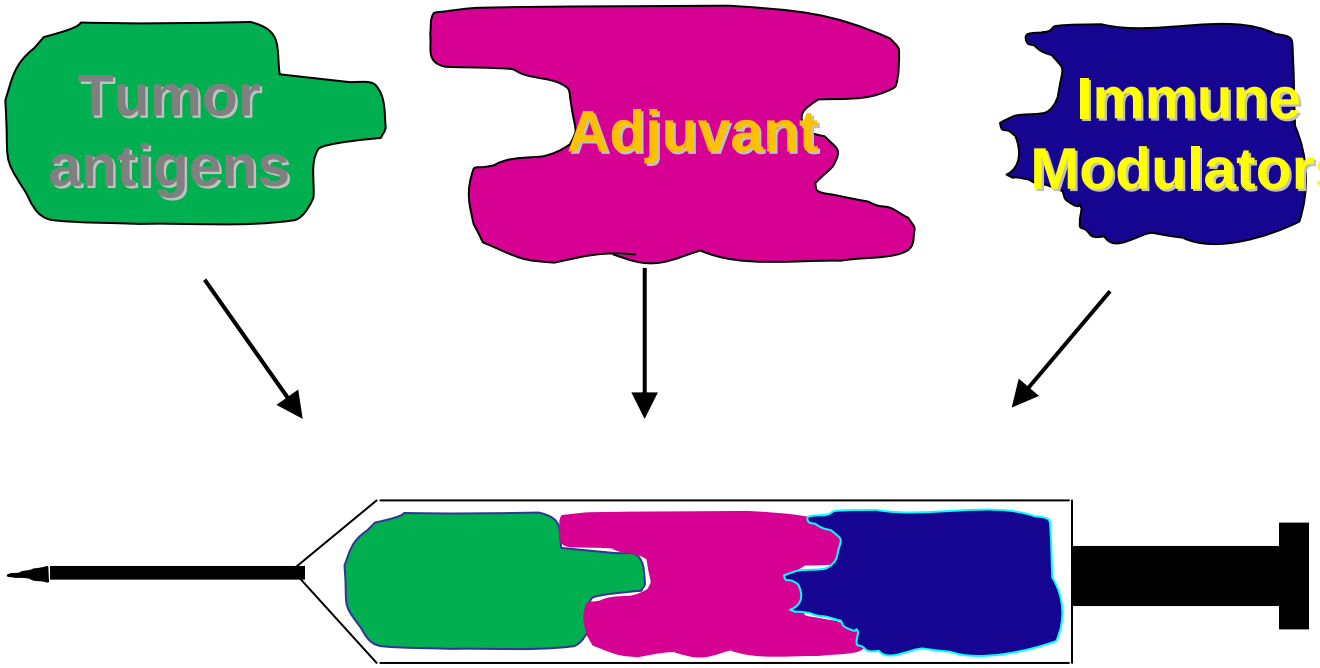
Sipuleucel-T Immunotherapy for Castration-Resistant Prostate Cancer

Philip W. Kantoff, M.D., Celestia S. Higano, M.D., Neal D. Shore, M.D., E. Roy Berger, M.D., Eric J. Small, M.D., David F. Penson, M.D., Charles H. Redfern, M.D., Anna C. Ferrari, M.D., Robert Dreicer, M.D., Robert B. Sims, M.D., Yi Xu, Ph.D., Mark W. Frohlich, M.D., Paul F. Schellhammer, M.D., for the **IMPACT Study** Investigators

N Engl J Med Volume 363(5):411-422 July 29, 2010

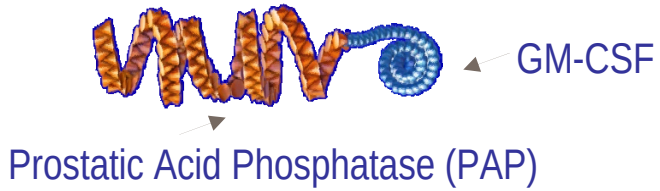
Vaccines: Teaching the immune system to recognize tumor cells

- Three components:

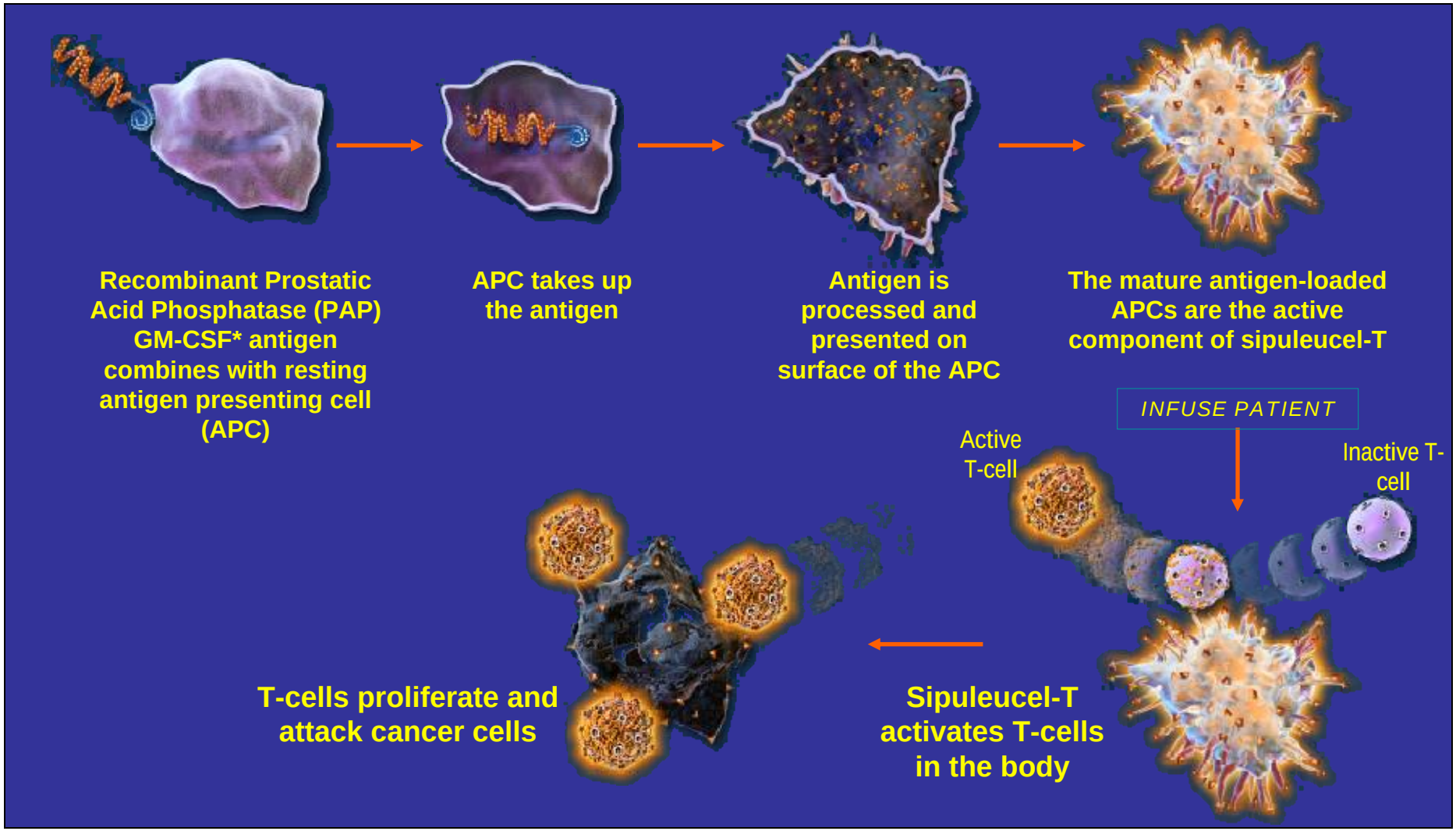


Recombinant Antigen

- Composed of prostatic acid phosphatase (PAP) linked to granulocyte-macrophage colony stimulating factor (GM-CSF)
- Manufactured as recombinant protein antigen



Autologous Cellular Immunotherapy with Sipuleucel-T



The precise mechanism of action of sipuleucel-T is not known.

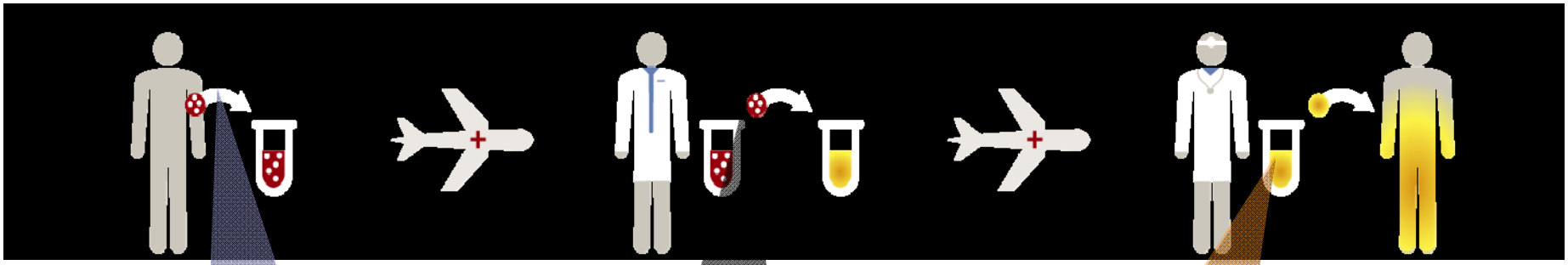
*GM-CSF; granulocyte-macrophage colony stimulating factor

Pre-Clinical Rationale

- Antigen-loaded APCs isolated from peripheral blood showed clinical promise in lymphoma[1]
- Prostatic acid phosphatase (PAP) is highly expressed in prostate tissue[2]
- Granulocyte Macrophage Colony Stimulating Factor (GM-CSF) activates APCs[3]
- Rat APCs, loaded with rat PAP+GM-CSF recombinant protein, induced prostatitis[4]

[1]Hsu et al., (1996) Nat. Med. 2:52-58
[2]Lam et al., (1989) Prostate 15(1): 13-21
[3]Markowicz et al., (1990) J. Clin. Invest. 85: 955-61
[4]Laus et al., (2001) Can Res. Ther. Cont. 11: 1-10

PROVENGE (sipuleucel-T) Production and Delivery



DAY 1
LEUKAPHERESIS

The patient gets standard blood collection where white blood cells are extracted for treatment.

DAY 2–3
PROVENGE (SIPULEUCEL-T) IS MANUFACTURED

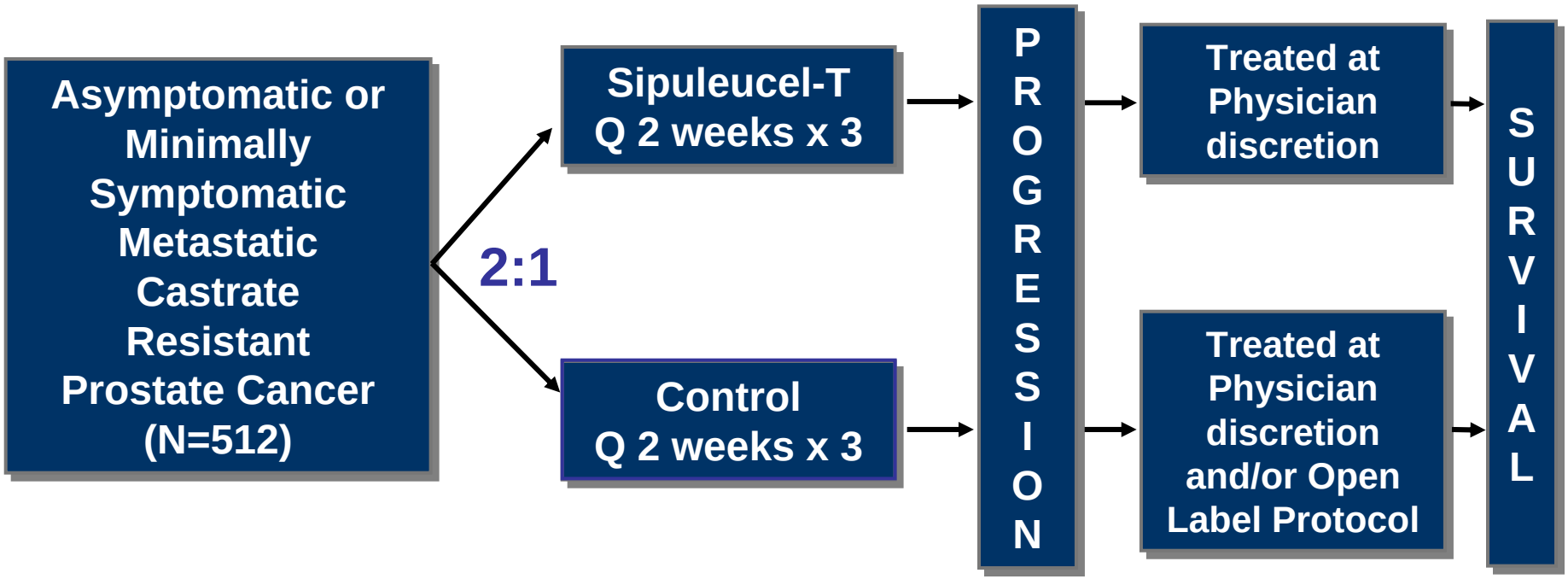
The patient's peripheral blood mononuclear cells (PMBCs) are separated from other white blood cells using proprietary technology.

DAY 3–4
PATIENT IN INFUSED

The physician administers the patient's PROVENGE intravenously.

Complete course of therapy: 3 cycles

Study Design: Phase 3 D9902B IMPACT Trial
(IMmunotherapy Prostate AdenoCarcinoma Treatment)

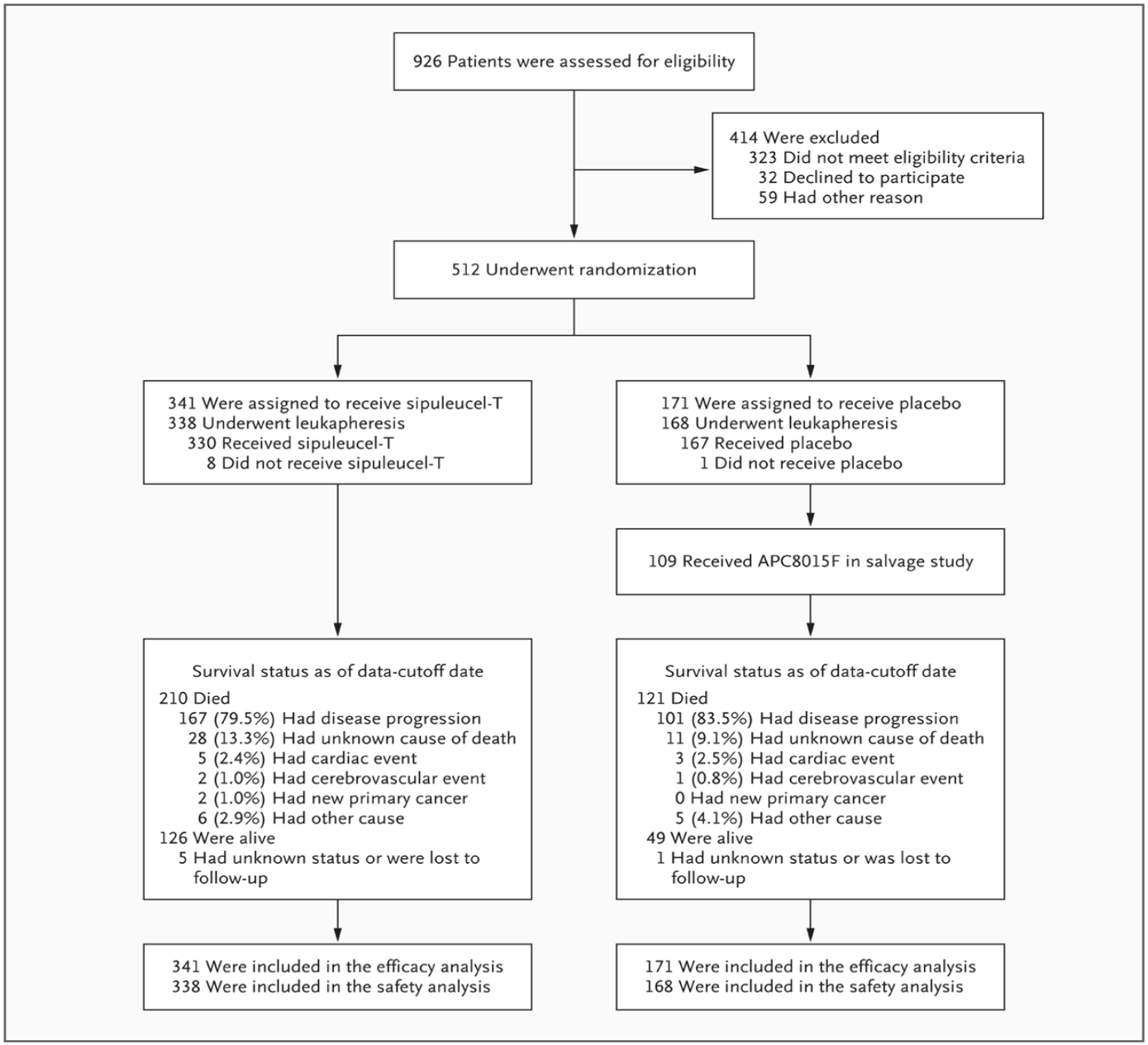


Endpoints for 9902B IMPACT

Primary endpoint: Overall Survival

Secondary endpoint: Time to Objective Disease Progression

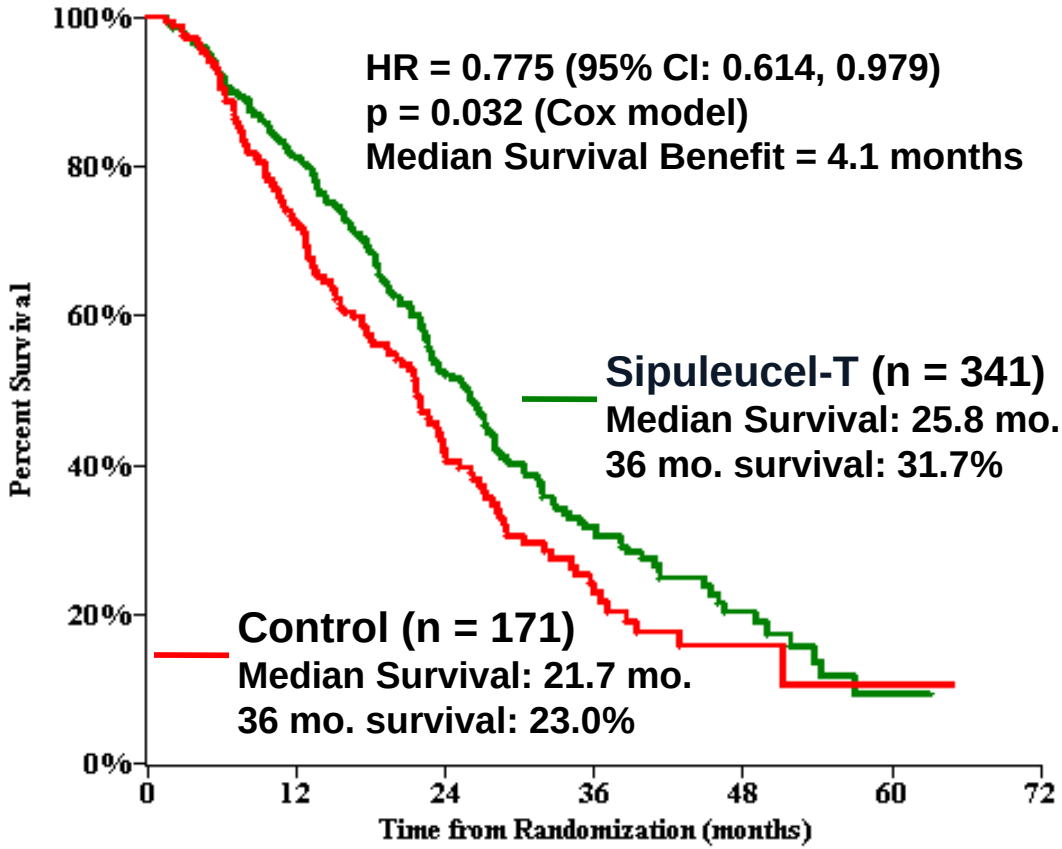
Enrollment and Outcomes



Kantoff PW et al. N Engl J Med 2010;363:411-422

The NEW ENGLAND JOURNAL of MEDICINE

Study D9902B (IMPACT): Overall Survival Primary Analysis (331 events)



No. at Risk

Sipuleucel-T	**341**	**274**	**129**	**49**	**14**	**1**
Control	**171**	**123**	**55**	**19**	**4**	**1**

Kantoff, ASCO-GU March 2010

Safety Profile: The Most Common Adverse Events[1]

	Any Grade		Grades 3-5	
	PROVENGE (n=601) (%)	Control[2] (n=303) (%)	PROVENGE (n=601) (%)	Control[2] (n=303) (%)
Any adverse event	**98.3**	**96.0**	**30.9**	**32.0**
Chills	**53.1**	**10.9**	**2.2**	**0.0**
Fatigue	**41.1**	**34.7**	**1.0**	**1.3**
Fever	**31.3**	**9.6**	**1.0**	**1.0**
Back pain	**29.6**	**28.7**	**3.0**	**3.0**
Nausea	**21.5**	**14.9**	**0.5**	**0.0**
Joint ache	**19.6**	**20.5**	**1.8**	**1.7**
Headache	**18.1**	**6.6**	**0.7**	**0.0**

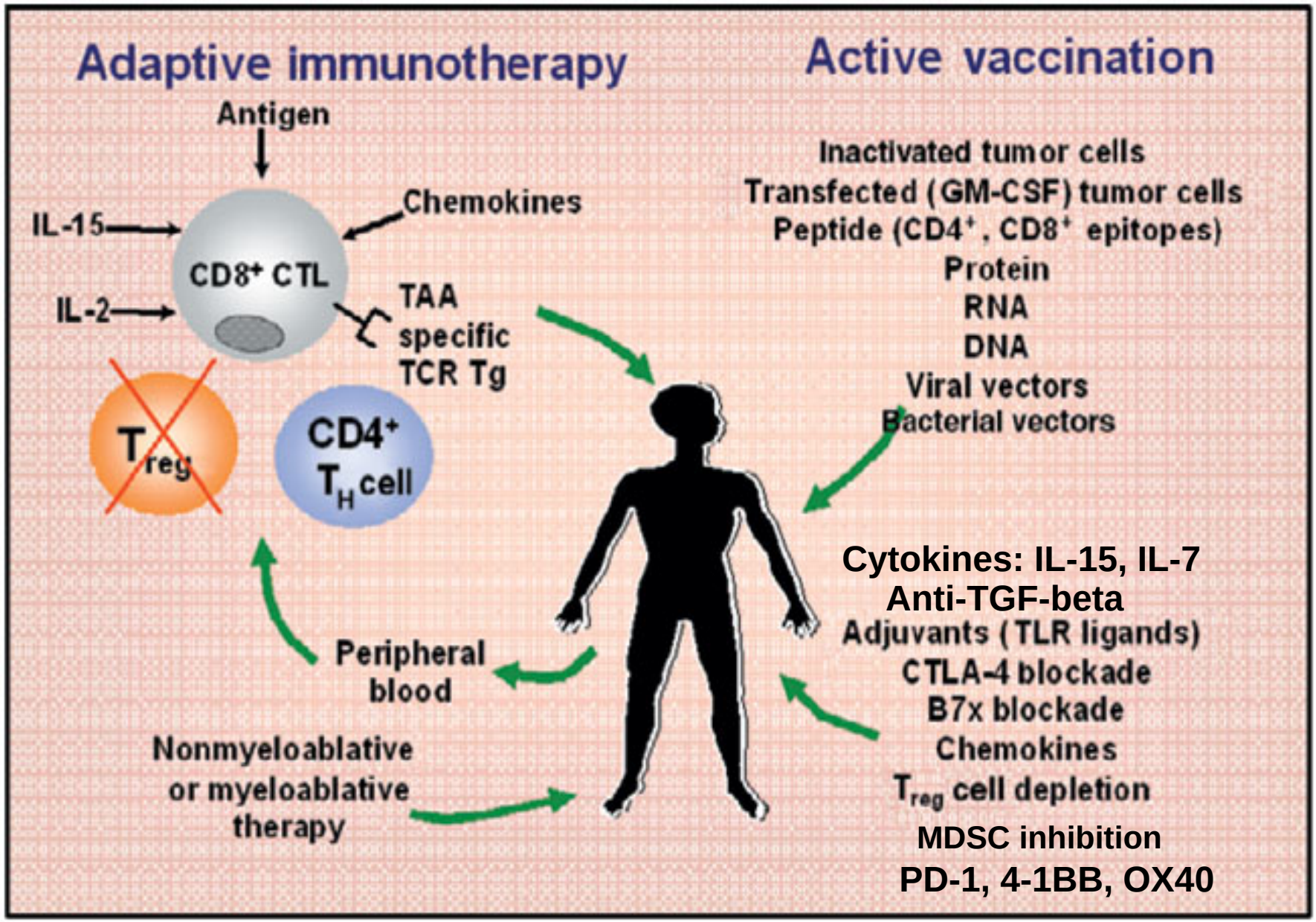
[1]All grades occuring in ≥ 15% of patients randomized to PROVENGE
[2]Control was nonactivated, autologous, peripheral blood mononuclear cells

1.5% of patients in the pivotal trial discontinued treatment with PROVENGE due to adverse events.

PROVENGE package insert-Dendreon Corporation; 2010

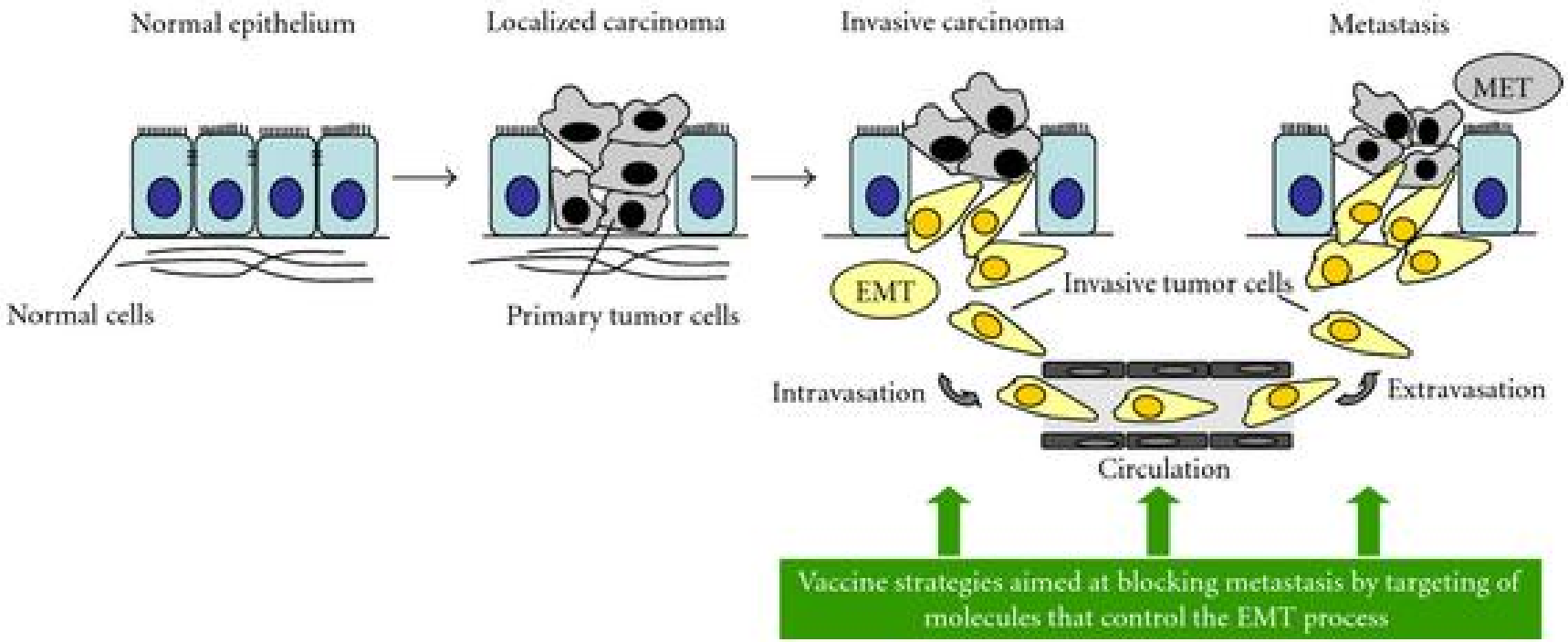
Studies of Humoral and Cellular Immune Responses

- A subset of the 512 patients from study D9902B, a phase 3, randomized, double-blind, control trial, were examined.
- Recombinant antigen prostatic acid phosphatase (PAP) was used as antigen source in the assays
- Humoral responses were assessed by ELISA
- Cellular responses were assessed by IFNγ-ELISPOT and ^{3}H-thymidine T cell proliferation assays

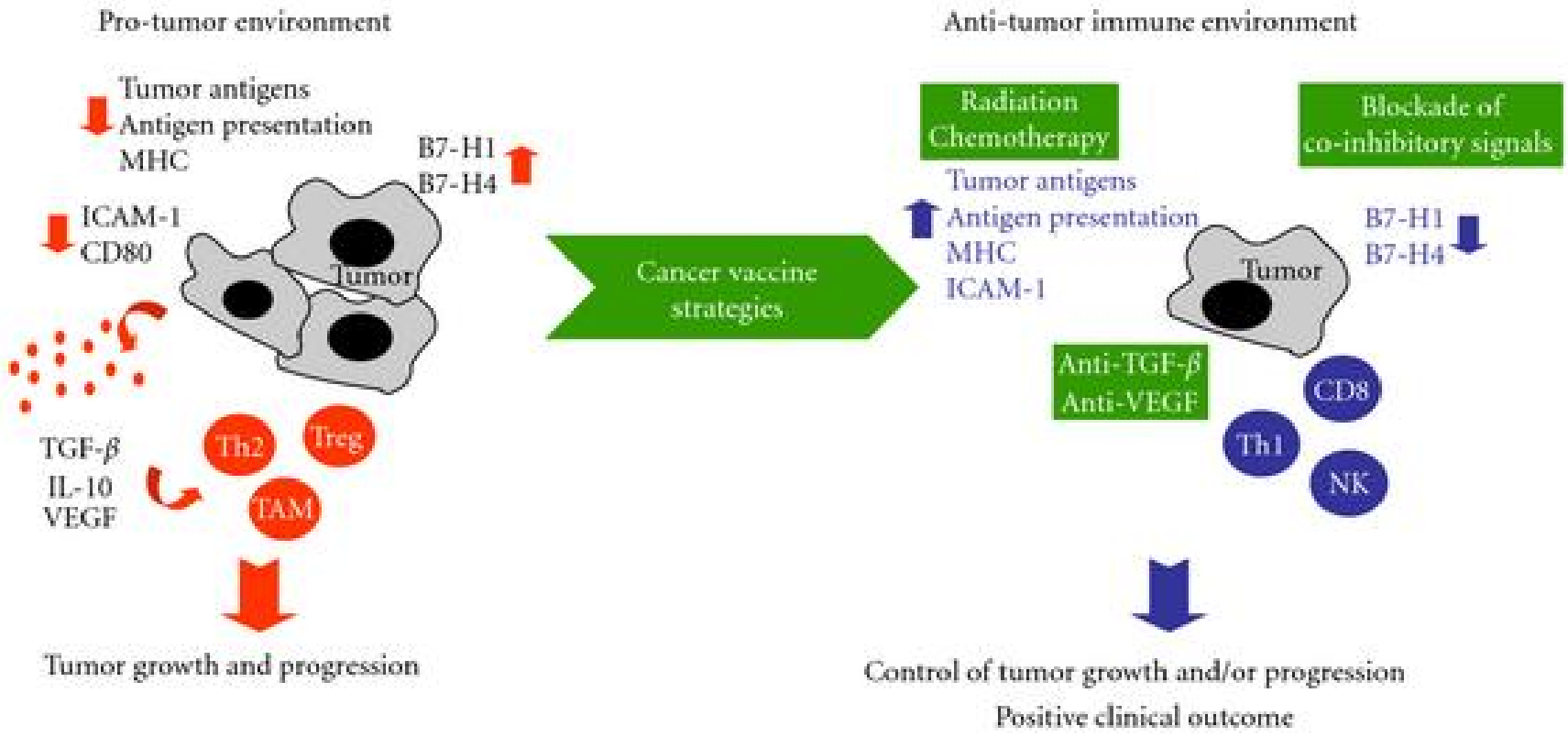


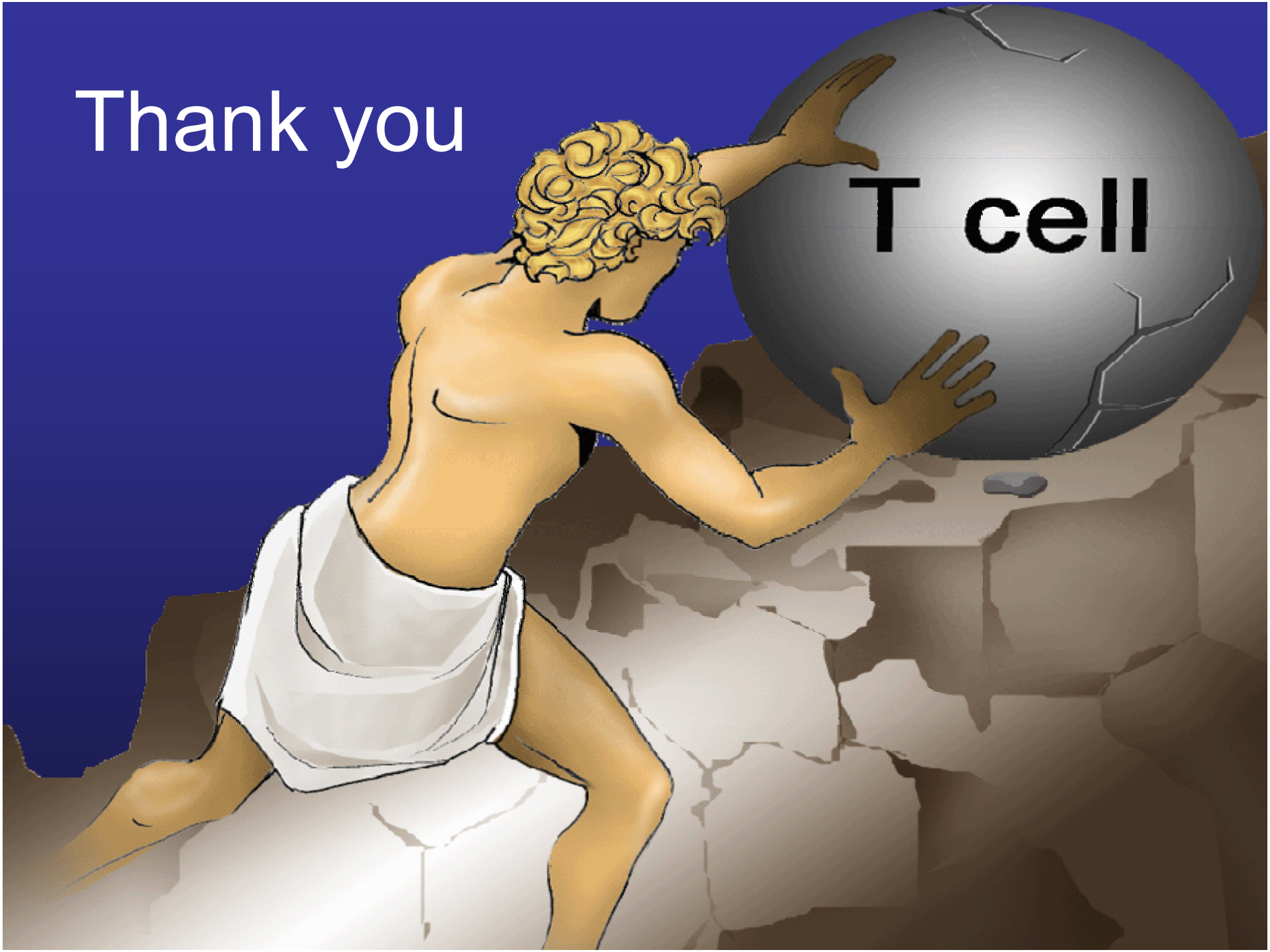
Modified from - Pure, Allison & Schreiber Nature Immunol 6:1207 (2005)

The tumor may not have to be the target



Combination with other effective therapies




Thank you
T cell