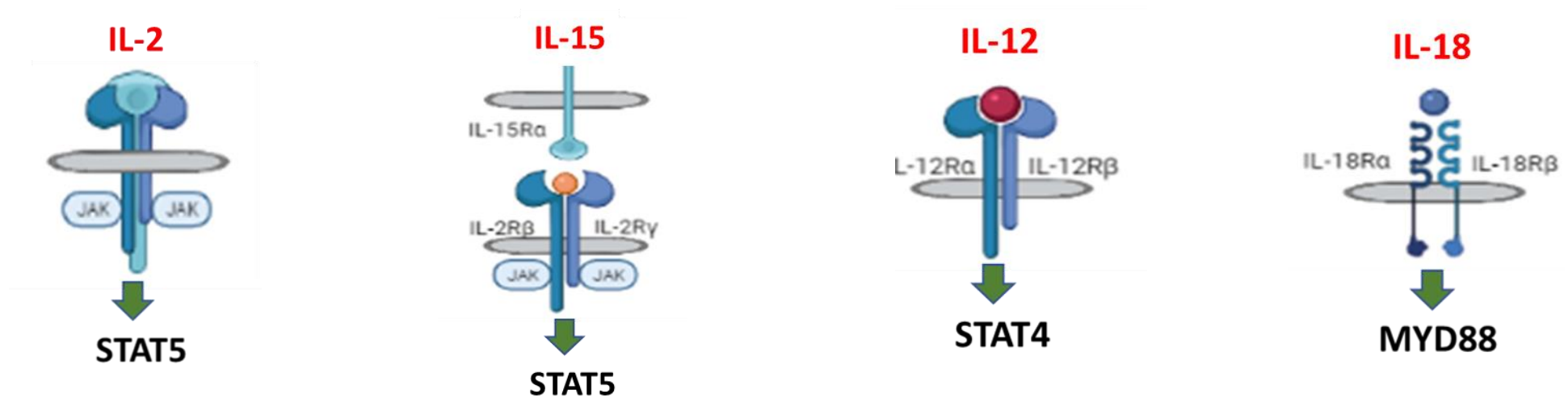




**COM503 - Differentiated approach to harness
cytokine biology for cancer therapeutics**

Cytokines powerful potential limited by therapeutic window



- Short half life
- Pleiotropy
- Vascular leak syndrome
- Cardiotoxicity

- Short half life

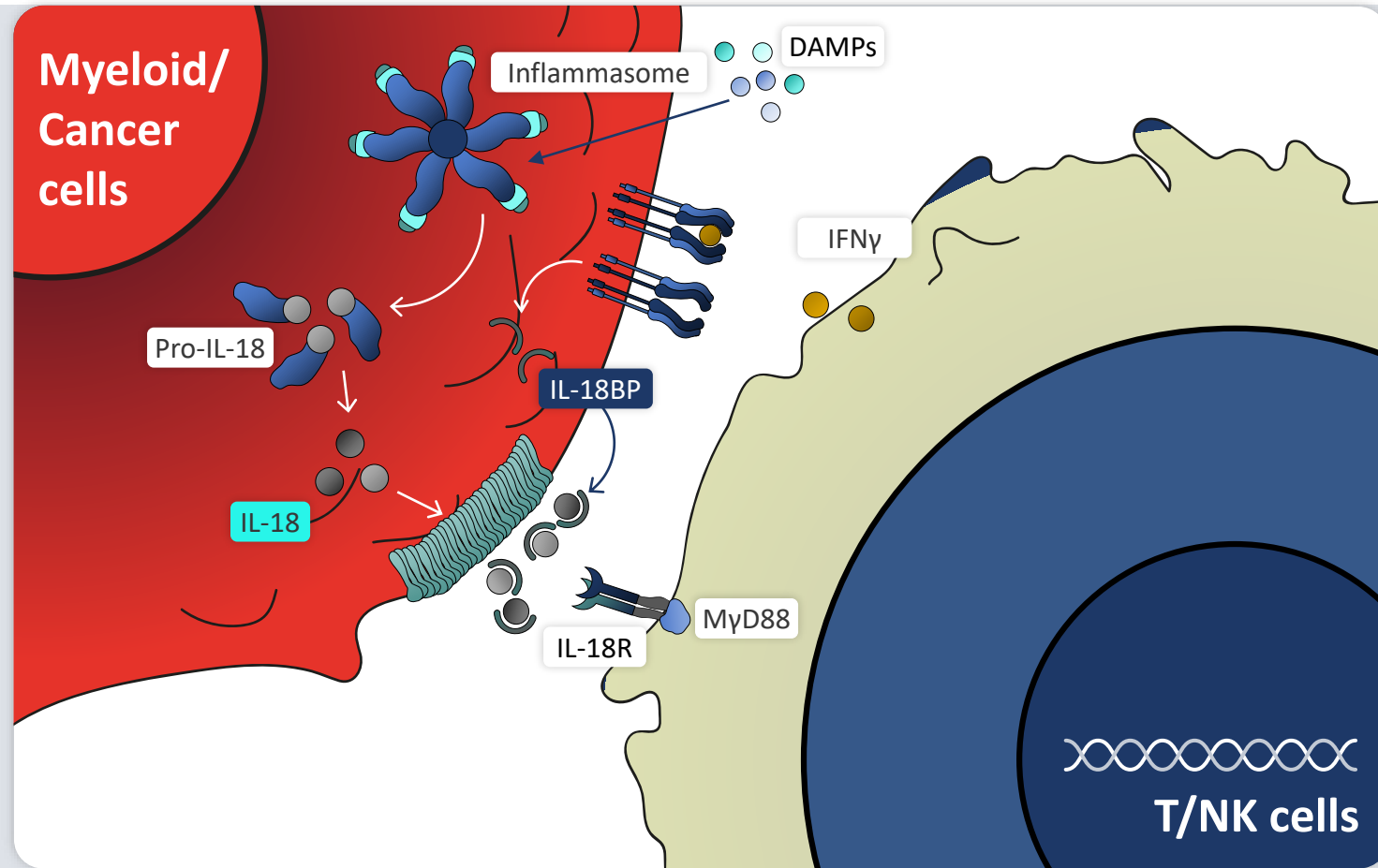
- Short half-life
- Systemic inflammation
- Myelotoxicity
- Hepatotoxicity

- High affinity binding protein
- Short half-life

Pleiotropy, toxicity, short half life severely limit the therapeutic use of cytokines

Compugen identified a potential dominant immunosuppression mechanism

Interleukin-18 binding protein, a natural inhibitor of interleukin-18



IL-18 is an effector cytokine, highly upregulated in tumor microenvironment

IL-18BP blocks IL-18 immune stimulatory activity via a negative feedback mechanism

COM503 A fully human, high affinity anti-IL18BP antibody restores human TIL and NK cell activity

Antibody characteristics



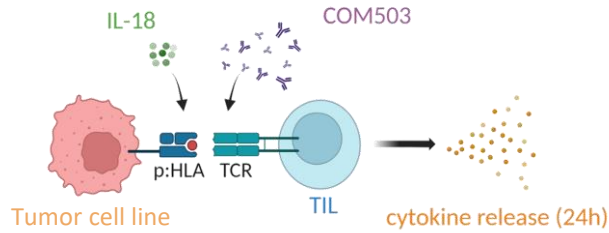
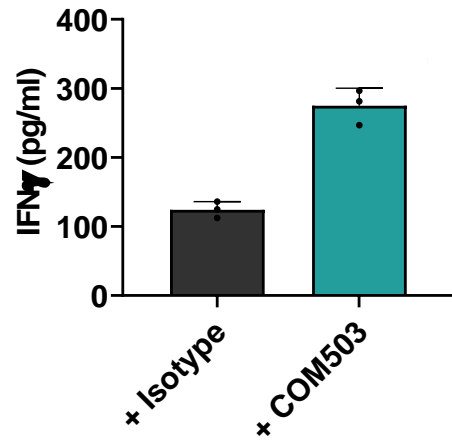
Humanized IgG4 antibody

High affinity (<1pM KD)

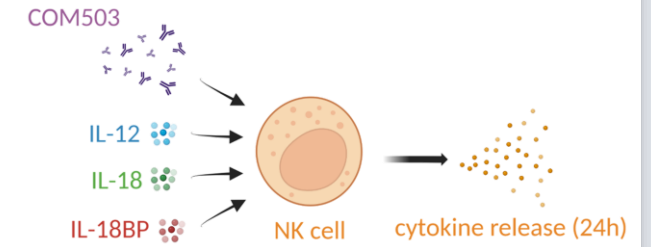
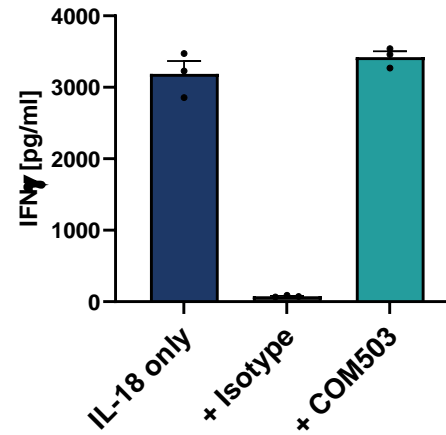
Release IL-18 from pre-formed IL-18:IL-18BP complex

Enhances T and NK cell activation

COM503 restores TILs activity

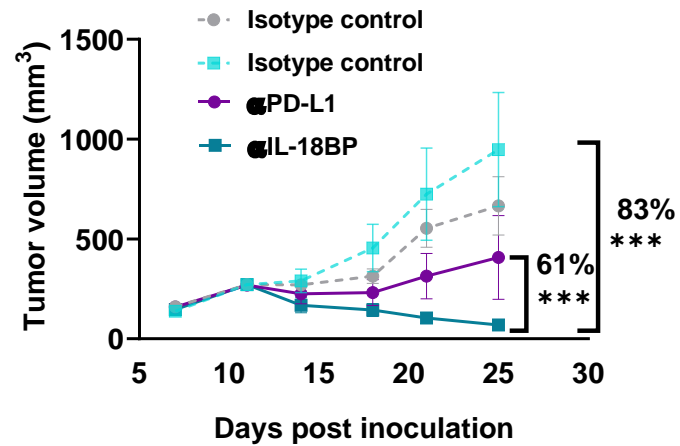


COM503 restores NK cell activity

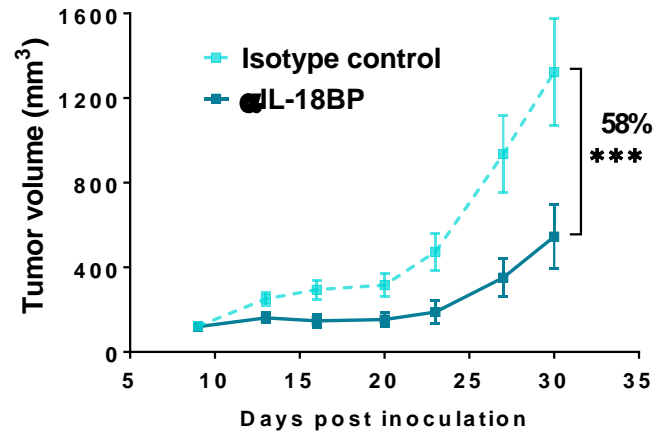


Anti-IL-18BP antibody demonstrates monotherapy activity across murine syngeneic tumor models

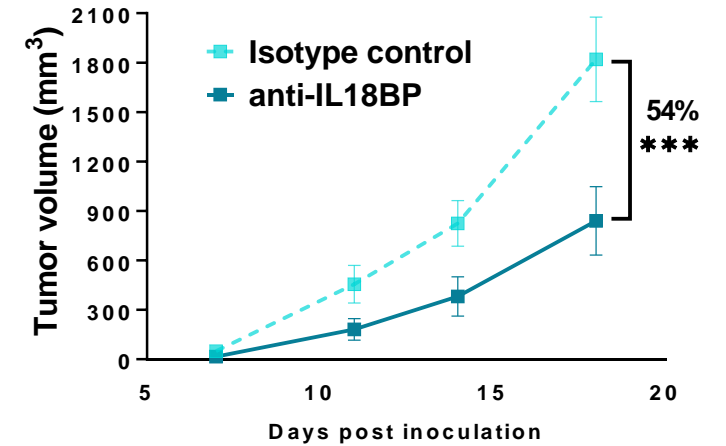
α IL-18BP Ab inhibits tumor growth in E0771 orthotopic mouse breast tumor model



α IL-18BP Ab inhibits tumor growth in MC38ova mouse CRC tumor model

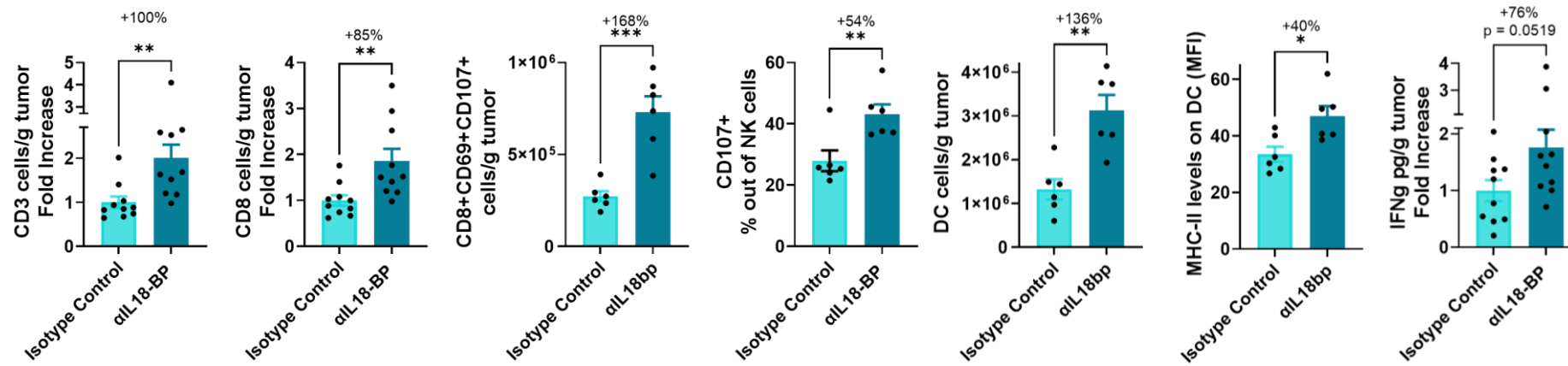


α IL-18BP Ab inhibits tumor growth in B16F10-hmgp100 mouse melanoma model

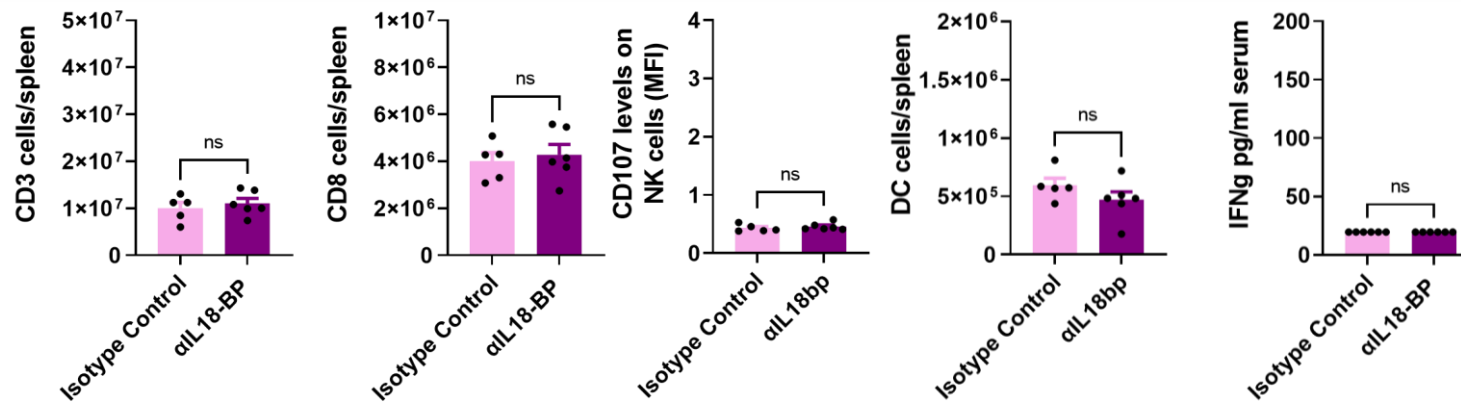


Anti-IL-18BP antibody modulates tumor microenvironment without effecting periphery in murine tumor model

Monotherapy with anti-IL-18BP Ab immune-modulated tumor microenvironment in MC38ova model



Monotherapy with anti-IL-18BP Ab doesn't modulate peripheral immunity



Immune modulation restricted to tumor site in contrast to therapeutic recombinant cytokines given systemically