Prophylactic Breast Cancer Vaccination

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Vaccine Renaissance Conference IV
Providence, RI
October 23, 2010

Cleveland - Home of the Rock and Roll Hall of Fame
We have several patents pending for the use of lactation proteins in breast cancer vaccination
Organs We Have Destroyed with Targeted Autoimmunity

- **Brain**: autoimmune encephalomyelitis – **Multiple Sclerosis**
- **Heart**: autoimmune dilated cardiomyopathy – **Heart Failure**
- **Inner Ear**: autoimmune inner ear disease – **Sudden Deafness**
- **Ovary**: premature ovarian failure (POF) – **Infertility**
- **Bladder**: autoimmune cystitis – **Interstitial Cystitis**
- **Prostate**: autoimmune prostatitis – **Prostatitis**

Cancer Vaccination

- The development of effective vaccines against the more common cancers like breast, prostate, colon, lung, *et al.* has been very frustrating and disappointing for well over 40 years

- Only recently did the FDA “approve” the first non-viral cancer vaccine, namely, **Provenge**, a dendritic cell vaccine against prostate acid phosphatase and metastatic prostate cancer that adds a median few months of overall survival

- The single most important reason for these modest results is the determined use of cancer vaccines to *Treat* established tumors rather than to *Prevent* the tumors from establishing themselves
The Center for Disease Control and Prevention identifies 16 different pathogens against which children may be vaccinated by age thirteen.

These vaccines target 16 different Non-Self pathogens that threaten our biologic integrity.

The Childhood Vaccination Program is Our Instruction Manual on How to Eliminate Diseases.

![Graph showing the decline in Hib disease incidence in the United States from 1990 to 2007.](image-url)
The Success of Childhood Vaccination is Rooted in Prophylaxis – Measles

![Measles - United States, 1950-2007 graph]

The Success of Childhood Vaccination is Rooted in Prophylaxis – Mumps

![Mumps - United States, 1968-2007 graph]
The Success of Childhood Vaccination is Rooted in Prophylaxis – Polio

Poliomyelitis – United States, 1950-2007

Polio Vaccine – Gone are the Rows of Iron Lungs
What About An Adult Prophylactic Vaccine Program to Protect us from Adult Diseases?

- Other than seasonal **Influenza** vaccination, there are no scheduled vaccinations after age 11-12 until **Herpes Zoster** at age 60 and **Pneumoccus** at age 65

- This represents an enormous **Hole in Our Adult Health Care**

- Is it possible to develop an **Adult Vaccination** program that prevents adult onset diseases in the same way the childhood vaccination program prevents childhood associated diseases?

- When we reach 40 years of age, can we have breast cancer, ovarian cancer, prostate cancer, and colon cancer vaccines designed to protect us from these adult diseases?

- Appropriate stimulation of the immune system through **Adult Vaccination** can keep us healthy during the course of our entire life and not just during childhood

Cancer Vaccines

- Most cancers are not directly caused by viruses and are therefore, not amenable to a traditional protective or prophylactic vaccine

- However, all cancers are diseases involving unregulated growth of self tissues

- Since there is no virus implicated in the majority of breast cancers, and since breast tumors are due to overgrowth of dysfunctional breast cells, then a prophylactic breast cancer vaccine must target **Breast Self**
Problem and Solution

**PROBLEM:** How do we target normal Breast Self so that breast tumors are killed as they form but normal breast cells are spared any autoimmune damage?

**SOLUTION:** By targeting “Retired” Breast Self that is no longer made in normal breast tissues but is made in dysfunctional breast tumors.

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Taking Advantage of the Normal Aging Process in Women

Two complementary events that normally take place as women age:

1) 95% of breast cancer cases in the USA occur in women aged 40 and older (American Cancer Society, Breast Cancer Facts and Figures 2009-2010)

2) 2.6% of children in the USA are born to women 40 years of age and older (Centers for Disease Control and Prevention, National Vital Statistics Reports, Births: Final Data for 2007)

Therefore, the vast majority of women after age 40 no longer breastfeed, and their lactation proteins become essentially “retired” at a time in life when risk for developing breast cancer rises rapidly.
“Retired” Lactation Proteins as Targets for Prophylactic Breast Cancer Vaccination

• We reasoned that vaccination against “retired” lactation proteins would not cause any damage to normal breast tissues because these proteins are no longer being made in any appreciable amounts

• We also reasoned that vaccination against “retired” lactation proteins would prevent any emerging breast tumors from growing because these proteins are expressed in the dysfunctional breast tumor cells

• WE WERE RIGHT!!! We found that vaccination against the “retired” lactation protein, α-lactalbumin, provides protection against the development of breast cancer in mice in the complete absence of any autoimmune breast inflammation and damage

• Thus, our vaccine is both effective and safe for prophylaxis

α-Lactalbumin

**Initial Experimental Design**

Purified recombinant mouse α-lactalbumin

Emulsion in complete Freund’s adjuvant (CFA)

Subcutaneous injection of 8 week old SWXJ female mice

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**Recall Responses to α-Lactalbumin Indicate a Predominant Th1-Like Proinflammatory Response**
CD3+ T Cells Infiltrate Lactating but Not Non-Lactating Mouse Mammary Glands

Real Time RT-PCR Shows Increased IFNγ, α-Lactalbumin, and α-Casein Expression in Lactating Breast Tissue 6 Weeks after Immunization with α-Lactalbumin
AUTOIMMUNE BREAST FAILURE: Pups Show a Failure to Thrive with Decreased Mean Pup Weights

Pups from α-Lactalbumin Immunized Mice Exhibit Kwashiorkor-Like Alopecia and Liver Toxicity
Prophylactic Vaccination with $\alpha$-Lactalbumin Inhibits the Growth of: 1) Autochthonous Breast Tumors in MMTV-neu Mice, and 2) Transplantable 4T1 Breast Tumors in BALB/c Mice

Vaccination of 2 Month Old MMTV-neu Mice

Vaccination 13 Days Before Inoculation of BALB/c Mice with 4T1 Tumor Cells

Treatment with $\alpha$-Lactalbumin Vaccination Inhibits the Growth of Established 4T1 Breast Tumors in BALB/c Mice but Protection Fades with Time After Inoculation

Delay Between Inoculation of 4T1 Tumor Cells and Vaccination

5 Days 14 Days 21 Days
Therapeutic Vaccination with $\alpha$-Lactalbumin at 6 Weeks Inhibits the Growth of Established Autochthonous Breast Tumors in MMTV-PyVT Mice

CD3+ T Cell Infiltration of 4T1 Tumors in BALB/c Females Vaccinated with $\alpha$-Lactalbumin
Analysis of Tumor Infiltrating Lymphocytes (TILs): Flow Cytometry

CD4+ TILs Produce IFN\(\gamma\)

CD8+ TILs Mediate Cytotoxicity
Inhibition of Tumor 4T1 Breast Tumor Growth is Mediated by $\alpha$-Lactalbumin Primed Lymph Node Cells (LNC)

Inhibition of 4T1 Breast Tumor Growth is Mediated by $\alpha$-Lactalbumin Primed CD4+ or CD8+ T Cells
Summary

• Vaccination with the lactation protein, α-lactalbumin, provides protection against the development of breast cancer in mice in the absence of any detectable autoimmune induced breast inflammation

• "Retired" self proteins that are no longer expressed in normal tissues but are overexpressed in tumors may substitute for Non-Self viral targets in developing prophylactic vaccination against diseases we confront as we age like breast cancer

• Our results provide a rational basis for the development of a safe and effective prophylactic vaccine against human breast cancer

Collaborators

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• Funded by NIH R01CA-14035 and support from the American Recovery and Reinvestment Act of 2009
Our Breast Cancer Vaccine Team

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“The future ain’t what it used to be.”

---- Yogi Berra