NOVEL NEOADJUVANT DENDRITIC CELL VACCINE IN EARLY HER-2+ BREAST CANCER

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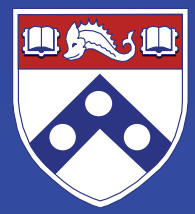
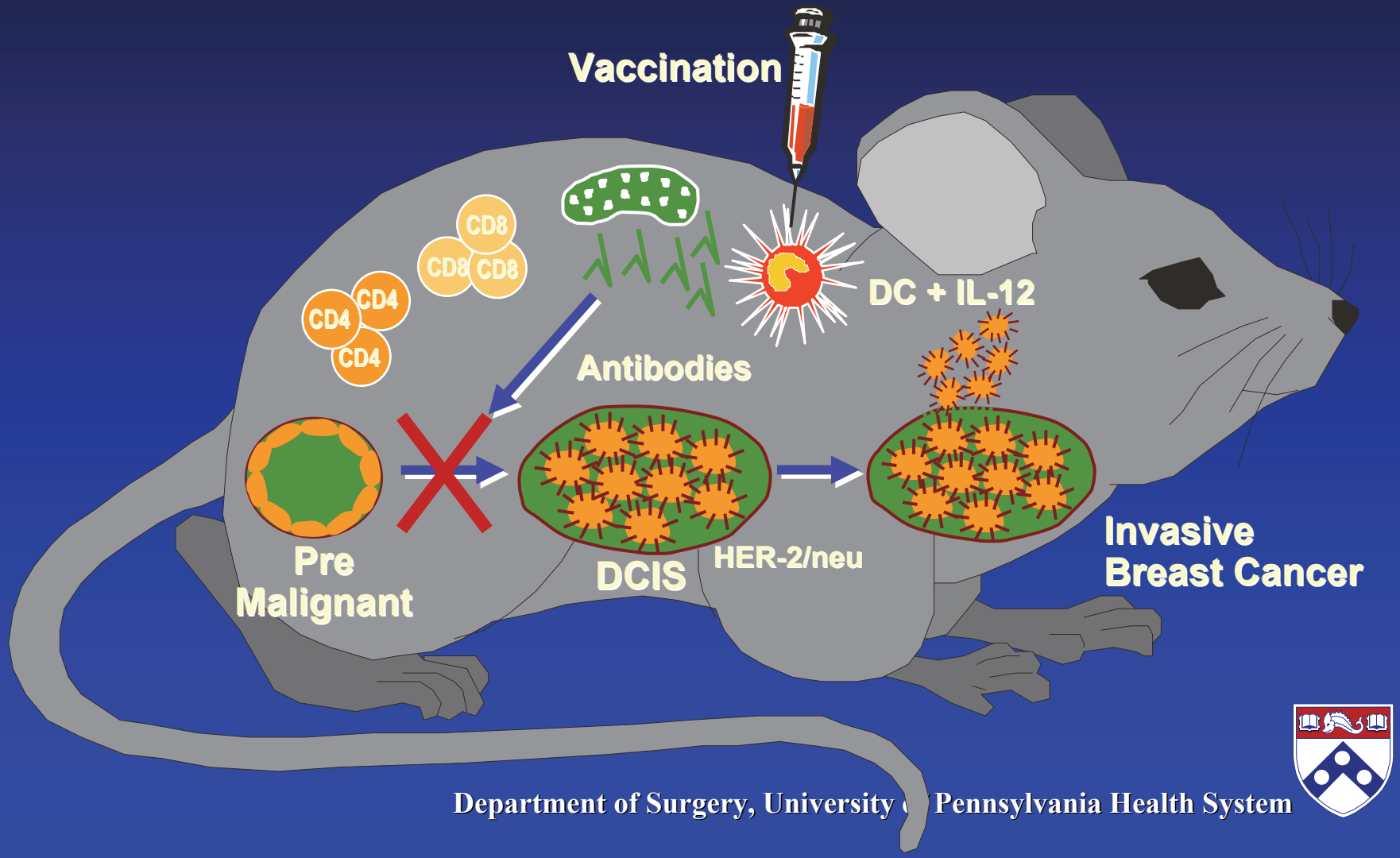


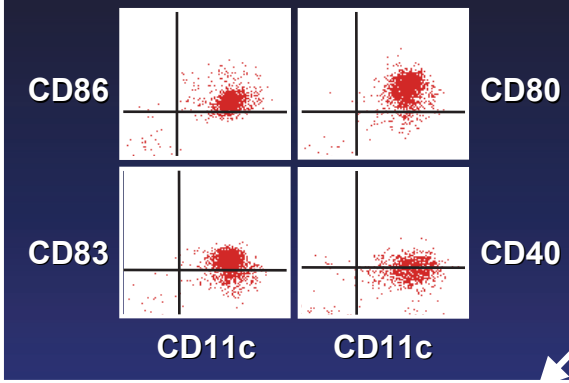
Pre-Clinical Breast Cancer Prevention Vaccines

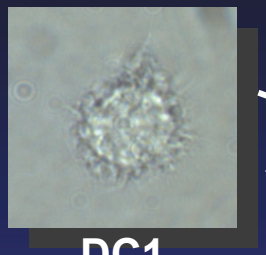


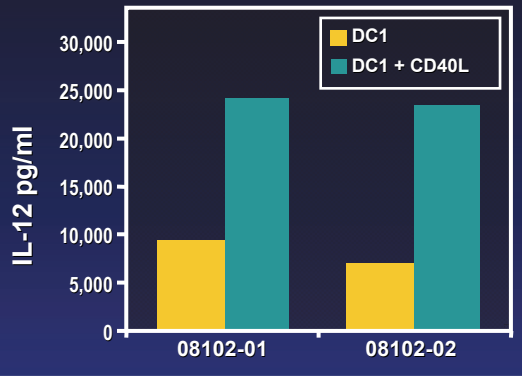
Department of Surgery, University of Pennsylvania Health System

HER-2/neu Peptide Pulsed DC1 Vaccine for DCIS

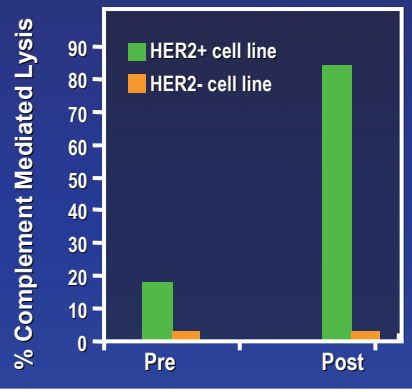
INNATE

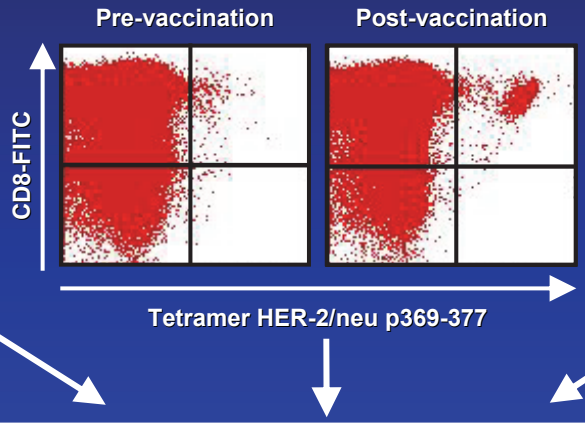


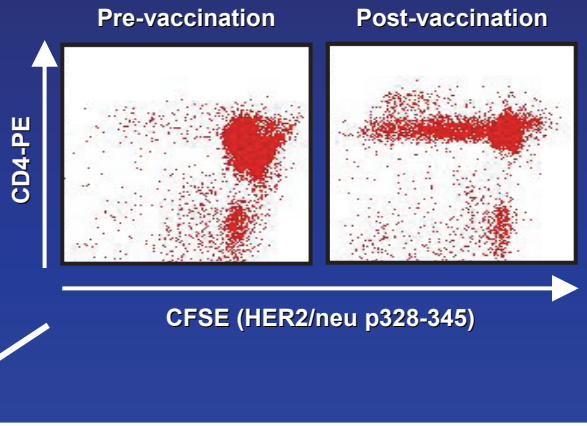




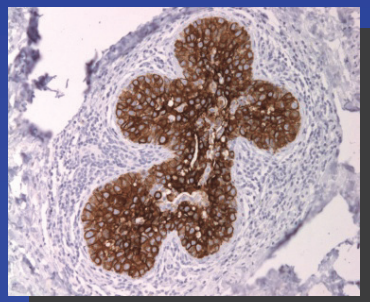
ADAPTIVE

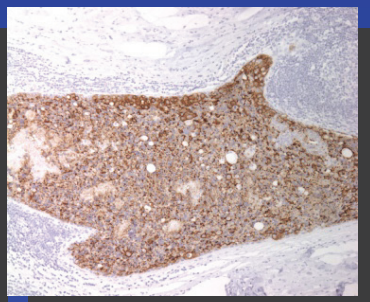




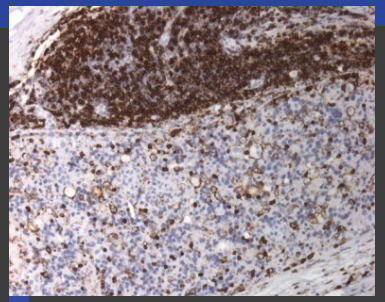


DCIS



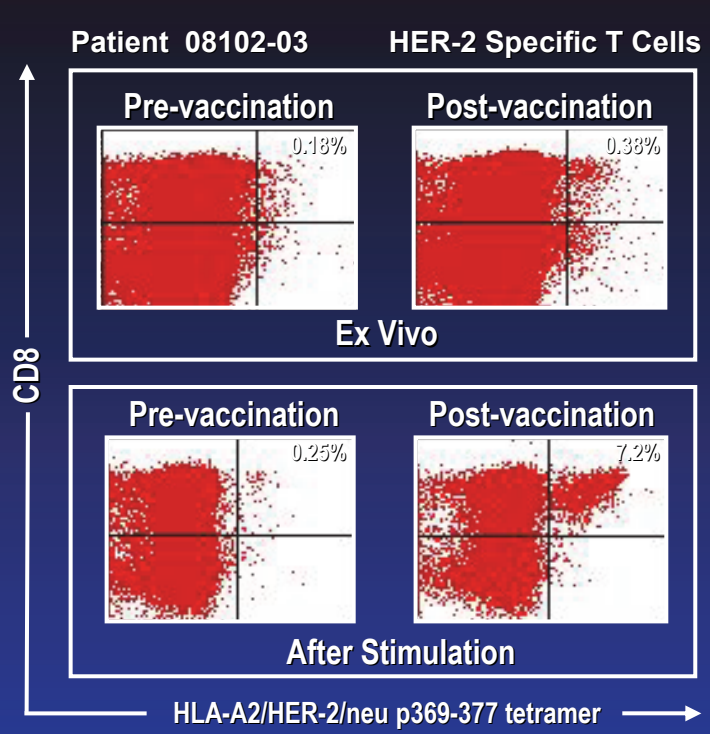


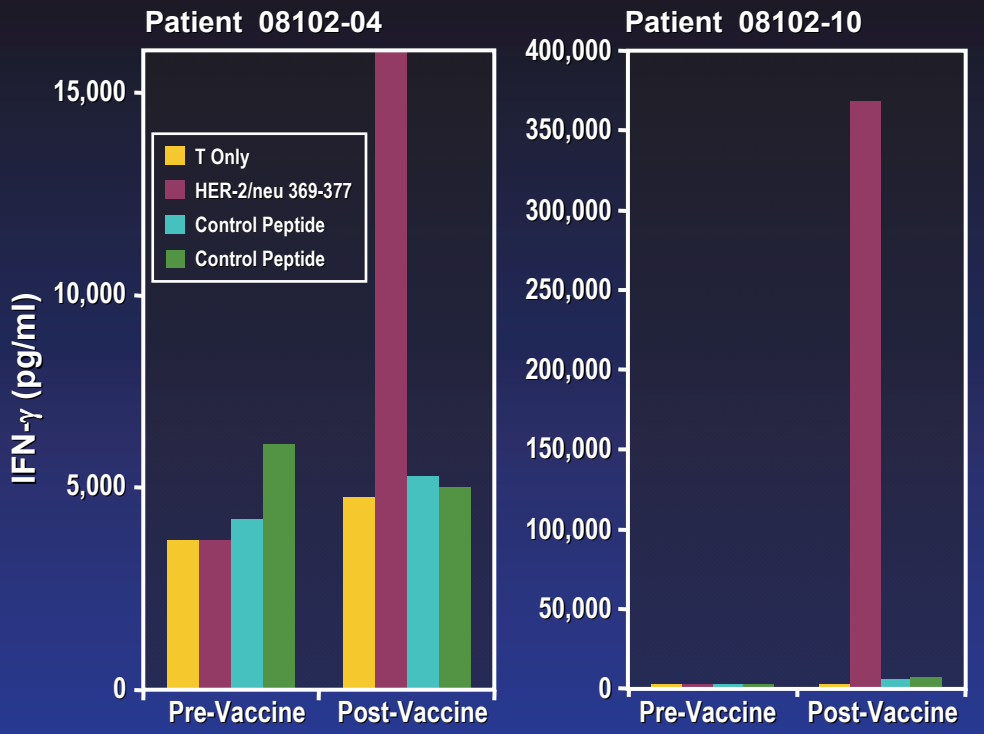
Post-Vaccine HER-2/neu



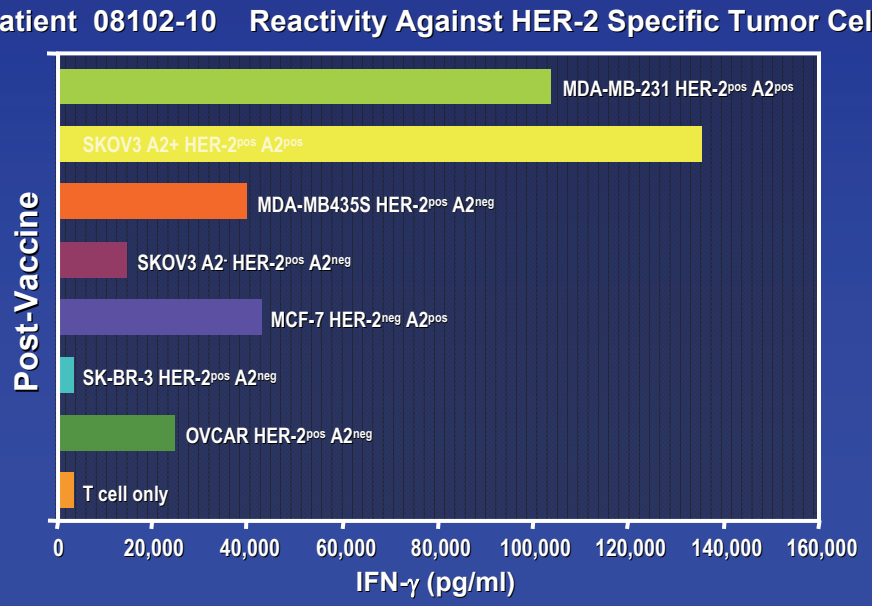
Safety of DC1 Vaccines

- Grade I, II - fevers, chills, headache, fatigue, injection site soreness
- Cardiac 5/57 patients Asymptomatic declines in MUGA 10-20% within normal range all resolved on repeat 30 days
- No long term sequela patients out range 6 months – 84 months

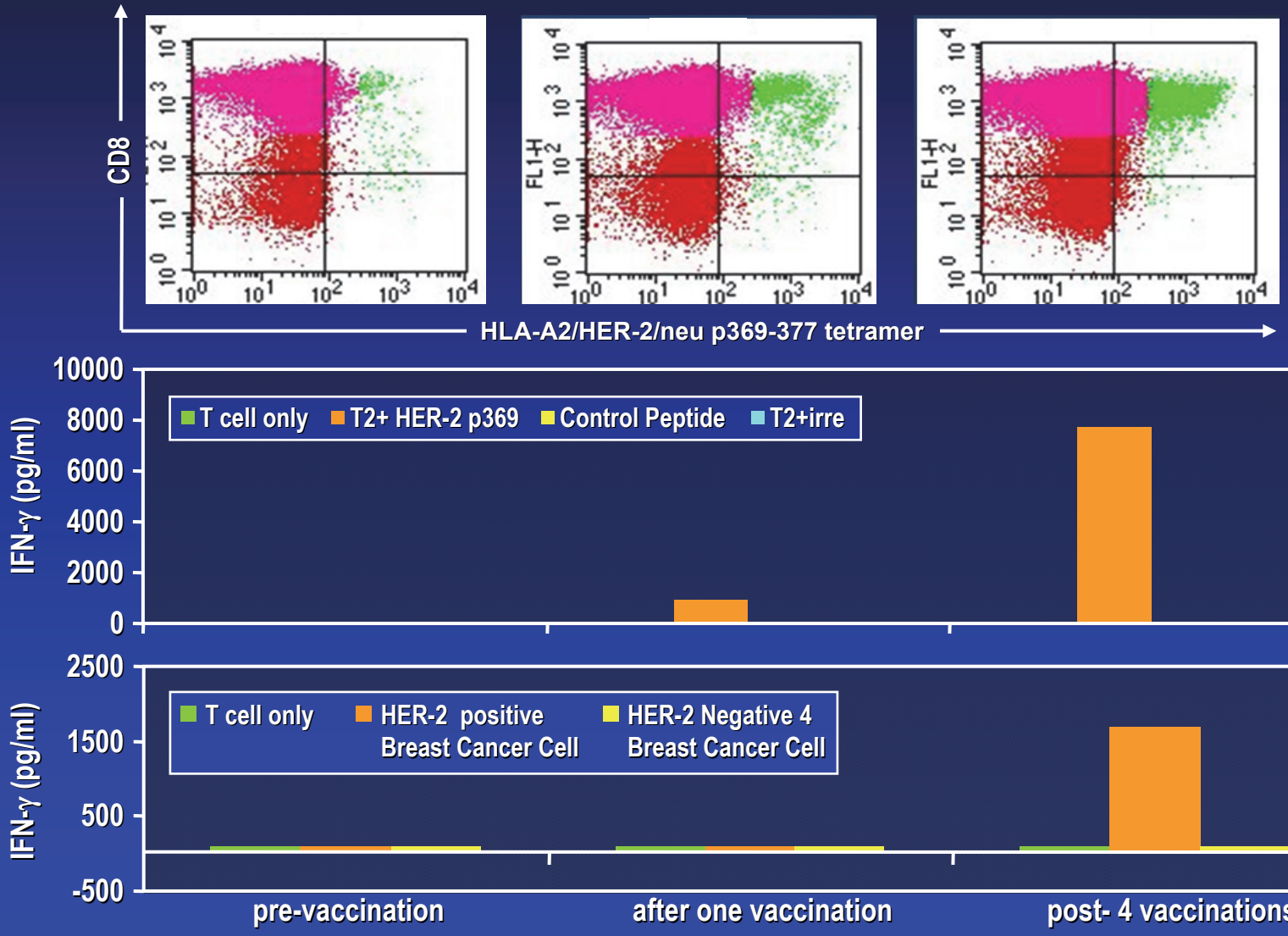




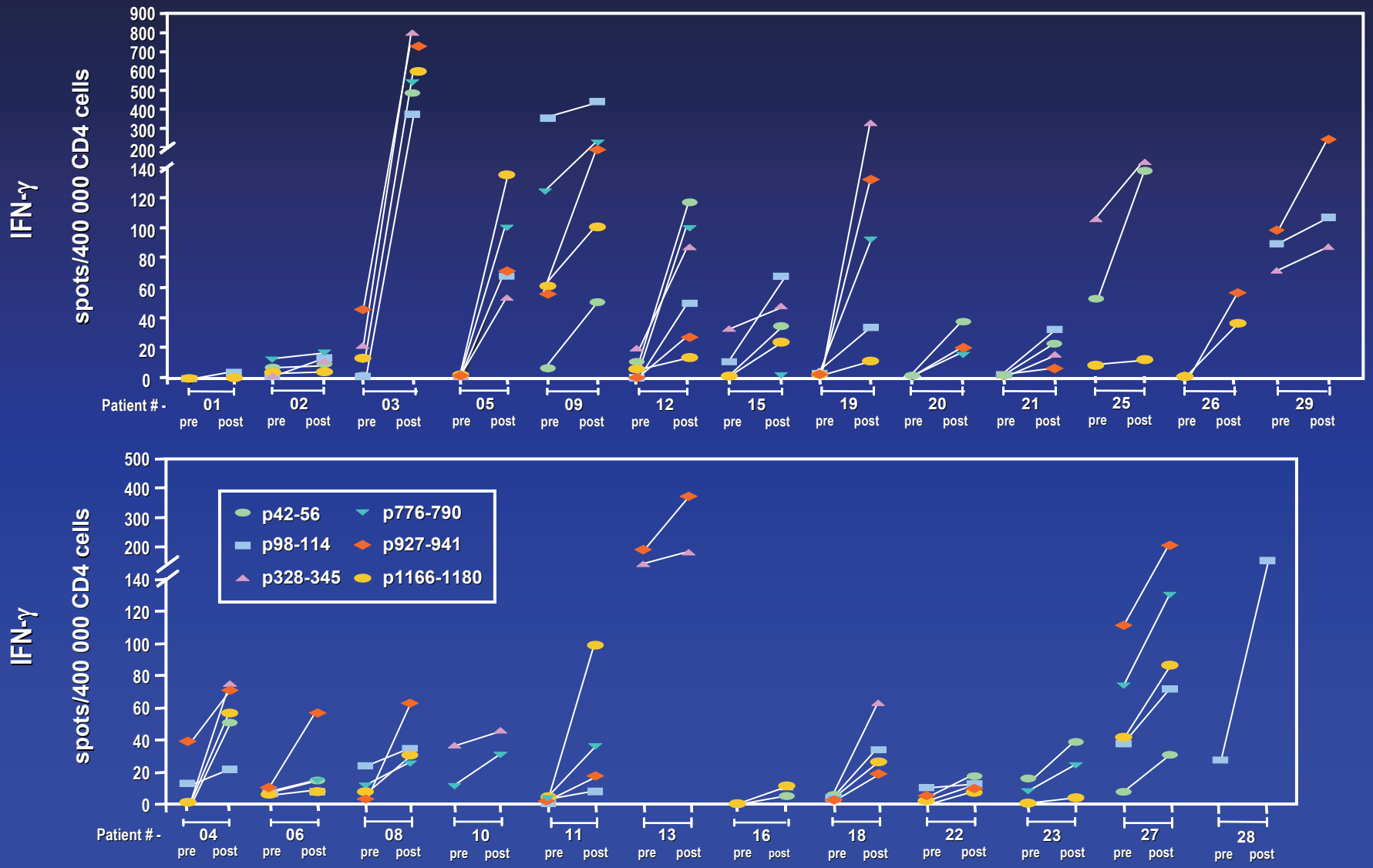
HER2/neu pulsed-ICAIT DC1 activate anti-HER2/neu CD8 T cells in DCIS patients



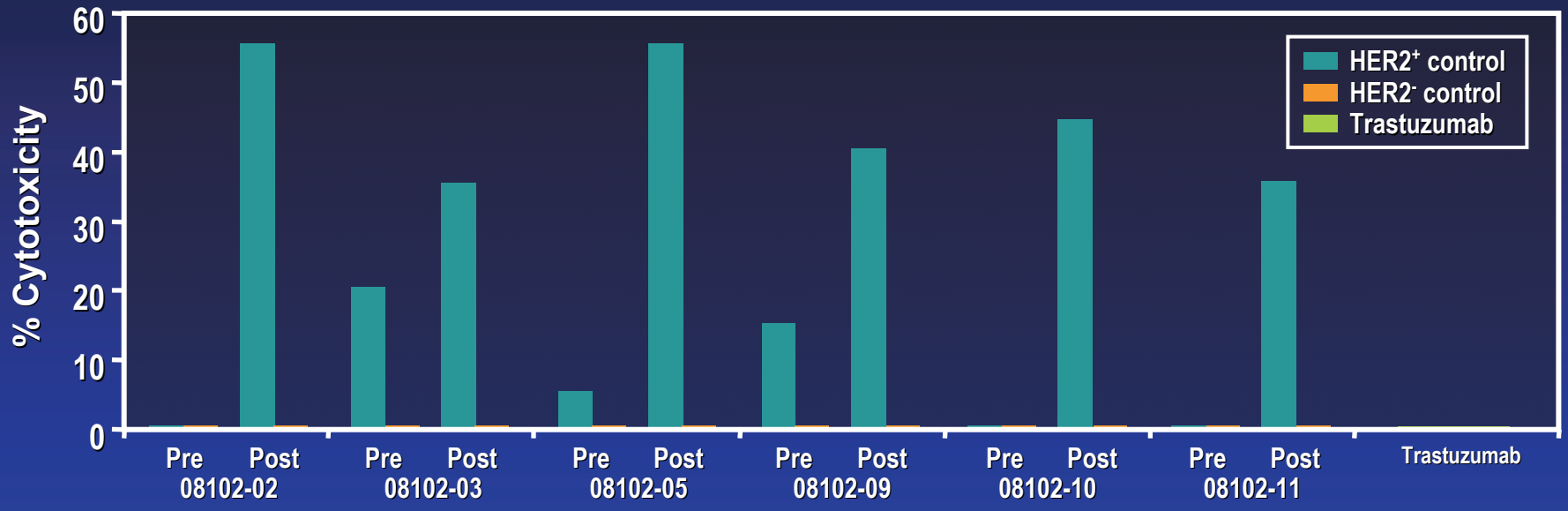
Optimal induction of anti-tumor effector CD8+ T Cell responses requires multiple vaccinations

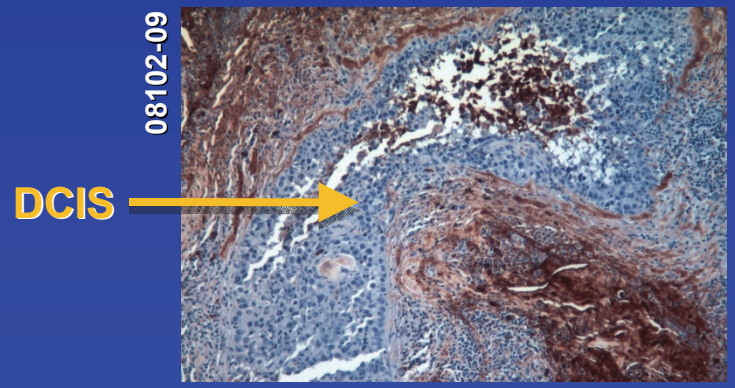


Induction of CD4 T cell anti-HER2 responses after ICAIT DC1 vaccination in DCIS patients

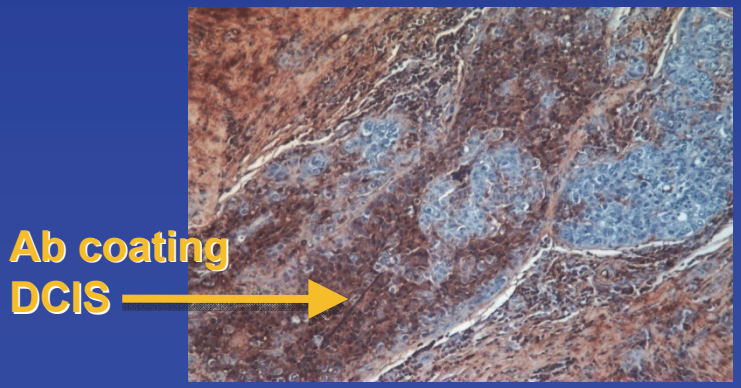


Induction of Complement fixing anti-HER2/neu ABs post-vaccine:
Direct antibody-mediated tumor cell killing





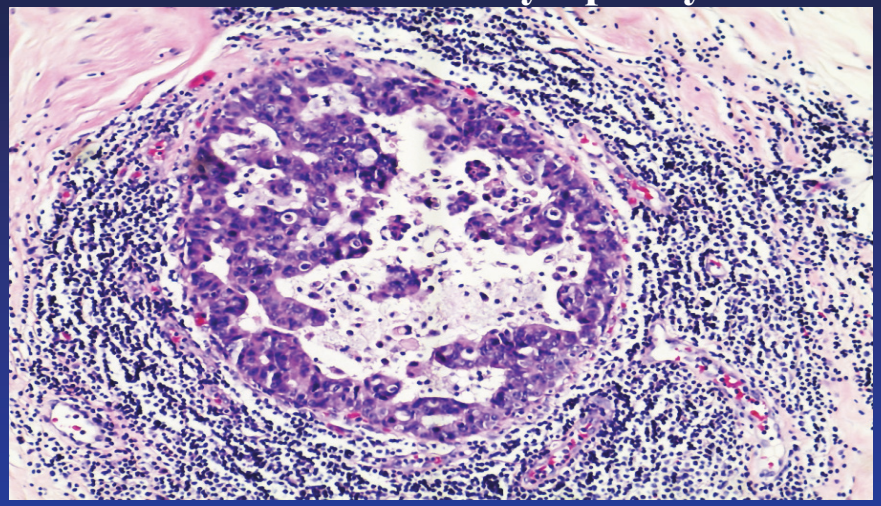
Pre-Vaccine



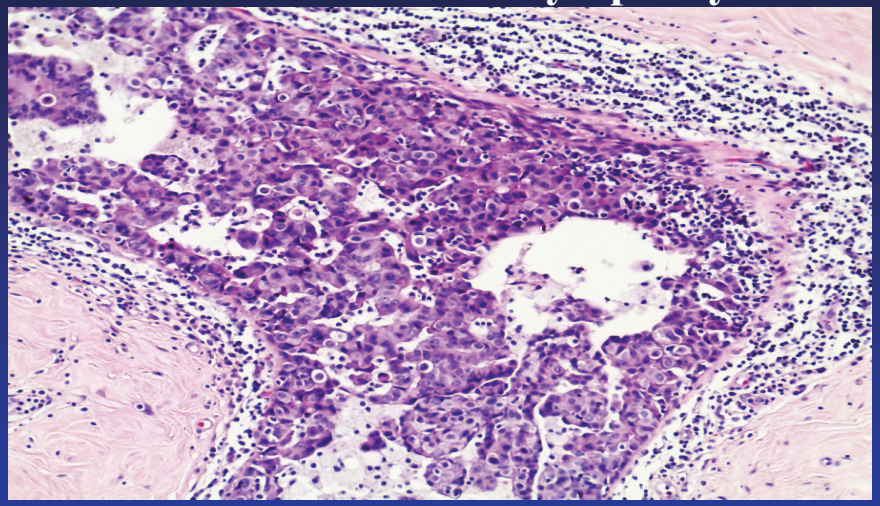
Post-Vaccine

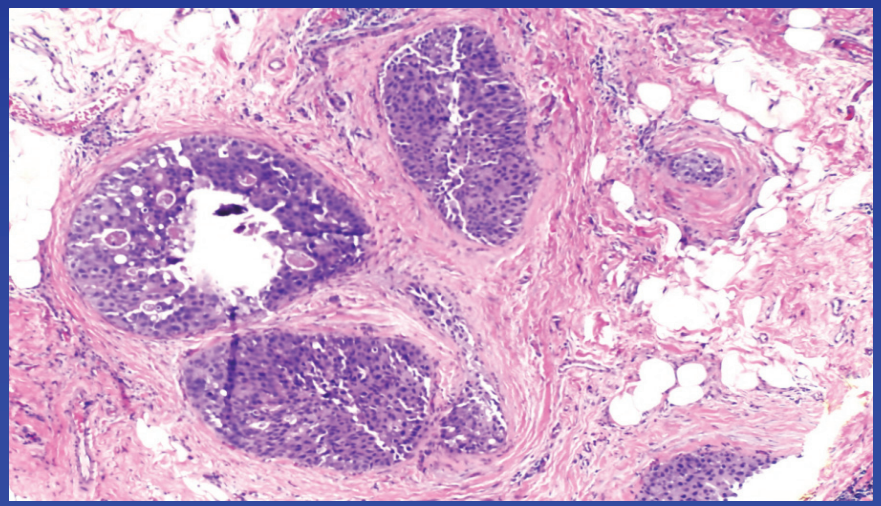
Immune Response in the DCIS to DC1 Vaccination

Post-Vaccine Lymphocytes

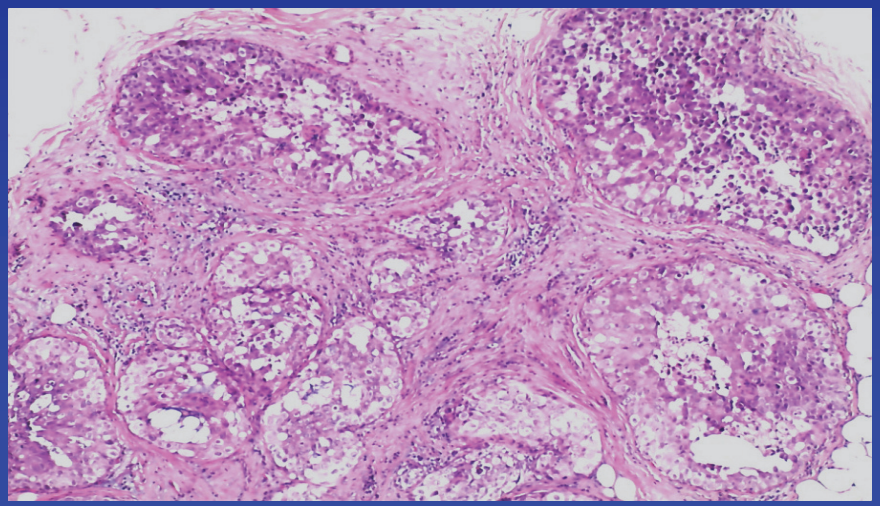


Post-Vaccine Lymphocytes



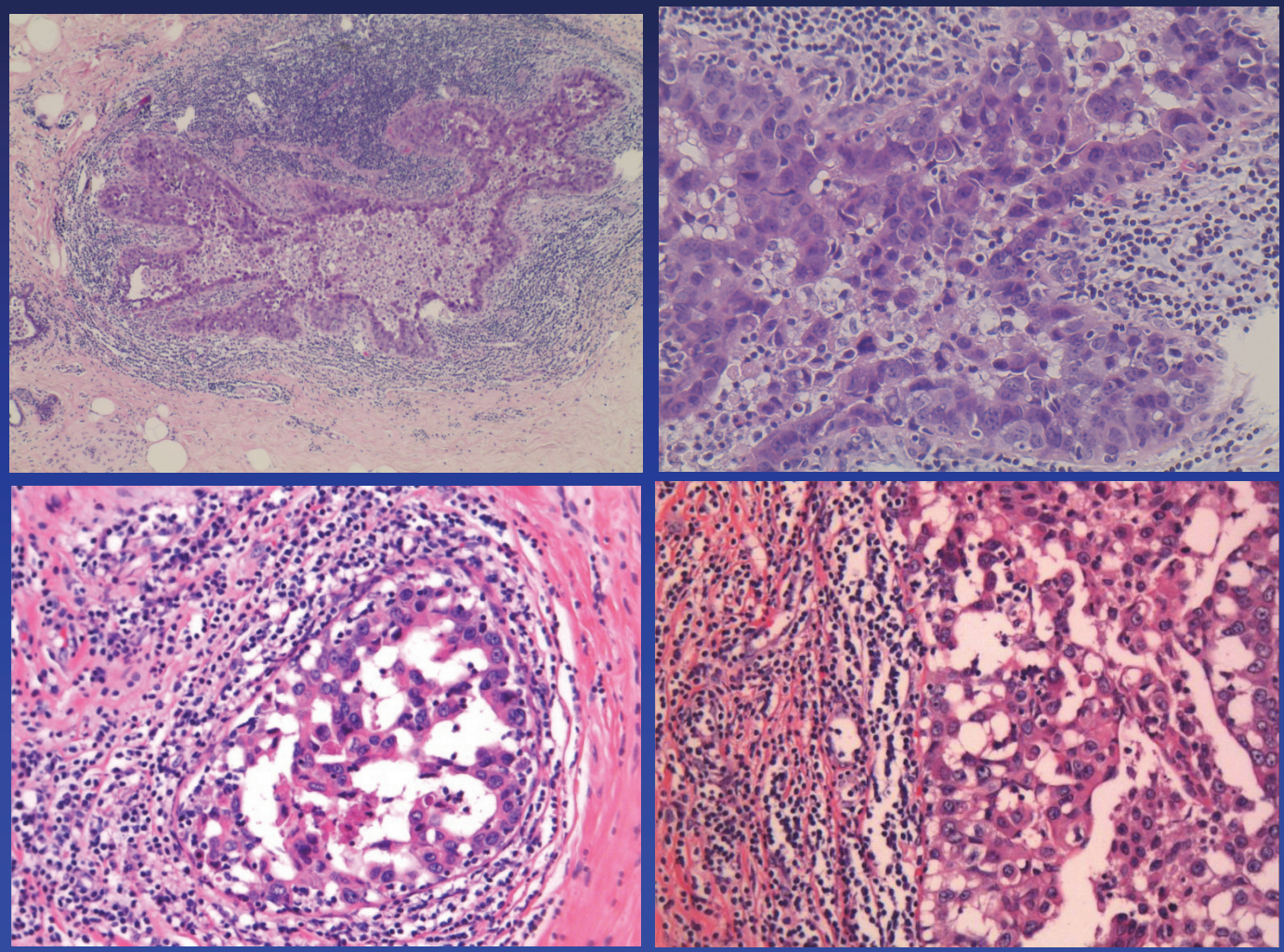


Pre-Vaccine

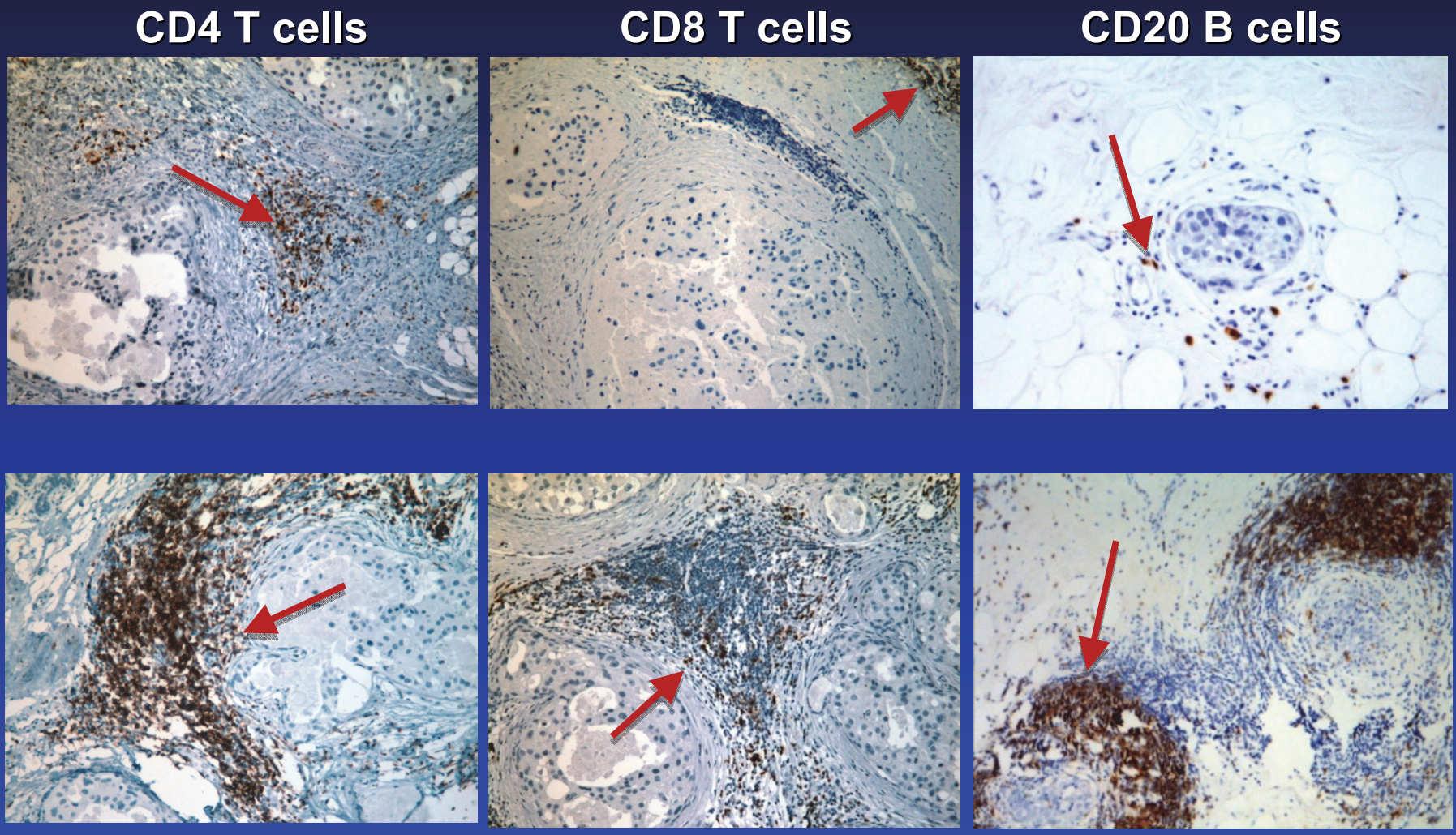


Post-Vaccine

Lymphocyte Infiltration Within Residual DCIS Ducts Following Vaccination



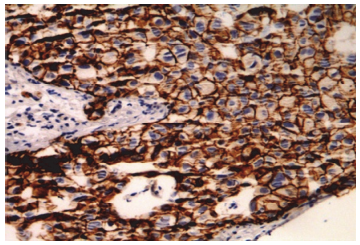
Trafficking of Lymphocytes into breast post-vaccination of DCIS patients



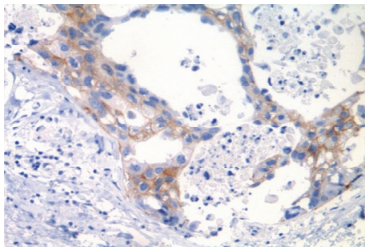
Response to Vaccines

A

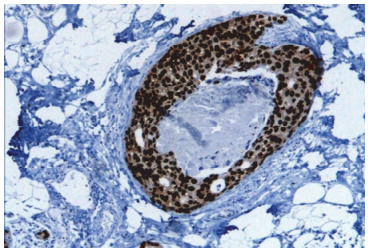
Pre Vaccine HER-2/neu



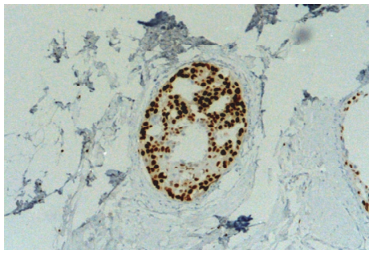
Post Vaccine HER-2/neu



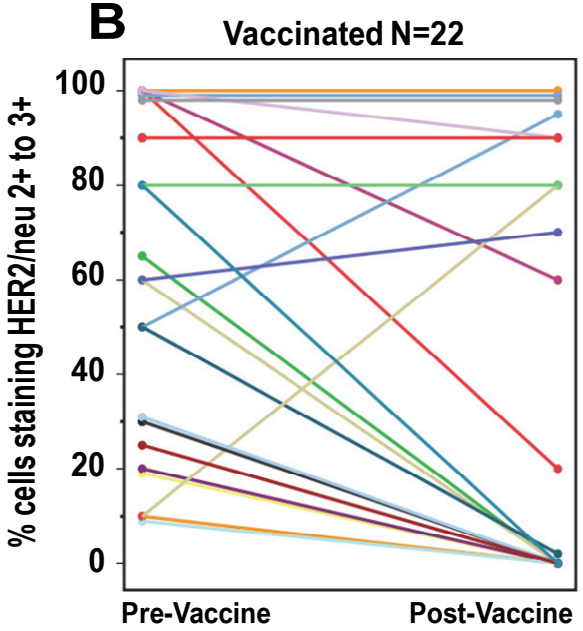
Pre Vaccine ER



Post Vaccine ER



B



C

Percent of cells staining HER-2/neu 2+ to 3+ Pre- and Post-vaccination
Patients sorted by Phenotype and Pre-vaccination HER-2/neu expression

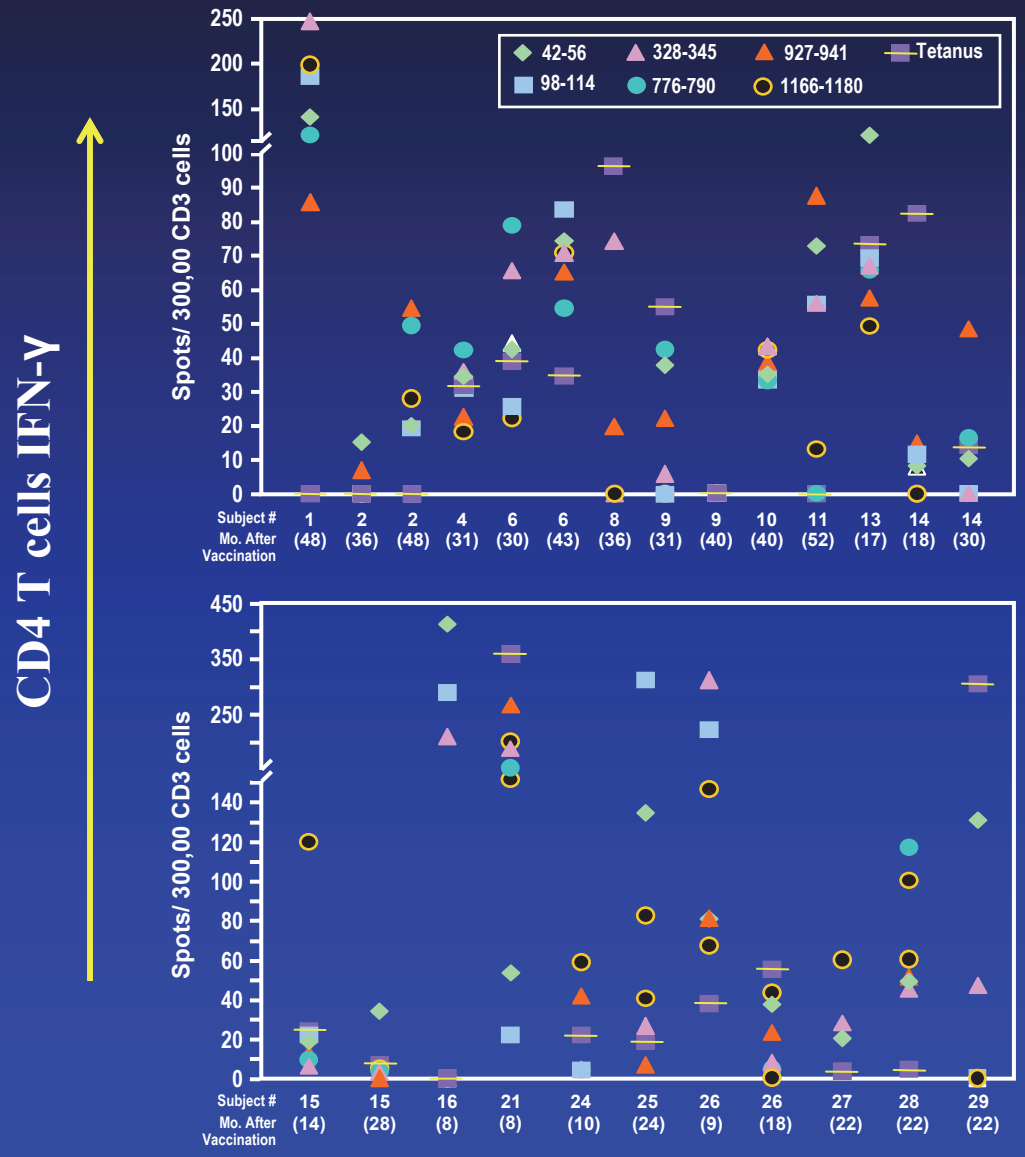
ER^{pos} $HER\text{-}2/neu^{pos}$					
% Pre-vaccine	% Post-vaccine	Percent Change	% Pre-vaccine	% Post-vaccine	Percent Change
10	0	-100%*	65	0	-100%*
20	0	-100%*	80	0	-100%*
20	0	-100%*	80	80	0%
25	0	-100%*	90	90	0%
30	0	-100%*	100	90	-10%
50	2	-96%*	100	>90	0%
50	95	+90%	100	100	0%
60	70	+17%	100	100	0%

ER^{neg} $HER\text{-}2/neu^{pos}$		
% Pre-vaccine	% Post-vaccine	Percent Change
10	0	-100%*
10	80	+700%
30	0	-100%*
60	0	-100%*
100	20	-80%
100	60	-40%

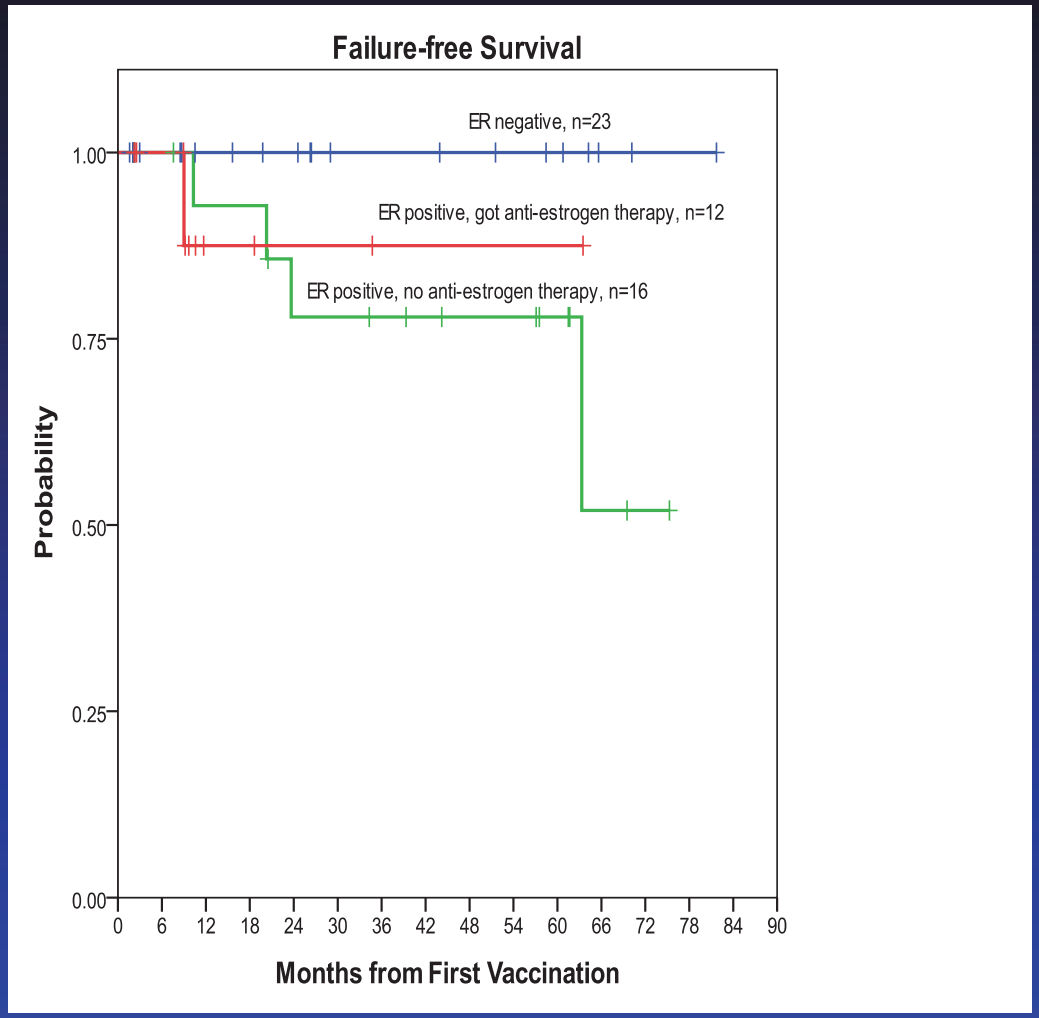
*patient scored as $HER\text{-}2/neu^{neg}$

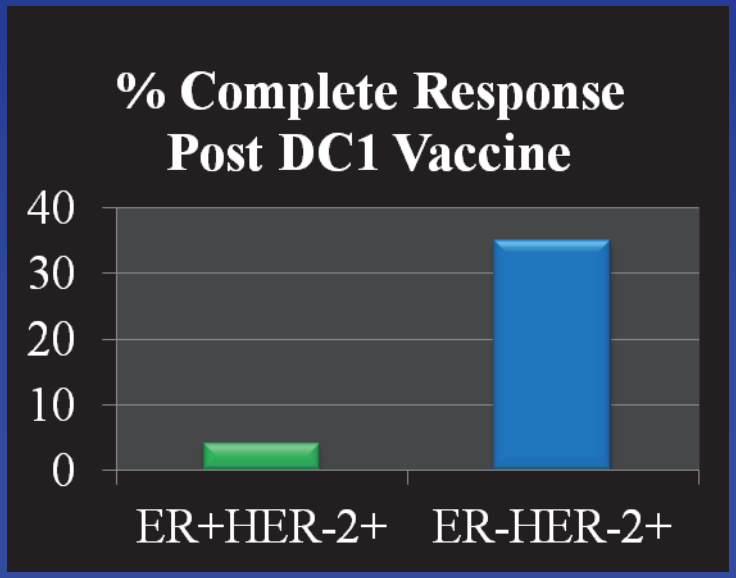
Induction of long-term anti-tumor immunity

Robust anti-HER2 responses more than 4 yrs post vaccination

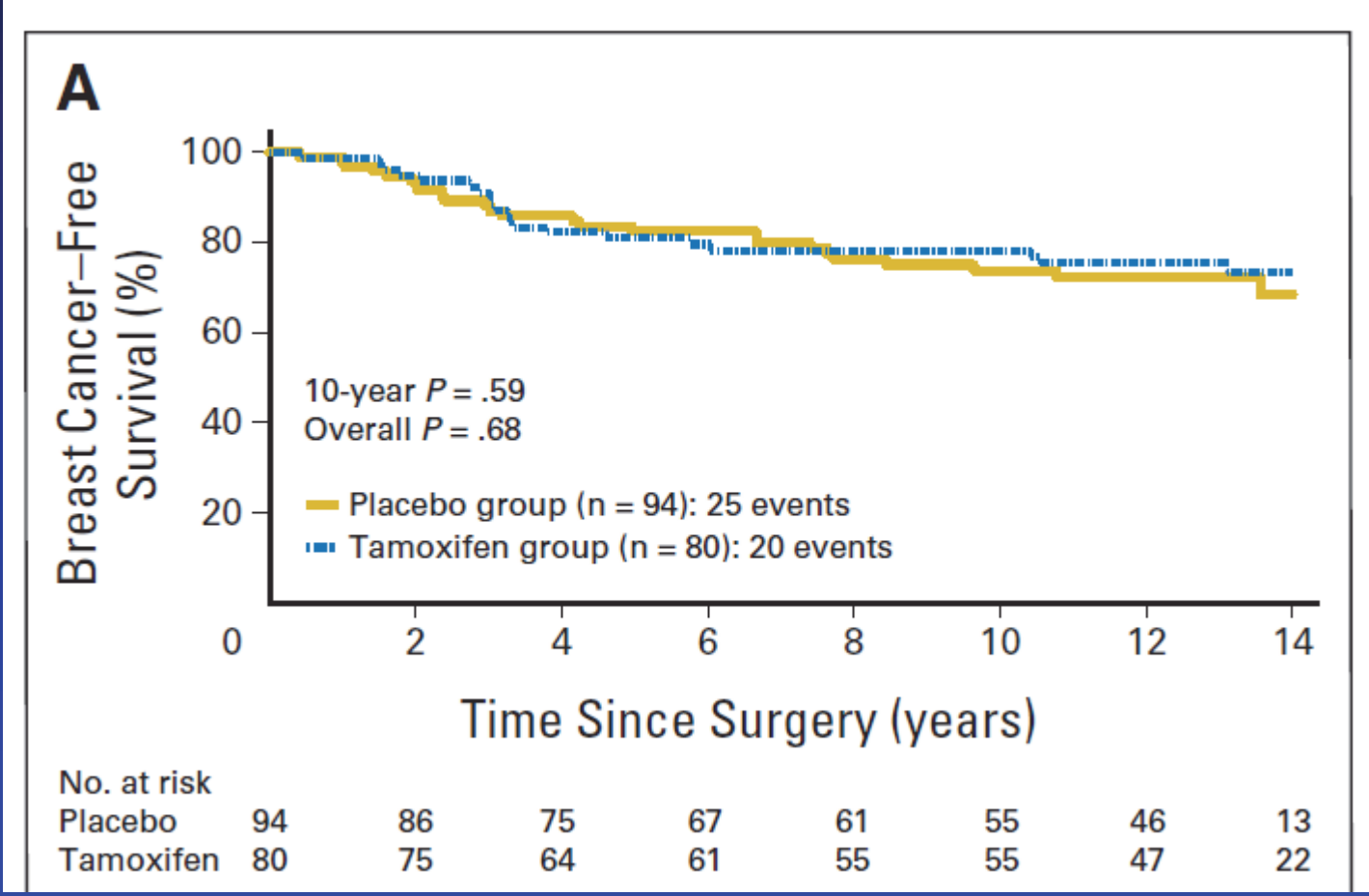


Comparison of Absence of Disease Post DC1 Vaccine with Disease Free Recurrence

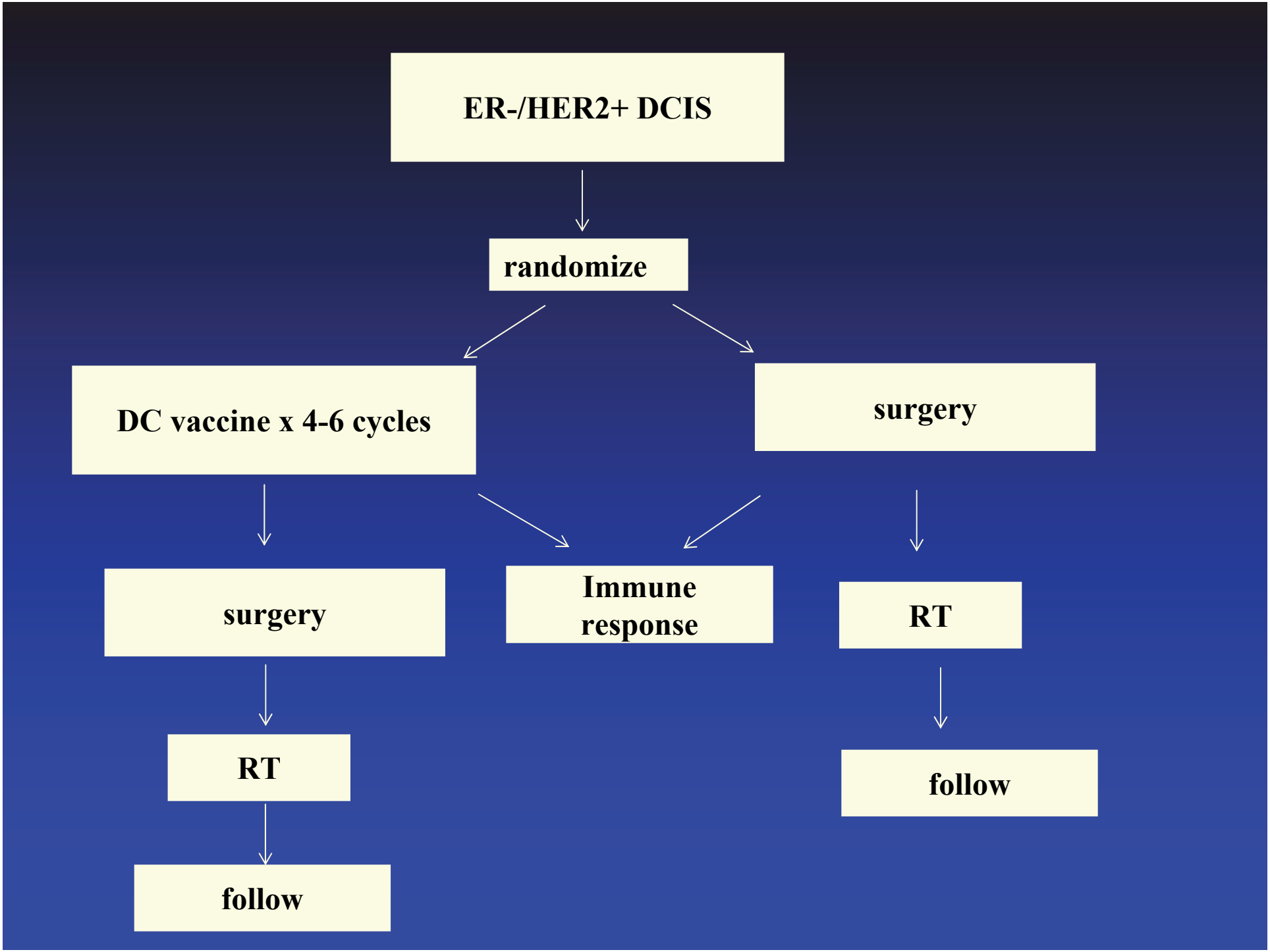




NSABP-B24: Outcomes of women with ER- DCIS



Allred, JCO, 2012


ER-/HER2+ DCIS
randomize
DC vaccine x 4-6 cycles
surgery
surgery
Immune response
RT
RT
follow
follow

Summary

- ICAIT DC1 Vaccines Induce Long Lasting Th1 CD4 and CD8 T cell responses
- They Induce Lymphocyte Migration into DCIS Ducts
- Induce Elimination of HER-2 Expressing DCIS
- Can Prevent Recurrence Of HER-2 Phenotype
- Suggest Vaccination Against Breast Cancer can be Effective if Targets are Right
- Caution that Multiple targets will be needed in true primary breast cancer prevention

Acknowledgements

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  - Shuwen Xu
  - Ursula Koldovsky
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  - Gary Koski
- NIH
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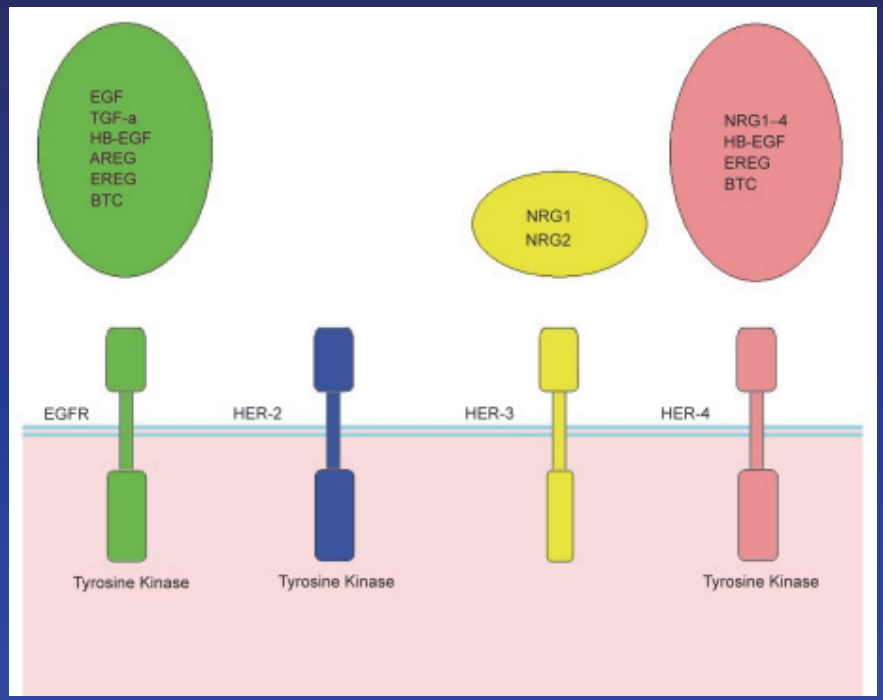
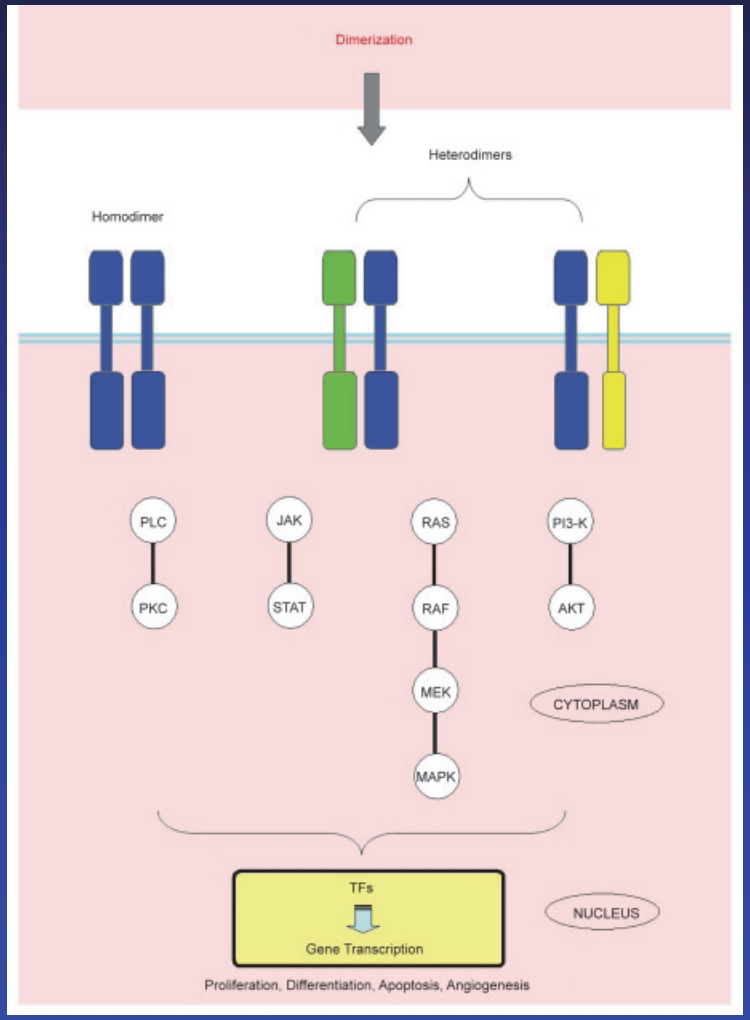
- Mayo Clinic
  - Peter A Cohen

HER Family





Koutras et al. Onco Targets and Therapy 2008; 1: 5-19

HER Family Pre and Post-Vaccination