

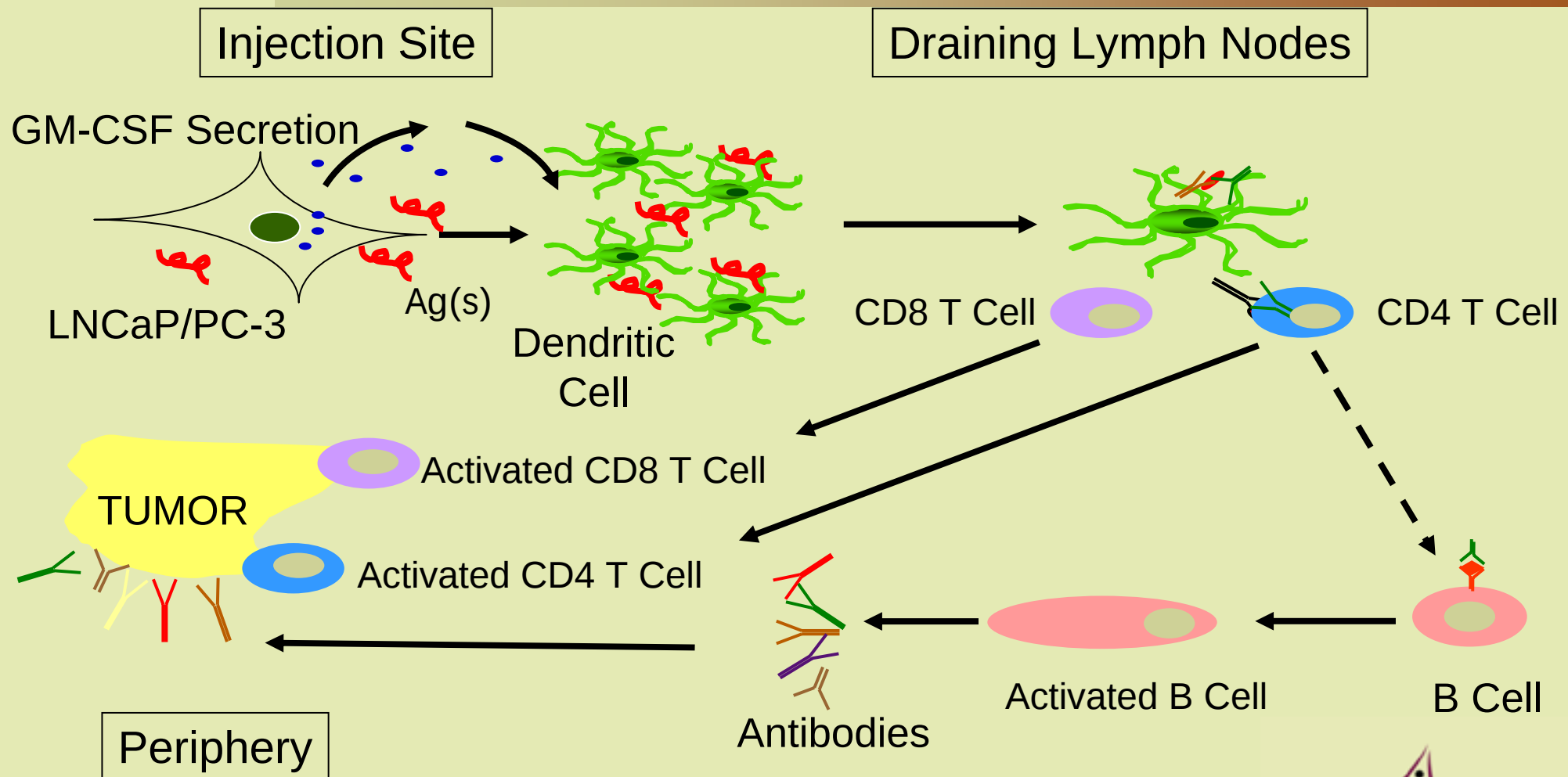
Anti-PD-1 antibody enhances the potency of GM-CSF-secreting tumor cell immunotherapy (mGVAX)

**Betty Li
iSBTC 2007**



CELL GENESYS

GVAX™ Platform: Proposed Mechanism of Action Based on Preclinical Models



PD-1: Facts

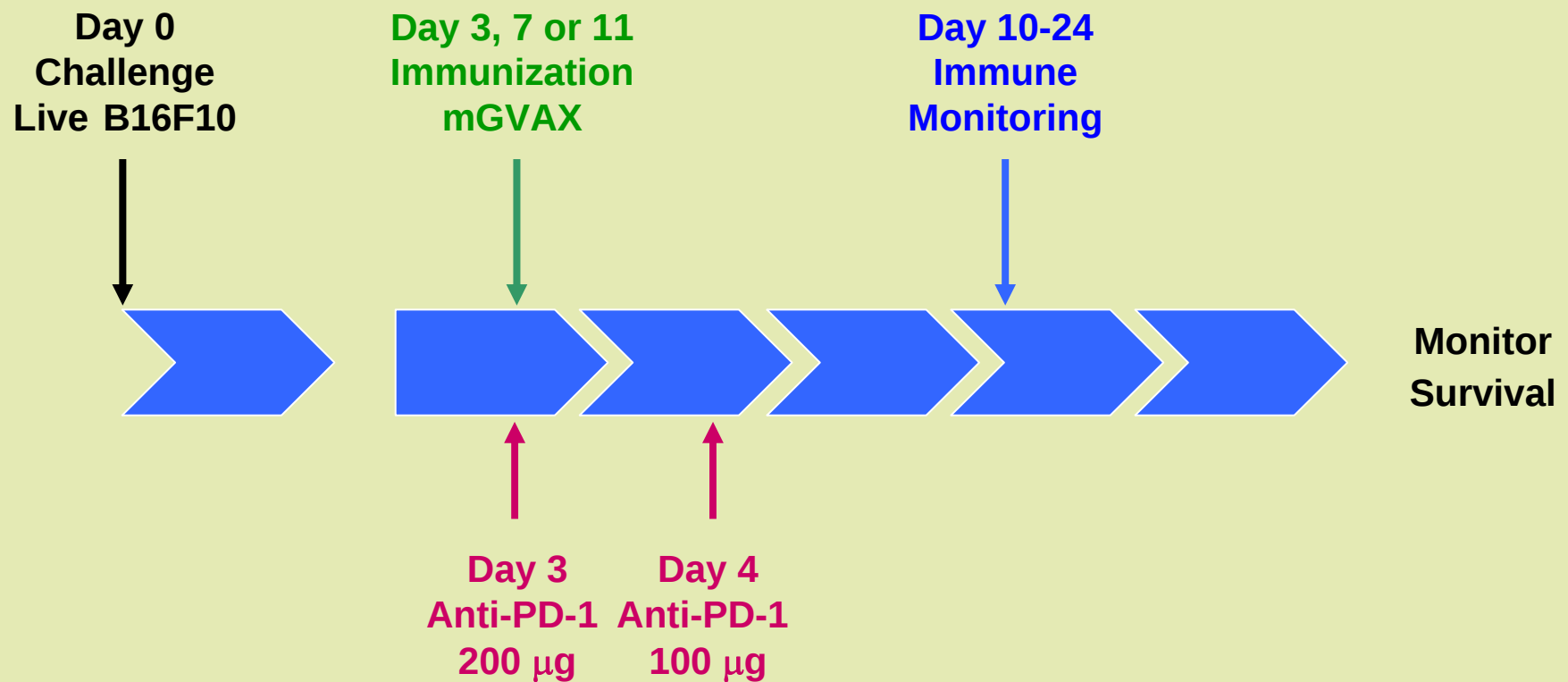
- ❖ Negative regulator of T cell activation that shares structural properties with members of the CD28 family
 - ❖ PD-1 blockade reverses T-cell exhaustion, restores cytokine production and augments the expansion of antigen specific T cells
- > Based on mechanism of PD-1 action, blockade of this pathway should potentially enhance the potency of cancer immunotherapies



Combination Therapy:

GM-CSF-secreting tumor cell Immunotherapy and anti-PD-1

Study Schematics

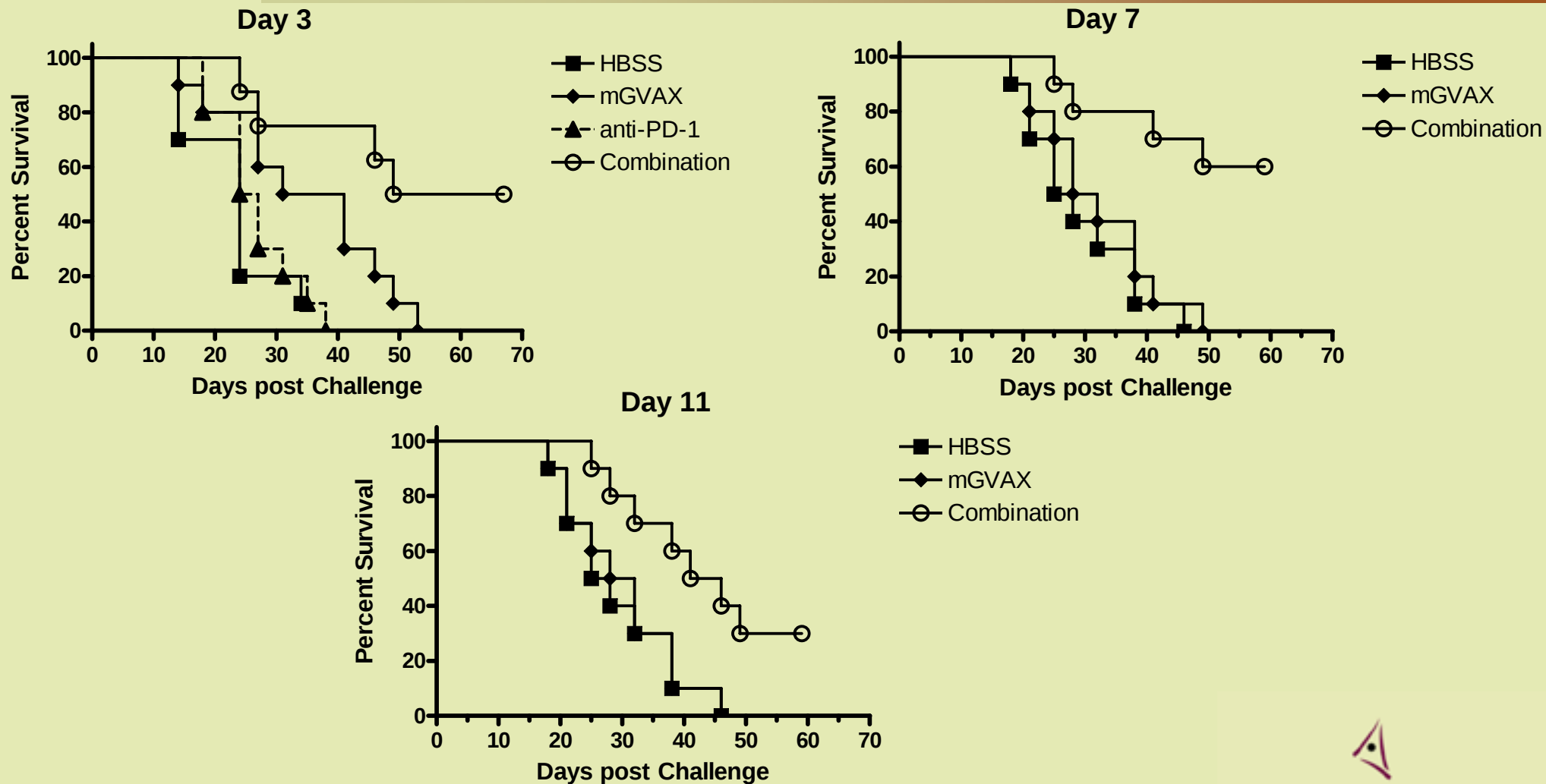


*Chimeric anti-mouse PD-1 antibody provided by Medarex



Anti-PD-1 prolongs survival of mGVAX treated animals

Survival (B16F10 model)

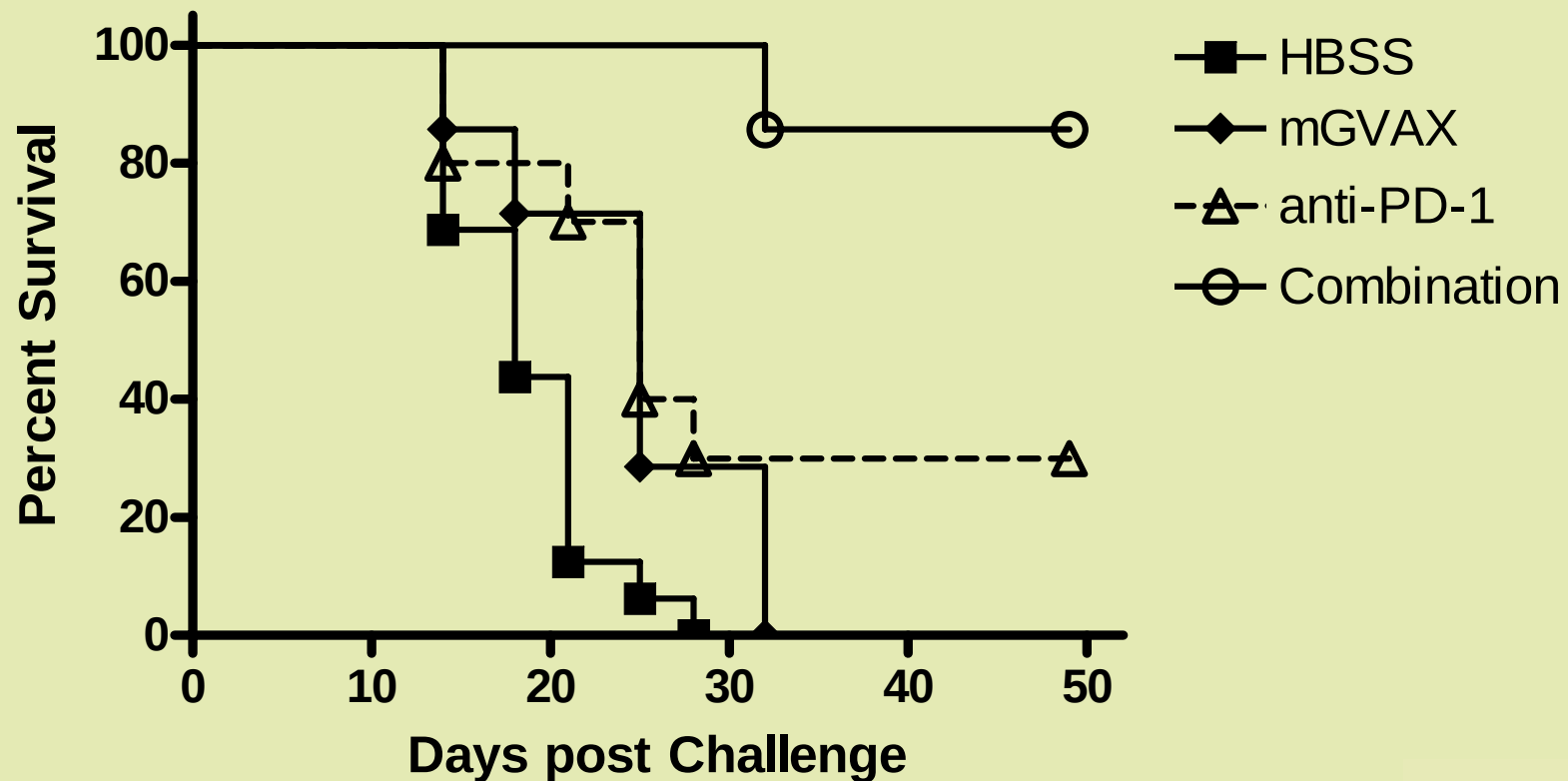


CELL GENESYS

***Anti-PD-1 monotherapy does not provide any therapeutic benefit in the non-immunogenic B16 model**

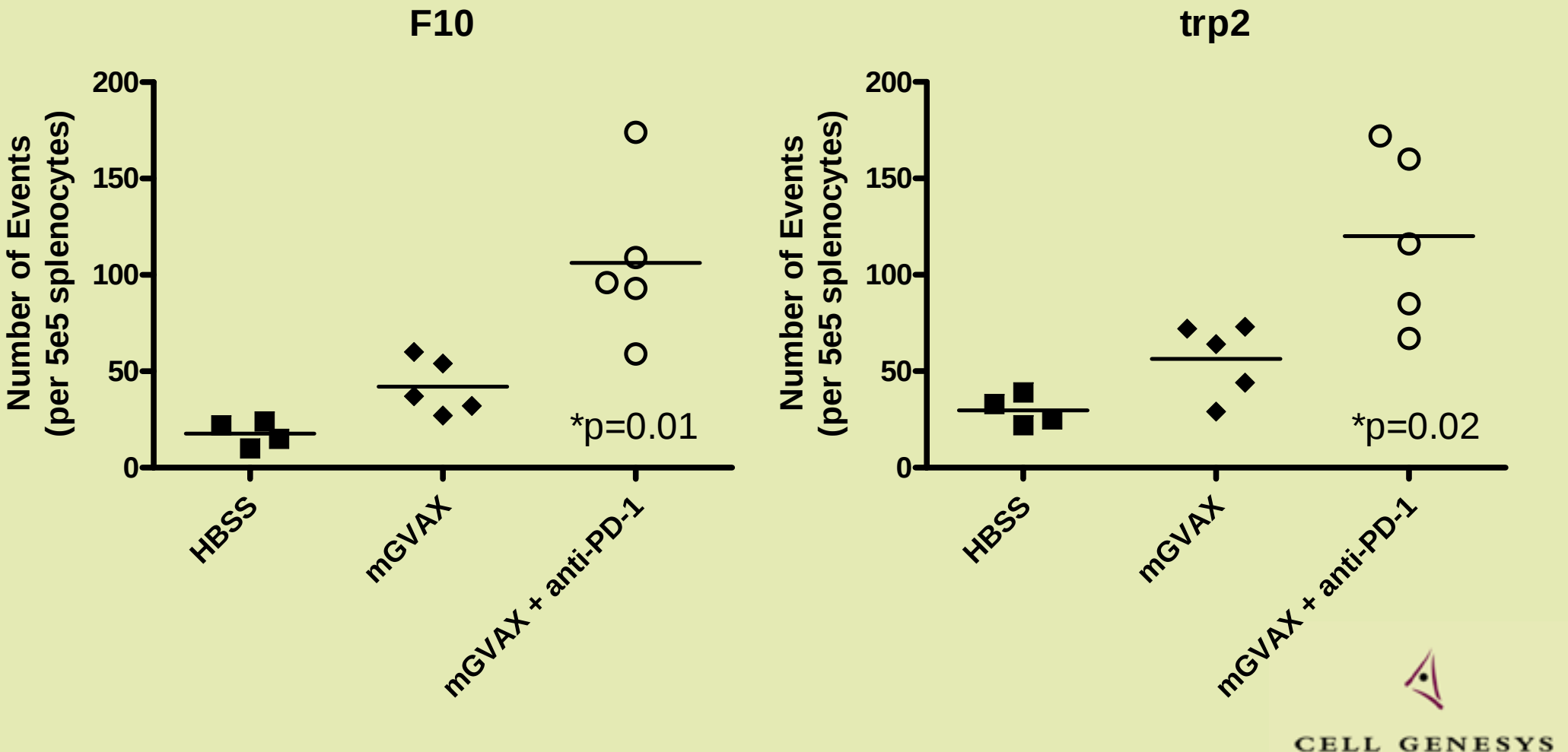
Anti-PD-1 prolongs survival of mGVAX treated animals

Survival (CT26 model): Day 3 treatment



Anti-PD-1 enhances mGVAX induced antigen-specific T- cell responses

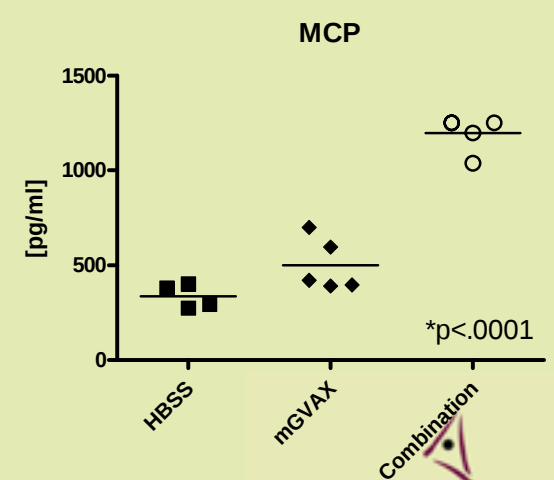
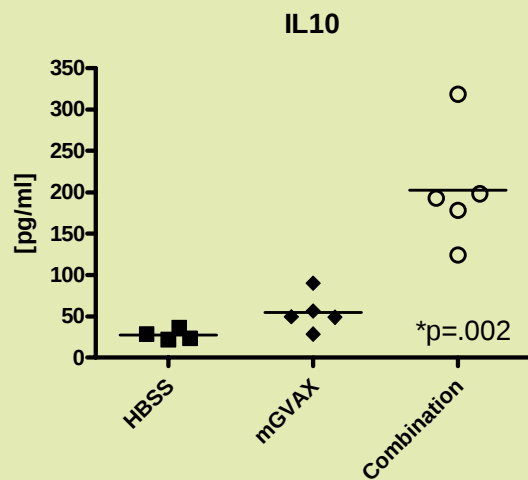
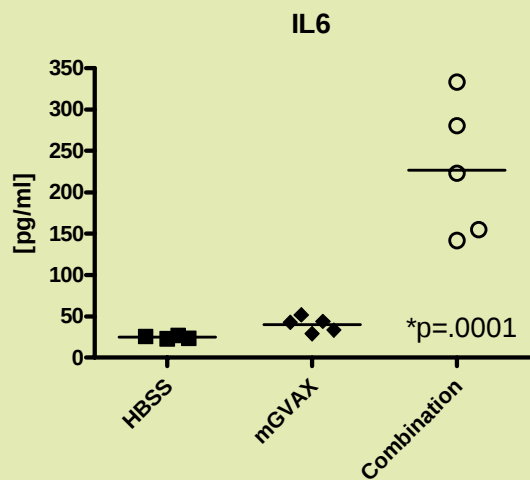
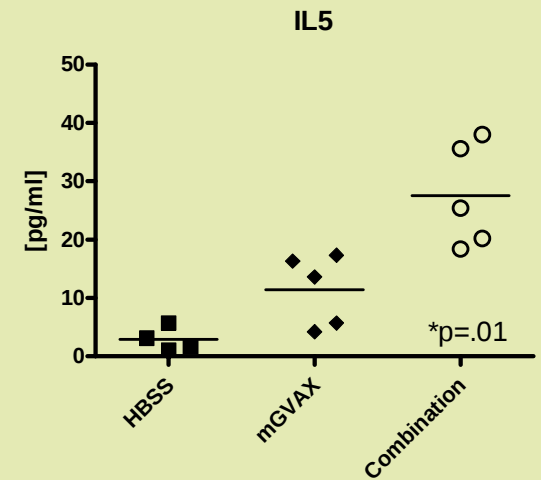
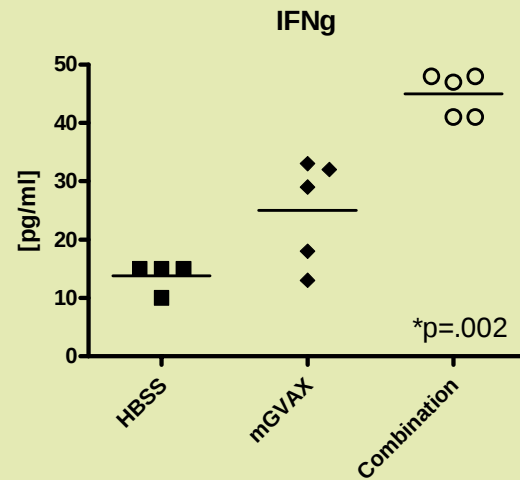
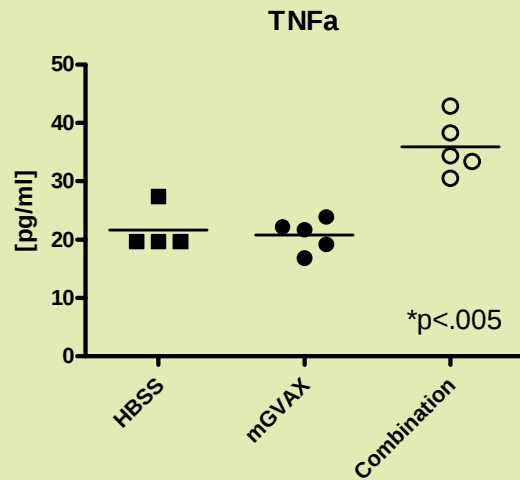
IFN γ ELISPOT (7 days post immunotherapy)



CELL GENESYS

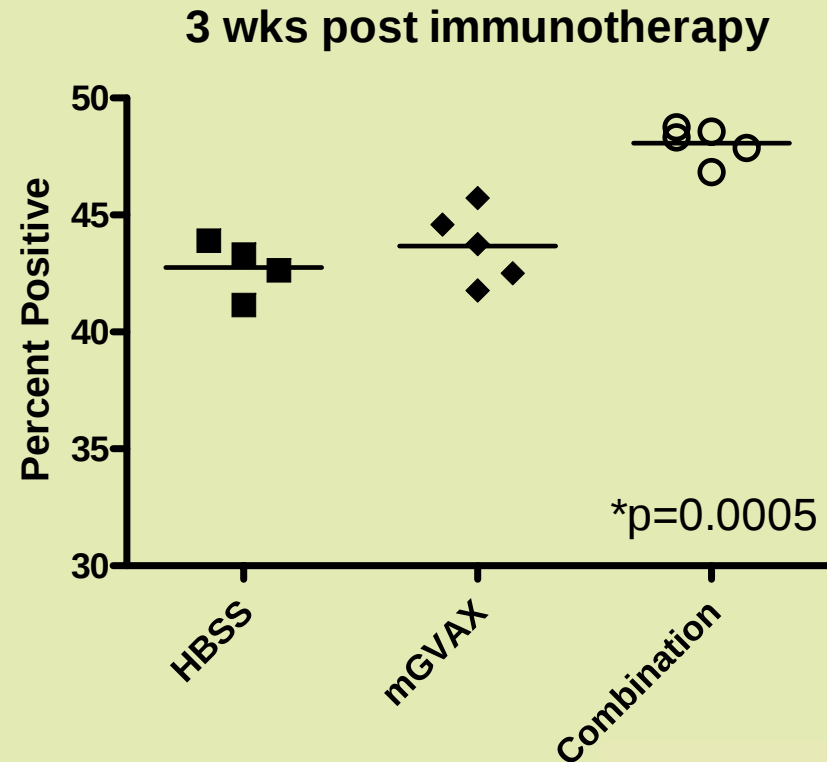
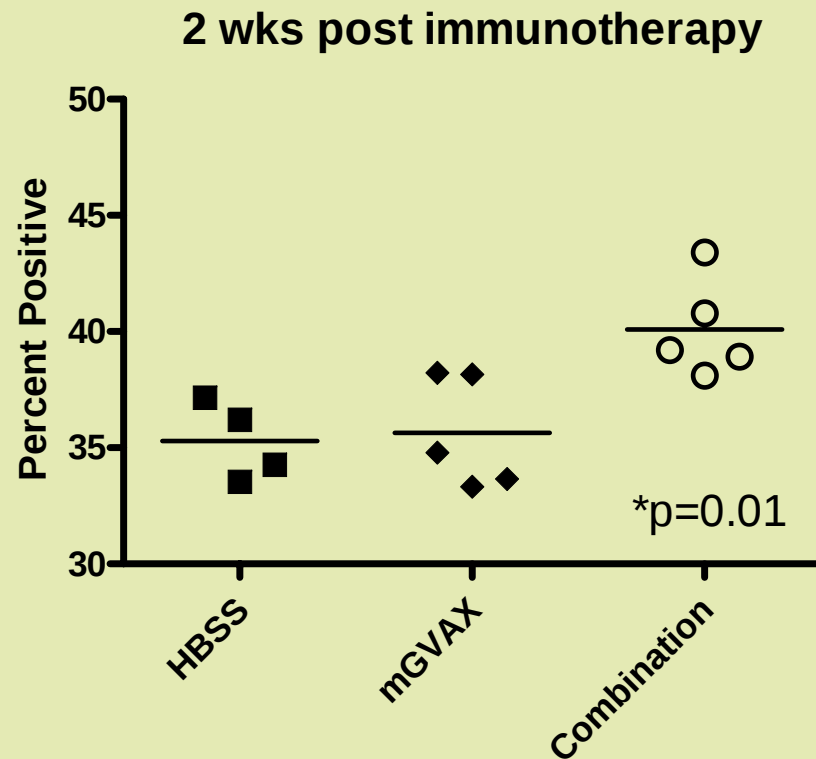
Anti-PD-1 enhances mGVAX immunotherapy induced cytokine production by splenocytes

Cytokine Analysis (7 days post immunotherapy)



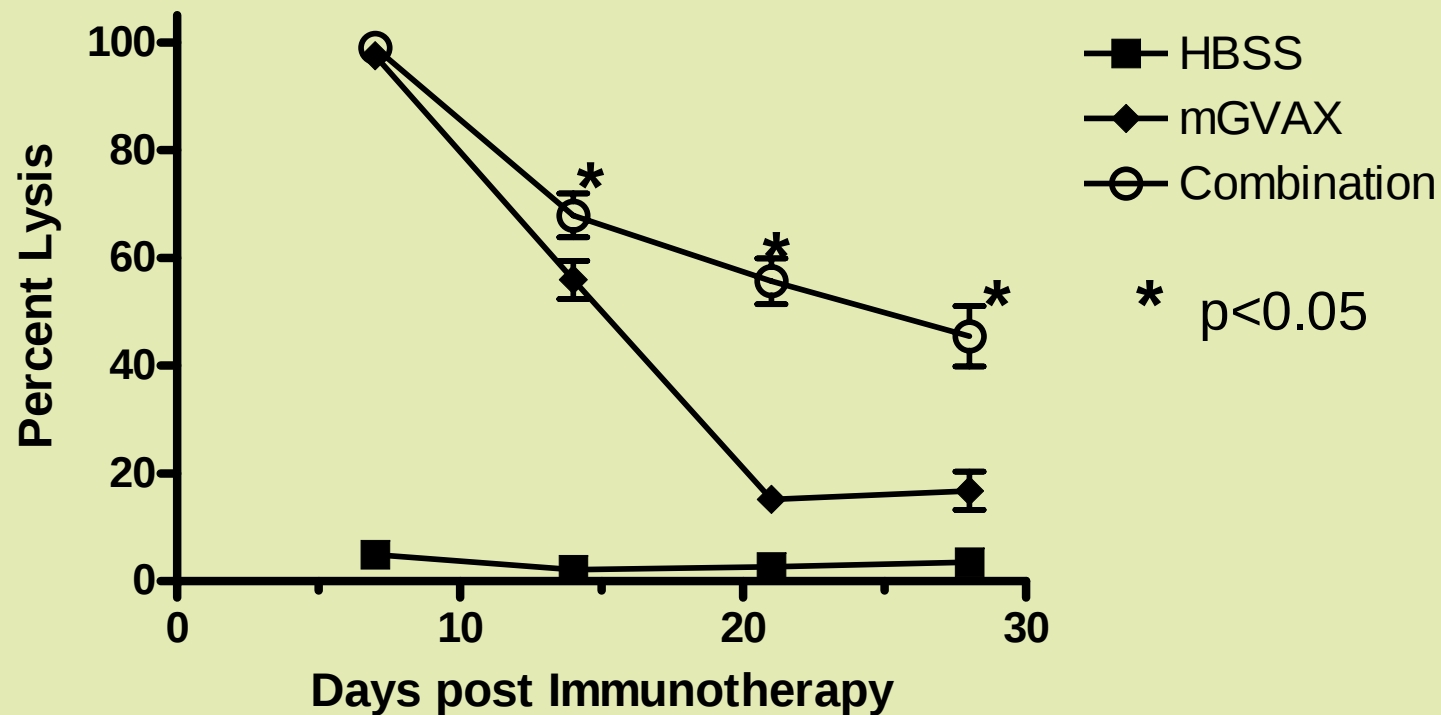
Anti-PD-1 increases the percentage of CD8 memory T-cells in mGVAX treated animals

Ly6C⁺/CD69⁻ (CD8 subpopulation)



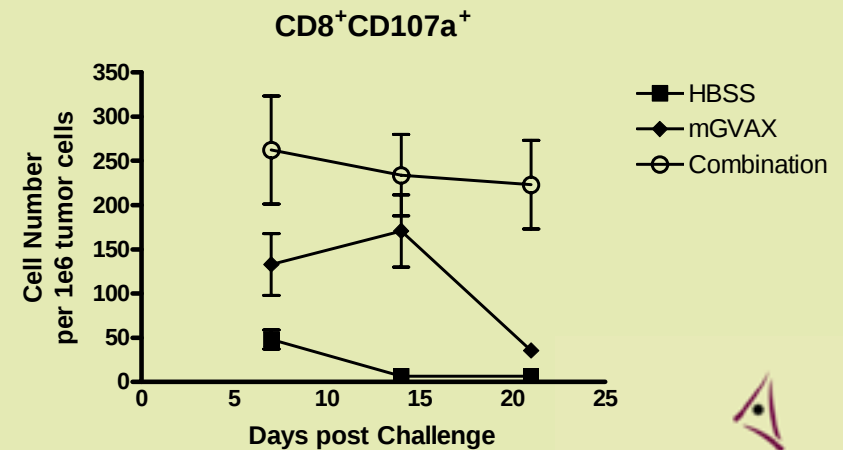
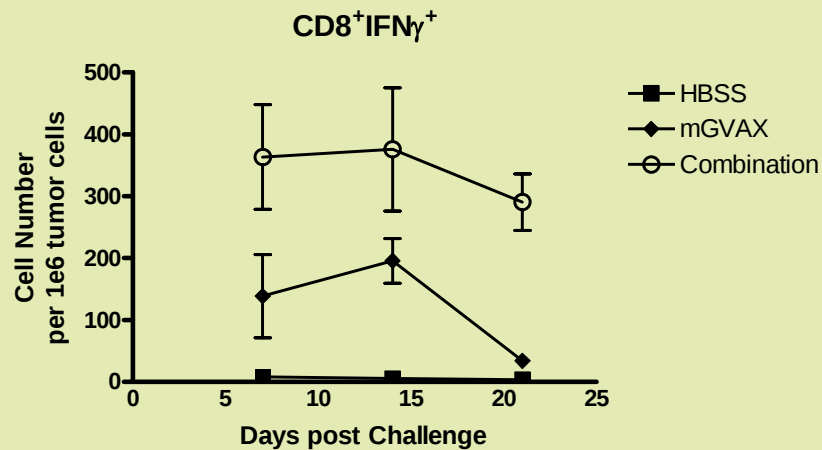
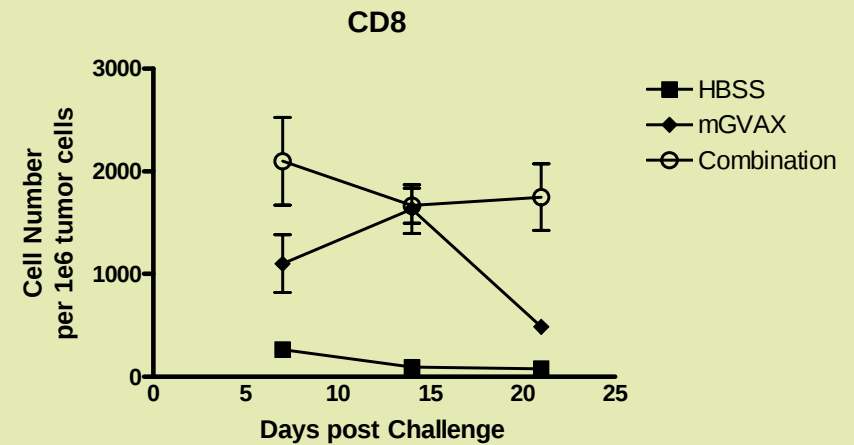
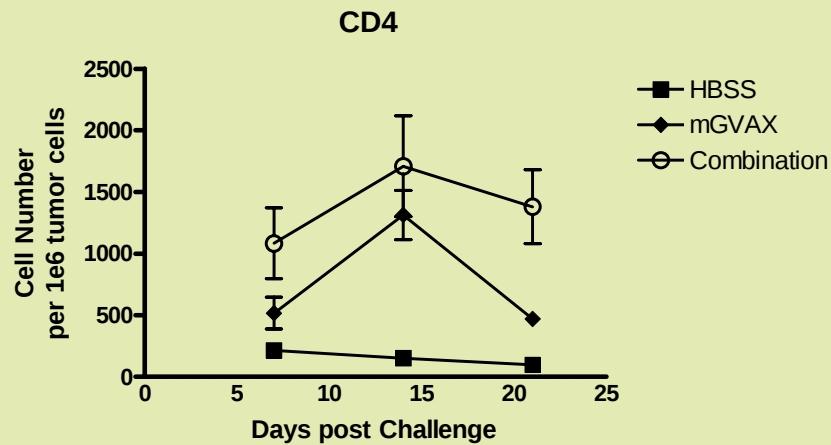
Anti-PD-1 enhances mGVAX induced, antigen-specific cytolytic T-cell responses

In vivo CTL (ovalbumin as surrogate antigen)



Anti-PD-1 enhances mGVAX induced, intratumoral CD8 T-cell infiltration

TIL kinetics



Summary

- ✳ mGVAX + anti-PD-1 combination therapy results in enhanced survival (B16F10 and CT26 tumor models)
- ✳ Anti-PD-1 therapy augments mGVAX mediated CD8⁺ T cell responses (cytolytic activity, pro-inflammatory cytokine secretion)
- ✳ Anti-PD-1 allows the persistent survival of mGVAX activated cytolytic T cells
- ✳ Anti-PD-1 increases the percentage of mGVAX induced memory T-cells within the CD8 subpopulation



Acknowledgements

Cell Genesys

Karin Jooss

Melinda VanRoey

Sheila Tanciongo

Bernadette Batiste

Jason Ho

Tammy Langer

Medarex

Alan Korman



CELL GENESYS