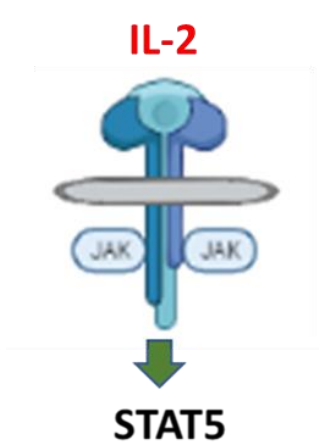
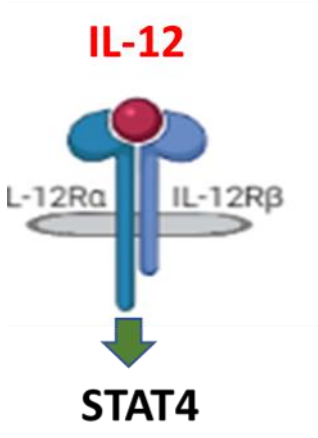
COM503 - Differentiated approach to harness cytokine biology for cancer therapeutics

Cytokines powerful potential limited by therapeutic window

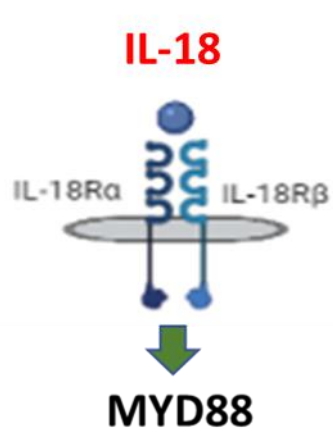


- Short half life
- Pleiotropy
- Vascular leak syndrome
- Cardiotoxicity

- Short half life



- Short half-life
- Systemic inflammation
- Myelotoxicity
- Hepatoxicity



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

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

Propper D J. et al, 2022

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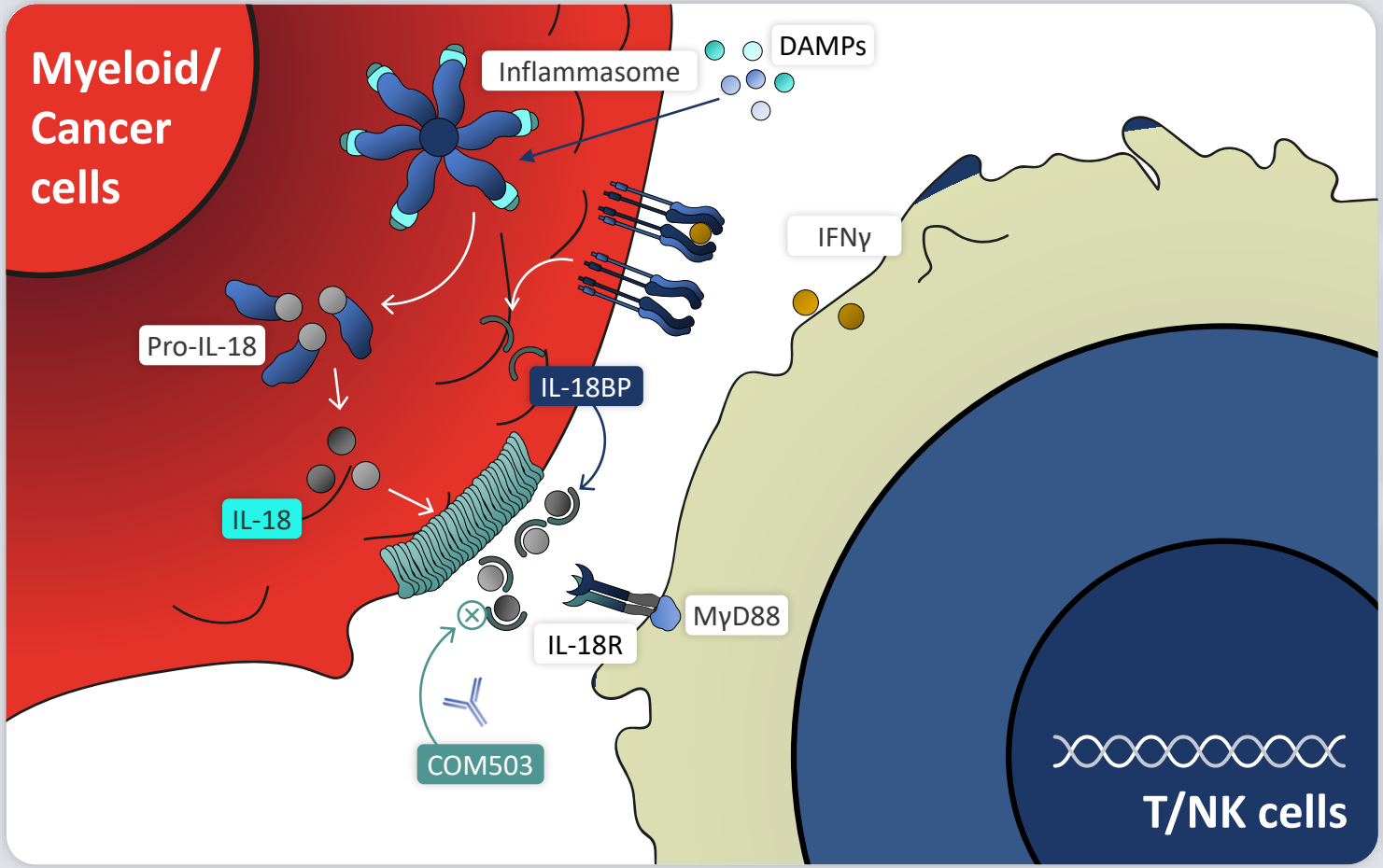
COM503: Compugen identified potential dominant immunosuppression mechanism and antibody therapeutic

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

DAMPs- Damage-associated molecular patterns

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COM503: advantages of a differentiated approach

	COM503 anti-IL-18 binding protein	Recombinant cytokines
Novelty	Novel antibody approach	Multiple challenges, no FDA approval in last 30 years
	Anti-IL-18BP releases endogenous IL-18 in the TME	Systemic administration of a recombinant protein
Pharmacokinetics	✓ Slow elimination	✗ Requires modification/engineering to overcome pharmacokinetic limitations
Immunogenicity	✓ Potentially low risk, human IgG antibody	✗ Modified/engineered recombinant cytokine, increases risk
Therapeutic window	✓ Immune modulation selectively targets TME, potential for better tolerance	✗ Systemic immune modulation, potential for unmanageable side effects

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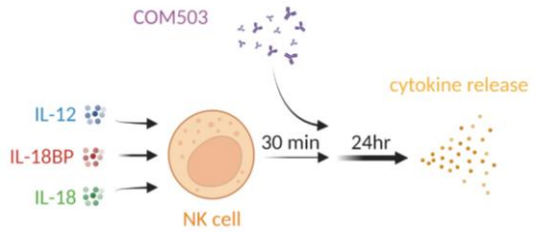
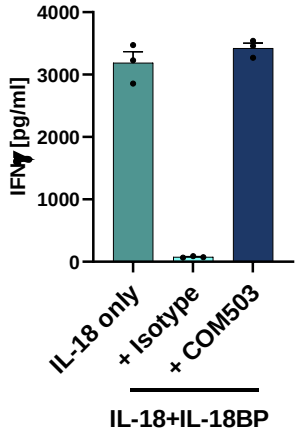
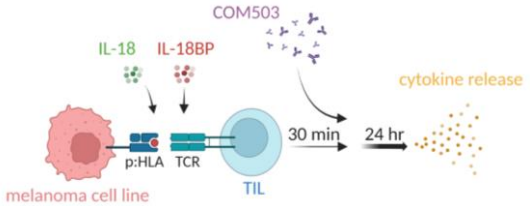
COM503, fully human, high affinity anti-IL-18BP antibody restores human TIL and NK cell activity in human assays

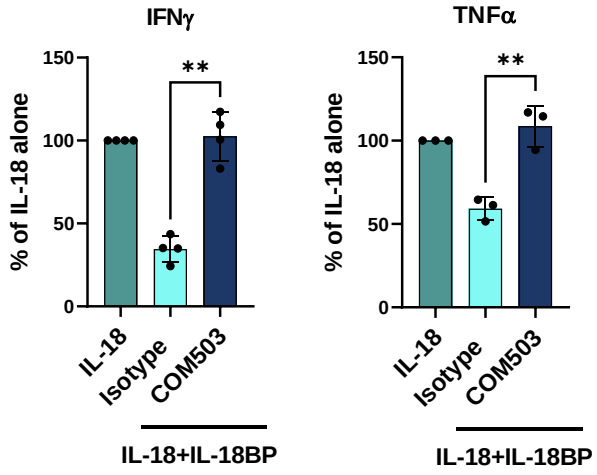
COM503 restored NK cell activity



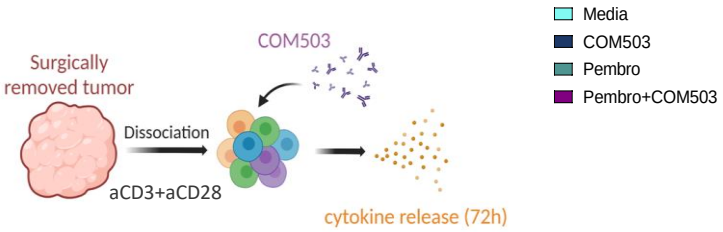


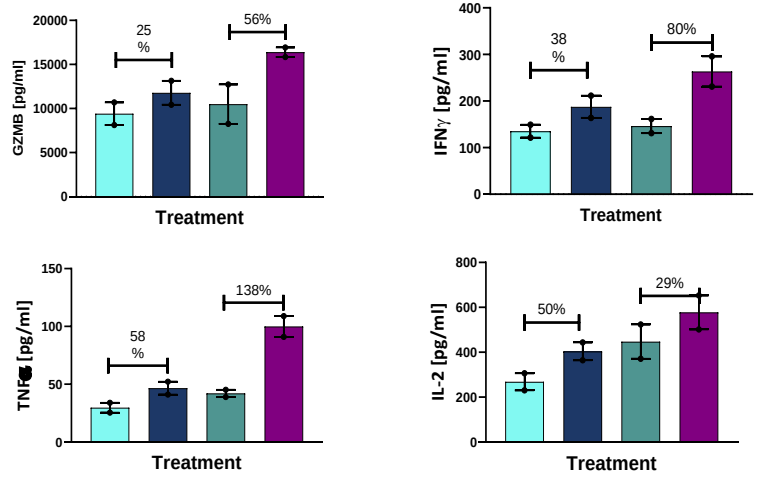
COM503 restored TILs activity





COM503 enhanced T cell activation in human dissociated tumor cells assay





TILs- tumor infiltrating lymphocytes
Ferre P, presentation, SITC, 2023, modified

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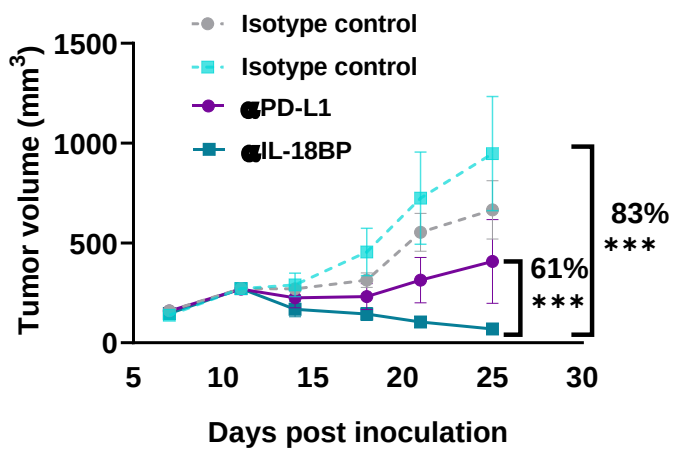
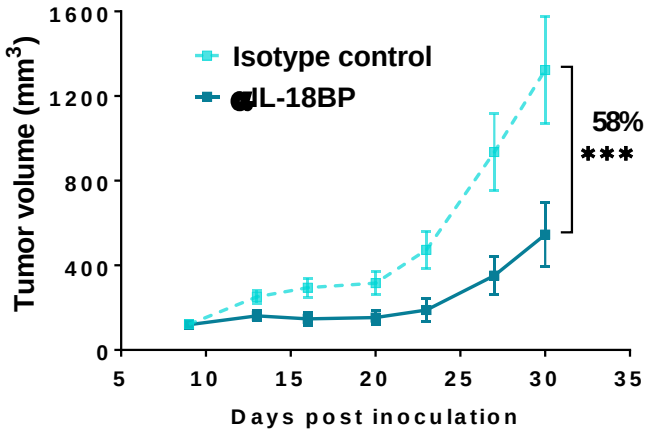
Anti-mouse IL-18BP antibody demonstrates monotherapy activity across murine syngeneic tumor models

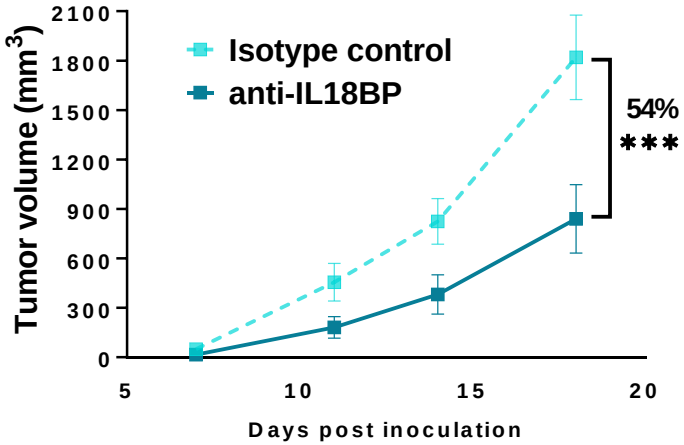
αIL-18BP Ab inhibits tumor growth in E0771 orthotopic mouse breast tumor model



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



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



Ophir E, presentation, CIMT 2023, modified

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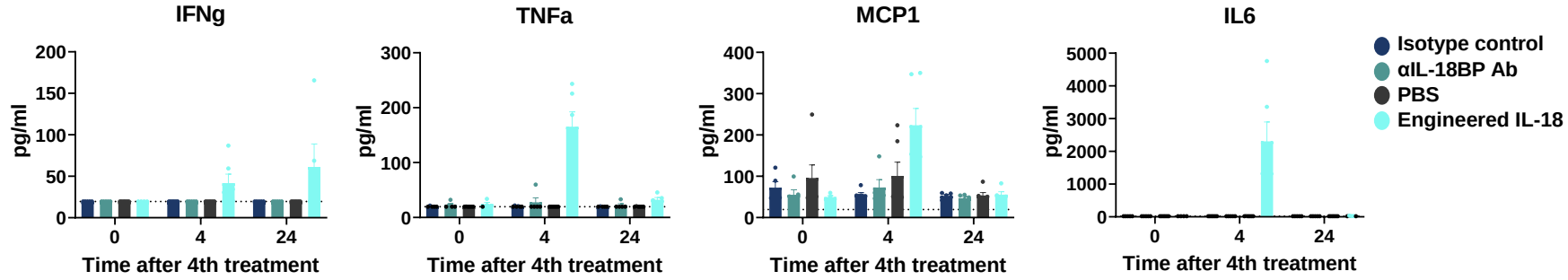
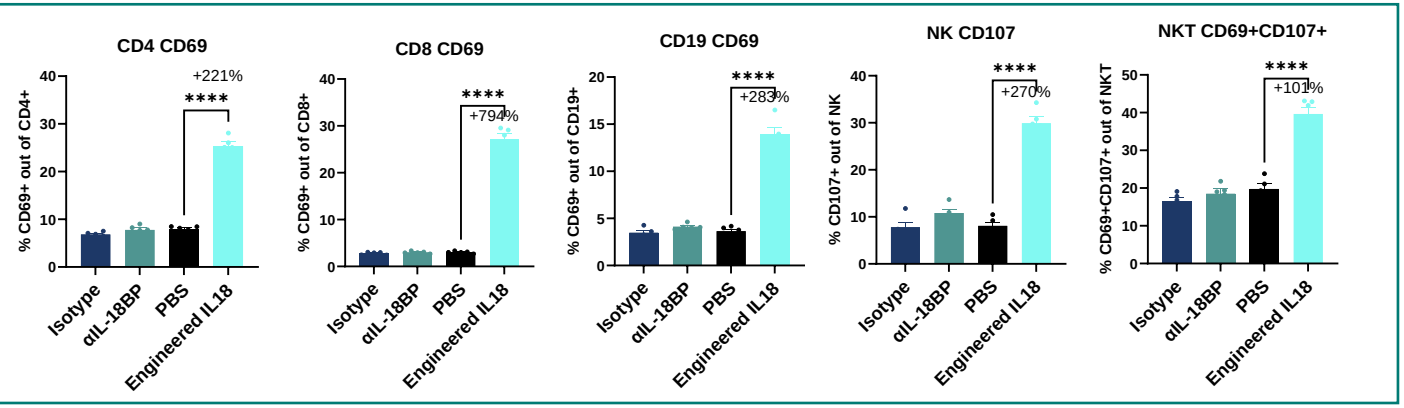
Anti-IL18BP Ab is expected to have a better therapeutic window than recombinant cytokines

Administration of anti-mouse IL-18BP Ab to mice did not affect serum cytokines in contrast to engineered mouse IL-18*

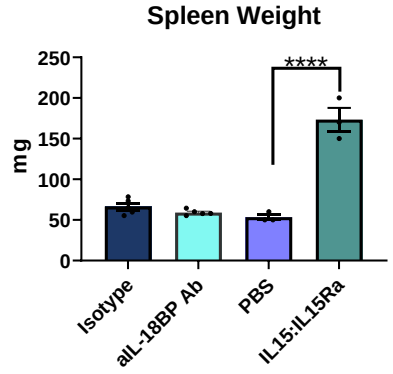


*Engineered IL-18 does not bind to IL18BP but retains its binding to IL-18R

Administration of anti-mouse IL-18BP Ab to mice did not affect lymphocytes activation in contrast to engineered mouse IL-18



Administration anti-mouse IL-18BP Ab to mice did not result in splenomegaly in contrast to rIL-15:IL15Ra



Ferre P presentation, SITC 2023, modified

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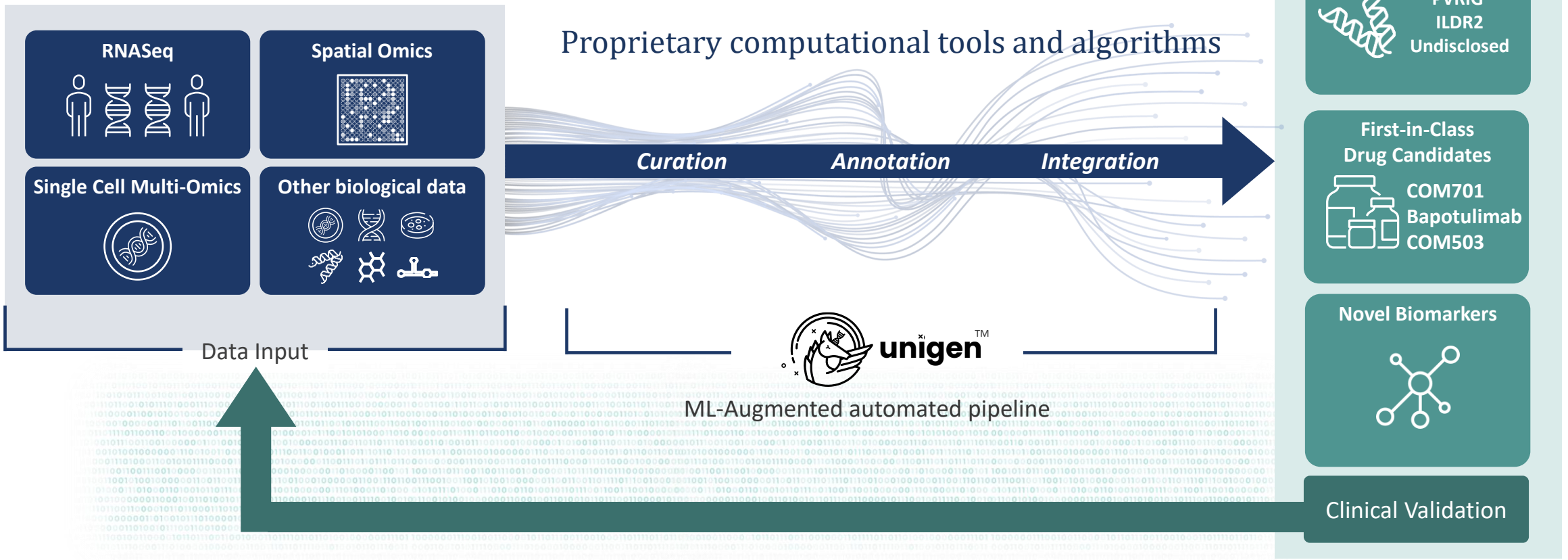

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