



## Novel Vaccine Strategies for Cancer and AIDS



TEDCO/NIH/NCI Technology Showcase  
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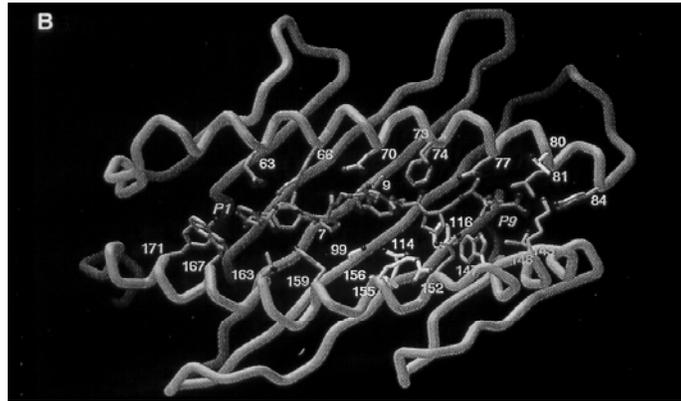
### *Technology: TARP Tumor antigen*



- **TARP (T-cell Receptor g chain Alternate Reading Frame Protein): A new tumor antigen expressed in 95% of prostate cancers and 50% of breast cancers (Essand et al. PNAS 1999; Wolfgang et al. PNAS 2000; Oh et al., Cancer Research 2004).**
- **High affinity HLA-A2-binding epitopes defined.**
- **Sequences modified to improve binding to HLA-A2 without losing recognition by the responding T cells, to make a more potent anti-cancer vaccine.**
- **Clinical trial in prostate cancer to open soon.**

Peptide Fragments of Viral Proteins Bind Specifically in the Groove of Major Histocompatibility Molecules such as HLA-A, B, C

### Sendai Virus Peptide Bound to H-2K<sup>b</sup>



From DH Fremont, M. Matsumura, EA Stura, PA Peterson, & IA Wilson. *Science* 257: 919-926, 1992

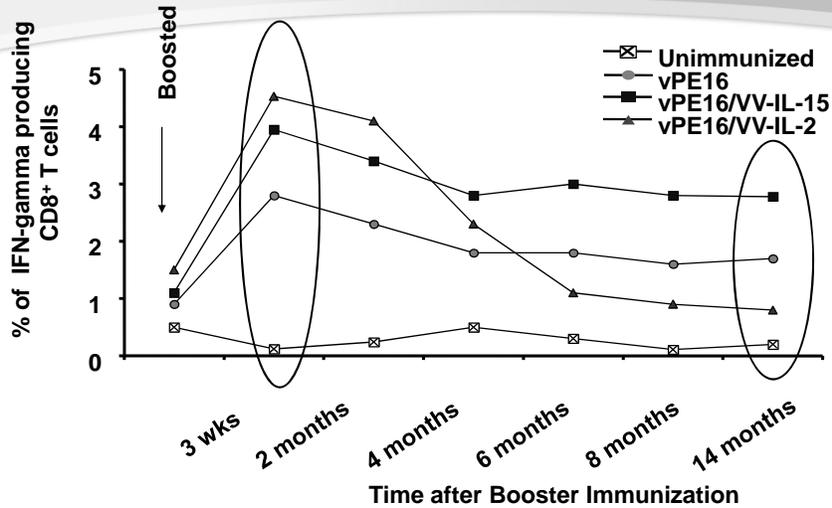
**Strategy: Epitope Enhancement by Sequence Modification to Increase Peptide Affinity for the MHC Molecule**

## IL-15 as a Vaccine Adjuvant

**Induction of long-lived cytotoxic T lymphocytes (CTL)**

**Induction of higher avidity CTL, more effective at clearing viruses or killing tumor cells.**

*IL-15 expression by a vaccine vector induced longer-lived memory CD8<sup>+</sup> CTL*

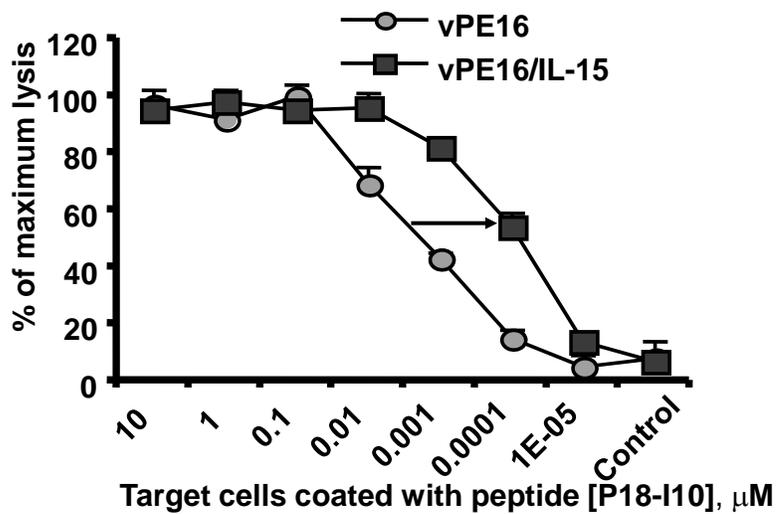


Oh et al., *PNAS* 2003

Explained by:

1. Higher IL-15R $\alpha$  expression
2. Greater homeostatic proliferation

*Immunization with antigen + IL-15 induces higher avidity memory CD8<sup>+</sup> CTL*

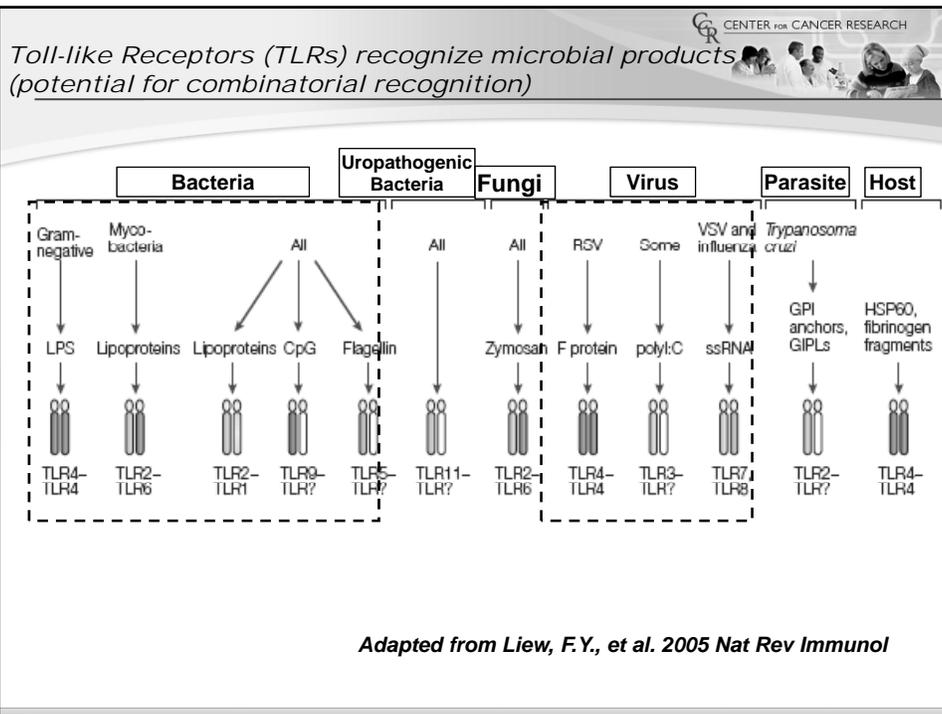


Oh et al., *PNAS* 2004

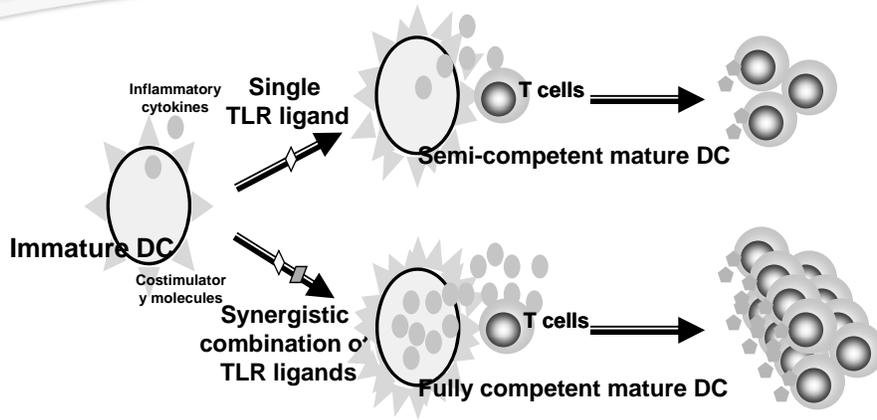
2 months after immunization



## Synergistic Combinations of Toll-like Receptor Ligands as Vaccine Adjuvants



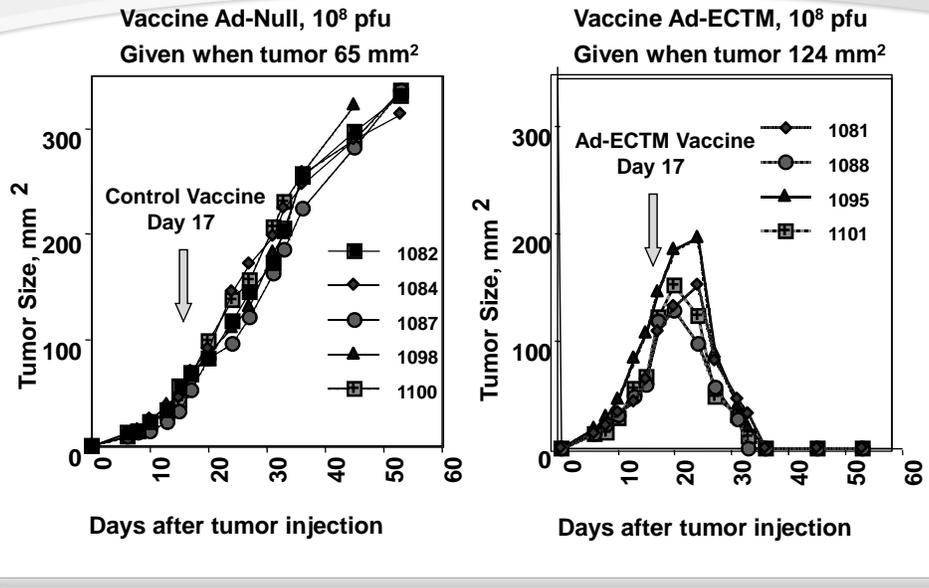
*Hypothesis for synergy in dendritic cell activation by TLR ligands*



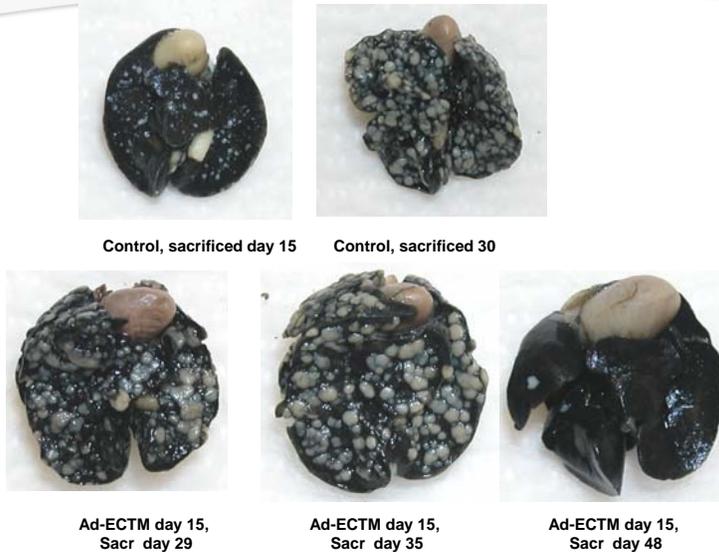
**Recombinant Adenovirus Expressing HER-2/neu (ErbB2)  
As a Vaccine for Breast Cancer**

**Treatment of large established mammary carcinomas in mice with an Adenovirus expressing the extracellular and transmembrane Domains (ECTM) of the *neu* oncogene (ErbB2) can induce Regression of subcutaneous tumors and lung metastases in a mouse model.**

# Ad-ECTM vaccine causes regression of large (> 1 cm<sup>2</sup>) tumors



# Ad-ECTM vaccine induces regression of established Lung tumors from IV injection of TUBO breast cancer cells



## *Technology Applications*

- **These all represent technologies to make more effective vaccines for cancer and/or HIV.**
- **None of these are yet licensed or part of an existing CRADA.**

## *Contact Information*

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