


 **CENTER FOR
CANCER
RESEARCH**
Connecting the Cancer Community




• Innovative Science • Breakthrough Therapies • Clinical Advances


Novel Vaccine Strategies for Cancer and AIDS

 **TECH**
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Technology Development Corporation

TEDCO/NIH/NCI Technology Showcase
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September 25, 2007

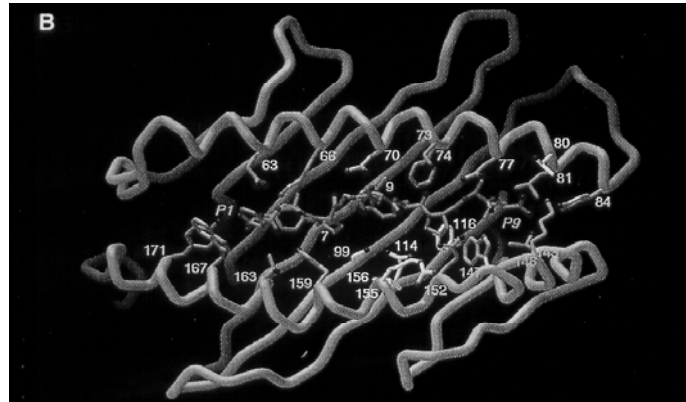


 **CENTER FOR CANCER RESEARCH**

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.**

Sendai Virus Peptide Bound to H-2K^b



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

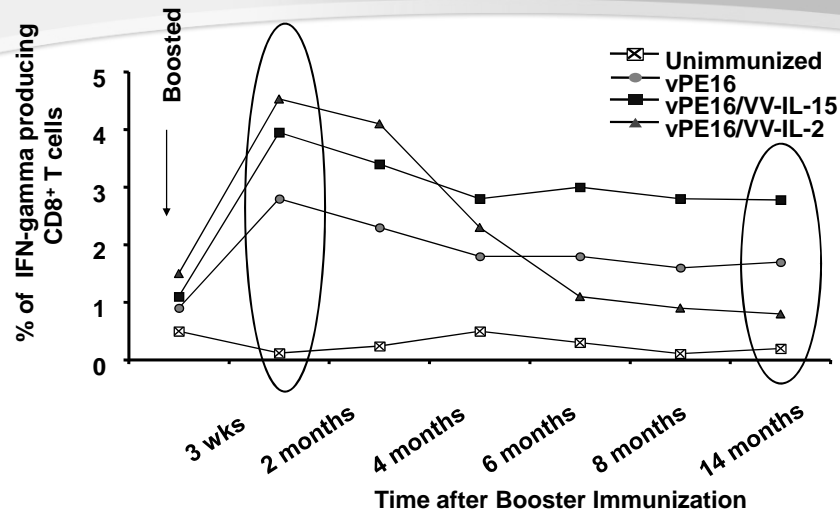
Strategy: Epitope Enhancement by Sequence Modification to Increase Peptide Affinity for the MHC Molecule

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⁺ CTL

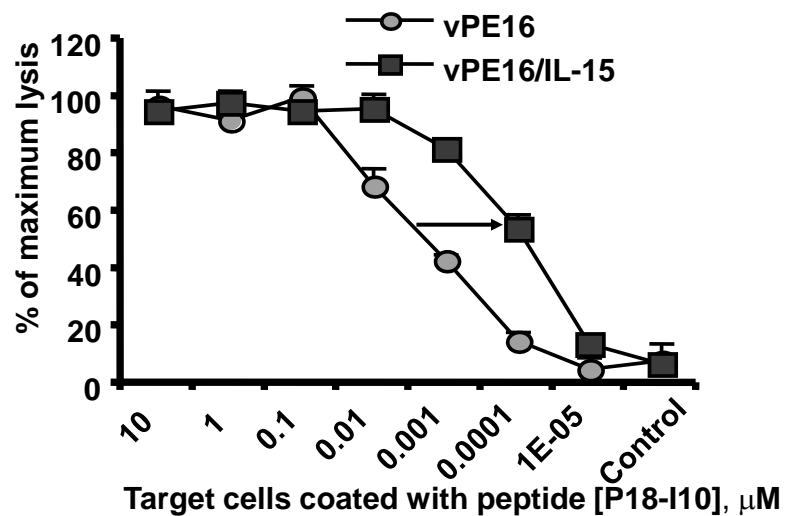


Oh et al., *PNAS* 2003

Explained by:

1. Higher IL-15R α expression
2. Greater homeostatic proliferation

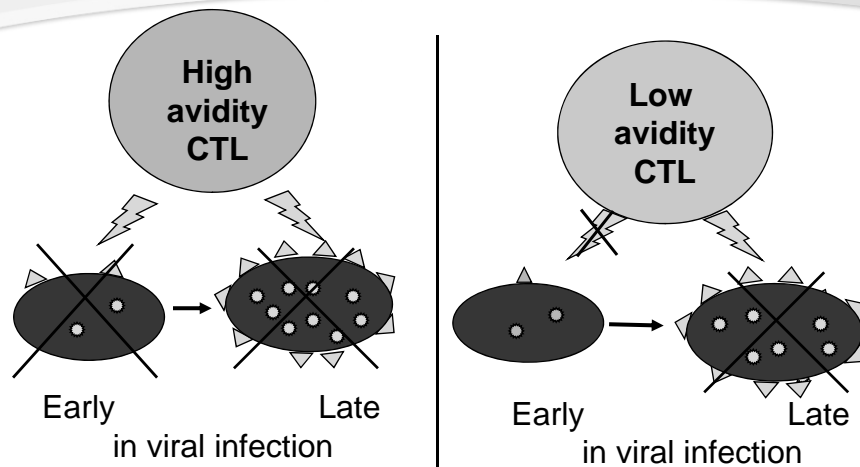
Immunization with antigen + IL-15 induces higher avidity memory CD8⁺ CTL



Oh et al., *PNAS* 2004

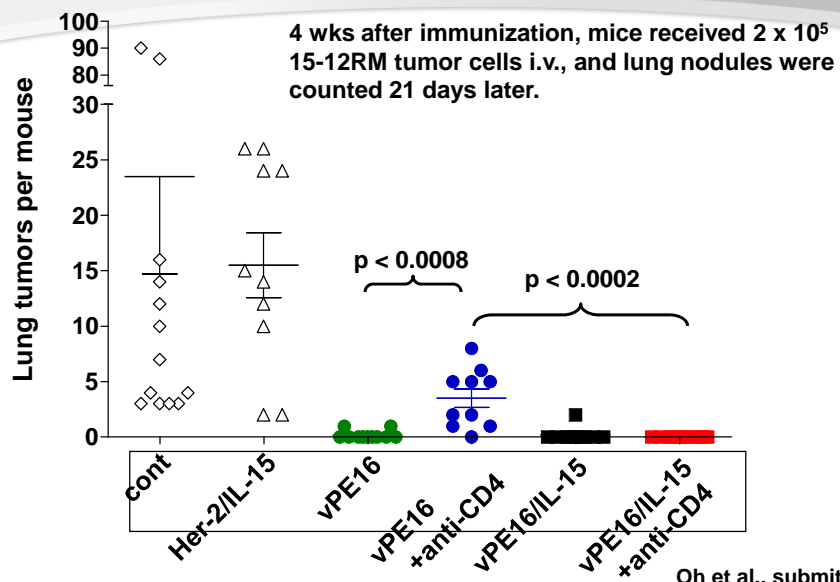
2 months after immunization

High avidity CTL are more effective at viral clearance

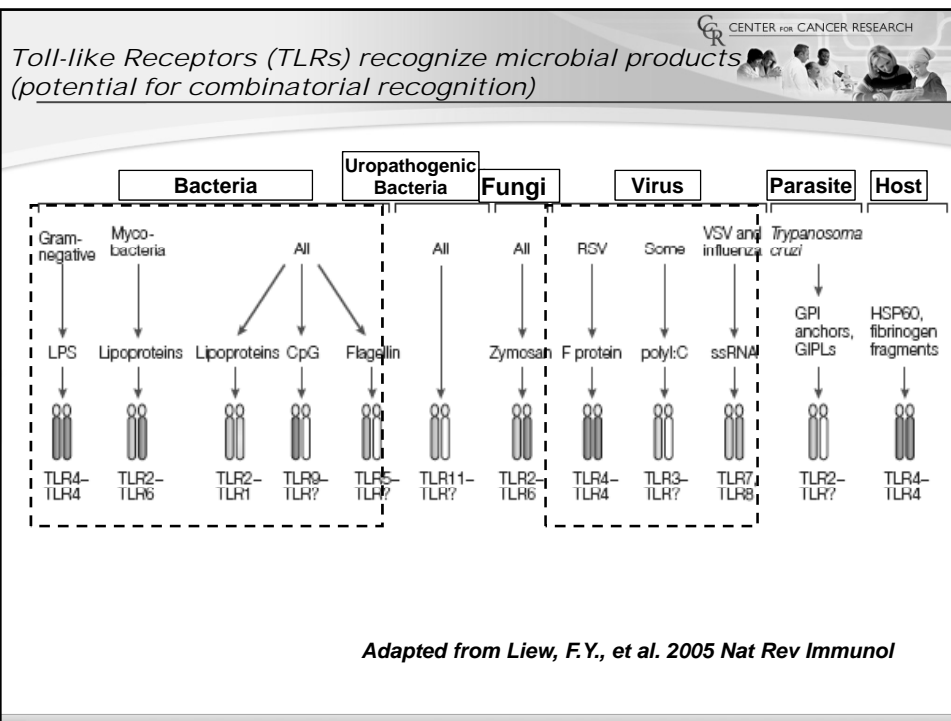


Alexander-Miller et al. *PNAS* 1996; Derby et al., *J. Immunol.* 2001; Belyakov et al, *Blood* 2006

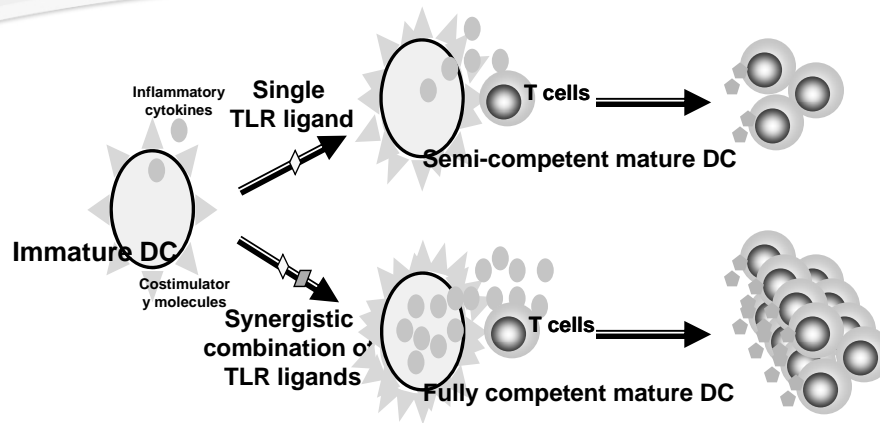
IL-15 overcomes CD4-deficiency to allow vaccine-induced protection against 15-12RM lung tumors



Synergistic Combinations of Toll-like Receptor Ligands as Vaccine Adjuvants



Hypothesis for synergy in dendritic cell activation by TLR ligands

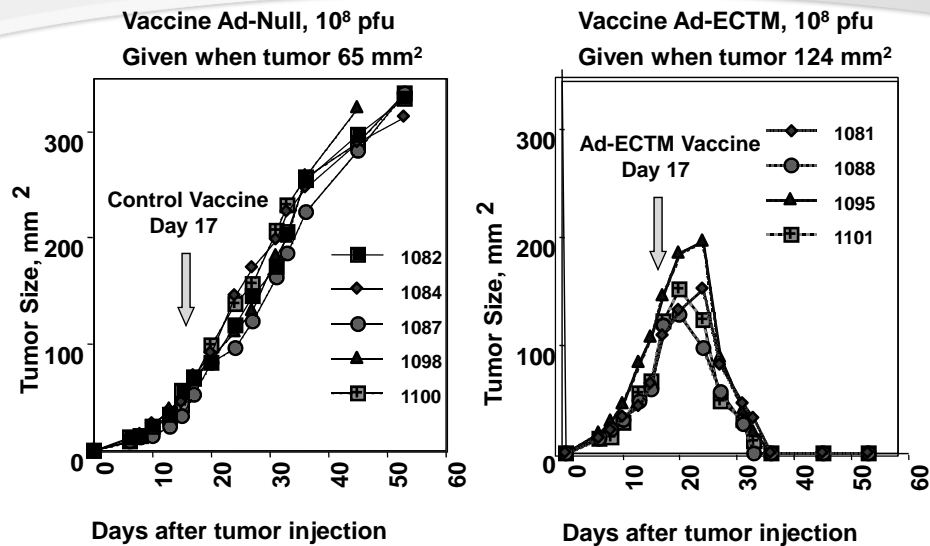


Recombinant Adenovirus Expressing HER-2/neu (ErbB2) As a Vaccine for Breast Cancer

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 ($> 1 \text{ cm}^2$) 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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