Cancer Immunotherapy

CANCER BIOLOGY
April 15, 2009

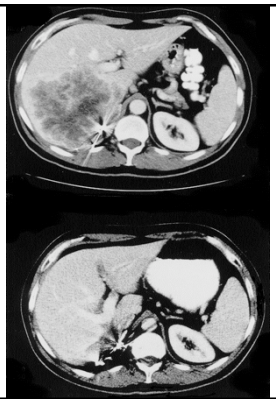
Can the immune system be harnessed to fight cancer?

- Can the immune system see cancer?
- What is the best way to turn on the immune system to fight cancer?
- Which cells of the immune system can destroy cancer?

Immunotherapy Can Work!

Objective responses Have been rare!

RCC pt 7 years out From IL-2
Surgery Branch, NCI

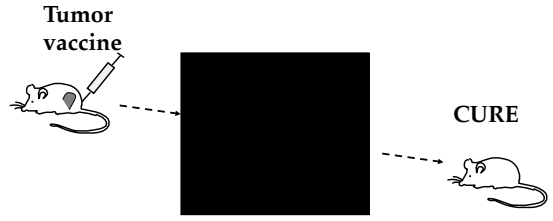


What is it? Immunotherapy

Active-specific immunotherapy
vaccines

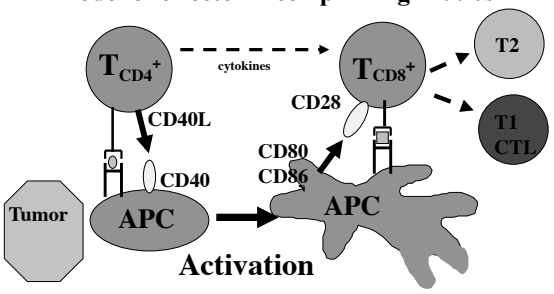
Adoptive immunotherapy
(passive transfer)
Transfer of active reagents/cells to the tumor-bearing host

Turning "on" the Immune System..



Turning "on" the Immune System..

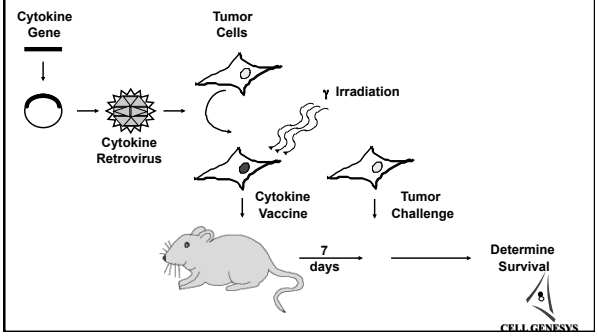
Model of effector T cell priming - 1990s



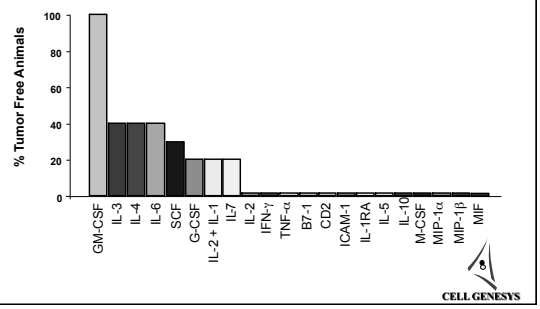
How can we model something as complicated as the immune system and cancer?

Animal tumor models provided key evidence that encouraged investigators to move forward with clinical trials

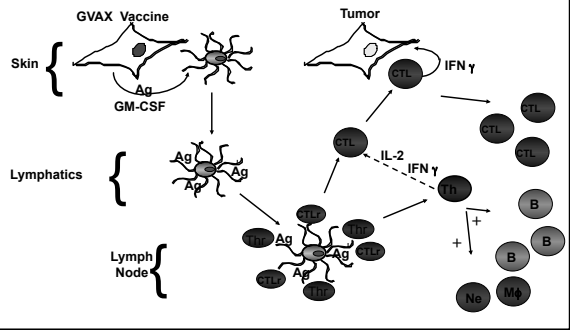
Screen for Induction of Anti-Tumor Immunity



GM-CSF Induces the Greatest Anti-Tumor Immunity



Mechanism of Action of GVAX®



Cancer Immunotherapy - Vaccines

- **Peptides, Proteins +/- cytokines**
- **viral vectors +/- cytokines**
- **Autol / allo Tumor +/- cytokines**
- **Dendritic Cells + Tumor (lysates) (only pediatric patients?)**

Cancer Vaccine Approaches

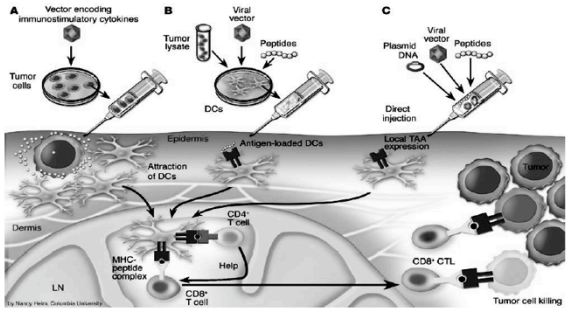


Table 2 Peptide vaccine immunization of patients with metastatic cancer

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$_{280-288}$(288SV)[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
gp100$_{11-25}$	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. [a]g209-2M. [b]g280-9V. [c]MART-1_{26-35}(27L). [d]Tyrosinase$_{368-376}$(370D).

Rosenberg, SA et al. Nature Medicine, 10:9, Sept 2004

Cancer Immunotherapy - Vaccines

- **Cancer Vaccines - Do Not Work!**

Peptides, proteins, TAA viruses, DC pulsed with TAA.

Or?? The way they "were" given didn't induce an immune response that was sufficient to see a therapeutic effect.

Cancer Immunotherapy - Vaccines

- **Some small studies with complex vaccines "appear" to have worked.. WHY??**
- **Gene-modified tumors expressing "sufficient" GM-CSF…**
- **But only with autologous vaccine?**

Autologous tumor vaccine - patient's tumor

1) Genetically engineered whole tumor cells
NSCLC, Melanoma, Renal, Myeloma, other

2) Antigen (HSP) from whole tumor cells:
Melanoma, Renal, other

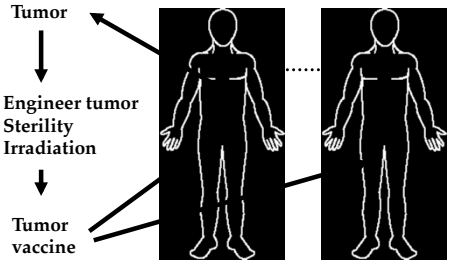
Autologous tumor vaccine - patient's tumor
Whole Cells - Gene-modified or….

Advantages: Everything that the tumor has should be expressed by the vaccine - unique antigens -

Disadvantages: Need tumor, variability, Hard!

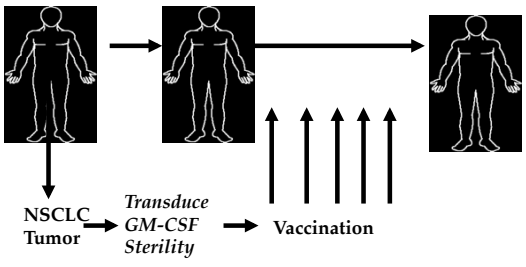
Requirements: Need Team of investigators to make it work! Some positive results - BUT.. not an easy commercial platform..
MAY become domain of Departments Surgery, Radiation Oncology, BMT.
surgeons, pathologists, oncologists, scientists, Inc, FDA, ..

Clinical Trial - Autologous Tumor Vaccine



mti 163

NSCLC GM-CSF gene-modified GVAX Autologous Tumor Vaccine



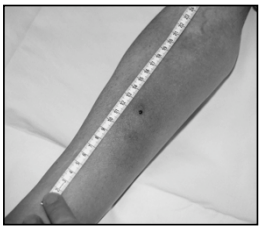
J Natl Cancer Inst. 2004 Feb 18;96(4):326-31.

GVAX® Lung Cancer Vaccine
Adverse Events

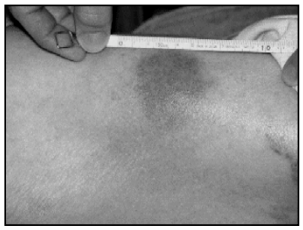
- **Vaccines well tolerated**
- **No dose limiting toxicity**
- **Most common adverse events**
  - **grade 1/2 vaccine site reactions (erythema, edema, pruritis, pain)**
  - **grade 1/2 constitutional symptoms (fever, chills, fatigue, myalgias)**
- **Serious, possibly related adverse events**
  - **dehydration necessitating brief hospitalization**
  - **progression of pre-existing pericardial effusion**
  - **pneumonia responsive to antibiotics**

GVAX® Lung Cancer Vaccine
Vaccine and Tumor DTH reactions

Vaccine Site Reaction



Autologous Tumor DTH Reaction



Tumor Response Data
Summary

- **42 initiated vaccinations**
  - **32 evaluable (received ≥ 3 vaccines) (9 cohort A; 23 cohort B)**
  - **4 ongoing (1 cohort A; 3 cohort B)**
  - **6 nonevaluable (all cohort B)**
- **Response data**

Cohort B (stage IIIB/IV)

Response	#	%
CR	3	13
PR	0	0
SD*	4	26
PD*	13	57
NED	1	4
Total	23	100

*2 patients with mixed tumor responses

Cohort A (stage IB/II)

Outcome	#	%
NED*	8	89
PD	1	11
Total	9	100

*NED = "no evidence of disease"

Median follow up 7 mo (range 4–16 mo)

*Stage IIa patient who surgical resection with no evidence of disease > 9 months

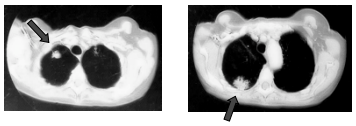
GVAX® Lung Cancer Vaccine
Summary of Responders

Patient	Response	Comments
VF2	Complete (> 6 mo)	72 yo F with stage IV bronchioalveolar ca with multiple lung disease. Failed Carbo/Taxol. Regression of 3 cm lung mass
CSV	Complete (> 2 mo)	53 yo F with stage IV bronchioalveolar ca with multifocal lung disease. Failed Carbo/Taxol and 2 investigational drugs. Regression of two lung masses (1.5 and 0.8cm).
AF2	SD (> 6 mo)	51 yo M with stage IIIB squamous cell ca with lung mass and malignant effusion. Failed Carbo/Taxol, s/p thoracic RT. Partial regression of 2cm lung mass.
HWV	Complete (> 2 mo)	62 yo F with stage IV squamous cell ca with brain, bone and s/p resection of brain mass, thoracic and brain RT. Resolution of all lesion on scans seen.
WJ6	Mixed	52 yo M with stage IV squamous cell ca with multiple lung nods. Failed Taxol/Cisplatin/Gemcitabine and Cisplatin/Navelbine. Resolution of 2 lung masses with progression of others. Underwent 2nd round of pneumonectomy and vaccination.
HEK	Mixed	70 yo F with stage IV NSCLC with multiple lung nods, s/p thoracic RT. Partial regression of 1.7cm lung mass and regression of 2nd lesion.

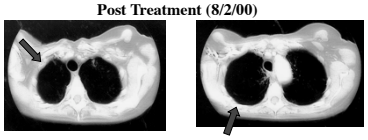
23

Complete Tumor Response
Patient VFD (bronchoalveolar ca)

Baseline (3/10/00)



Post Treatment (8/2/00)



Survival of patients receiving vaccines secreting "optimal" levels of GM-CSF was higher

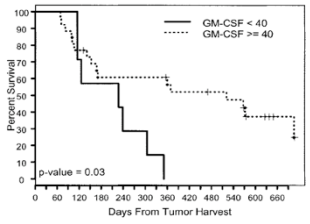


Fig. 3. Kaplan–Meier estimates of overall survival in cohort B. Treated advanced-stage patients analyzed by vaccine-associated granulocyte–macrophage colony-stimulating factor (GM-CSF) secretion. **Dashed lines** = at least 40 ng/24 h per 10^6 cells (26 patients); **solid lines** = less than 40 ng/24 h per 10^6 cells

Nemunaitis J., et al., JNCI 96;326-31, 2004

Hypothesis

These vaccine strategies failed because of variability in GM-CSF production by the patients autologous tumor cells -

Question?

How can you insure high production of GM-CSF by the tumor vaccine

Need approach to obtain consistent high level of GM-CSF secretion at vaccine site:

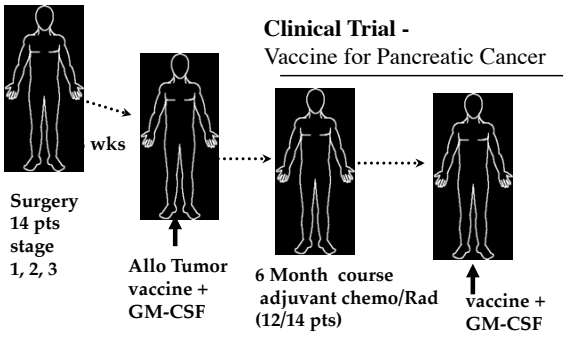
- **New generation viral vectors**
- **Local release**
  - **copolymers**
  - **mini-pumps**
- **Transfected allogeneic tumor cell lines.**

Allogeneic tumor vaccine - same histology

1) Genetically engineered whole tumor cells
Breast, prostate, pancreatic cancer

Advantages: Standardized product, stability, identity, the vaccine has wide spectrum of tumor-associated antigens. Easier! Prevention trials possible.

Disadvantages: missing unique antigens - critical?



Clinical Trial -
Vaccine for Pancreatic Cancer

Jaffee et al, JCO 19(1) 145-156 January 2001

Clinical Trial - Vaccine for Pancreatic Cancer

Preliminary Results:

- **Three patients developed DTH**
- **These Three patients disease free 25 months following diagnosis**
  Jaffee et al, JCO 19(1) 145-156 January 2001
- **All three developed mesothelin-specific T cell responses**
  Thomas et al., J Exp Med. 2004 Aug 2;200(3):297-306.
- **Phase II trial open at JHU**

Dendritic Cells (DC) are the most potent APCs / Nature's adjuvant?

Can DC help prime an antitumor immune response?

Dendritic Cells used to present tumor "antigens"

1) Tumor specific peptides
2) Proteins / fusion proteins {Dendreon}
3) Transduced with tumor RNA
4) Tumor-pulsed DC or
5) DC tumor fusions

Dendritic Cells used to present tumor "antigens"

1) Tumor-specific peptides

Positive: Defined antigen,
easy to monitor patient's response -
tetramers, ELISpot, other..
Objective responses when combined with IL-2
Rosenberg et al. Nat. Med 1998

Negative: Need to match patients HLA-
Generate variants that loose antigen expression

Dendritic Cells used to present tumor "antigens"

2) Tumor-specific proteins

Positive: Defined antigen, don't need to match patient's HLA. Possible to monitor patient's response

Negative: May still generate variants that loose antigen expression. Early /in clinical trials

*** Dendreon Results.. Press Release 04/14/09

Thomson Reuters

BEFORE THE BELL-Dendreon surges after trial results

04.14.09, 10:22 AM EDT

REUTERS NEW YORK, April 14 (Reuters) - Shares of Dendreon Corp more than tripled to $24.75 on Tuesday after the company said its experimental Provenge prostate cancer drug met the main study goal of a Phase III clinical trial.

(Reporting by Chuck Mikolajczak; Editing by James Dalgleish)
Keywords: MARKETS STOCKS BEFORETHEBELL

World's Scariest Stock: Dendreon

By Brian "Mad Scientist" Orelli, Ph.D.
October 31, 2008 | Comments (2)

Recs

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Rec This

Stock Advisor

Since 2002, *Motley Fool Stock Advisor* has outperformed the S&P 500 by 37 percentage points. Join David and Tom Gardner in Stock Advisor today.

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Bet got your tongue? We dare you to keep reading our special series on the World's Scariest Stocks.

Investors are a lot like a girl in a horror movie. The reason that the girl is screaming -- in my analogy, the reason investors are selling -- isn't because of what's outside her house. She's screaming because she doesn't *know* what's outside the house.

The fear of the unknown makes investing scary, and things don't get much more unknown than the future of Dendreon (Nasdaq: DNDN). The biotech is up for its second nomination as the World's Scariest Stock in as many years, and being a year older hasn't made it any less so.

Dendritic Cells used to present tumor "antigens"

3) Tumor-specific RNA

Positive: Broad spectrum of possible Ags - less likely to get escape variants. Don't need to match patient's HLA. Possible but difficult to monitor patient's antitumor response.

Negative: Not defined antigen. Not an off the shelf reagent. Need some "good" source of RNA.

Twenty patients DC + hTERT mRNA
J Immunol. 2005 Mar 15;174(6):3798-807.

Dendritic Cells used to present tumor "antigens"

3) Tumor-specific RNA - continued

hTERT-specific CD8+ T cells in PBL (0.9-1.8% - 19/20)

LAMP hTERT vaccine - higher frequencies of hTERT-specific CD4+ T cells and increased CTL-mediated killing of hTERT targets

Reduction of prostate-specific Ag velocity and molecular clearance of circulating micrometastases
J Immunol. 2005 Mar 15;174(6):3798-807.

Dendritic Cells to present tumor "antigens"

4) Tumor-pulsed DC or fusion products

Positive: Broad spectrum of possible Ags - less likely to get escape variants. Don't need to match patient's HLA.

Negative: Not defined antigen. Not an off the shelf reagent. Need viable autologous tumor for vaccine. Early /in clinical trials
Nestle et al. Nat. Med 1998
Tumor-DC fusion - controversy - new trials (CCF)

IN April 2009 - DC vaccines HAVE NOT SHOWN convincing evidence of therapeutic efficacy..

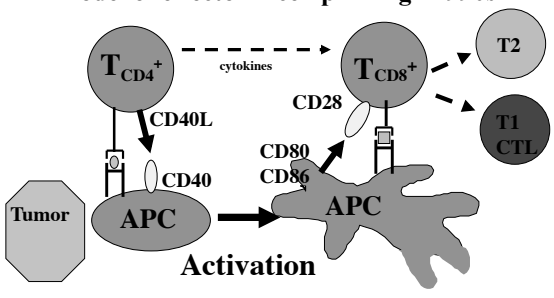
Hypothesis

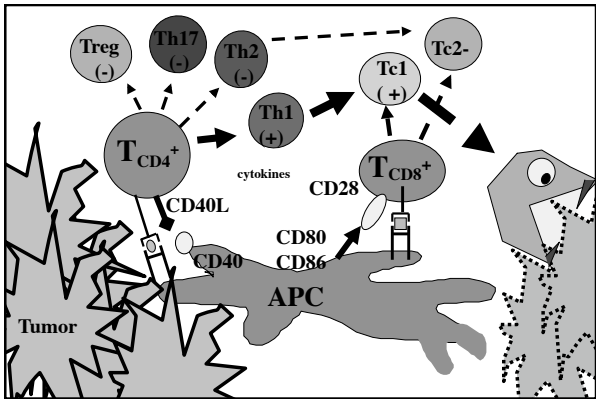
Clinical vaccine strategies fails when the patient does not develop a strong anti-tumor immune response.

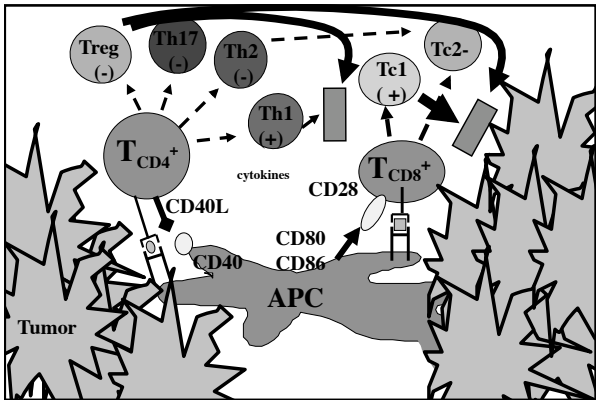
Questions?

What is the "correct" type of response?
How strong a response do you need?

Turning "on" the Immune System..
Model of effector T cell priming - 1990s







Hypothesis

Clinical vaccines fail when patients do not develop a strong anti-tumor immune response.

Questions?

How can you induce a stronger anti-tumor immune response?

Increase Immune response..

1) Block Negative Signals / improve Costimulation : Anti-CTLA4
2) Create Space for immune response… Homeostasis-driven proliferation (chemotherapy / radiation)
3) Reduce Treg cells / function.. (chemo, IL-2 toxins, other mAbs)

Biological Function (CTLA-4; CD152)

- **Regulation of peripheral T-cell tolerance.**
- **Induction of T-cell anergy.**
- **Attenuation of T-cell responses in inflammatory environment.**
- **Regulation of the composition of a polyclonal T-cell response.**

Antibodies or ligands that costimulate the immune response
Anti-OX40
Anti-4-1BB

Antibodies or ligands that block inhibitory signals
Anti-CTLA-4..
(Possible approval in 2009?)

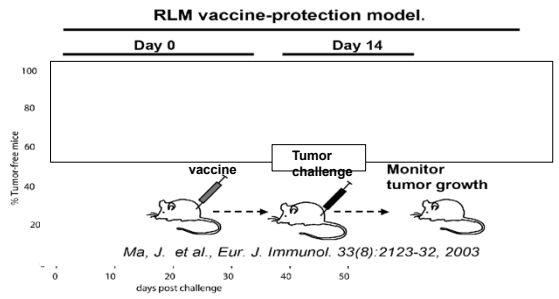
But there are others.. Anti-B7-H1, anti-PD-1,…

- **Homeostasis-driven proliferation**

Naïve T-cell repertoire can be skewed toward a specific antigen, resulting in a dramatic expansion of antigen-specific T cells

Mackall, CL et al. J Immunol 1996.
Borrello, IK, et al. Blood 2000.
Hu, H-M, et al. J. Immunother, 2000
Asavaroengchai and Mule'. PNAS 99:93, 2002
Dummer et al., J. Clin Inv. 110:185, 2002
Hu, H-M, et al. Cancer Research, 2002

Experimental Design for "reconstitution" of lymphopenic host prior to vaccination.

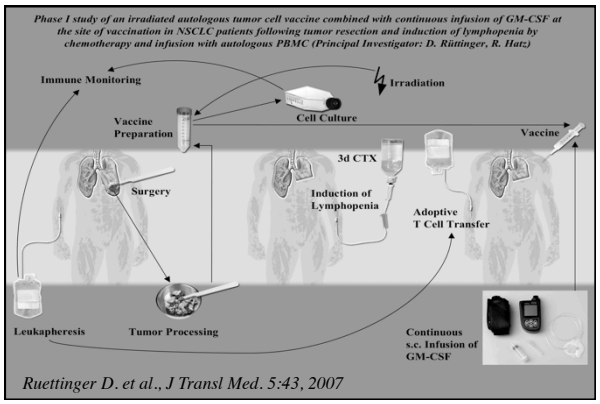


Clinical trials:

- **Combining Chemotherapy with vaccinations**

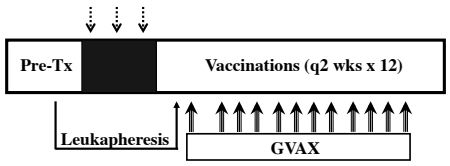
  Prostate, Melanoma, Breast, NSCLC, Myeloma, Pancreatic cancer.

  Still early but some promising results in pancreatic CA



Phase I/II study of allogeneic prostate GVAX™ in advanced prostate cancer patients made lymphopenic by chemotherapy and infused with autologous PBMC - DOD PC020094 / PHS 02-200

1) None
2) Cytoxan 350 mg/m^2 d 1-3
3) Cytoxan + Fludarabine 20 mg/m^2 d 1-3



Workshop on Future Opportunities for Combination Biological Therapy of Cancer

Workshop Main Page | Presentations Slides & Schedules | Published Documents & News Releases | CME Information | Faculty

November 1, 2007
Seaport World Trade Center
Boston, Massachusetts

Drawing on dialogue initiated among leaders in the field at a highly successful planning workshop sponsored by the iSBTc in 2006, this in-depth program provided an assessment of state-of the-art opportunities for combining immune-stimulating agents with other cancer biologics as well as conventional antineoplastic agents. This highly interactive program provided a venue for intensive scientific dialogue among key stakeholders regarding both strategic opportunities and central obstacles to realizing the potential of combination approaches for the biological therapy of cancer. It is anticipated that participants in this important program will include broad representation by investigators from academia, industry and regulatory agencies in the U.S., Europe and beyond.

Organizers

Bernard A. Fox, PhD
Earle A. Chiles Research Institute

Thomas F. Gajewski, MD, PhD
University of Chicago

Rachel W. Humphrey, MD
Bristol-Myers Squibb Company

Hyam I. Levitsky, MD
Johns Hopkins University School of Medicine

Jon M. Wigginton, MD
Merck & Co., Inc.

http://www.isbtc.org/meetings/workshop07/

Clinical trials:

- **Combining Treg depletion with vaccinations**

  very early… Used IL-2-Dipteria toxin to eliminate IL-2 R + (CD25+) Tregs…

Problem is that after one vaccine tumor-specific "killer cells" also express IL-2R and are eliminated ..

New reagents, COX2 inhibitors, anti-TGFb,..

Preclinical data : VERY PROMISING!!!

Clinical trials:

- **Combining Treg depletion with vaccinations**
  - **Anti-CD4**
  - **Anti-GITR**
  - **Anti-Lag3**

All of these….

Preclinical data : VERY PROMISING!!!

Immunotherapy

Active-specific immunotherapy
vaccines

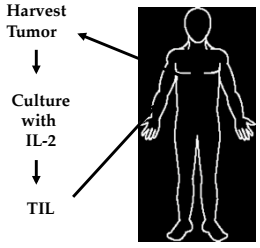
Adoptive immunotherapy
(passive transfer)
Transfer of active reagents/cells to the tumor-bearing host

Tumor-Infiltrating Lymphocytes - TIL 1986 -1997

Isolated by culturing fresh tumor suspensions in high dose IL-2.
Murine TIL exhibit specific cytotoxicity and cytokine release. *Spies et al JNCI*

Human TIL cells exhibit a similar profile.
Muul et al. J. Immunol

Adoptive immunotherapy TIL



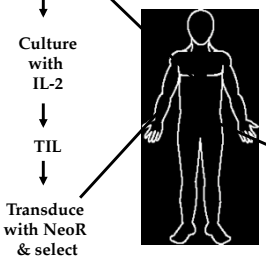
TIL cells infused i.v.
IL-2 administered t.i.d.

Tumor-Infiltrating Lymphocytes - TIL

TIL cells can cure animals of large tumor burdens . *Rosenberg et al. Science 1986*

TIL cells have therapeutic activity in patients. *Rosenberg et al. NEJM 1988*

Adoptive immunotherapy "Gene-marked" TIL



TIL cells infused i.v.
IL-2 administered t.i.d.

Biopsy tumor
1) PCR for Neo
2) culture with IL-2 and G418 to study TIL function / phenotype

Neo Labeled TIL - Results Human Gene Transfer Experiment

One patient had CR. Blood & tumor biopsies cultured under selection. TCR heterogeneity of recovered cells different from infused. ???

Aebersold et al. Hu Gene Tx 1990;1(4):373-84

Tumor Antigens - 1990s TIL help define these antigens

Class I restricted
MAGE. *Boon et al.*
MART-1/MelanA. *Rosenberg et al., Boon et al.*

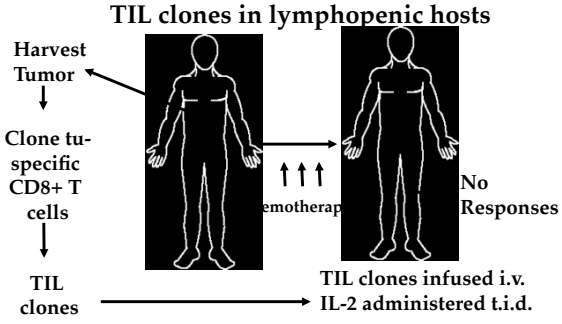
Class II restricted
Topalian et al.

Can the immune system see cancer?

YES! TIL studies identify that the immune response can detect cancer cells!

Question:
If we transfer more tumor-specific T cells will this therapy be more effective?

Adoptive immunotherapy - CD8+ TIL clones in lymphopenic hosts



Dudley et al., J. Immunother 2002 25:243-51

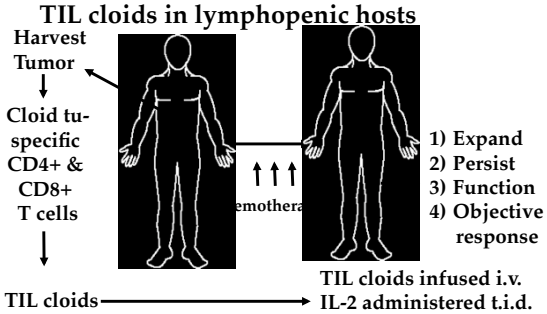
Give Cloned Tumor-Specific CD8+ T cells

No substantial improvement.

Give Cloned Tumor-Specific CD8+ T cells to immunosuppressed patients with "room" for T cells to expand in vivo

No objective responses.
Dudley M, et al., 2002, J. Immunotherapy

Adoptive immunotherapy - CD4+ & CD8+ TIL cloids in lymphopenic hosts



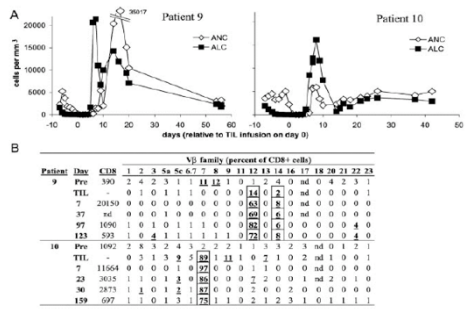
Dudley et al., Science 2002 / J Clin Oncol. 2005 Apr 1; 23(10):2346-57.

Give Tumor-Specific CD8 and CD4 T cells

T cells survive, expand in vivo, maintain anti-tumor function
50% objective response rate..

Evidence that T cells (TIL) can mediate tumor regression in humans??

Can this work at other centers??
Will this work in other diseases??



Patient	Day	CD8	1	2	3	5a	5c	6.7	7	8	9	11	12	13.1	13.6	14	16	17	18	20	21	22	23
9	Pre	390	2	4	2	3	1	1	11	12	1	0	1	2	4	0	nd	0	4	2	3	1	
	TIL	-	0	1	0	1	1	1	0	0	0	0	14	0	2	0	nd	0	0	0	0	1	
	7	20150	0	0	0	0	0	0	0	0	0	0	63	0	8	0	nd	0	0	0	0	0	
	37	nd	0	0	0	1	0	0	0	0	0	0	69	0	6	0	nd	0	0	0	0	0	
	97	1090	1	0	1	0	1	1	1	0	0	0	82	0	6	0	0	0	0	0	4	0	
	123	593	1	0	4	1	1	1	1	1	1	0	72	0	8	0	0	0	0	0	4	0	
10	Pre	1092	2	8	3	2	4	3	2	2	2	1	1	3	3	2	3	nd	0	1	2	1	
	TIL	-	0	3	1	3	9	5	59	1	11	1	0	7	1	0	2	nd	1	0	0	1	
	7	11564	0	0	0	0	1	0	97	0	0	0	1	1	0	0	0	nd	0	0	0	0	
	23	3035	1	1	0	1	3	0	86	0	0	0	7	2	0	0	1	nd	2	0	1	0	
	30	2873	1	1	0	1	2	1	87	0	0	0	2	0	0	2	0	0	0	0	0	0	
	159	697	1	1	0	1	3	1	75	1	1	0	2	1	2	3	1	0	1	1	1	1	

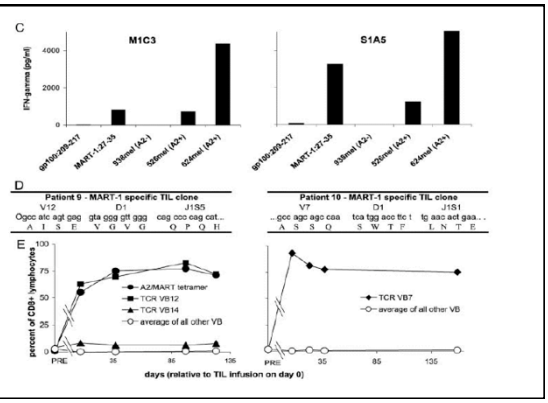
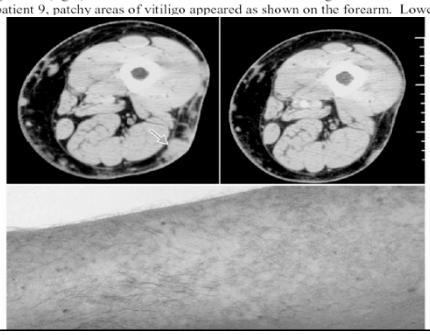
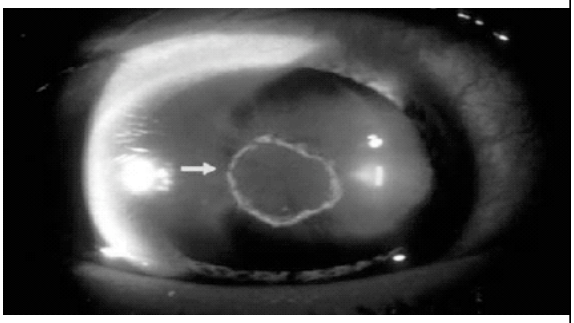


Figure S1. Antitumor and autoimmune manifestations following the transfer of lymphocytes with anti-MART-1 reactivity. Upper: CT scan of the lower extremity of patient 9 showing multiple melanoma metastases (arrow) in the skin and subcutaneous tissue (left) that underwent regression (right) after cell transfer. Middle: As cancer regressed in the lower extremity of patient 9, patchy areas of vitiligo appeared as shown on the forearm. Lower: Two





Evidence that T cells (TIL) can mediate tumor regression in humans??

Can this effect be induced without adoptive transfer of large numbers of activated T cells?

HOW!

COMBINATION STRATEGIES…

Combination Strategies are the FUTURE!

Collaborations - Need to get Investigators, Companies, FDA to all work together.

Concerns - SAE that will taint product
Intellectual property
? FDA ? too much testing?

Alternative strategy to generate tumor-specific T cells..

Genetically Engineered T cells?

Re direct them… TCR gene Transfer

Protect them from Bad signals..
Cortisone resistance gene.. Sangamo

Alternative strategy to generate tumor-specific T cells..

Re Directing T cells..
MicroMet Technology.

Antigens… Autophagy..
Li. Y, et al., Cancer Research 2008
Li, Y. et al., Autophagy 2009

Tumor Regression in Cancer Patients by Very Low Doses of a T Cell–Engaging Antibody

Ralf Bargou,[1,2]* Eugen Leo,[3]*† Gerhard Zugmaier,[3] Matthias Klinger,[3] Mariele Goebeler,[1,2] Stefan Knop,[2] Richard Noppeney,[4] Andreas Viardot,[5] Georg Hess,[6] Martin Schuler,[7] Hermann Einsele,[2] Christian Brandl,[3] Andreas Wolf,[3] Petra Kirchinger,[3] Petra Klappers,[3] Margit Schmidt,[3] Gert Riethmüller,[8] Carsten Reinhardt,[3] Patrick A. Baeuerle,[3]‡ Peter Kufer[3]

Combination Strategies: FDA is helping..

- **Adaptive trial designs - alter trials based on data accumulated..**
- **"Qualified" Biomarkers (not validated)**
- **Exploratory INDs -(Not CBER.. Yet)**

J. Immunother 30:1-15, 2007

www.isbtc.org Boston, Nov 1-4, 2007 DC 2008 / San Diego 2008..

Was there a tumor-specific immune response?

Potential Solution:

Screen Patients pre/post sera for antibody via protein array

Rationale:

Antibody response requires T cell help.

Can then go back and evaluate T cell response.

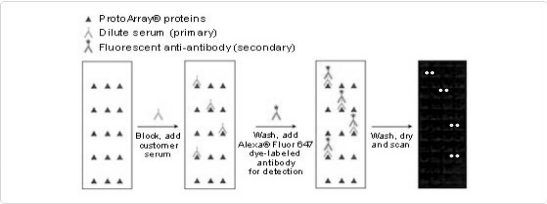
Was there a tumor-specific immune response?

Invitrogen's ProtoArray® Immune Response Biomarker Array

Human Protein Microarray v4.1 contains over 8,000 unique human proteins, purified from our baculovirus based expression system, arrayed in duplicate on a 1 inch x 3 inch nitrocellulose-coated glass slide.

Profiling service can rapidly profile 10 to over 100 serum samples for immunoreactivity to over 8,000 human proteins.

Screen Patients pre/post sera for antibody via protein array



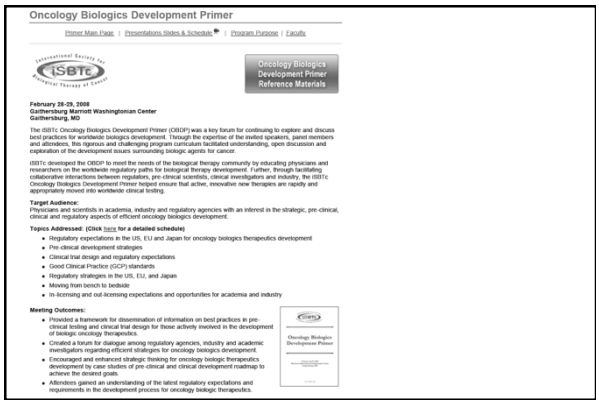
Immunotherapy may develop like other specialized areas of Medicine..

Vision..
Not so much "off the shelf".. Specialized Departments..
BMT / Surgery / Rad. Onc

Possibly greatest problem in field is……

Possibly greatest problem in field is……

Paucity of TRANSLATIONAL INVESTIGATORS



Oncology Biologics Development Primer

Primer Main Page | Presentations Slides & Schedule | Program Purpose | Faculty

ISBTc

Oncology Biologics Development Primer Reference Materials

February 28-29, 2008
Gaithersburg Marriott Washingtonian Center
Gaithersburg, MD

The ISBTc Oncology Biologics Development Primer (OBDP) was a key forum for continuing to explore and discuss best practices for worldwide biologics development. Through the expertise of the invited speakers, panel members and attendees, this rigorous and challenging program curriculum facilitated understanding, open discussion and exploration of the development issues surrounding biologic agents for cancer.

ISBTc developed the OBDP to meet the needs of the biological therapy community by educating physicians and researchers on the worldwide regulatory paths for biological therapy development. Further, through facilitating collaborative interactions between regulators, pre-clinical scientists, clinical investigators and industry, the ISBTc Oncology Biologics Development Primer helped ensure that active, innovative new therapies are rapidly and appropriately moved into worldwide clinical testing.

Target Audience:
Physicians and scientists in academia, industry and regulatory agencies with an interest in the strategic, pre-clinical, clinical and regulatory aspects of efficient oncology biologics development.

Topics Addressed: (Click here for a detailed schedule)

- Regulatory expectations in the US, EU and Japan for oncology biologics therapeutics development
- Pre-clinical development strategies
- Clinical trial design and regulatory expectations
- Good Clinical Practice (GCP) standards
- Regulatory strategies in the US, EU, and Japan
- Moving from bench to bedside
- In-licensing and out-licensing expectations and opportunities for academia and industry

Meeting Outcomes:

- Provided a framework for dissemination of information on best practices in pre-clinical testing and clinical trial design for those actively involved in the development of biologic oncology therapeutics
- Created a forum for dialogue among regulatory agencies, industry and academic investigators regarding efficient strategies for oncology biologics development.
- Encouraged and enhanced strategic thinking for oncology biologic therapeutics development by case studies of pre-clinical and clinical development roadmap to achieve the desired goals.
- Attendees gained an understanding of the latest regulatory expectations and requirements in the development process for oncology biologic therapeutics.