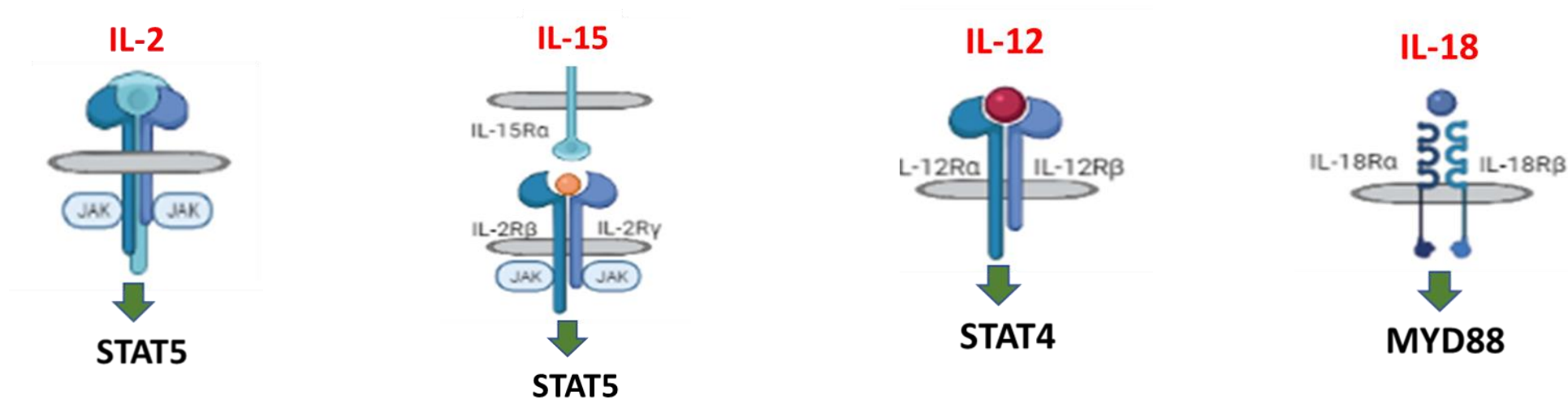




**COM503 - Differentiated approach to harness
cytokine biology for cancer therapeutics**

Cytokines powerful potential limited by therapeutic window



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

- Short half life

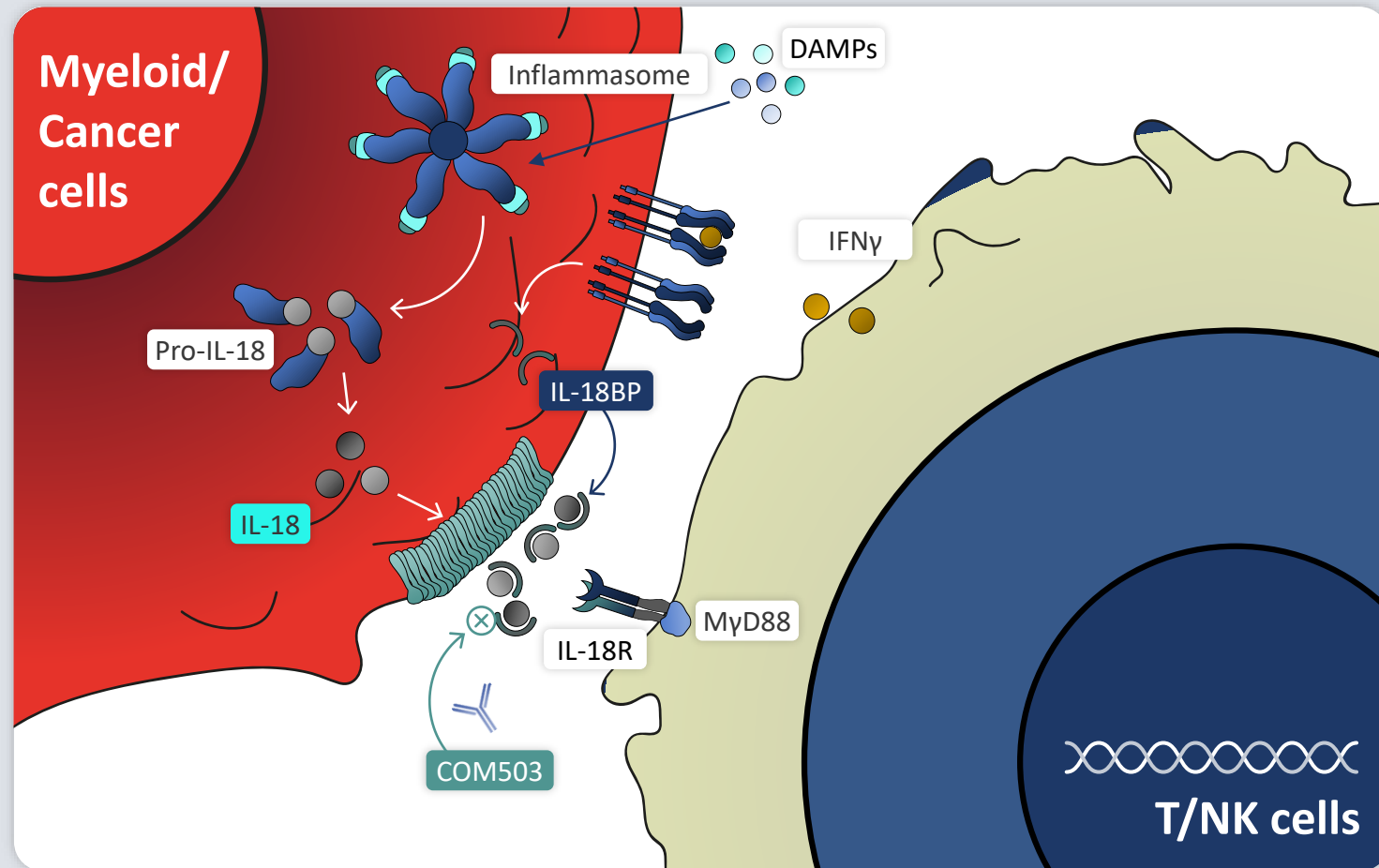
- Short half-life
- Systemic inflammation
- Myelotoxicity
- Hepatotoxicity

- Short half-life
- Bound to IL-18BP inhibiting activity in TME

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

COM503: Compugen identified potential dominant immunosuppression mechanism and antibody therapeutic

Interleukin-18 binding protein, an endogenous inhibitor of interleukin-18









IL-18 immune stimulatory cytokine upregulated in tumor microenvironment

IL-18BP blocks IL-18 activity

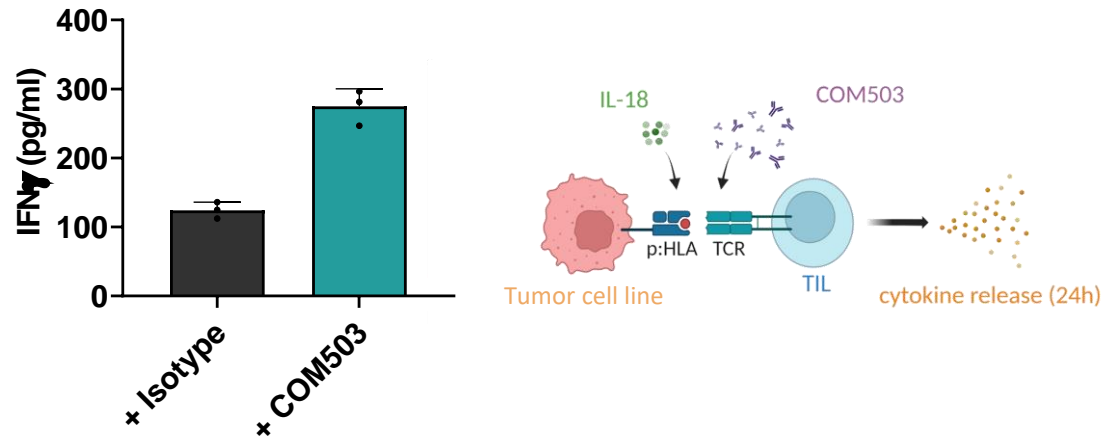
COM503 potential first-in-class high affinity antibody releases IL-18 to enhance T and NK cell activation

COM503: advantages of a differentiated approach

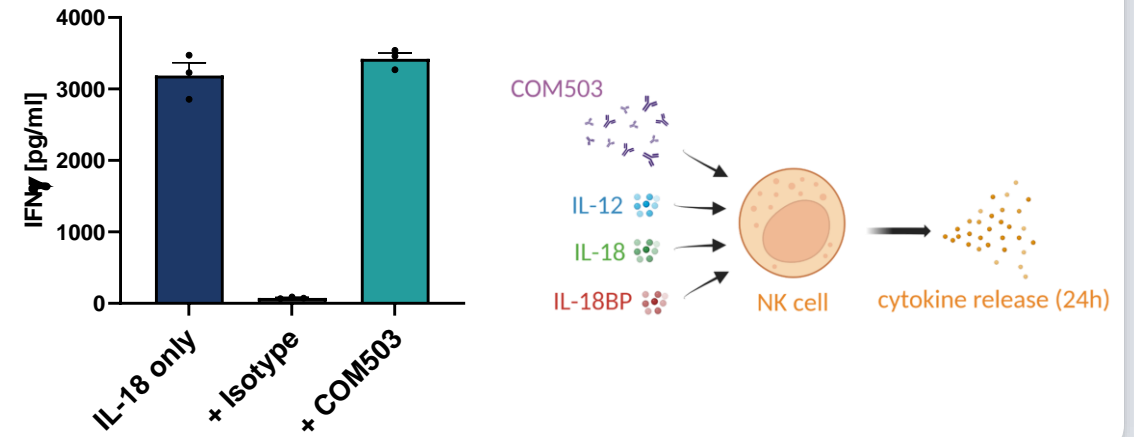
	COM503 anti-IL-18 binding protein	Engineered IL-18
Novelty	Novel antibody approach	Conventional cytokine approaches limited success to date, no FDA approval in last 30 years
	Anti-IL-18BP releases endogenous IL-18 in the TME	IL-18 mutated recombinant protein
Pharmacokinetics	 Slow elimination	 Requires modification/engineering to overcome pharmacokinetic limitations
Immunogenicity	 Low risk, human IgG antibody	 Increased risk, modified/engineered recombinant cytokine
Therapeutic window	 Immune modulation selectively targets TME, potential for better tolerance	 Systemic immune modulation, potential for unmanageable side effects

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

COM503 restores TILs activity

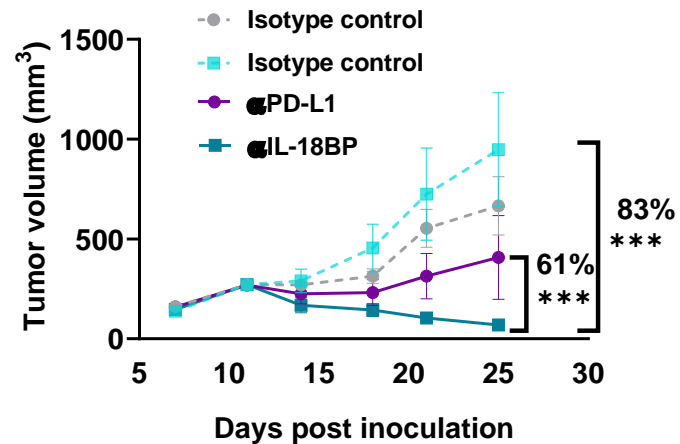


COM503 restores NK cell activity

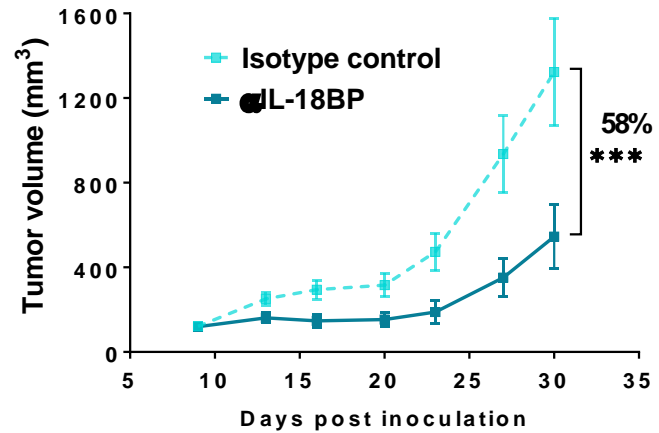


Anti-IL-18BP antibody demonstrates monotherapy activity across murine syngeneic tumor models

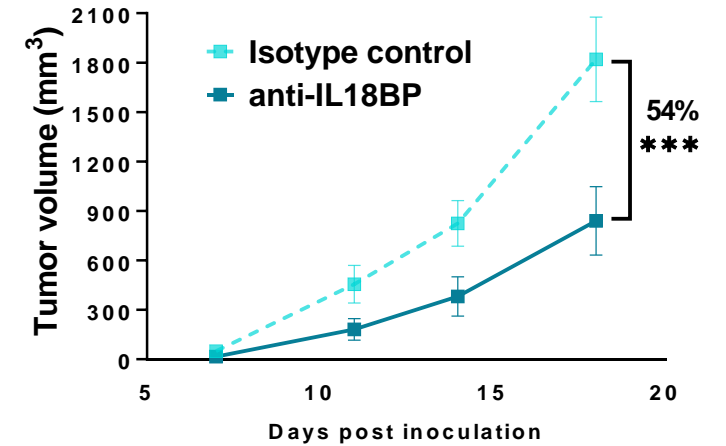
α IL-18BP Ab inhibits tumor growth in E0771 orthotopic mouse breast tumor model



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

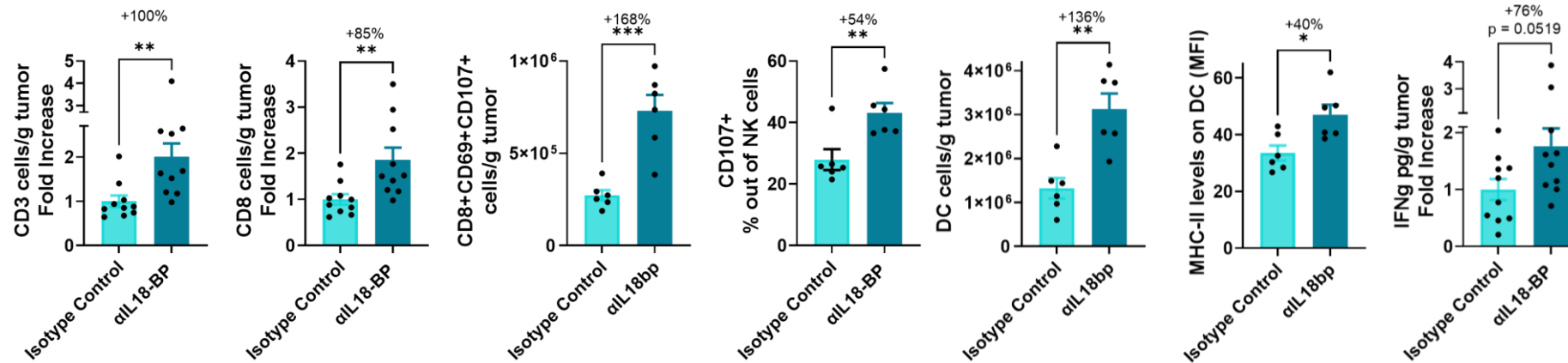


α IL-18BP Ab inhibits tumor growth in B16F10-hmgp100 mouse melanoma model

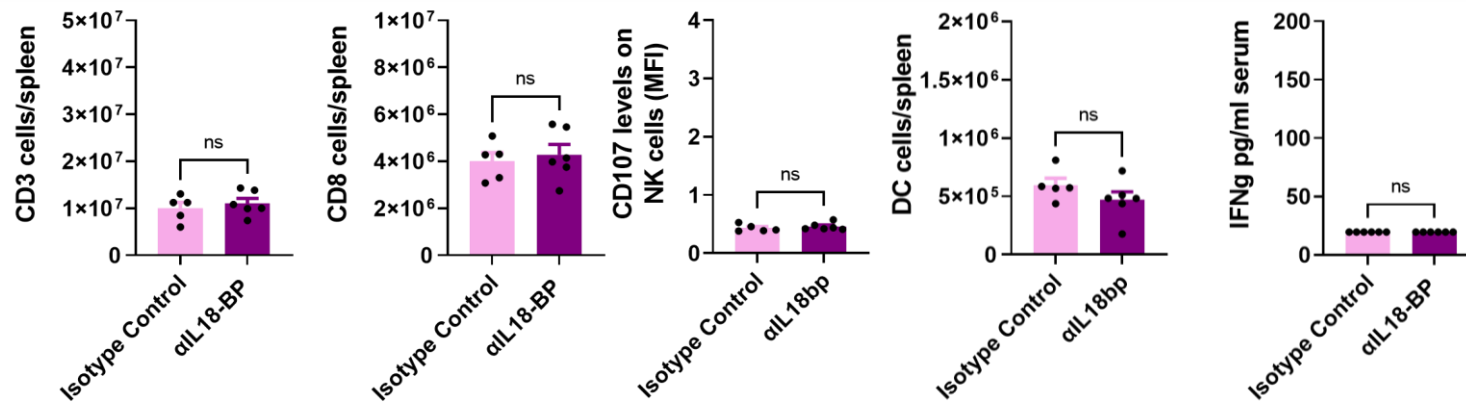


Anti-IL-18BP antibody modulates tumor microenvironment without affecting the periphery in murine tumor model

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 differentiated from therapeutic recombinant cytokines given systemically