

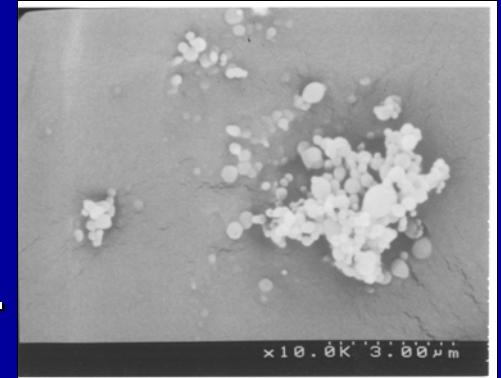
Regression of Advanced Spontaneous Mammary Tumors and Induction of Systemic Anti-tumor T- and B-Cell Immunity in Her-2/neu Transgenic Mice After Intra-tumoral IL-12 + GM-CSF Microsphere Therapy

Nejat Egilmez, Ph.D.

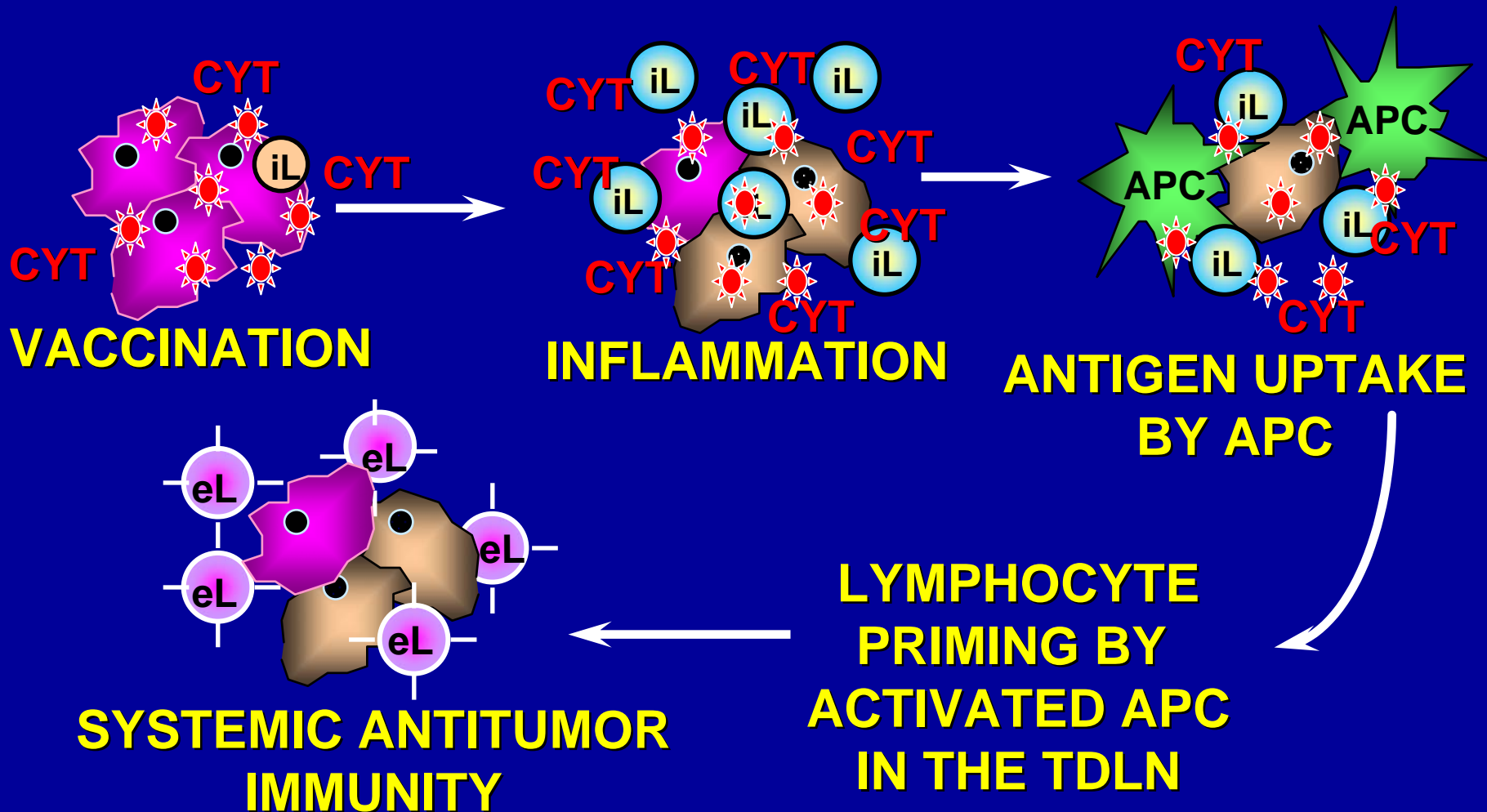
**J.G. Brown Cancer Center and the Department
of Microbiology & Immunology, School of
Medicine, University of Louisville, KY**

Biodegradable Controlled-Release Microsphere Adjuvants

- Biodegradable polymer (poly-lactic acid).
- Injectable (0.1-5 micron in size).
- Local, sustained release of macromolecules.
- Biological activity of macromolecules preserved.
- Storage stability depends on macromolecule.
- A clinically feasible alternative to gene- modification.

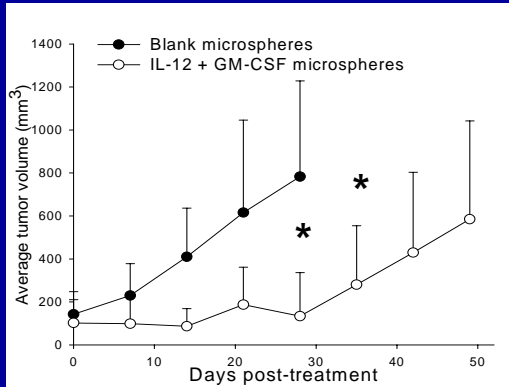


IN SITU TUMOR VACCINATION WITH CYTOKINE-ENCAPSULATED MICROSPHERES

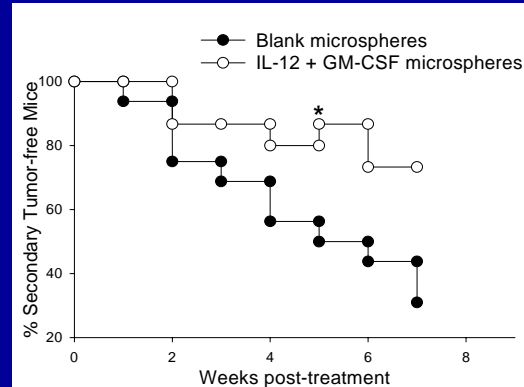


A Single Treatment w/IL-12 + GM-CSF Microspheres Induces Potent But Transient Tumor Suppression in FVB/neuN Mice

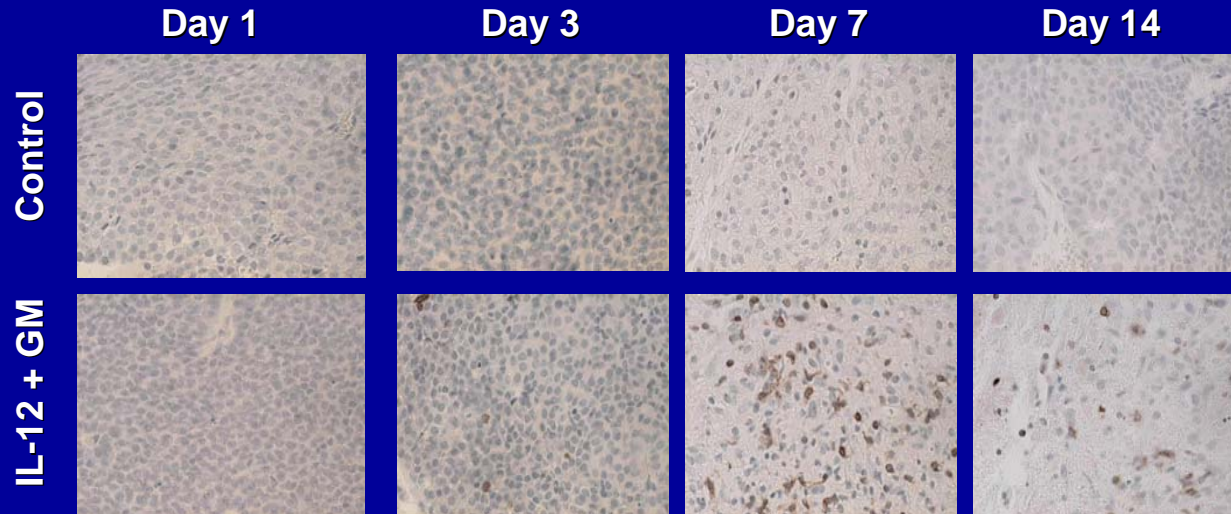
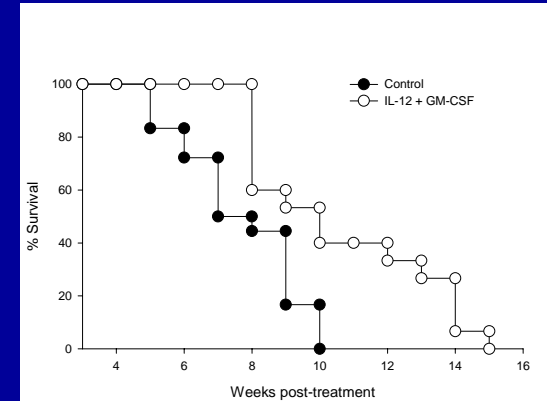
Primary Tumor



Secondary Tumor

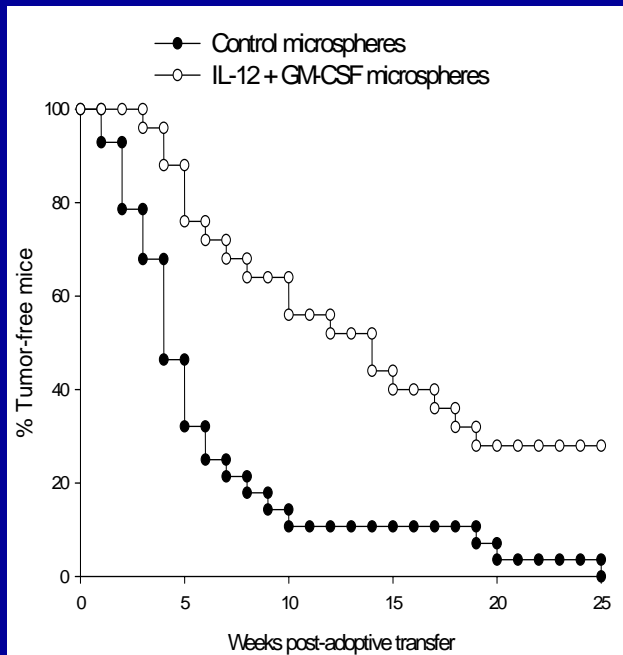


Survival

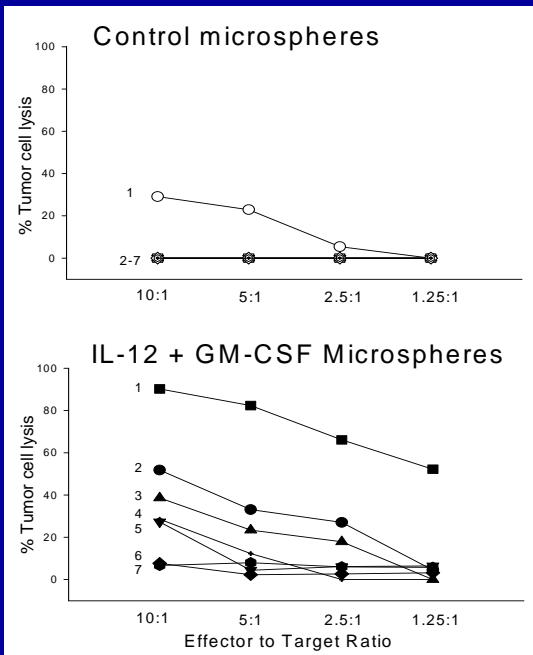


A Single Intra-tumoral Injection of IL-12 + GM-CSF Microspheres Induces Systemic Anti-tumor Immunity in FVB/neuN Mice

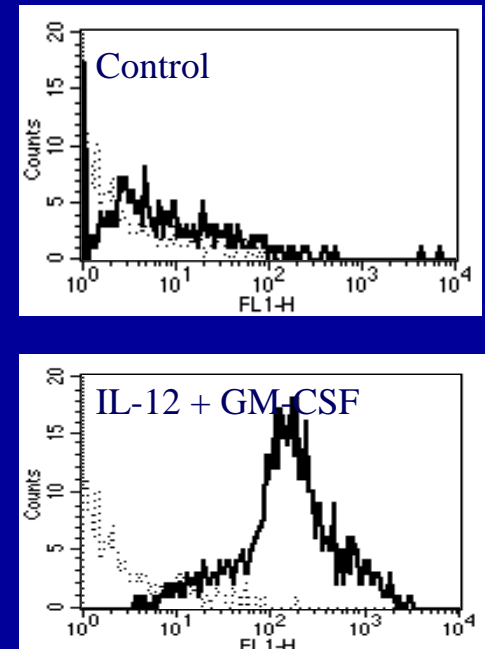
Adoptive transfer



Anti-tumor CTL



Anti-tumor Antibodies

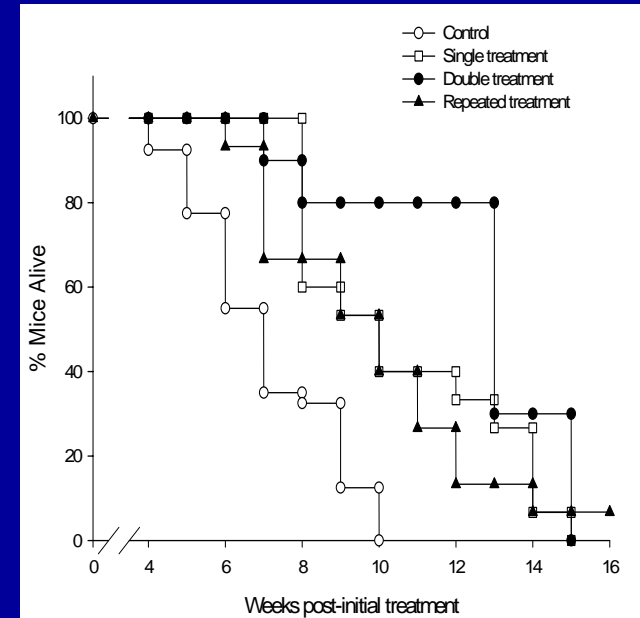


Chronic Immune Therapy with IL-12 + GM-CSF Microspheres Enhances Short-term Tumor Suppression But Does not Achieve Cure

8-weeks Post-first Treatment

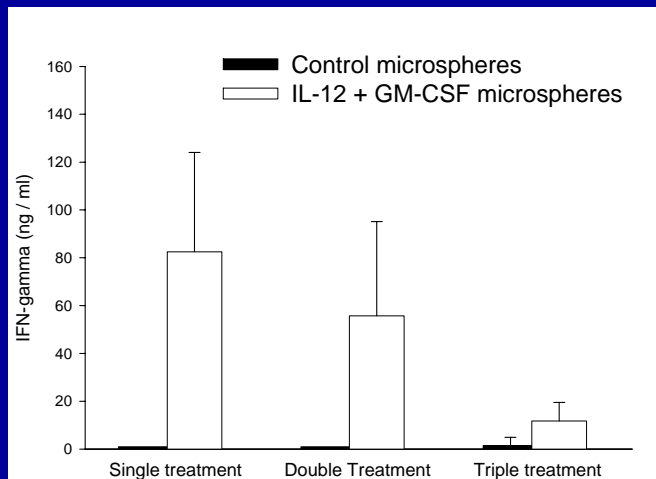
Rx	1 ^o Tumor growth	% 1 ^o Regression	% w/2 ^o Tumor
0	N/A	0	31
1	13-fold	0	73
2	2.7-fold	20	90
3	3.9-fold	14	73

Long-term Survival



Repeated Treatment Results in a Progressively Weaker T-cell Response

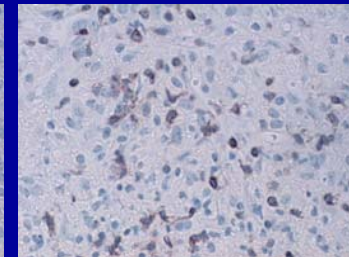
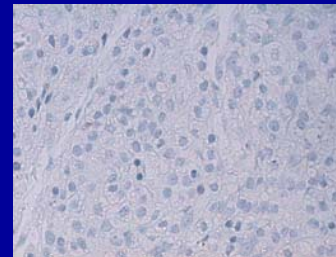
IFN- γ response



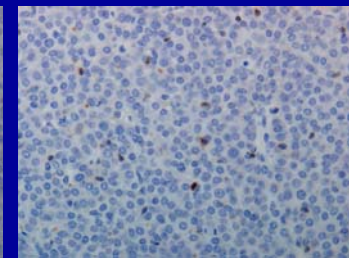
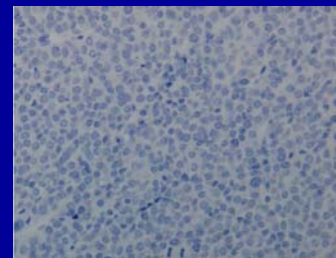
T-cell infiltration

Control

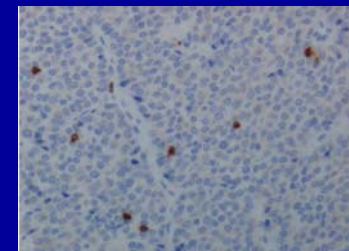
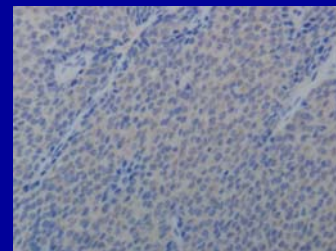
IL-12 + GM-CSF



Day 7



Day 28



Day 49

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- **Wyeth, Inc.**

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