

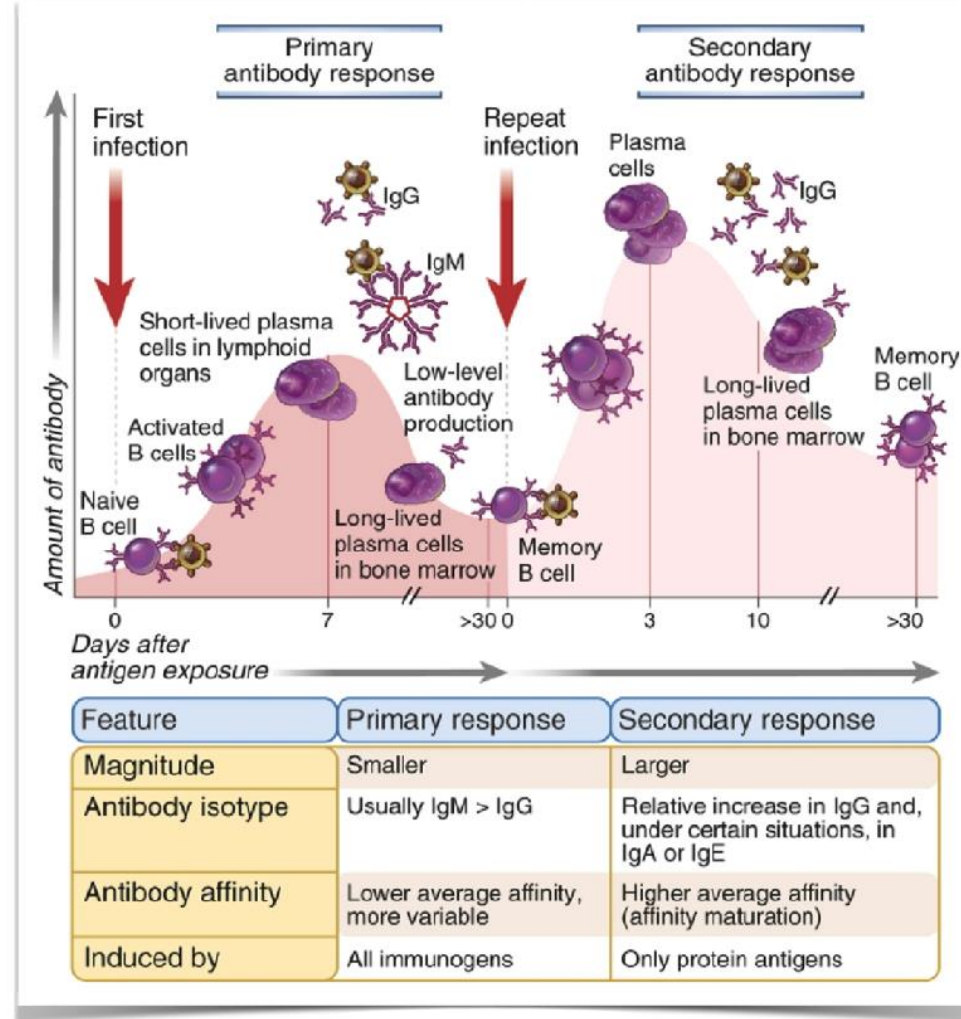
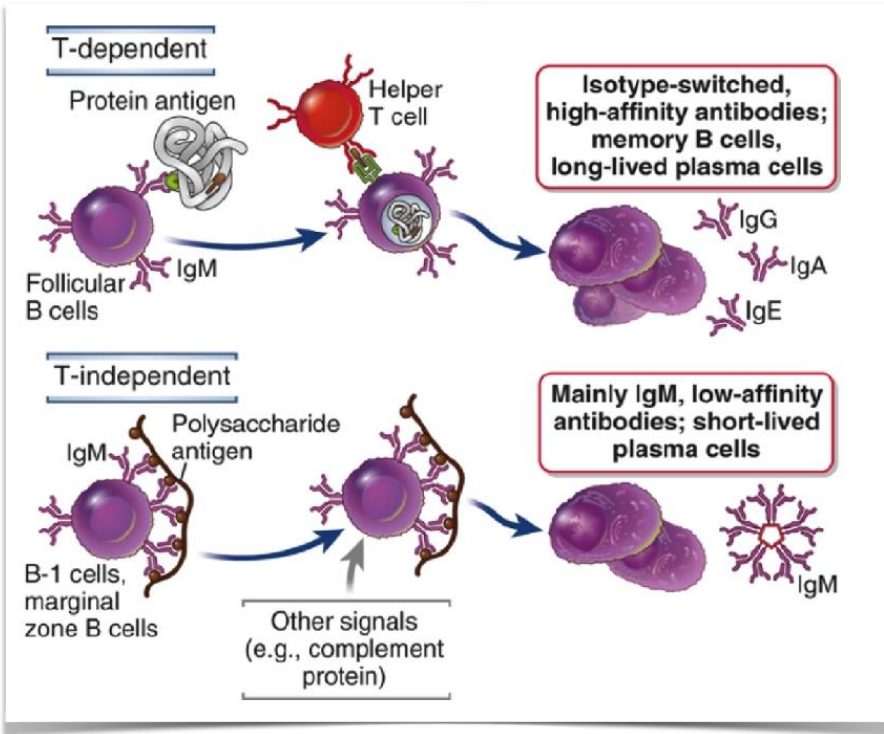
BIO-479 Exercise 8

# Lecture 6-7 Recapitulation

# Overview of humoral immune responses

- Which statement(s) about soluble effector molecules of innate immunity below are correct?
- 1, A primary antibody response is characterized by a high magnitude of antibody production, with IgG being the dominant isotype
- 2, Antibodies secreted by plasma cells have a different antigen specificity than the receptor on the naive B cell that was originally activated.
- 3, T-independent responses, often induced by polysaccharide antigens, are primarily characterized by the production of low-affinity IgM antibodies and short-lived plasma cells.
- 4, Polysaccharide antigens generally elicit stronger responses when presented with helper T cells.
- 5, All immunogens, including proteins and polysaccharides, are capable of inducing a robust secondary antibody response upon repeat infection.
- 6, A secondary immune response is induced only by protein antigens and results in antibodies with a higher average affinity than the primary response.

# Overview of humoral immune responses



During secondary responses, **memory cells** that have already undergone isotope switching and affinity maturation produce *more IgG with higher affinity*.

# B Cell Signalings

- Which statement(s) below are correct?
- 1, Antigens must always be processed into small peptides by dendritic cells before they can be recognized by the B cell receptor (BCR) on a naive B cell.
- 2, Follicular B cells are the primary subset that responds to T-independent polysaccharide antigens, mounting rapid IgM responses.
- 3, During T-dependent B cell activation, the B cell internalizes a protein antigen and presents its peptides on Class II MHC molecules to helper T cells.
- 4, The hapten-carrier effect works because the B cell receptor is specific for the protein carrier, while the helper T cell is specific for the linked hapten.
- 5, B cell receptor (BCR) signaling can be significantly enhanced when the co-receptor CR2 (CD21) binds to C3d complement fragments attached to the antigen.

# Germinal Center Reactions and Antibody Diversification

- Which statement(s) below are correct?
- 1, Isotype switching alters the variable (V) regions of the antibody heavy chain, thereby changing the antibody's specificity for its antigen.
- 2, Follicular dendritic cells (FDCs) are a specialized type of dendritic cell that presents processed antigen peptides on MHC Class II molecules to Tfh cells.
- 3, The enzyme Activation-Induced Deaminase (AID) is essential for both somatic hypermutation and heavy chain isotype switching.
- 4, Somatic hypermutation occurs primarily in the germinal center's dark zone, whereas the selection of B cells based on affinity occurs in the light zone.
- 5, The cytokine IFN-gamma is the primary signal from Tfh cells that induces B cells to switch to producing IgE.

## B Cell differentiation and T-independent responses

- Which statement(s) below are correct?
- 1, Long-lived plasma cells are primarily generated in extrafollicular B cell foci, while short-lived plasma cells arise from the germinal center reaction.
- 2, T-independent antigens are typically non-protein antigens, such as lipids and polysaccharides, that can activate B cells without T cell help.
- 3, TI-2 antigens, which have highly repetitive structures, are particularly effective at inducing strong antibody responses in infants.
- 4, Dendritic cells and macrophages can provide a co-stimulatory signal (BAFF) that augments the TI-1 antigen response and induces class-switching.
- 5, B-1 cells and marginal zone B cells are key responders to T-independent antigens, differentiating into short-lived plasma cells that produce mainly low-affinity IgM.

# Hapten-Carrier Effect

Mice are primed with DNP conjugated to ovalbumin (DNP–OVA). Weeks later, they are challenged with DNP–OVA, DNP–BSA, or native OVA, and anti-DNP antibody responses are measured. Which two statements best reflect the immunological principles governing T–B cell collaboration in this system?

- 1, Upon secondary challenge with DNP–BSA, robust anti-DNP IgG is observed only if the mouse was previously primed with a carrier that shares T cell epitopes with BSA.
- 2, Memory anti-DNP B cells can be reactivated by DNP–BSA even in the absence of carrier-specific T cells, because memory B cells no longer require T cell help for differentiation into antibody-secreting cells.
- 3, The requirement for physical linkage between hapten and carrier ensures that only B cells whose BCR binds the hapten internalize the entire conjugate, thereby restricting T cell help to B cells specific for the hapten—a process essential for epitope focusing in germinal centers.

# Hapten-Carrier Effect

Mice are primed with DNP conjugated to ovalbumin (DNP–OVA). Weeks later, they are challenged with DNP–OVA, DNP–BSA, or native OVA, and anti-DNP antibody responses are measured. Which two statements best reflect the immunological principles governing T–B cell collaboration in this system?

- 4, Secondary immunization with native ovalbumin boosts anti-DNP antibodies because memory T follicular helper (Tfh) cells specific for OVA can recognize free carrier protein and secrete cytokines that non-specifically enhance all nearby plasma cells.
- 5, During the primary response, B cells that bind DNP with low-affinity BCRs are excluded from receiving T cell help because Tfh cells selectively recognize high-affinity BCR–antigen complexes through co-receptors such as CD28.
- 6, The hapten–carrier effect demonstrates that T cell help is antigen-specific but not B cell receptor–dependent, as soluble carrier protein can activate carrier-specific T cells that then help any B cell presenting carrier peptides—even if that B cell’s BCR binds an unrelated antigen.

# Antigen Recognition and Antibody Structure-Function Relationships

- Which statement(s) are correct?
- 1, Because T cells recognize only linear peptides presented by MHC class II, effective vaccine must include a protein component that can be processed by antigen-presenting cells to provide T cell help, even though the protective B cell epitope is conformational
- 2, The conformational epitope can be mimicked by a short synthetic peptide, as long as the peptide contains the same amino acid side chains that contact the antibody's CDRs in the native protein
- 3, Antibody effector functions (e.g., complement activation) are determined by the CDR sequences in the variable region, so engineering the CDRs can simultaneously optimize both antigen binding and downstream immune activation

# Antigen Recognition and Antibody Structure-Function Relationships

- Which statement(s) are correct?

- 4, High-affinity antibody responses require germinal center reactions, which depend on B cells internalizing the intact antigen via BCR binding and presenting processed peptides to T follicular helper cells—thus the conformational epitope and T cell epitopes must be physically linked in the same molecule
- 5, Since B cells can recognize non-protein antigens such as carbohydrates, the conformational epitope could be replaced with a polysaccharide mimic to bypass the need for T cell help and still generate long-lived plasma cells.
- 6, The hinge region of IgG is essential for high-affinity binding to conformational epitopes because it allows the Fab arms to rotate and accommodate irregular antigen surfaces.

# Antibodies

- Which statement(s) below are correct?
- 1, IgG's long serum half-life is due to FcRn-mediated recycling in endothelial cells, a mechanism that can be exploited to extend the half-life of recombinant therapeutic proteins fused to IgG Fc domains.
- 2, During B cell development, co-expression of IgM and IgD on naïve mature B cells results from alternative splicing of a single primary RNA transcript encoding both heavy chain constant regions.
- 3, Hybridoma technology reliably produces monoclonal antibodies against any antigen, including highly conserved self-proteins, because myeloma fusion overcomes B cell tolerance mechanisms.
- 4, Secreted IgA functions primarily in systemic circulation as a monomer, while its dimeric form is restricted to intracellular compartments of plasma cells.

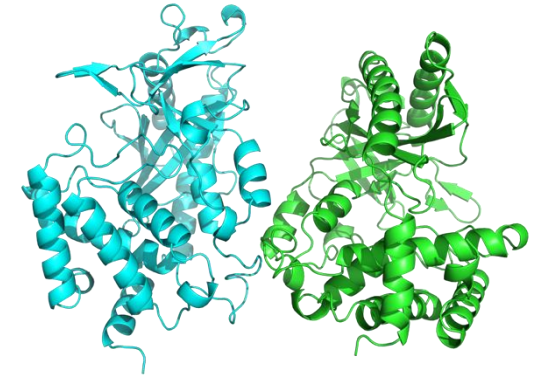
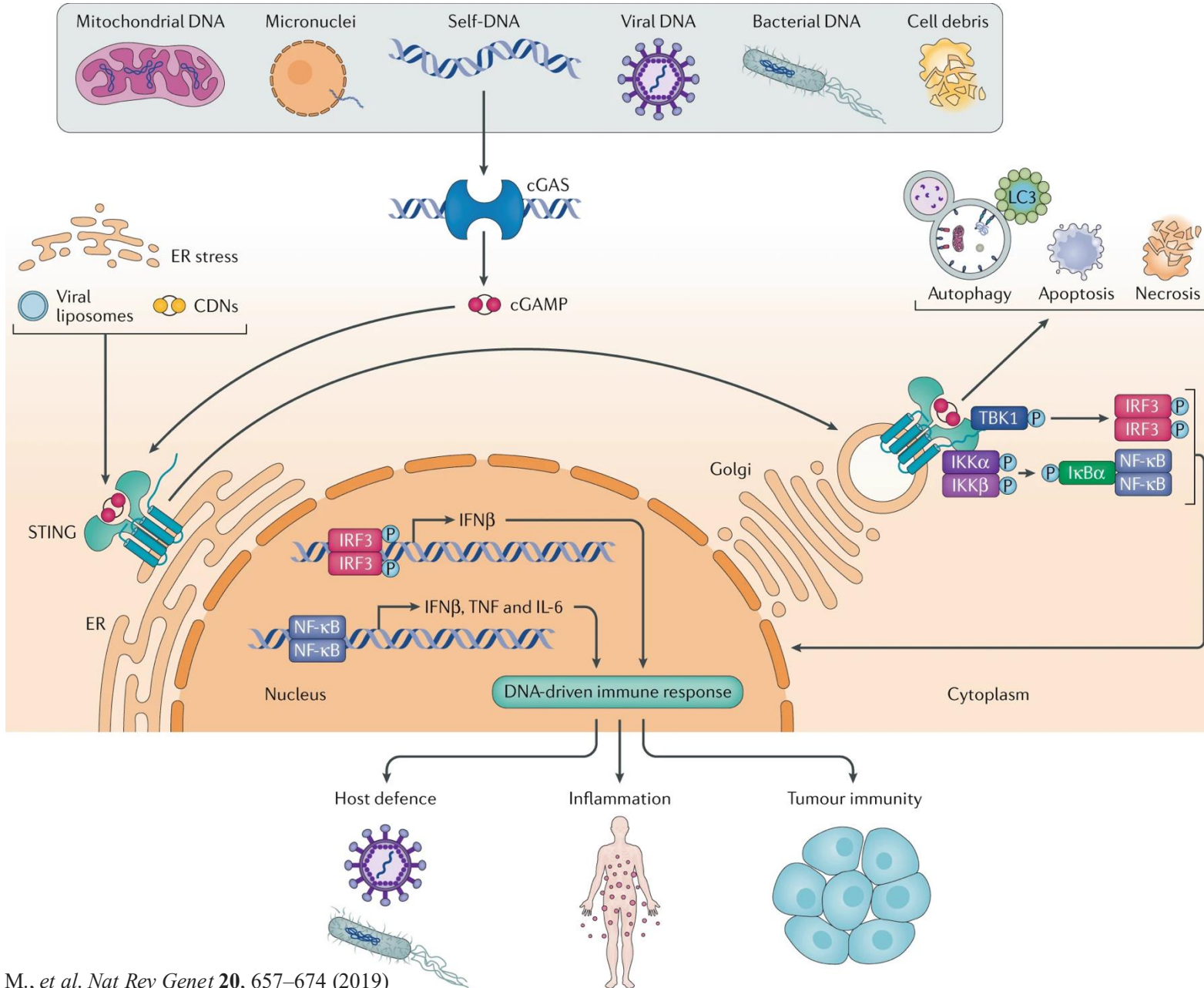
# Antibody and Antigen Interactions

- Which statement(s) below are correct?
- 1, Although IgM has lower intrinsic affinity for antigen than IgG, its pentameric structure provides high avidity, enabling efficient complement activation and pathogen clearance early in a primary response before affinity maturation occurs
- 2, Antibodies against conformational epitopes on native viral glycoproteins are typically elicited in T cell-independent responses because the intact folded protein can directly cross-link BCRs.
- 3, High-affinity antibodies generated after affinity maturation enhance FcγR-mediated effector functions such as ADCC because tighter antigen binding increases the dwell time of the antibody on the target cell surface, thereby promoting sustained Fc receptor clustering and signaling
- 4, In helminth infection, IgE's protective role depends on its high-affinity binding to FcεRI on eosinophils and mast cells; Its effectiveness relies on local production and FcεRI-mediated amplification rather than systemic neutralization
- 5, Opsonization by IgG requires bivalent binding to the microbe to induce conformational changes in the Fc region that enhance FcγR affinity on phagocytes—a process that is independent of complement and unaffected by antigen density on the pathogen surface

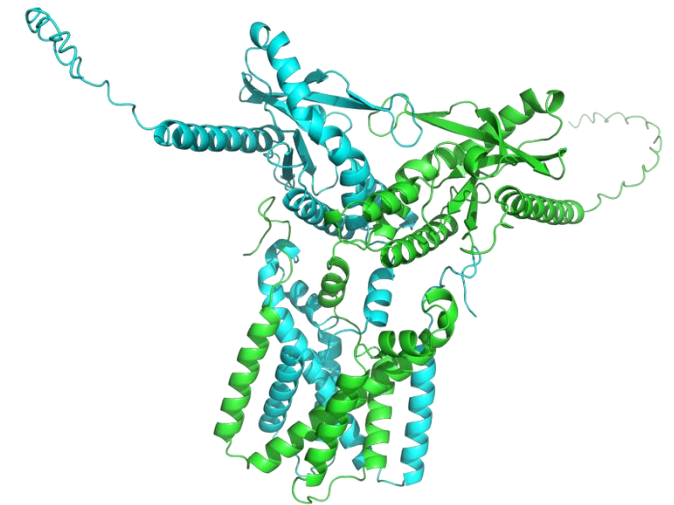
## BIO-479 Seminar 2

# **STING-induced Regulatory B cells Compromise NK Function in Cancer Immunity**

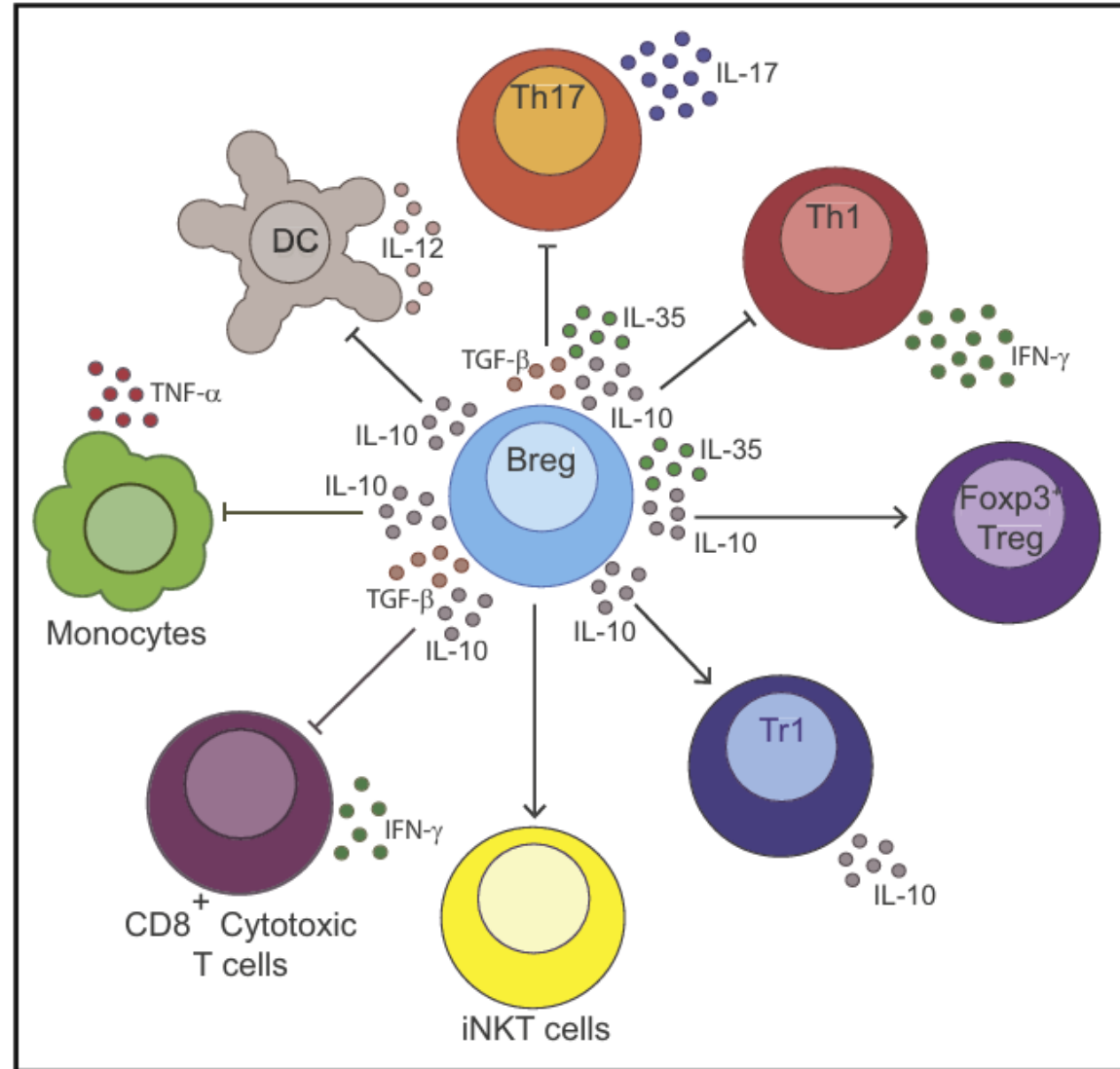
# cGAS-STING Signaling Pathway



cGAS dimer



STING dimer



Article

# STING-induced regulatory B cells compromise NK function in cancer immunity

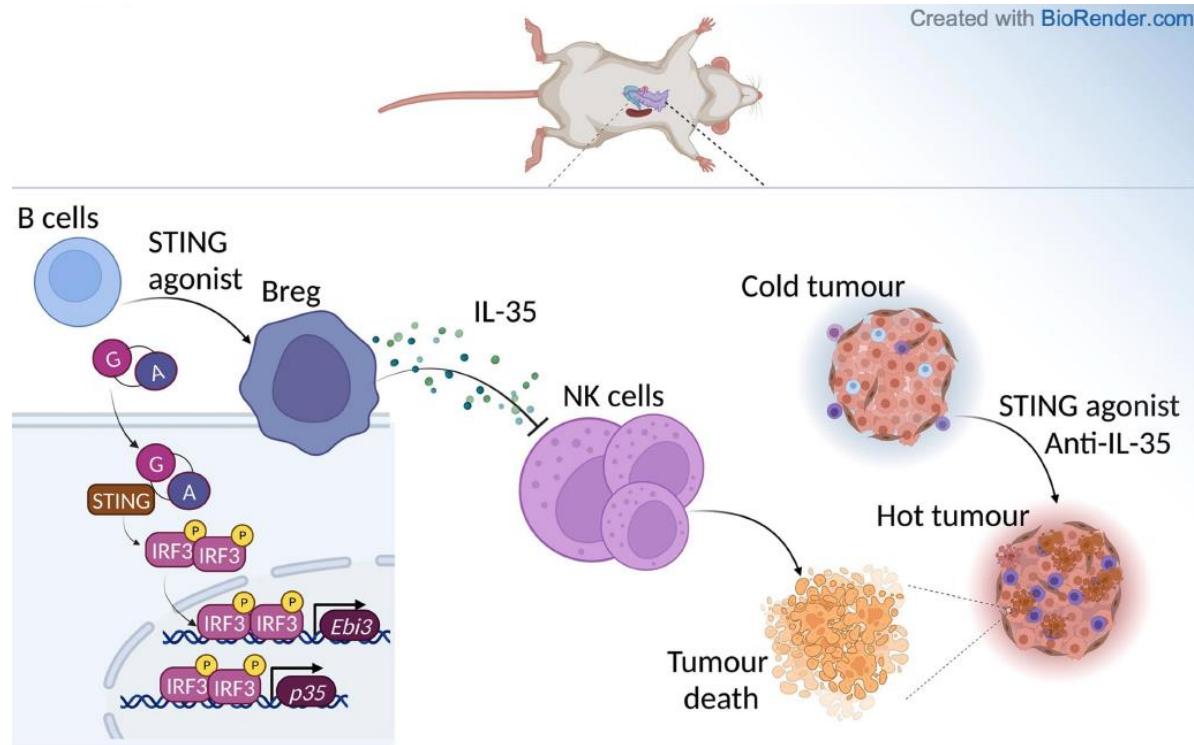
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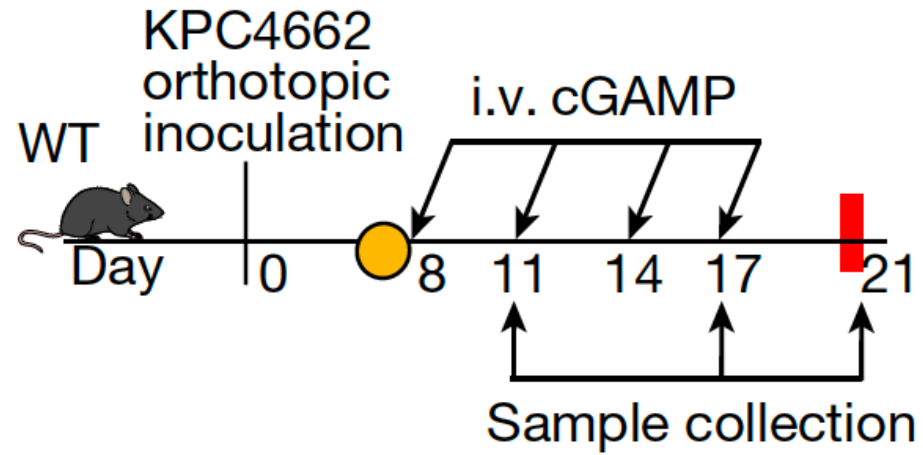
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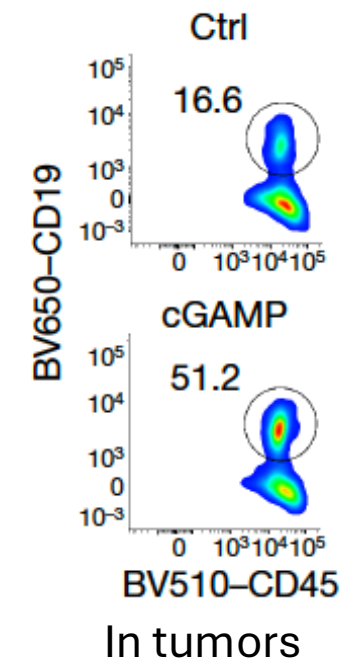
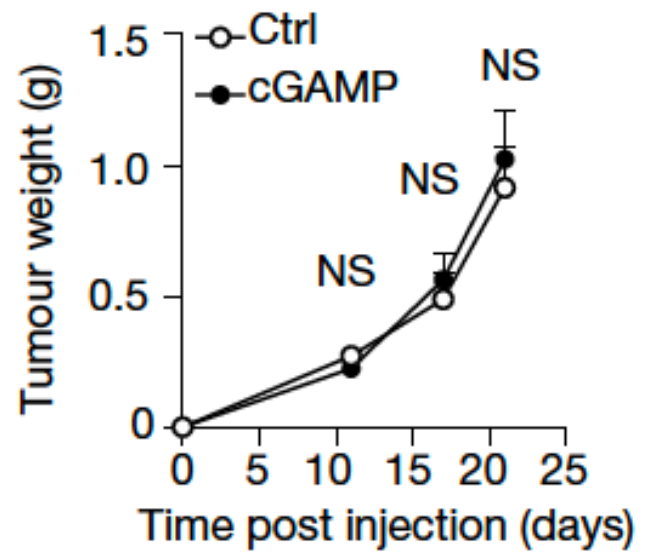
Published online: 5 October 2022

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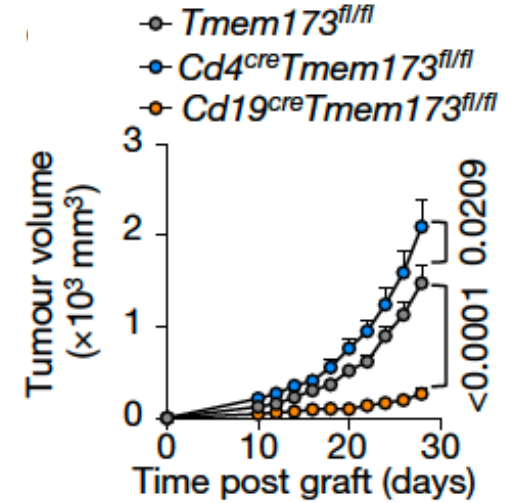
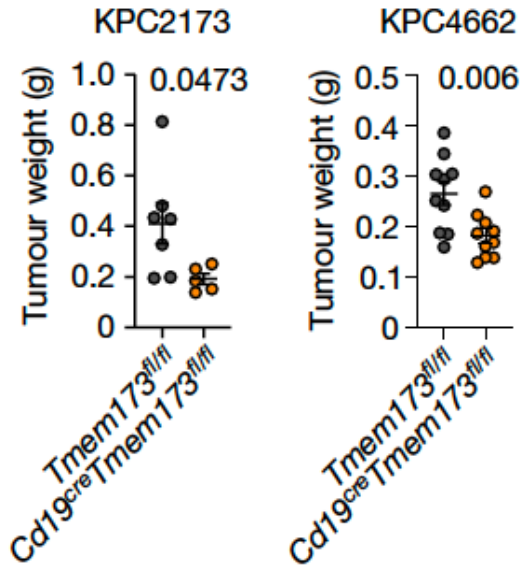




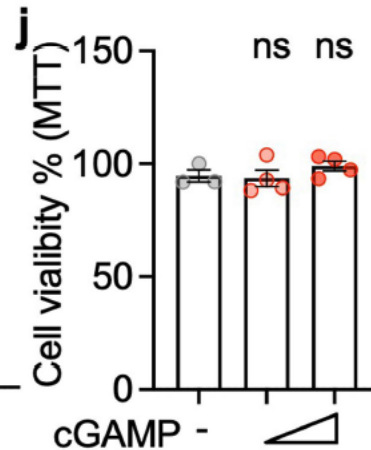
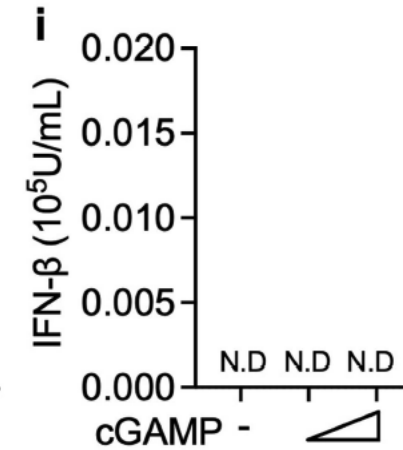
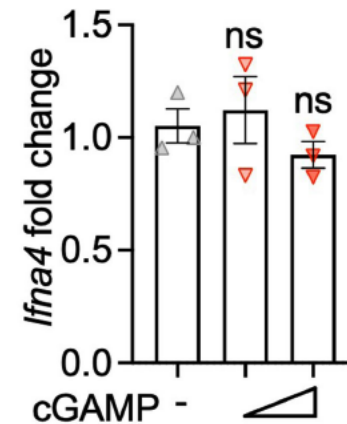
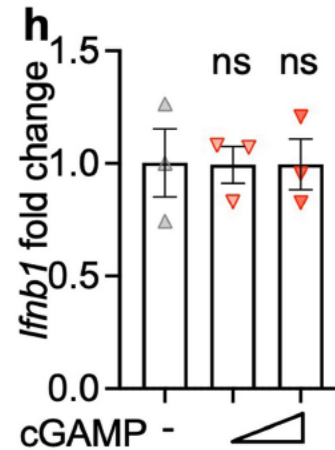
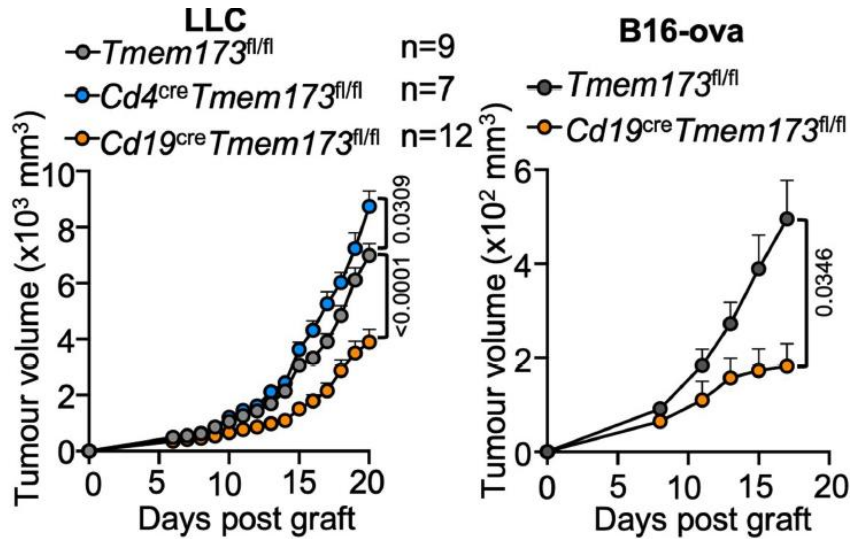
KPC Mice: Pancreatic Ductal Adenocarcinoma(PDAC) Model Mice

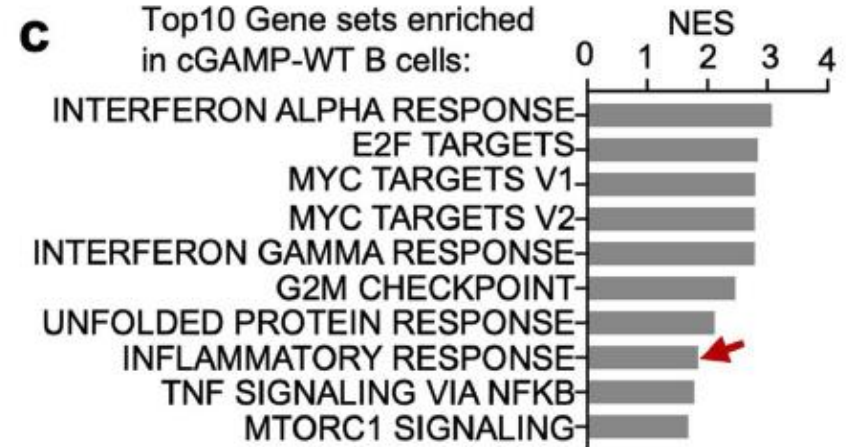
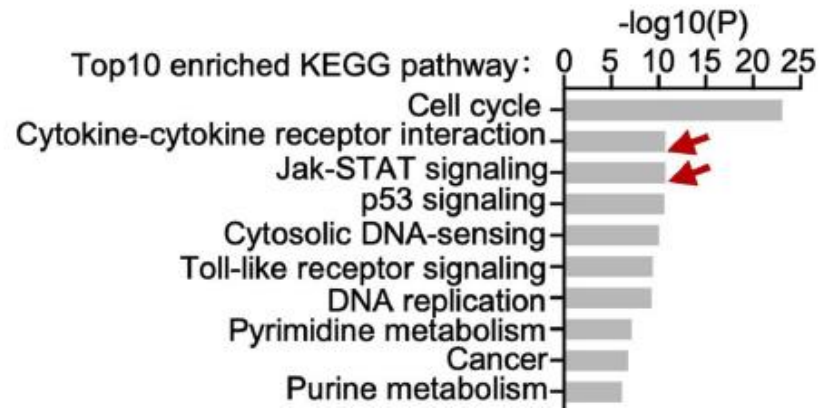
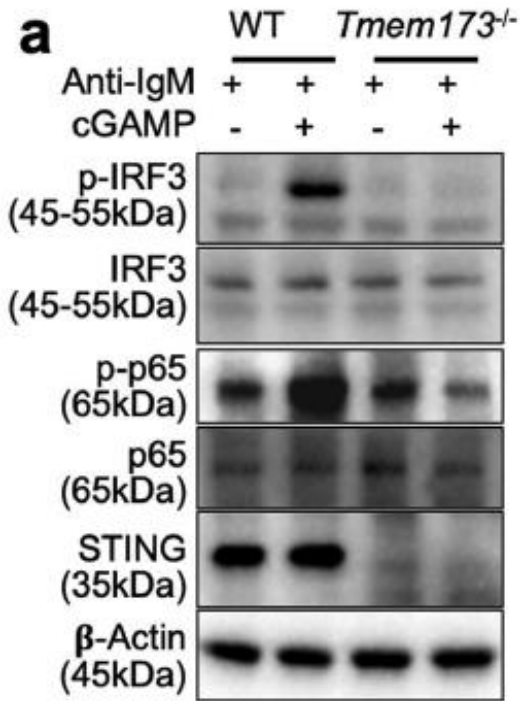


# STING Activation Enhances B Cells

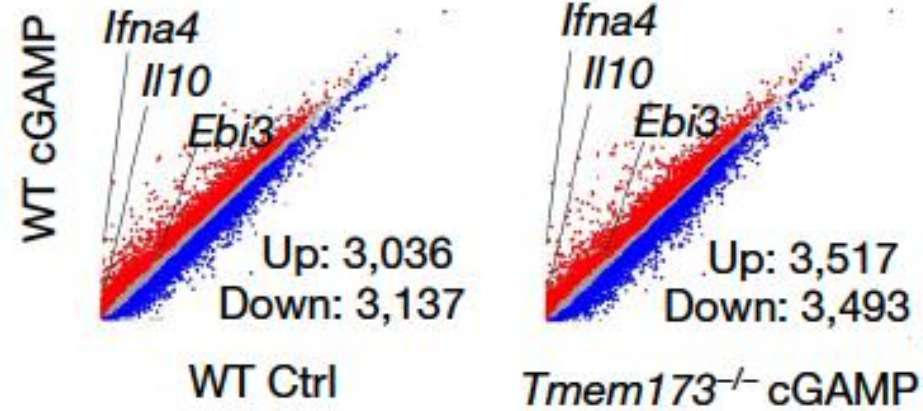


Triple-Negative Breast Cancer Model

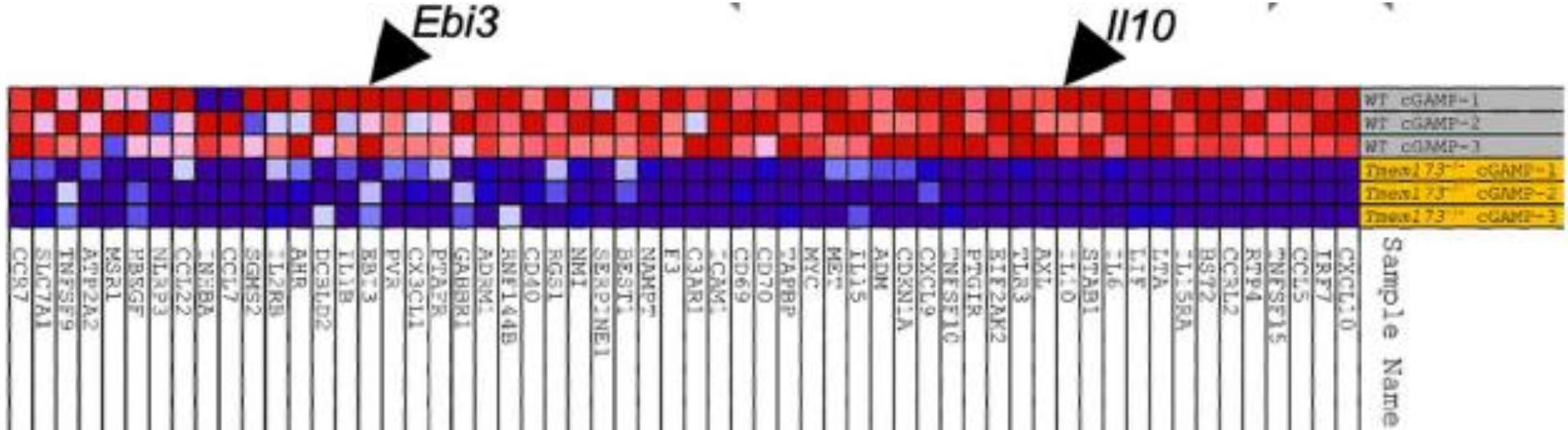




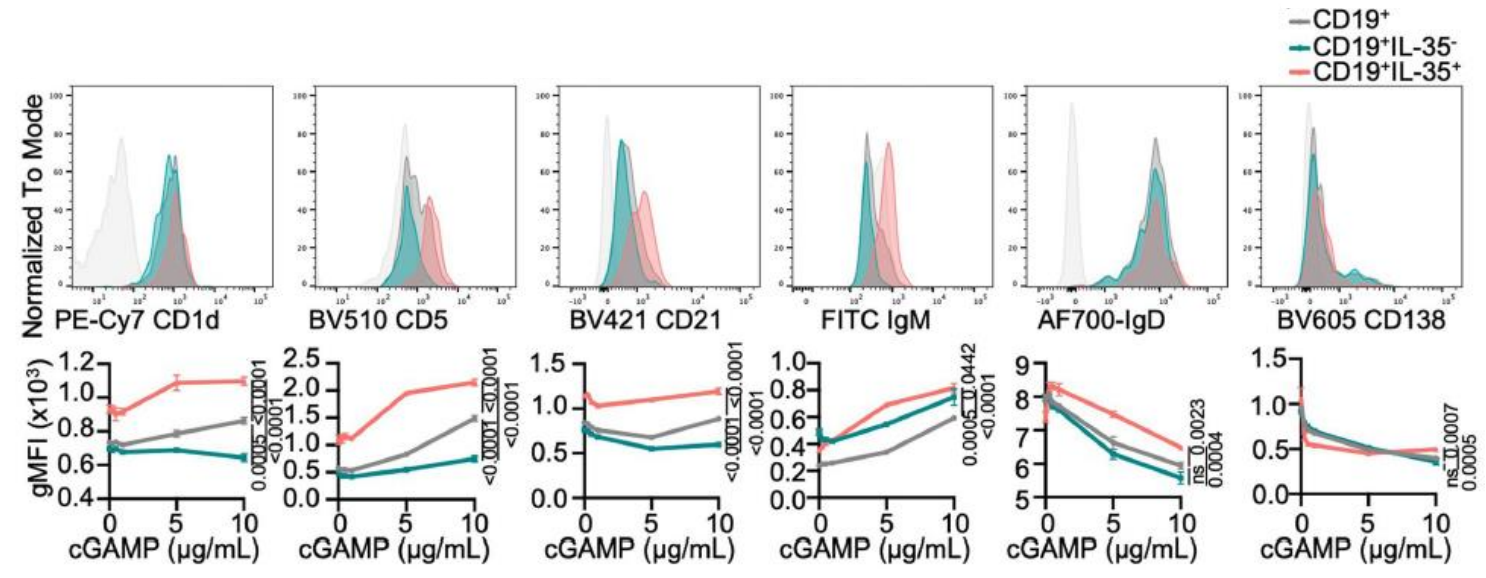
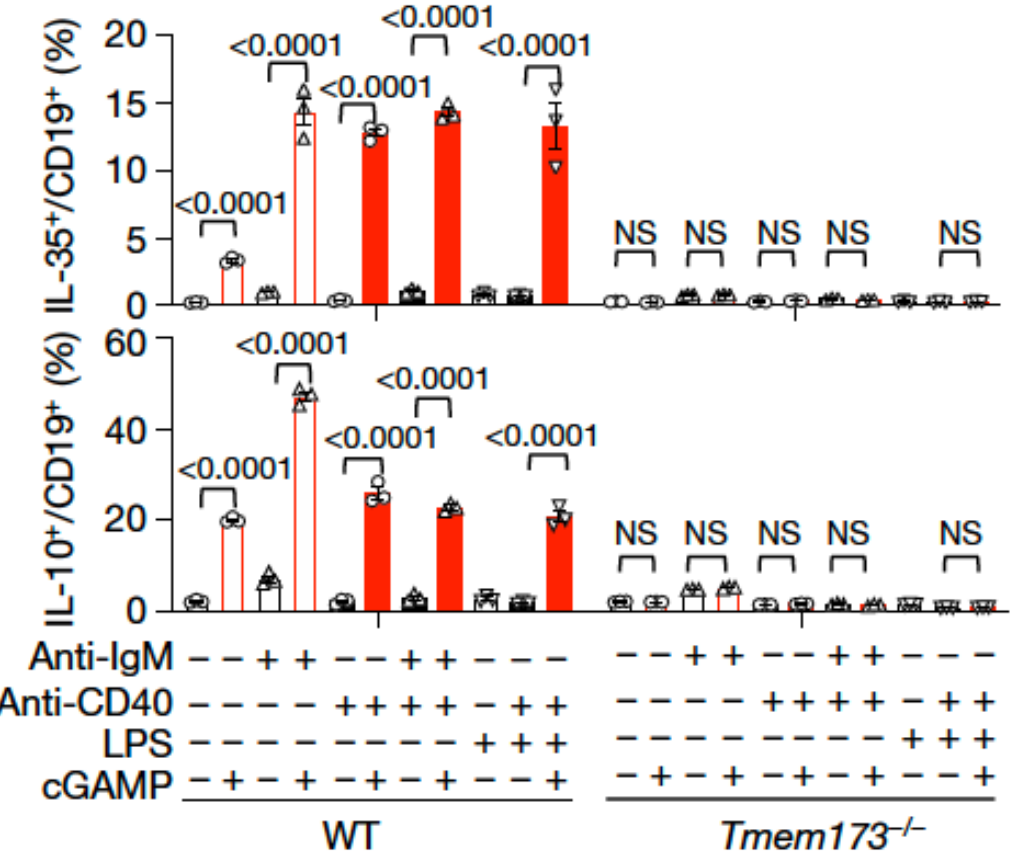
# ➤ STING Activation Enhances B Cells



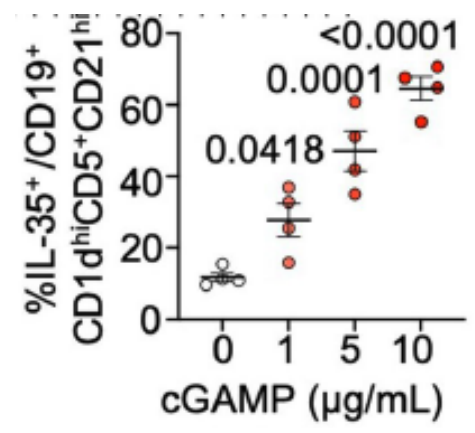
(subunit of immunosuppressive cytokines IL-27 and IL-35)

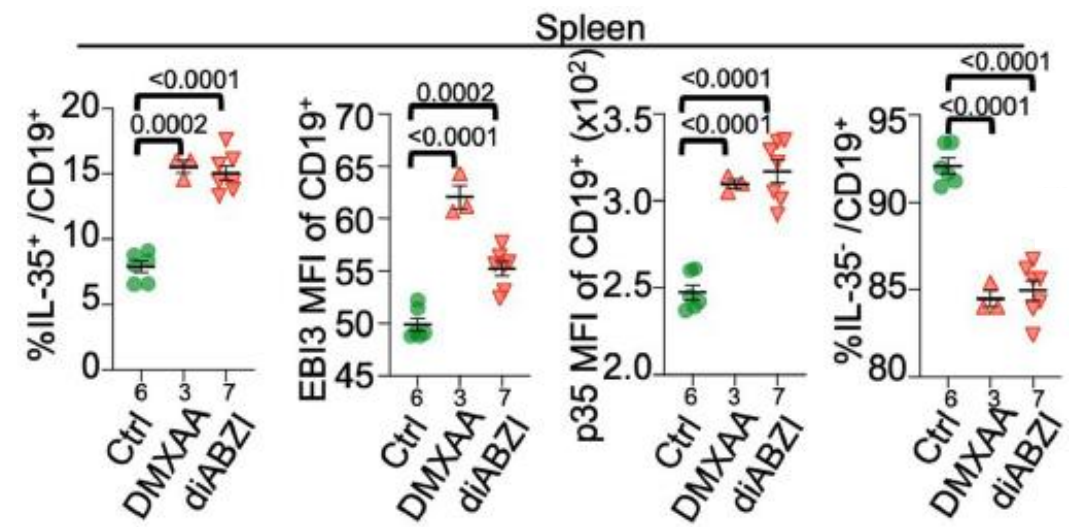
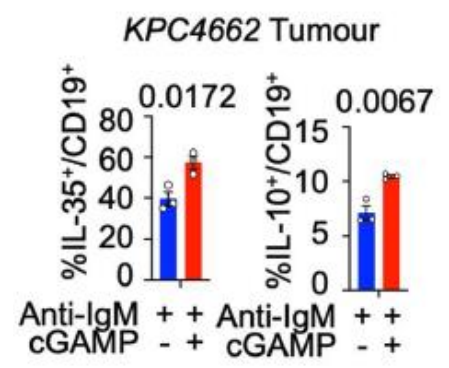
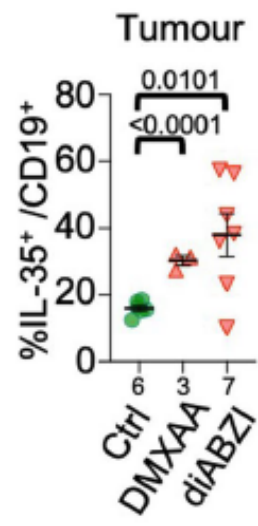
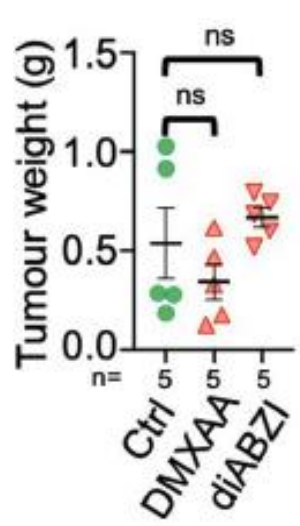
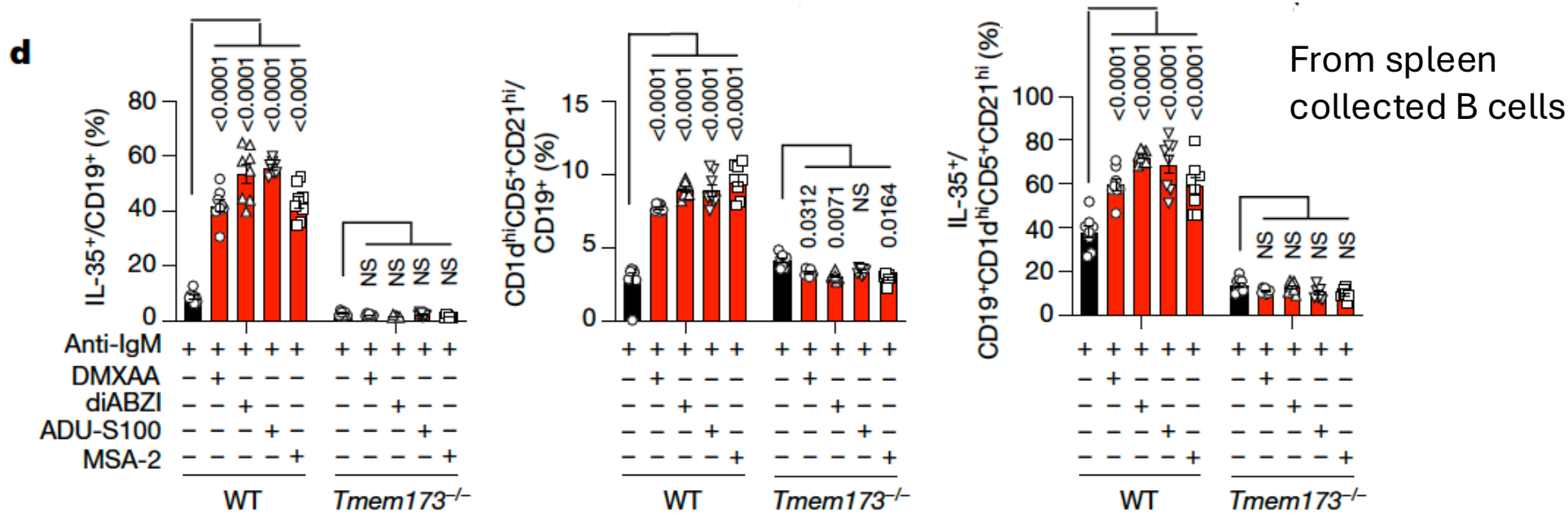


# STING Induces B<sub>reg</sub> Cells



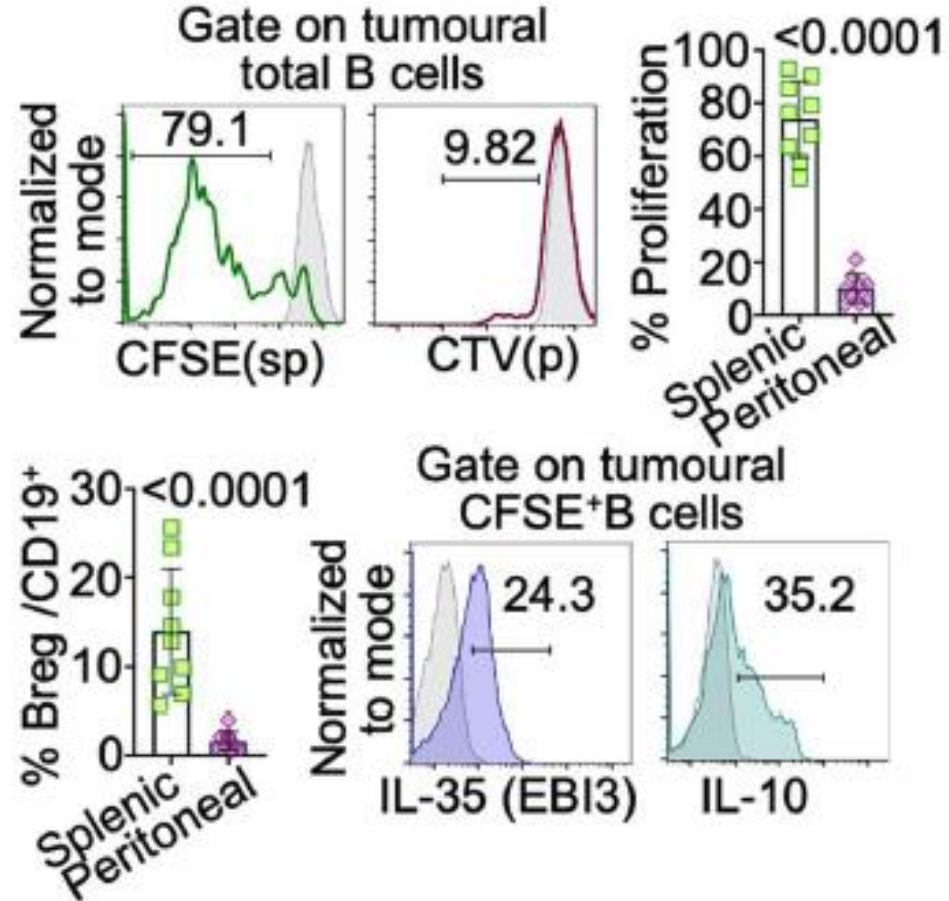
CD19<sup>+</sup>IL-35<sup>+</sup> cells are CD1d<sup>hi</sup>CD5<sup>+</sup>CD21<sup>hi</sup> B cells  
 This is a phenotype characteristic of mouse B<sub>reg</sub> Cells



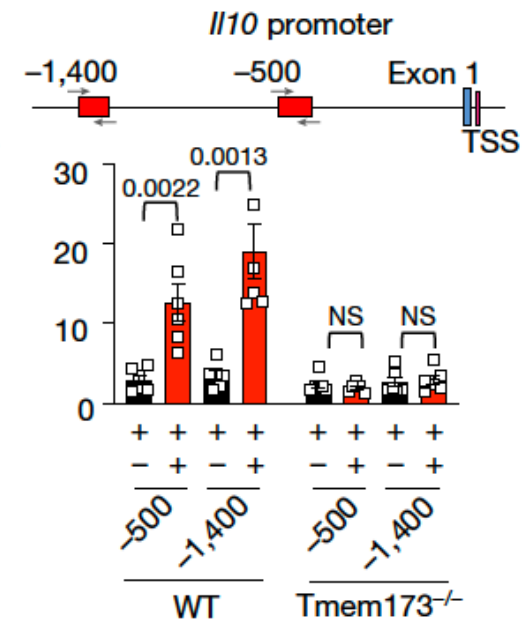
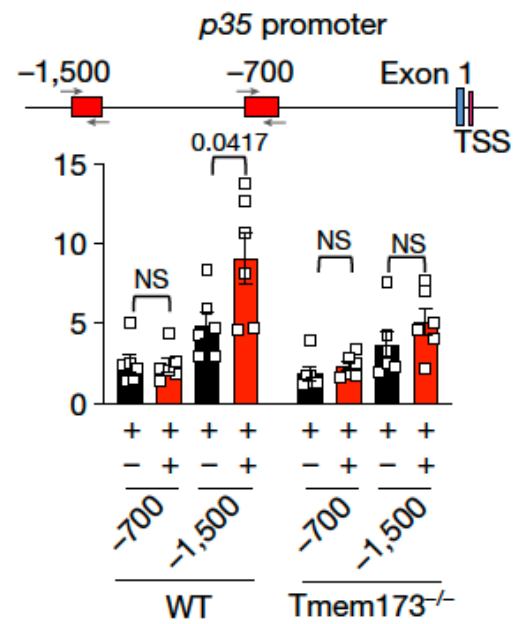
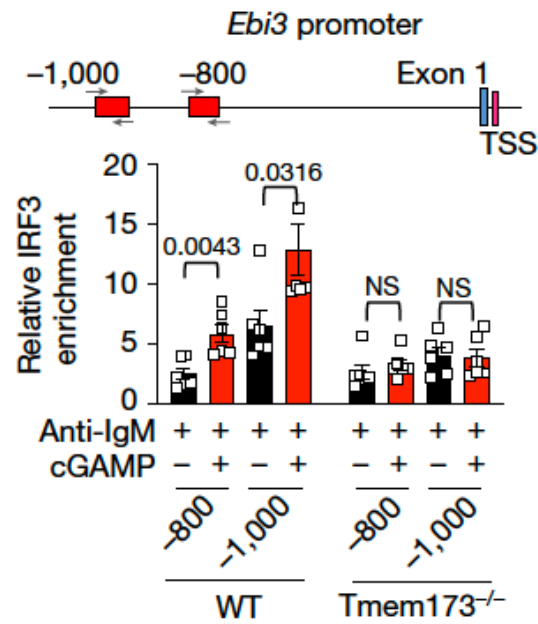
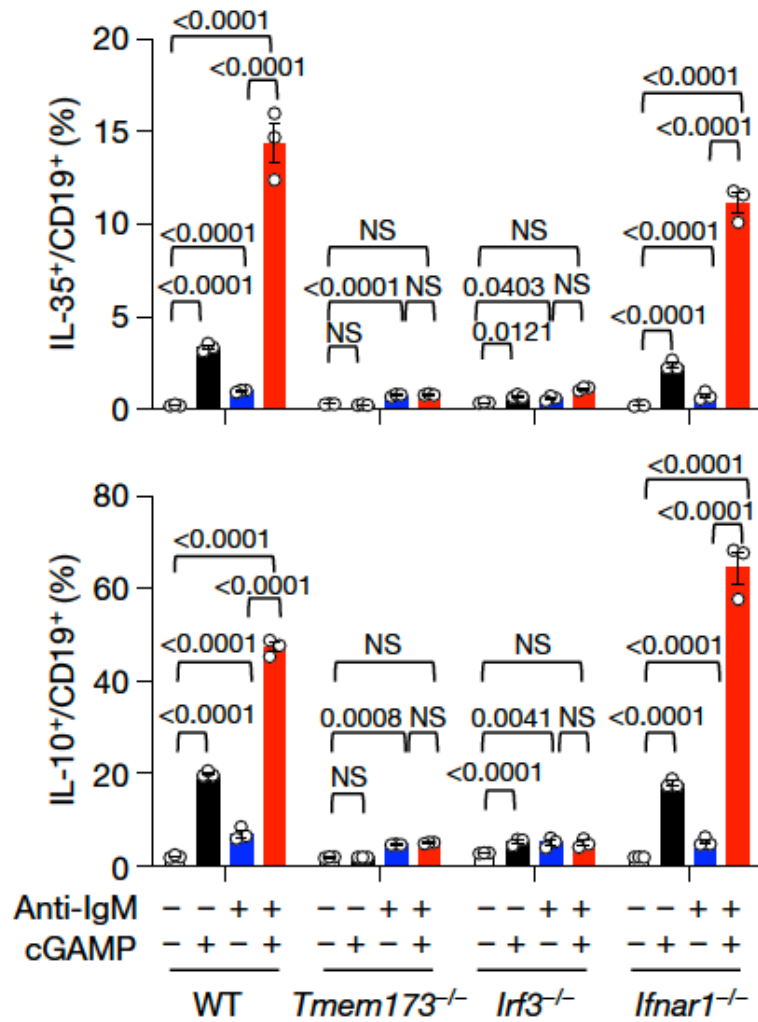


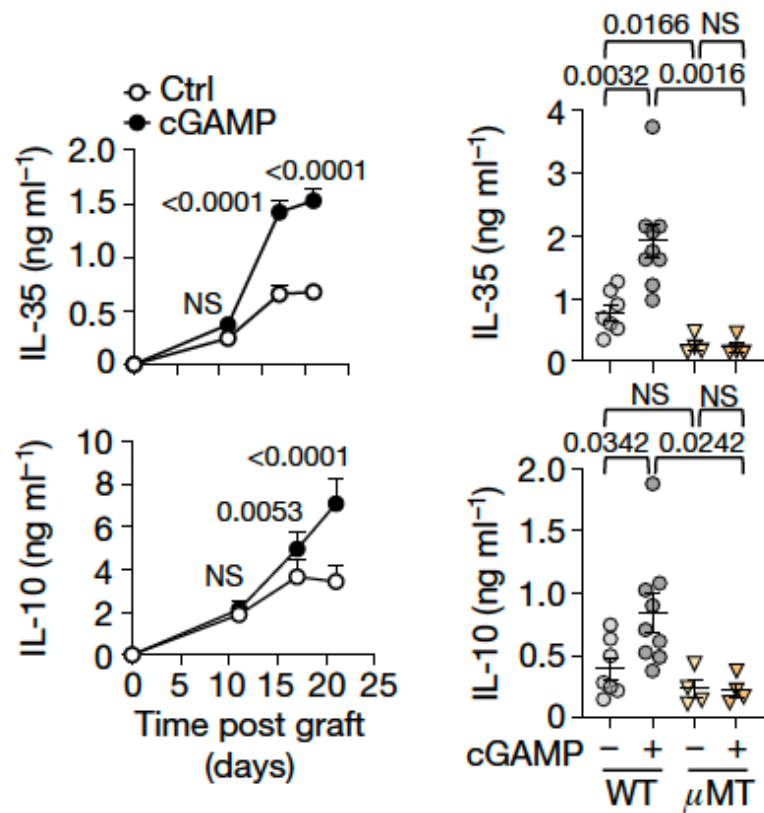
Source of the B cells in PDAC

Splenic B Cells: labeled with CFSE  
Peritoneal B Cells: labeled with CTV

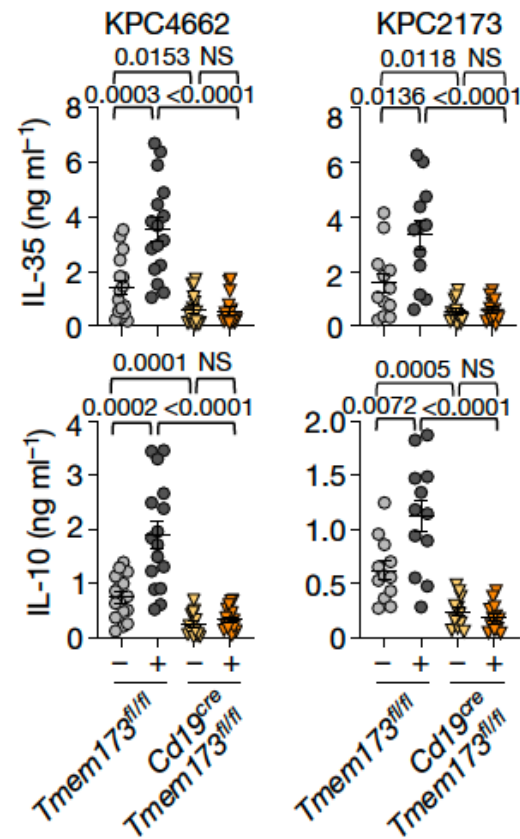


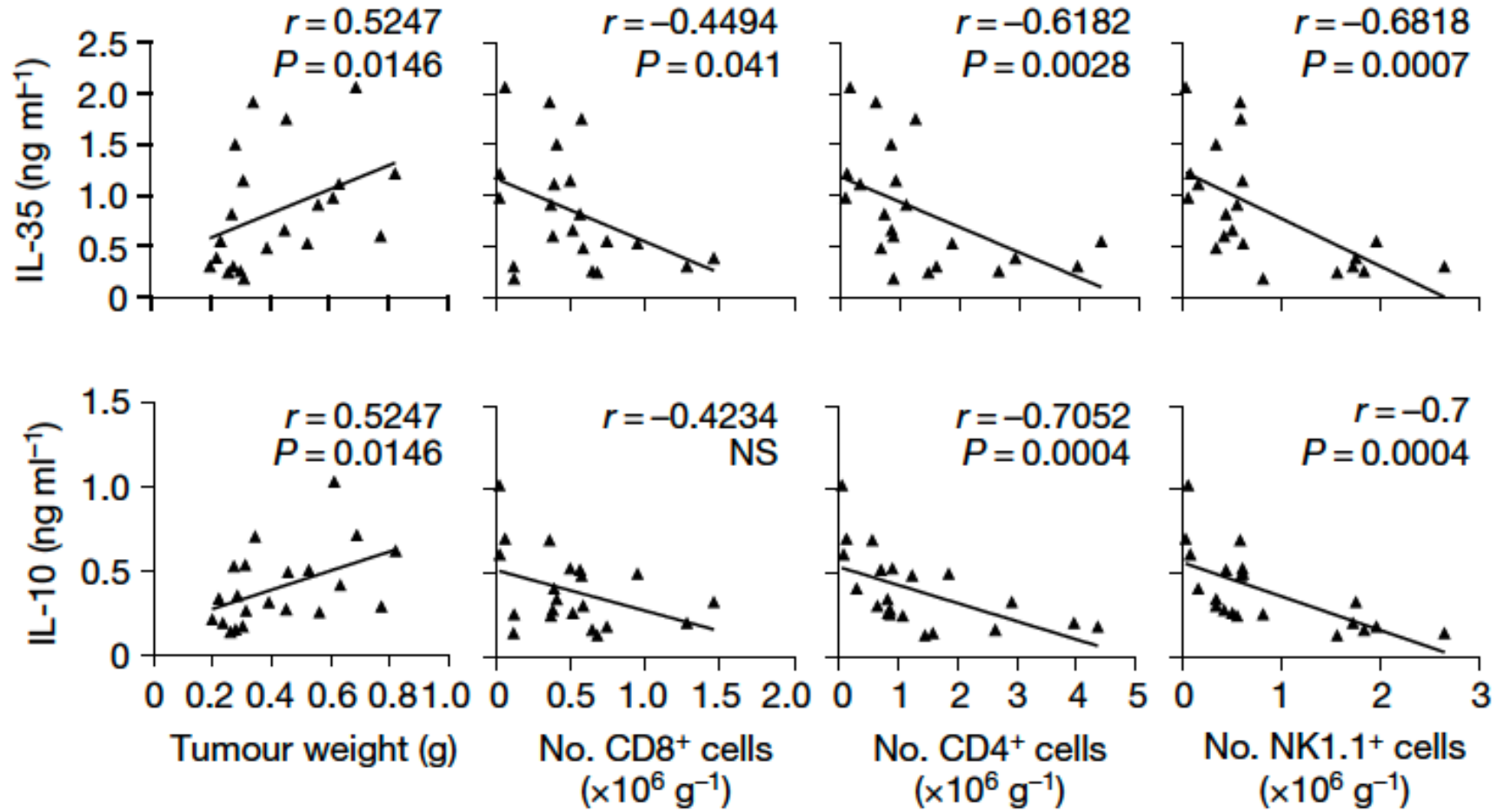
# STING-IRF3 Mediates B<sub>reg</sub> Cytokines



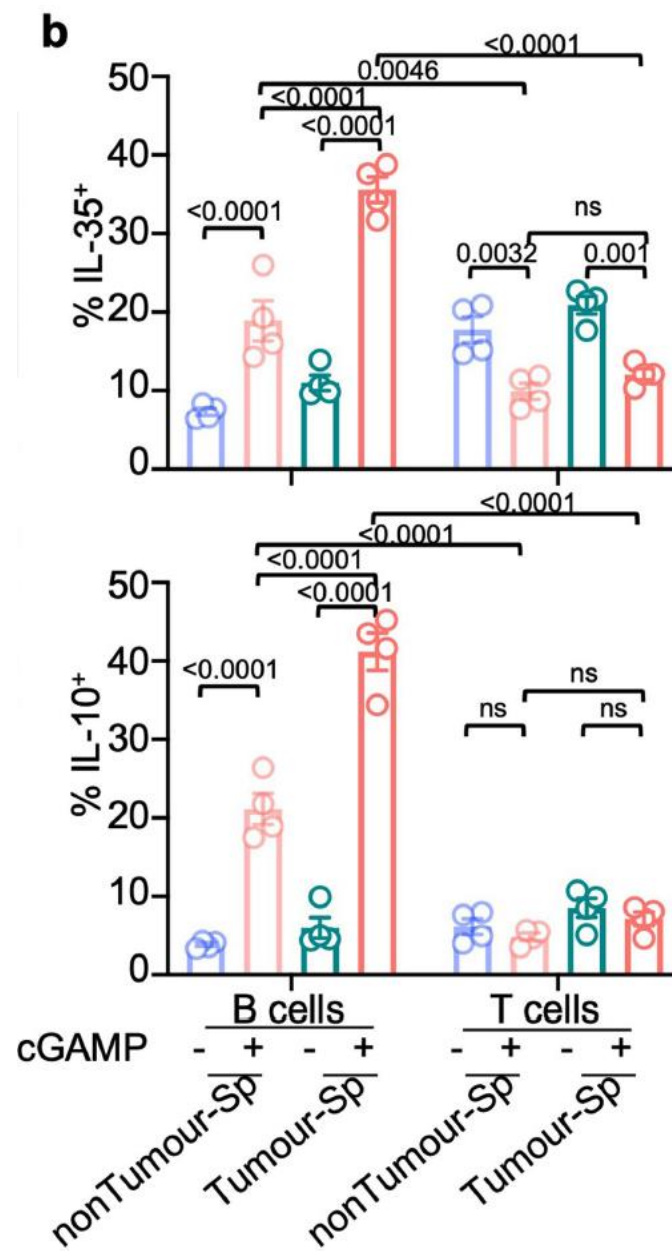
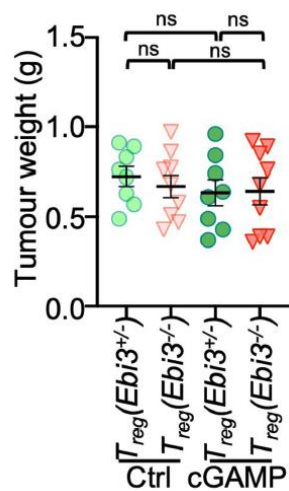
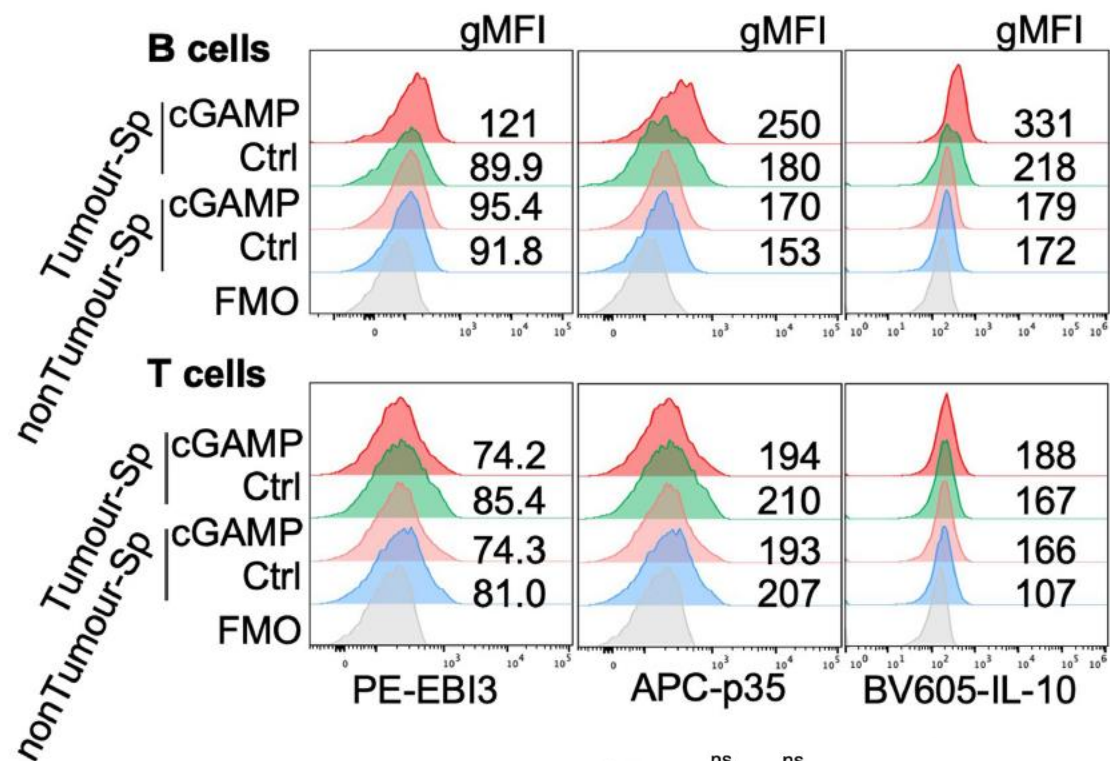


$\mu$ MT: B Cell abrogated mice

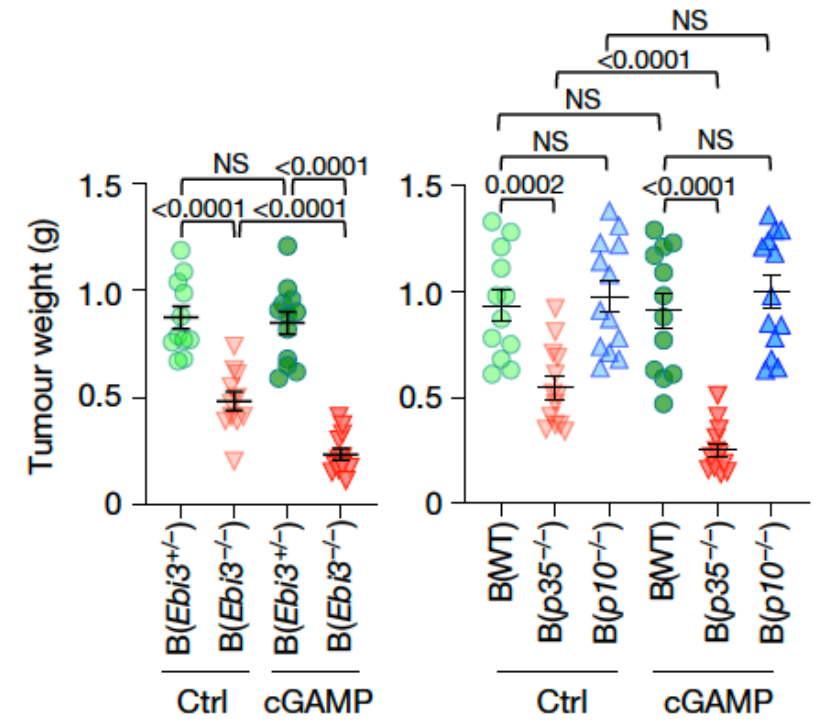
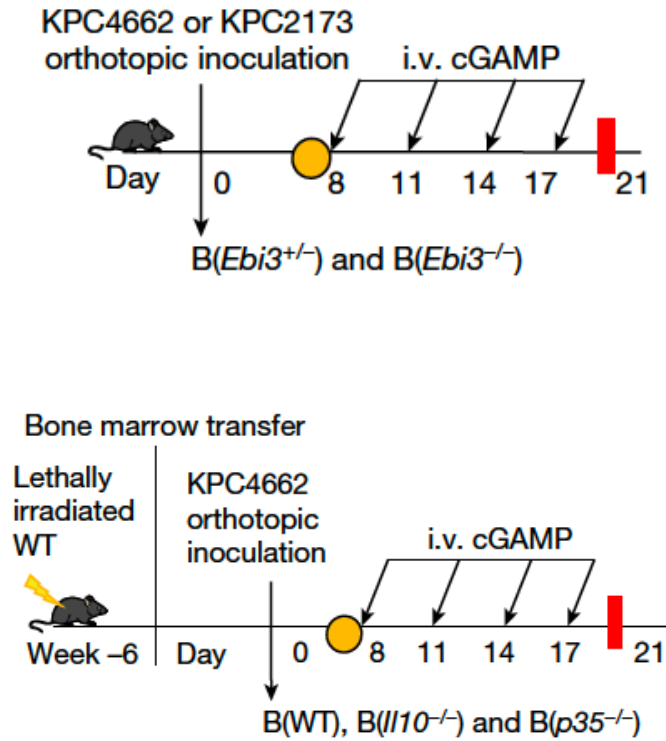




# STING-IRF3 Mediates B<sub>reg</sub> Cytokines

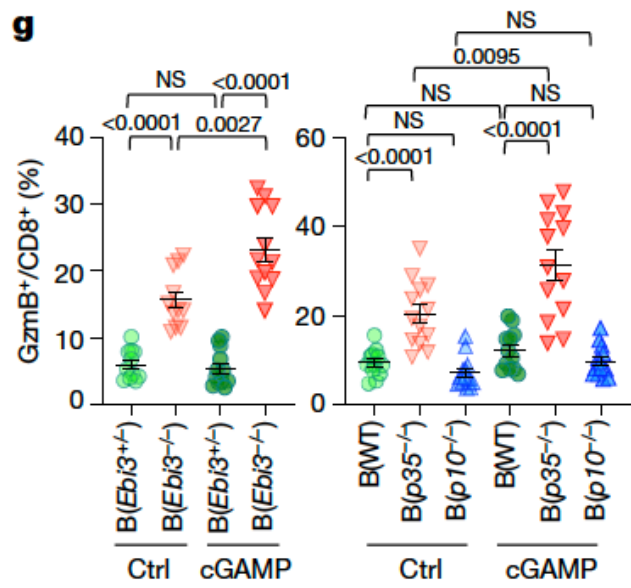


# IL-35<sup>+</sup> B Cells Subdue NK cell responses

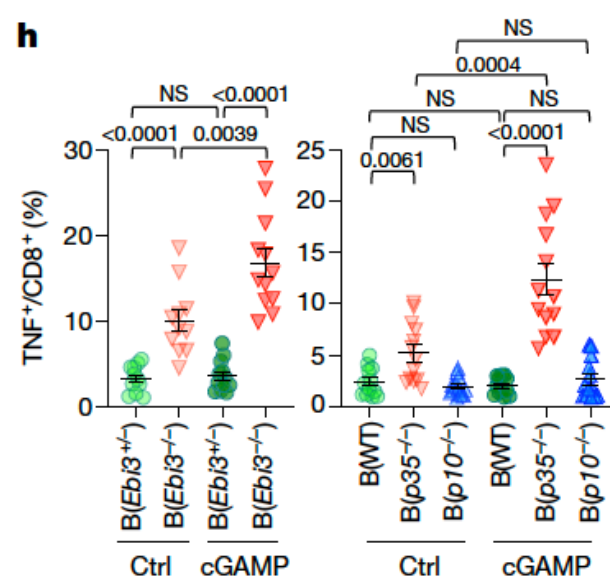


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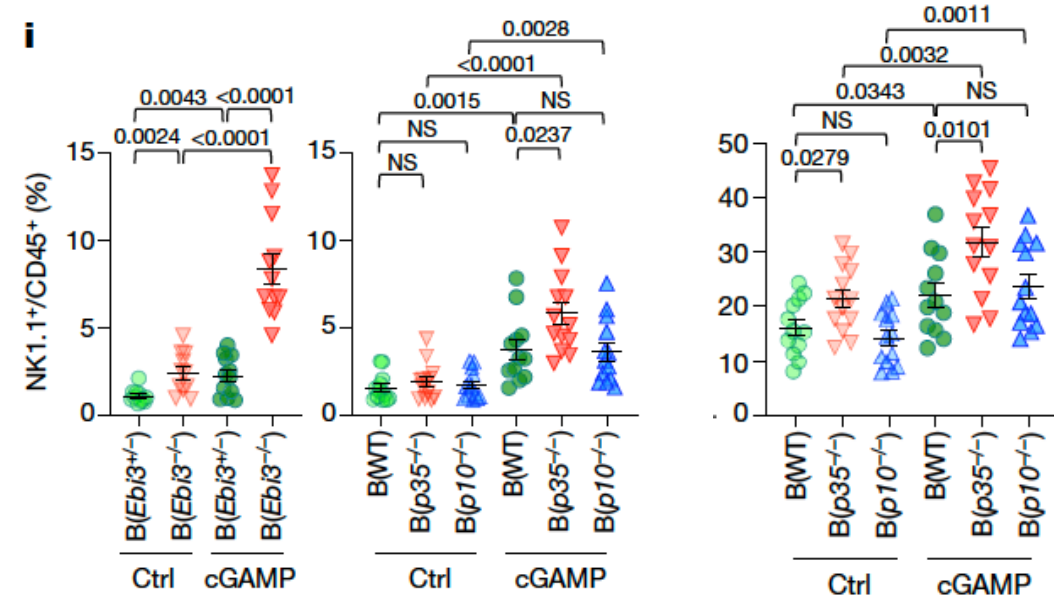
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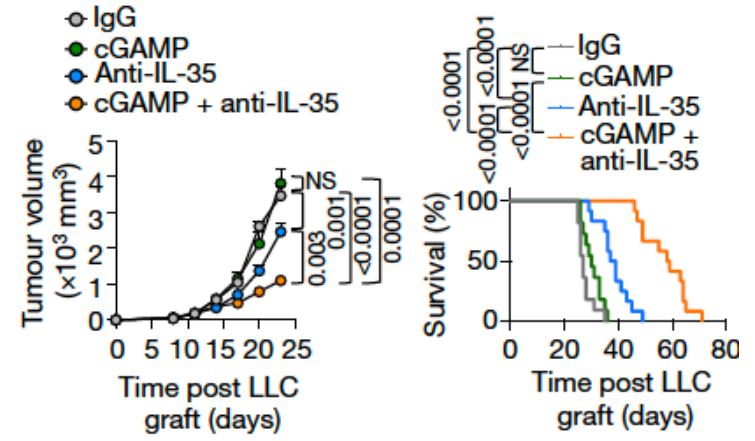
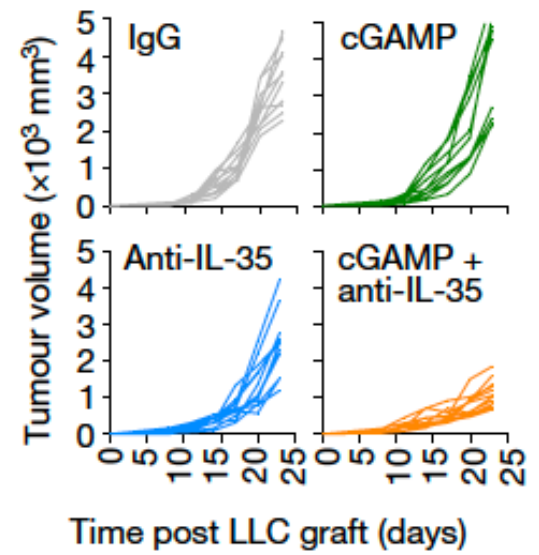
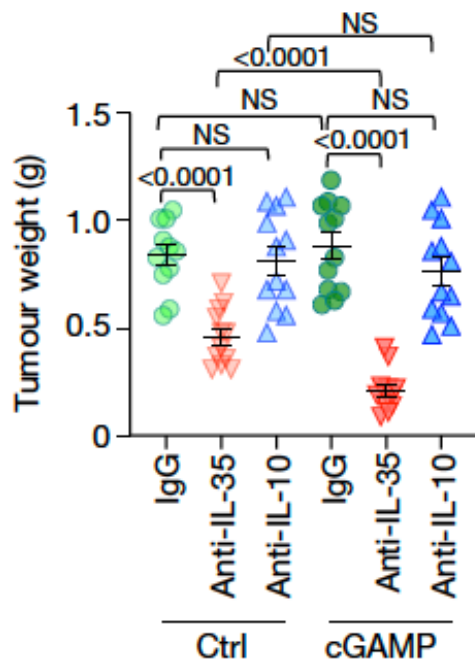
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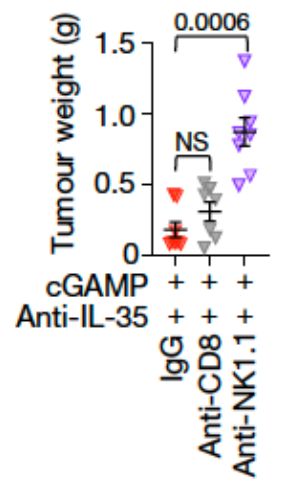
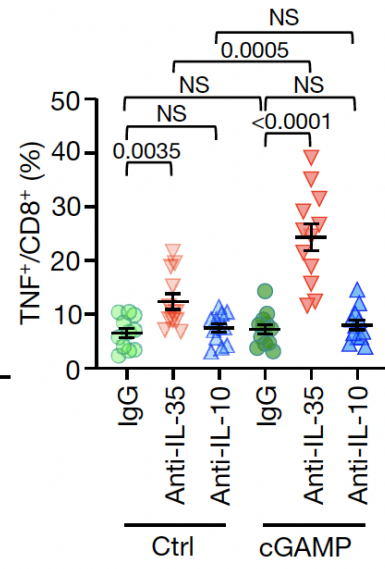
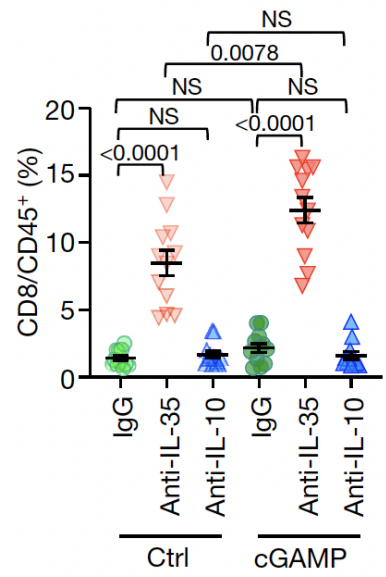
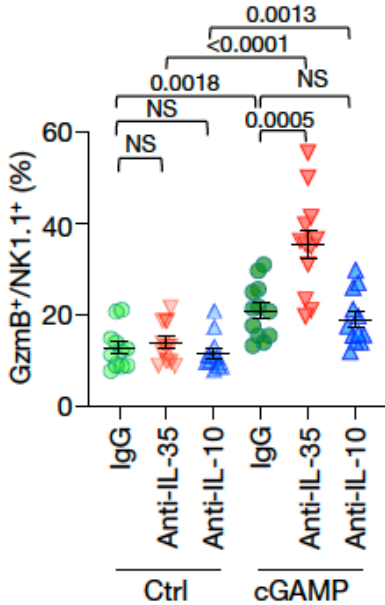
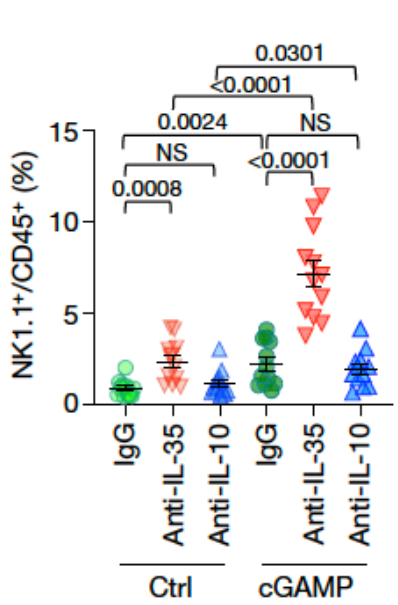
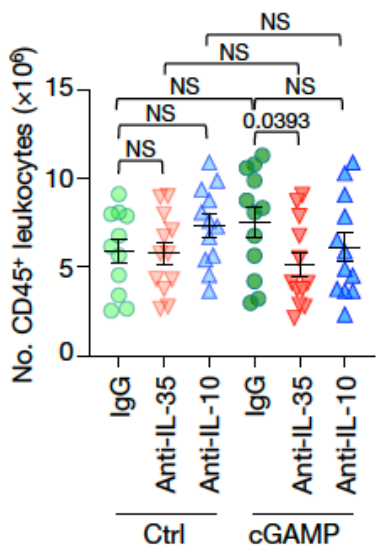
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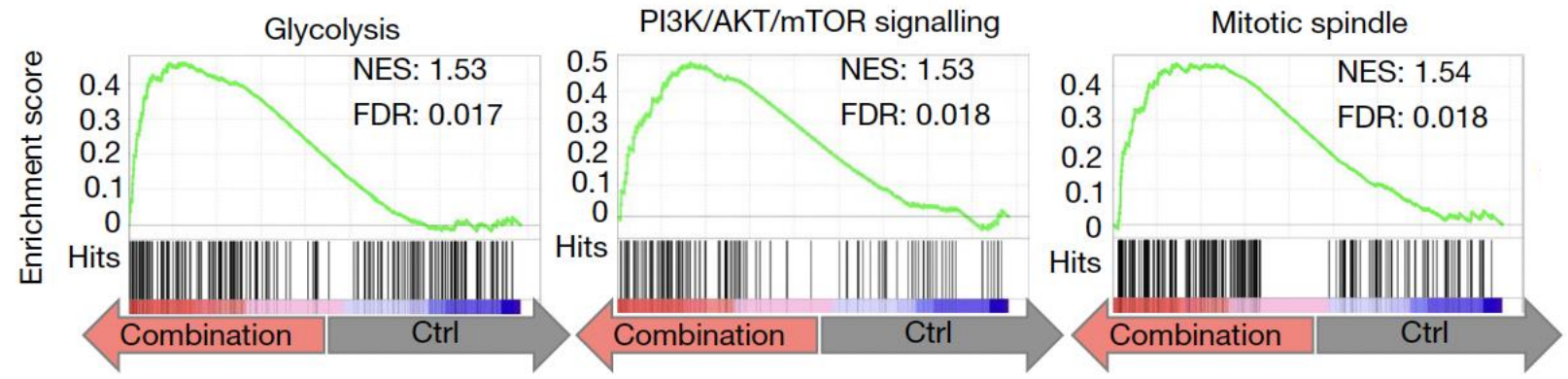
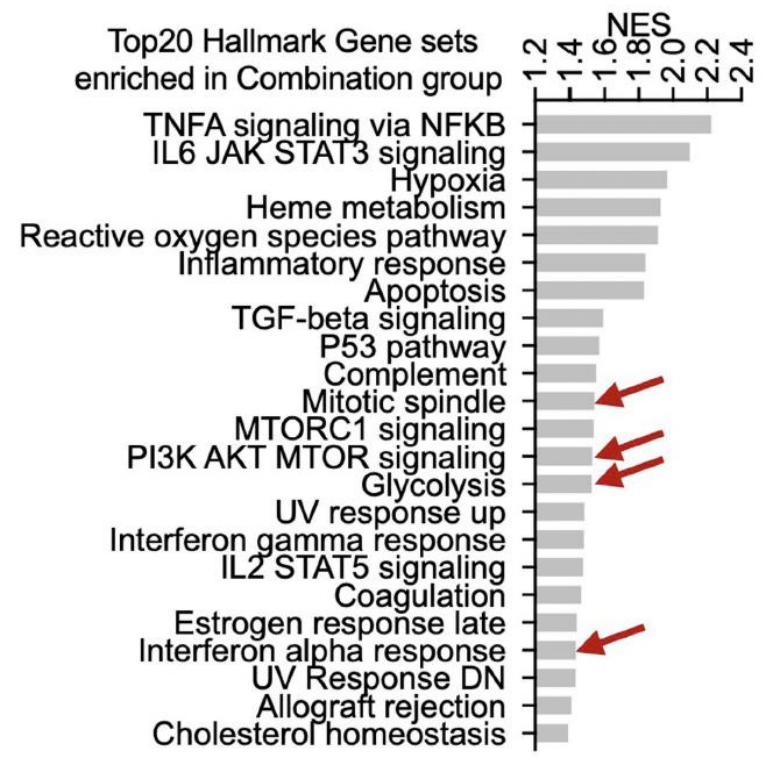
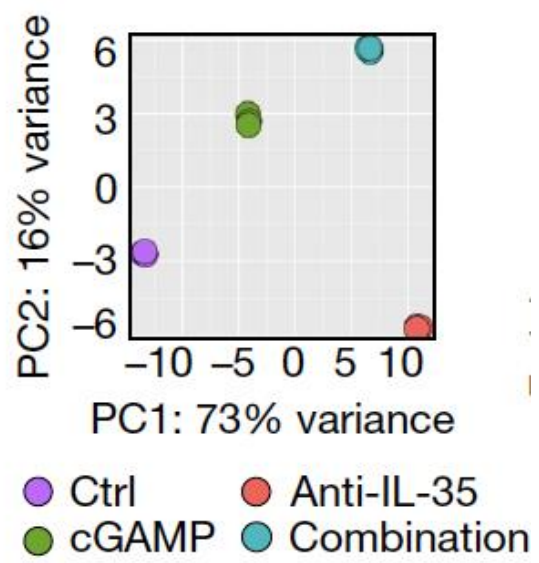
# IL-35<sup>+</sup> B Cells Subdue NK cell responses



# ➤ IL-35<sup>+</sup> B Cells Subdue NK cell responses



# IL-35<sup>+</sup> B Cells Subdue NK cell responses

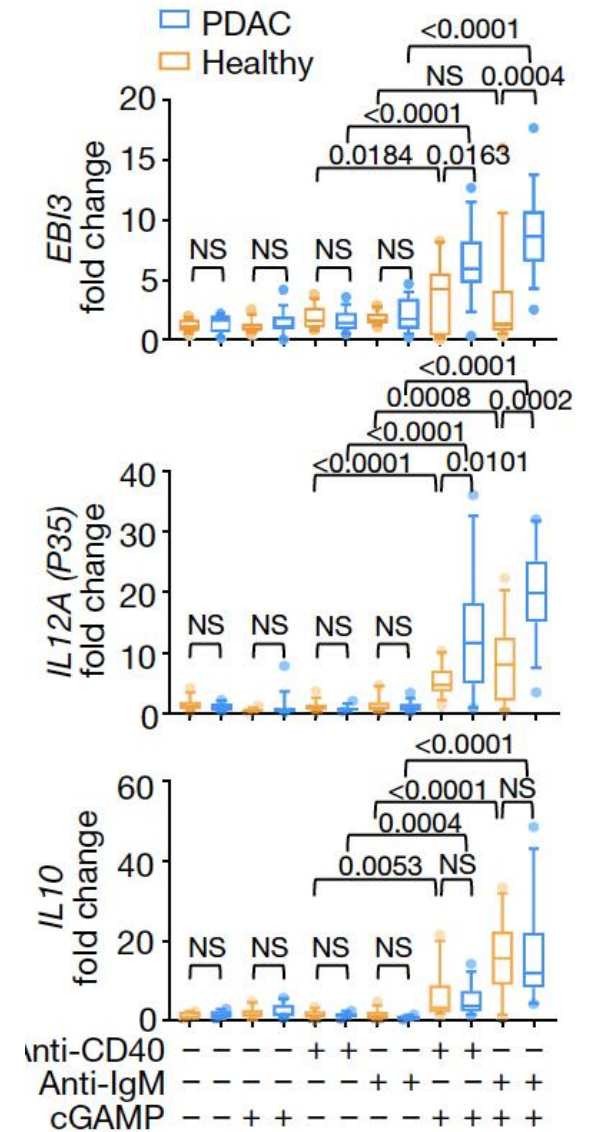
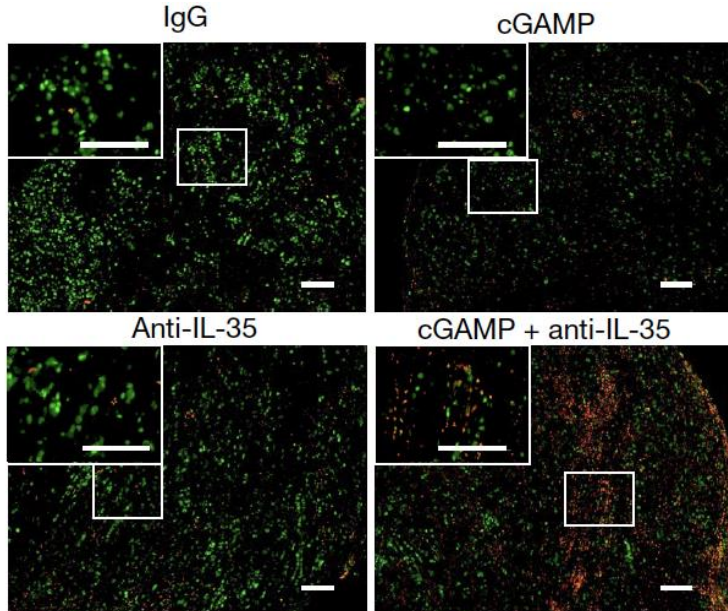
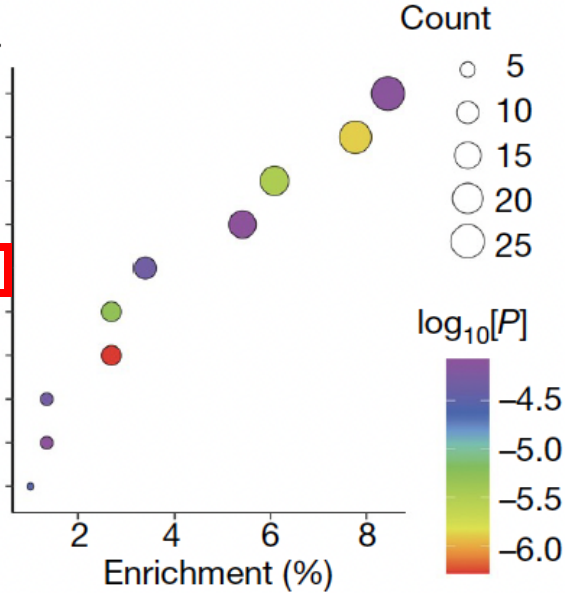


# ➤ IL-35<sup>+</sup> B Cells Subdue NK cell responses

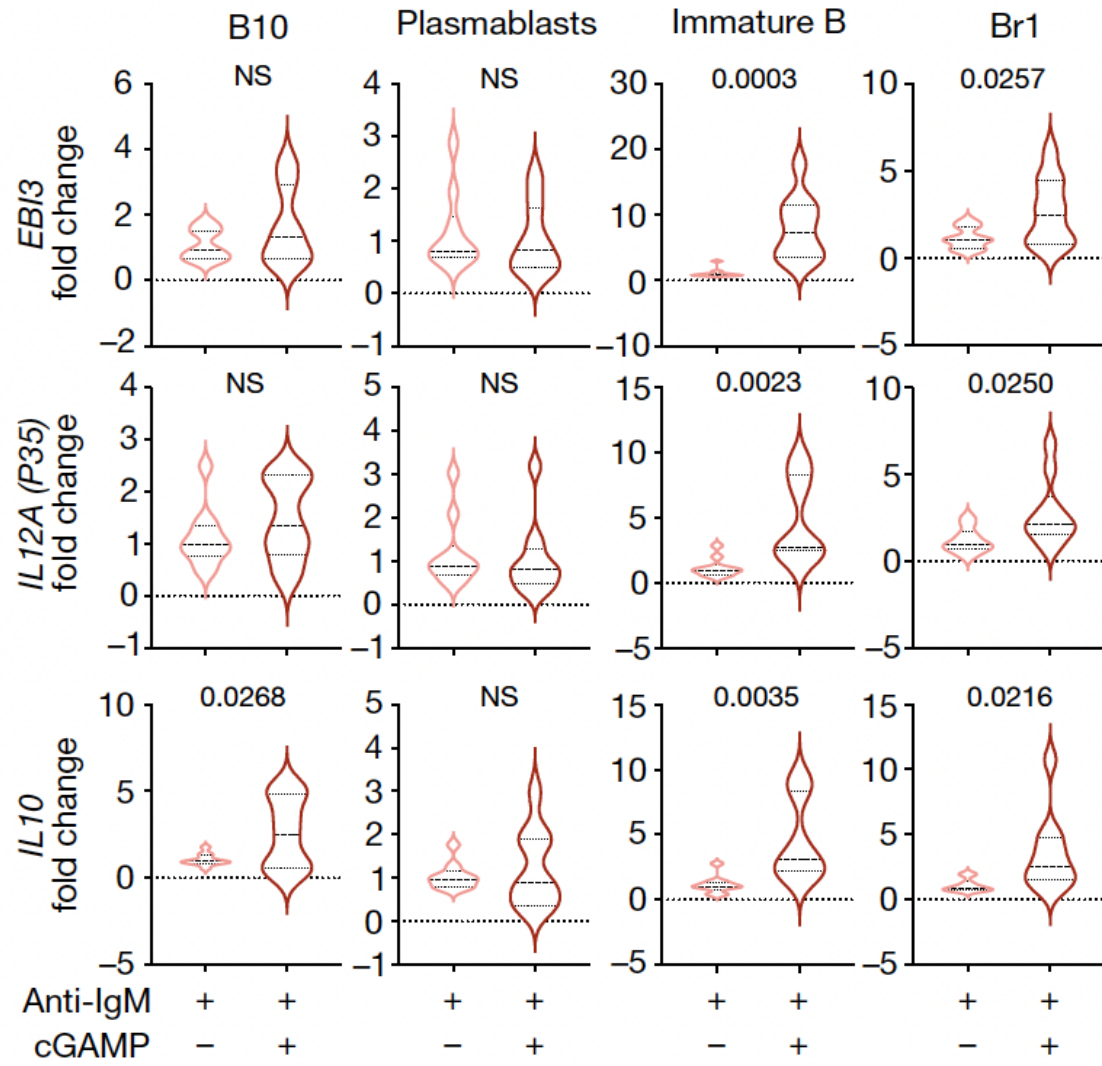
Changes that happens in double treatment only

Top 10 enriched terms

- Regulation of plasma membrane bounded cell projection organization
- Haemostasis
- Regulation of body fluid levels
- Histone modification
- Mitotic cell cycle phase transition**
- Regulation of blood coagulation
- HSP90 chaperone cycle for steroid hormone receptors (SHR) in the presence of ligand
- Protein refolding
- Postsynaptic actin cytoskeleton organization
- Glucocorticoid receptor signalling pathway



# ➤ IL-35<sup>+</sup> B Cells Subdue NK cell responses



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