

# IGFR Family Members are Immunologic Targets in Breast Cancer

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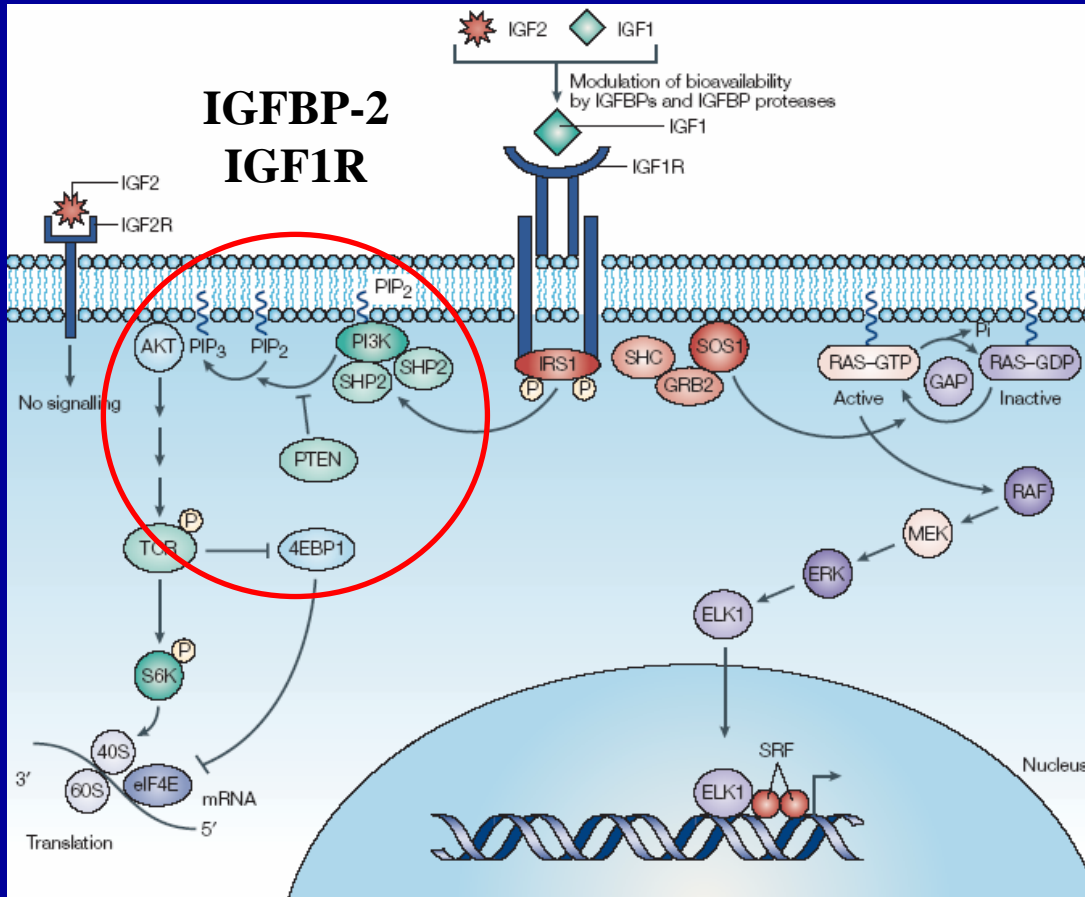
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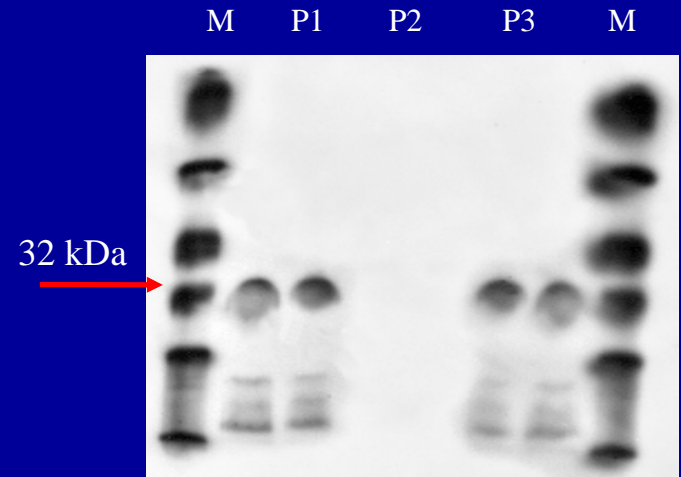
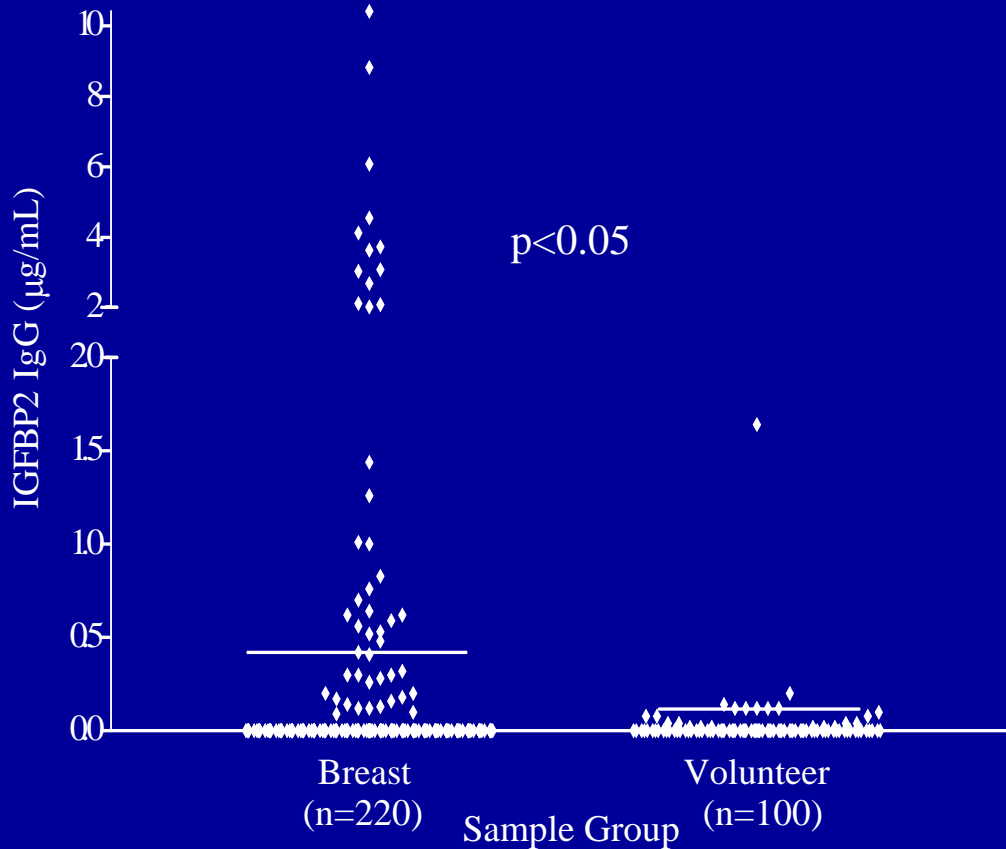
# IGFR1 Regulation of Breast Cancer



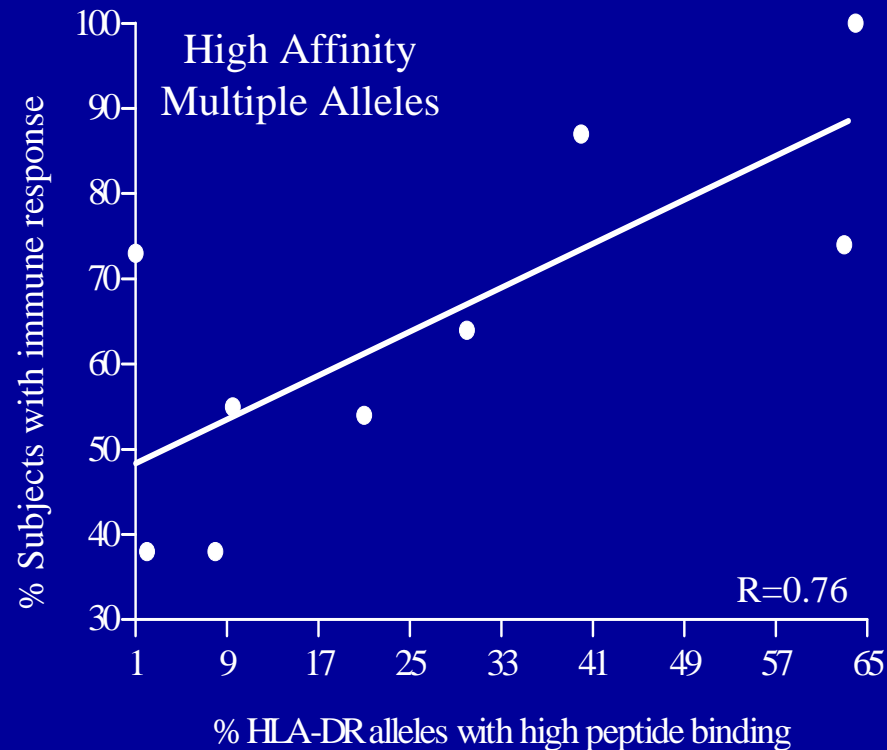
- Increased proliferation
- Decreased apoptosis
- Increased invasion
- Enhanced metastatic potential
- Plays a role in both hormone and trastuzumab resistance

Both IGFBP-2 and IGF1R proteins are overexpressed in breast cancer

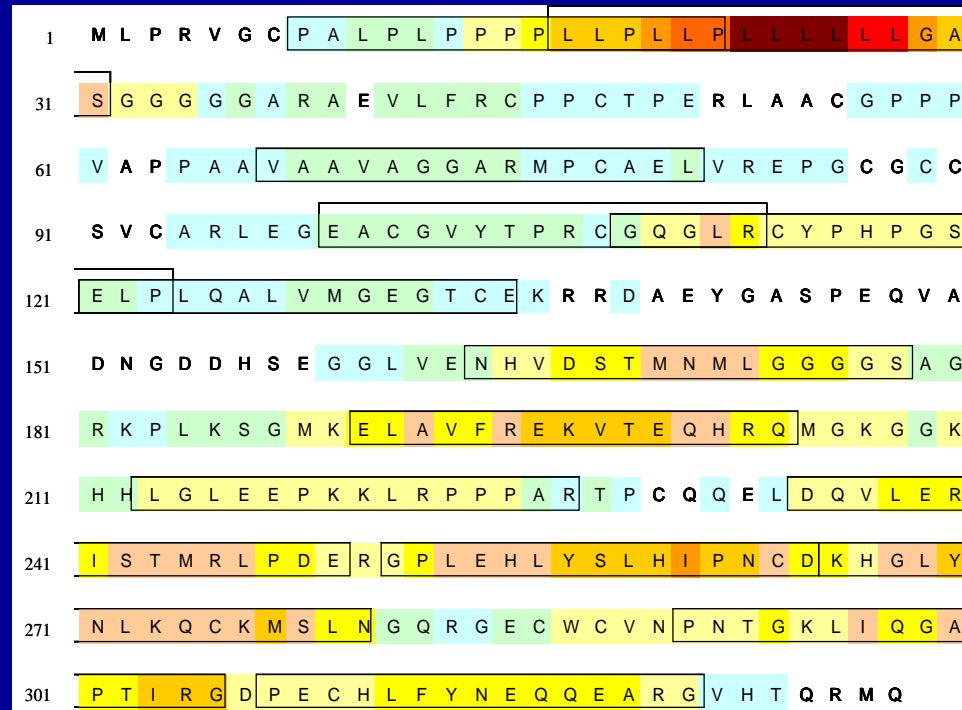
# Breast Cancer Patients Can Have Immunity to IGFBP-2



# Prediction of Potential Class II Epitopes

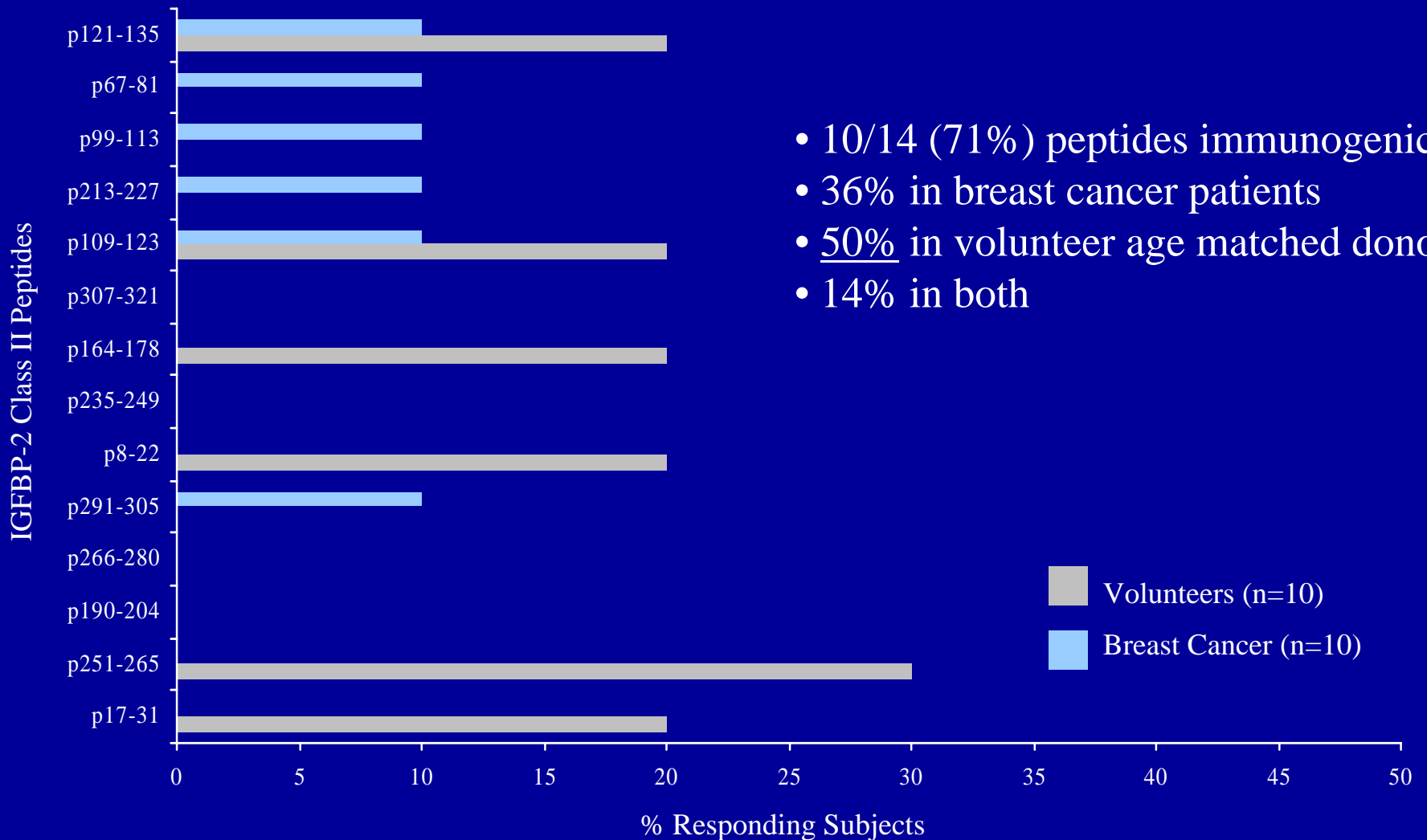


## IGFBP-2 Protein Sequence

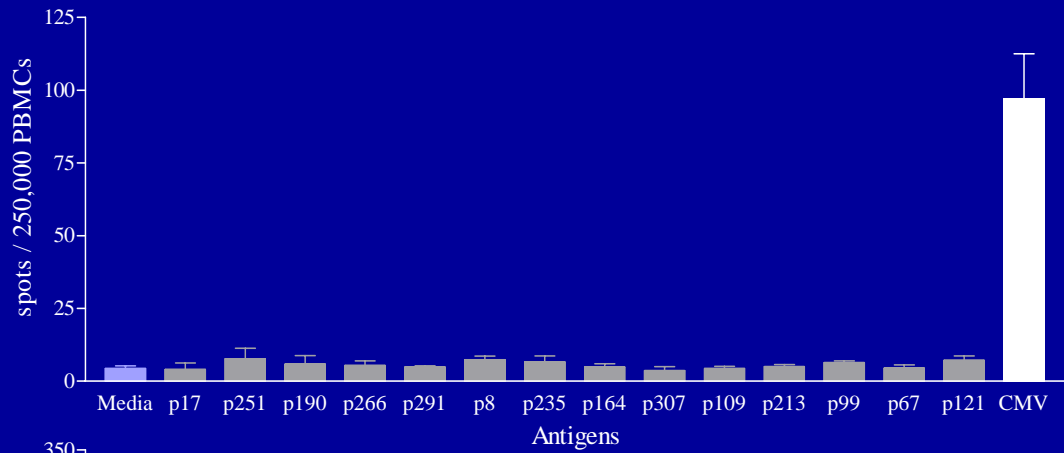


1. SYFPEITHI
2. Propred
3. MHC-Thread
4. Average Binding matrix method
5. Rankpep

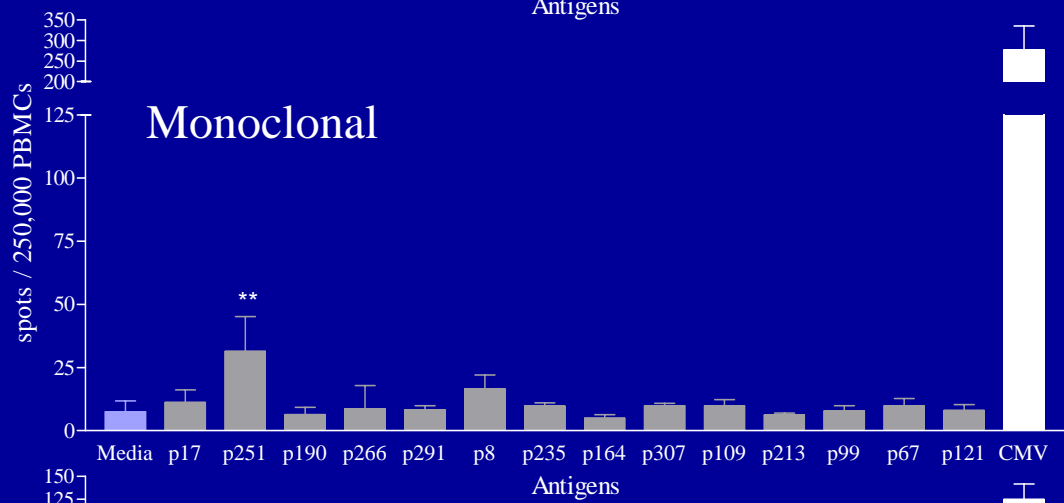
# T Cell Response to IGFBP-2 Peptides



IFN- $\gamma$  ELISPOT

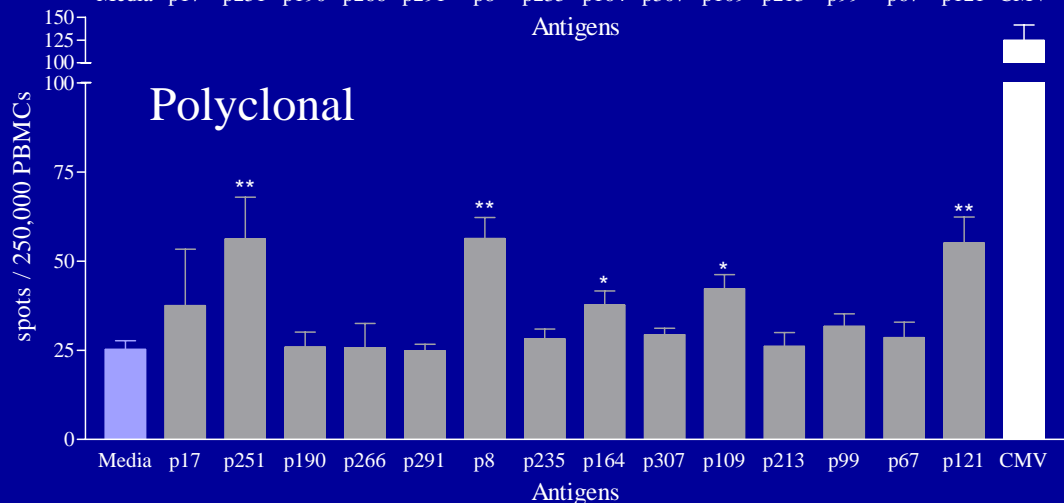


12/20 (60%)  
No response



Monoclonal

8/20 (40%)  
Response



Polyclonal

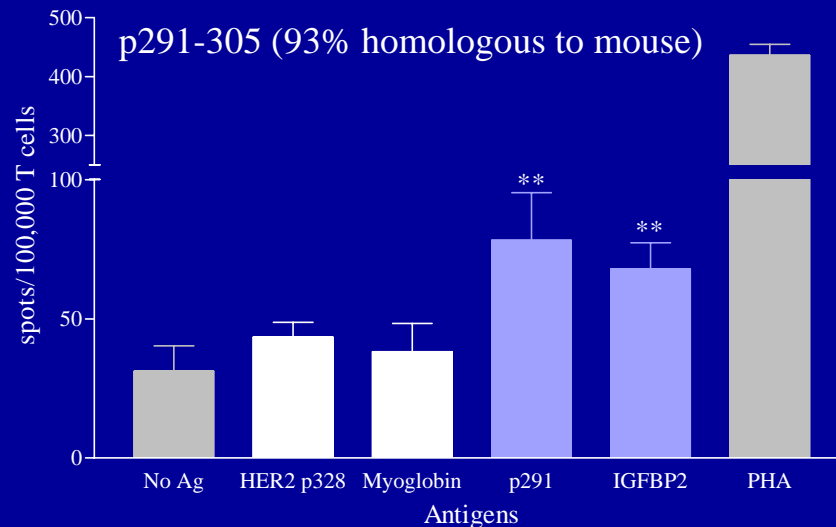
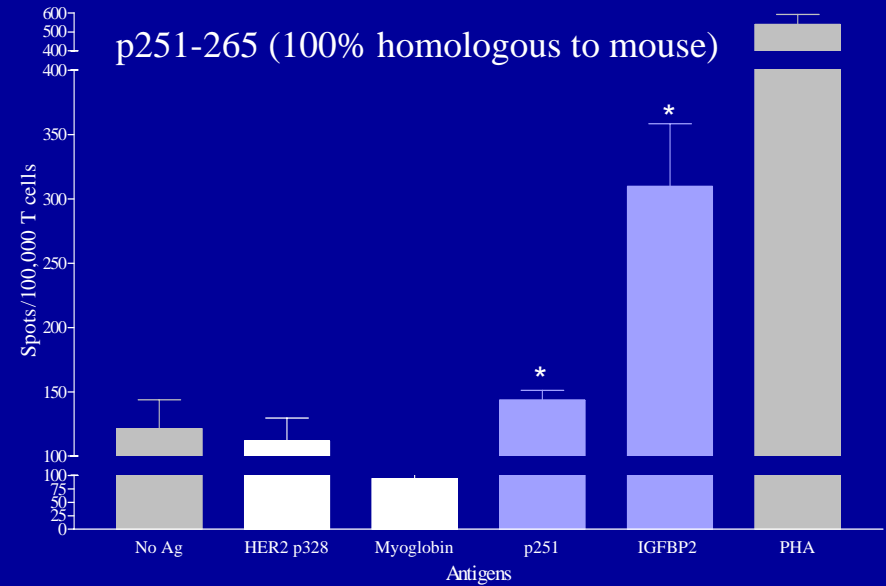
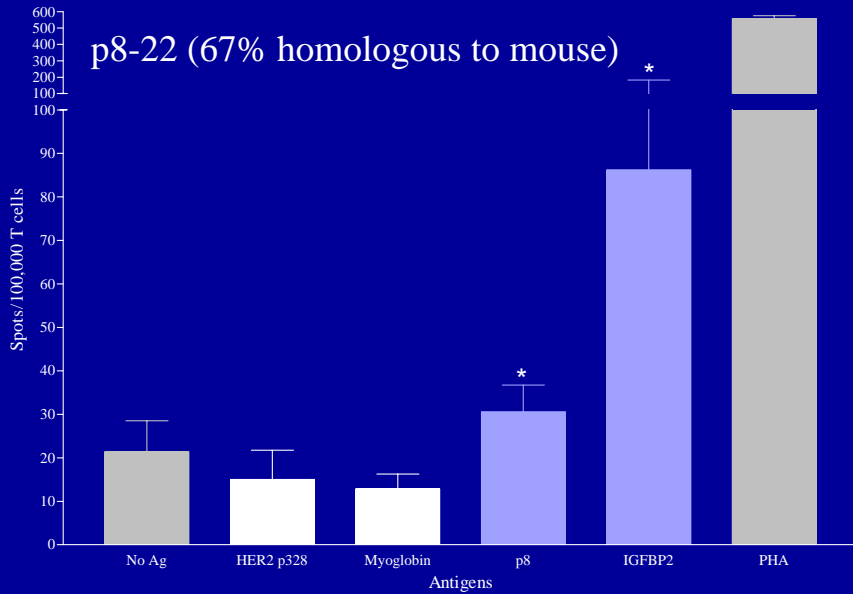
\* p<0.05  
\*\* p<0.005

# Immunogenic IGFBP-2 Peptides are Highly Homologous with Bacterial Antigens

60% of responders  
“molecular mimicry”

IGFBP-2 Peptides	Homologous protein		% Homology with mouse IGFBP-2
	Protein source of species	% Homology	
p17-31	<i>Candida albicans</i>	67	0
p251-265	<i>Pseudomonas aeruginosa</i>	47	100
p190-204	<i>Trypanosoma cruzi</i>	73	93
p266-280	<i>Lactobacillus reuteri</i>	47	100
p291-305	<i>Schistosoma japonicum</i>	60	93
p8-22	<i>Aspergillus oryzae</i>	67	67
p235-249	<i>Candida albicans</i>	53	93
p164-178	<i>Trypanosoma cruzi</i>	53	86
p307-321	<i>Staphylococcus aureus</i>	47	80
p109-123	<i>Pseudomonas fluorescens</i>	53	80
p213-227	<i>Aspergillus oryzae</i>	67	93
p99-113	Human, murine, canine IGFBP3, 4, 5	67-80	80
p67-81	<i>Propionibacterium acnes</i>	60	0
p121-135	<i>Pseudomonas aeruginosa</i>	60	80

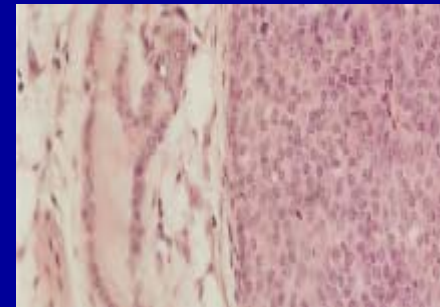
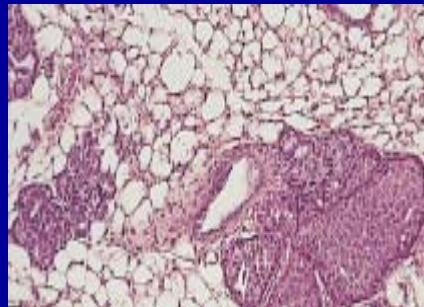
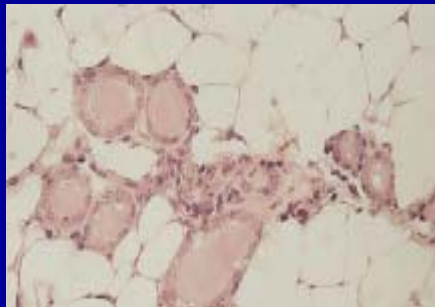
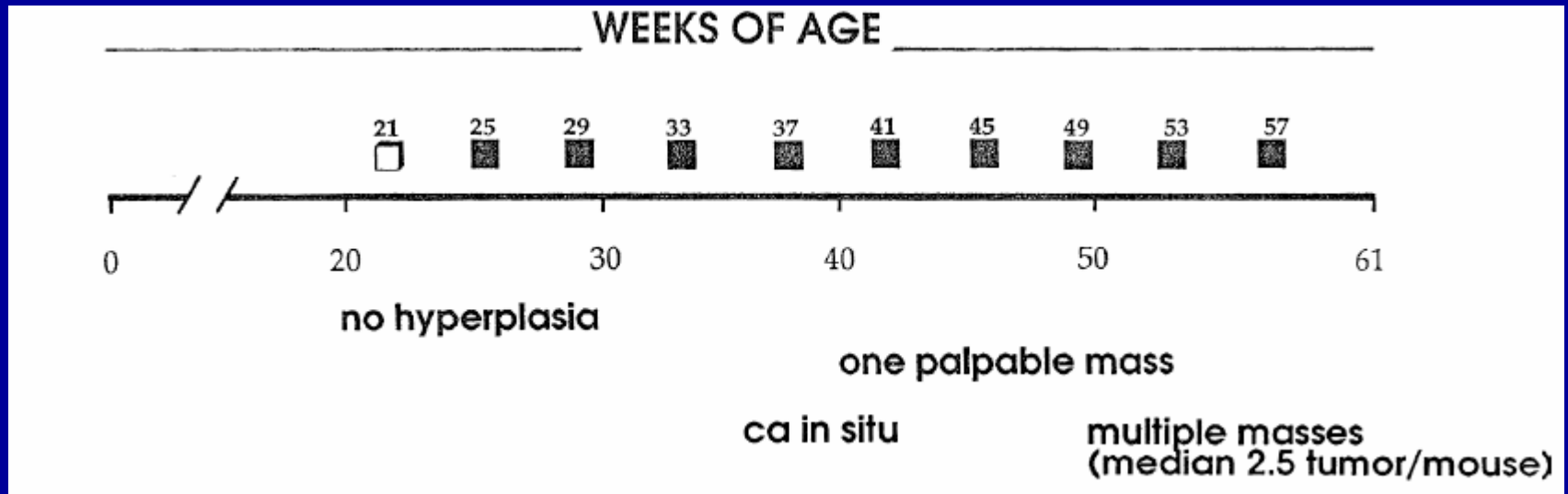
# IGFBP-2 Peptide Specific T Cell Lines Respond to Protein



\*  $p < 0.05$   
 \*\*  $p < 0.005$

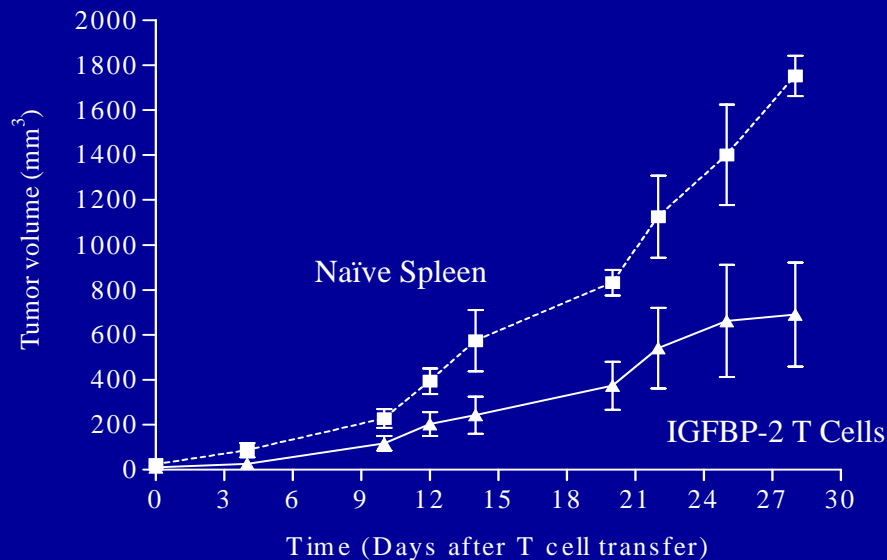
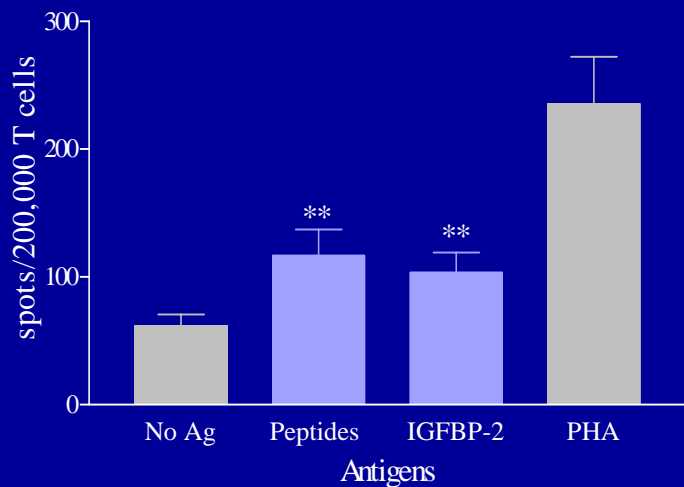
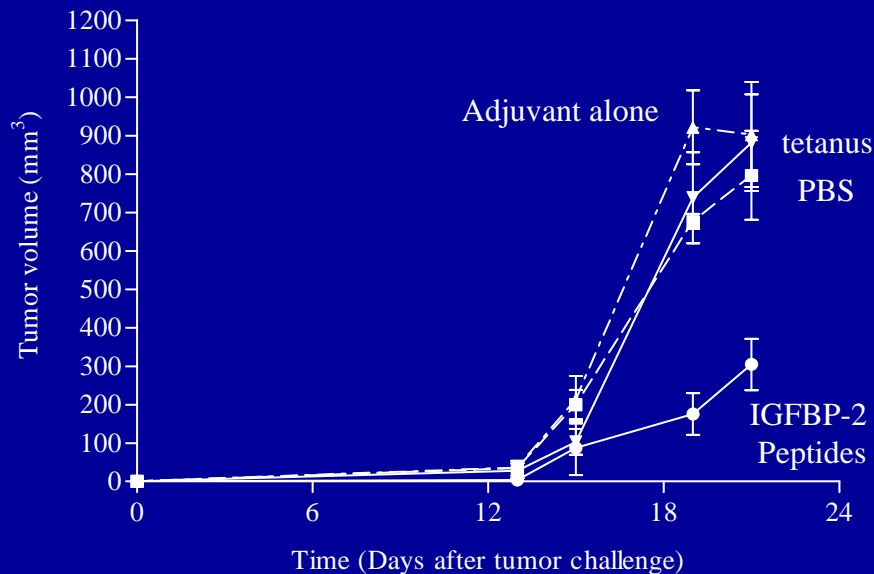
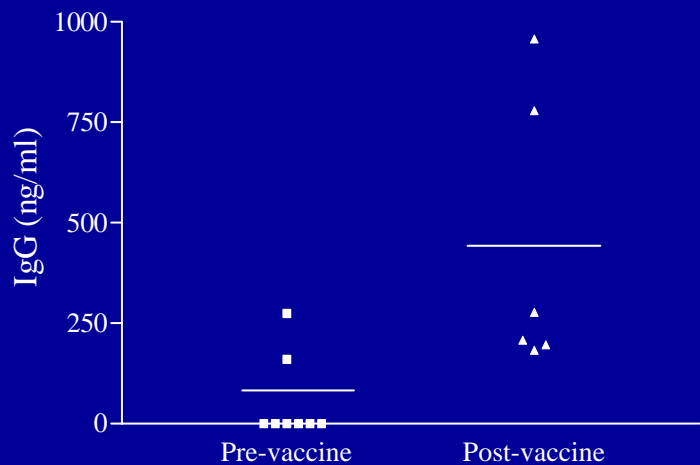


# neu Transgenic Mice: Model of HER2<sup>high</sup>/ER<sup>low</sup> Breast Cancer



Expression of both neu and murine IGFBP-2 and IGF1R

# IGFBP-2 Specific T Cells Inhibit Tumor Growth



\*\* p<0.005, n=5-6 mice/group

Park et al, 2007

# *Acknowledgements*

## Tumor Vaccine Group

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