BIOMUNEX pharmaceuticals

Disruptive biological approaches in immunotherapy, based on next generation BiXAb® bi- and multi-specific antibody platform for cancer treatment

Corporate deck for Galien start-up prize:
Deck4: Innovation
May 2023

Comparison of T-cell redirection modalities: the MAIT engager approach could provide a clear superiority to other T cell engagers

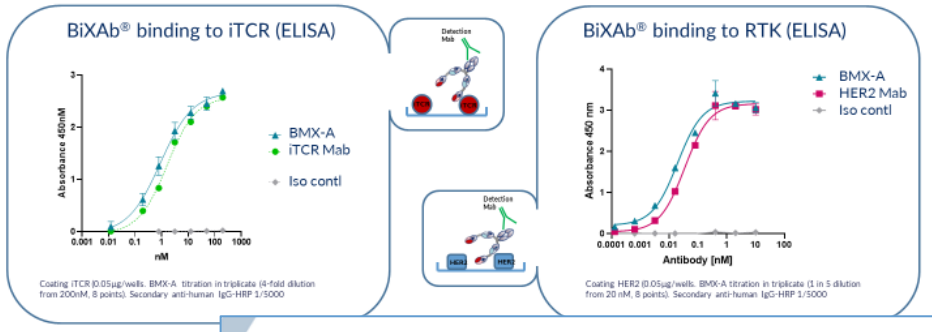
Feature	MAITs	α/β T-cells	γ/9δ2 T cells
Treg activation	No	Activate Tregs	γ9δ2 can potentially differentiate into Tregs (in response to TGFβ and IL-15).
Cytokine release	Limited	Widespread	Limited
Resistant to chemo-therapy (MDR gene)	Resistant	Not resistant	Not resistant
TCE activation	Restricted to MAITs	Activate all T cells	Restricted to γ/δ T cells
Subsets	Very limited subsets	Variety of subsets	limited subsets (but could be Treg)
Tissue resident	Naturally resident in barrier tissues (and others)	Traffic through tissues and resident	γ9δ2 are not naturally tissue resident
Abundance	Up to 20% of circulating T cells	Majority of T cells	<3% of circulating T cells
Cytotoxic function	Strong cytotoxic activity	Strong cytotoxic activity	Strong cytotoxic activity
TCR repertoire	Very limited: semi-invariant	Vast	Limited
Global Landscape	First-of-its-kind BsAb to MAIT cell engagers BIOMUNEX pharmaceuticals	Crowded space, with unsolved problems	Several examples: Lava Therapeutics, (Nasdaq), Adaptate, Maverick Ther., Gamma-Delta Ther. (acquired by Takeda)

Growing evidence strongly suggests that MAIT cell redirection would significantly impact solid tumors

The BiXAb® is able to effectively bind both targets

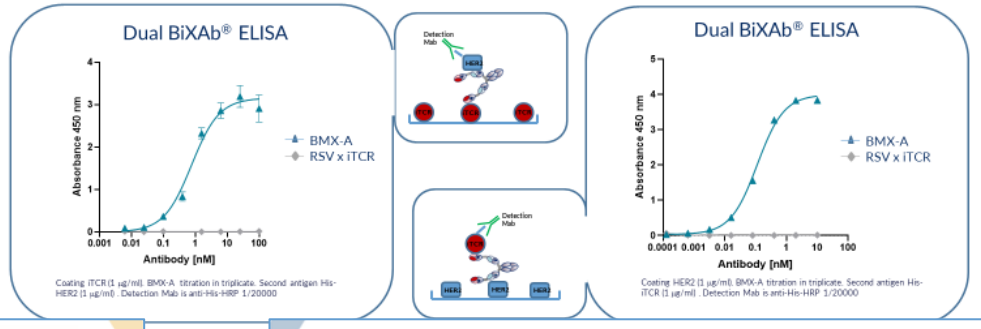
The BiXAb® is able to effectively bind the two recombinant proteins

- Binding of BiXAb® to target proteins, measured by ELISA.



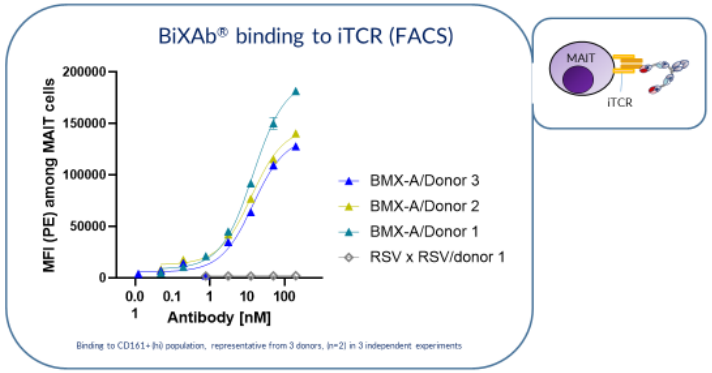
The BiXAb® can bind both targets simultaneously (ELISA)

- Dual ELISA shows (in both coating orientations) that the BiXAb® is able to bind both target proteins simultaneously.



The BiXAb® is able to bind the iTCR on MAIT cells

- BiXAb® binding to MAIT cells, by FACS



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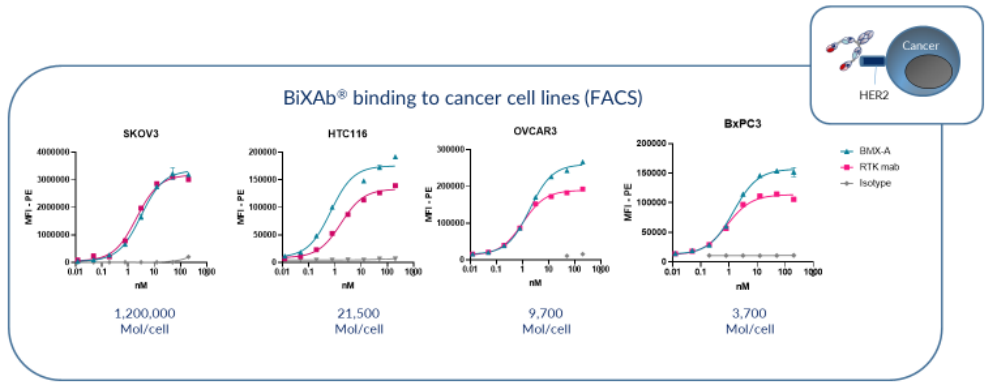
The BiXAb® binds to the RTK on cancer cells lines as effectively as the parental Mab

- The BiXAb® binds to Cancer cell lines over a wide expression range of HER2 expression



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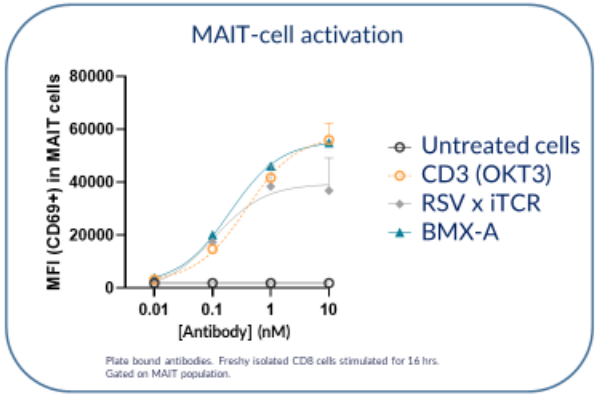
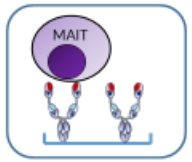
The BiXAb® activates MAIT cells

The BiXAb® can activate MAIT cells similarly to OKT3 (CD3 agonist)

- BiXAb® induced MAIT cell activation (Plate bound).
- Similar level of activation seen between iTCR (BMX-A) and epsilon chain binding (OKT3) on MAIT cells





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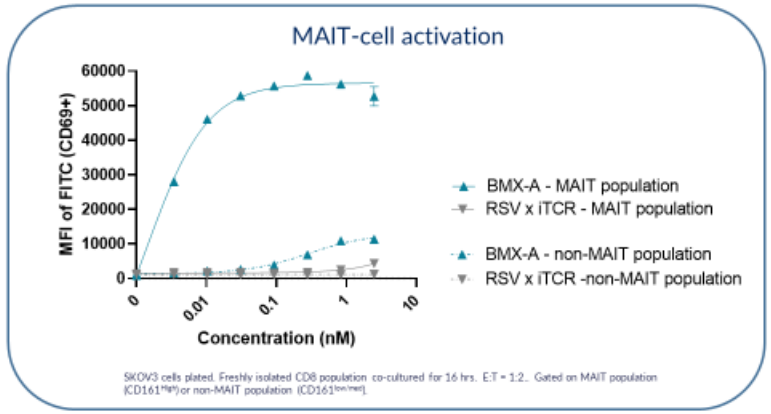
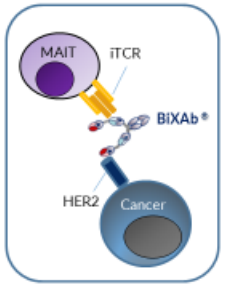
The BiXAb® activates only CD8+ MAIT cells and not other CD8 cells when co-cultured with cancer cells expressing HER2

- In a population of CD8 cells, only the MAIT cells are activated in the presence of the BiXAb® and cancer cells expressing HER2.
- The BiXAb® does not activate non-MAIT CD8 T-cells.





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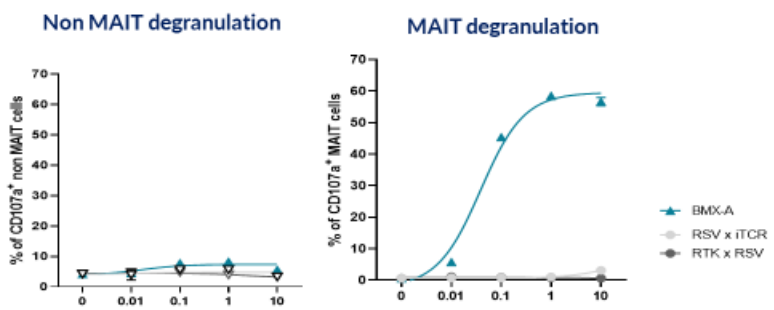
The BiXAb® is able to induce MAIT cell degranulation upon binding and MAIT-cell proliferation

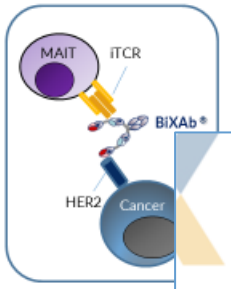
The BiXAb® induces MAIT cell degranulation upon binding and to cancer cells

- BiXAb® mediated degranulation is specific to the MAIT-cell population

Measurement of degranulation (CD107a)



Freshly prepared CD8 population.HCT-116 cancer cell line co-cultured with CD8s and BiXAb® s for 5h days. E:T ratio = 1:2. FACs read out gaited on MAIT ($CD161^{High}$) or non MAIT ($CD161^{low/med}$) population.



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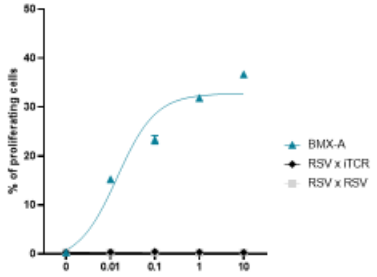
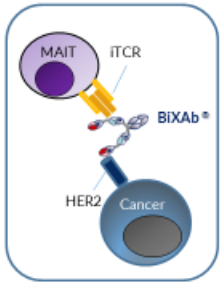
The BiXAb® can induce MAIT cell proliferation when co-cultured with cancer cells expressing HER2

- BiXAb® engagement of MAITs and target cancer cells induces MAIT-cell proliferation (measured by FACs on CD161 high population).

MAIT cell proliferation (FACS)



Freshly prepared CD8 population.SKOV3 cancer cell line co-cultured with CD8s and BiXAb® s for 5 days. E:T ratio = 1:1. FACs read out gaited on MAIT population.



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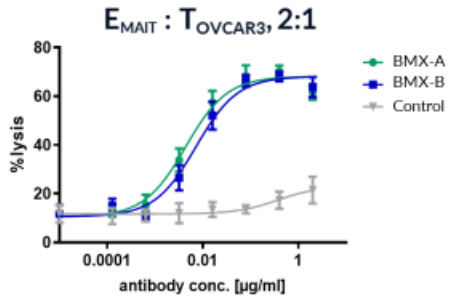
The BiXAb® is able to kill cancer cells expressing TAA (HER2) thanks to MAIT cell redirection

The BiXAb® can redirect MAIT cells to directly kill cancer cells (BMX 501 : HER2 x iTCR MAIT engager)

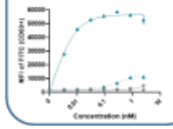
- BiXAb® induced MAIT redirection and killing of cancer cells
- **Ca 70% killing in 18 hrs**

BiXAb ® -mediated MAIT-cell redirected killing of OVCAR3 cancer cells

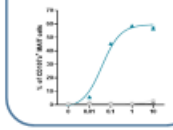


Freshly prepared CD8 population. OVCAR3 cancer cell line co-cultured with CD8s and BiXAb® s for 18 hrs. Cell lysis measured by Chromium release assay (data in triplicate). Combined data from 3 independent experiments and donors.

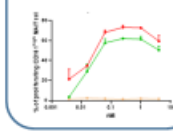
MAIT activation

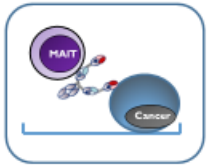


MAIT degranulation



MAIT proliferation





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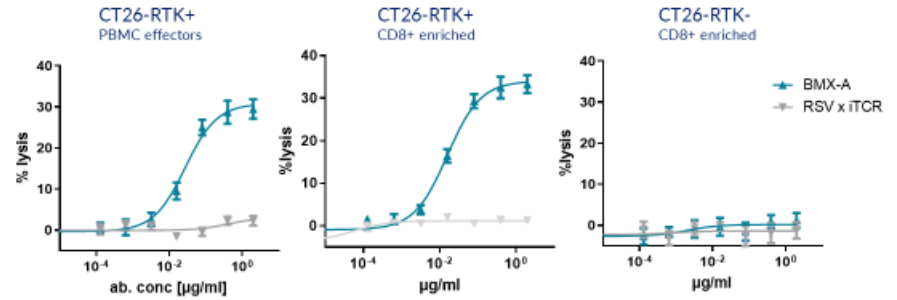
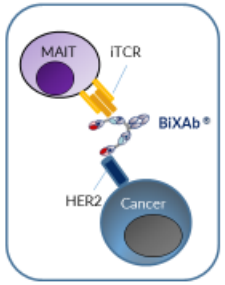
BiXAb® mediated MAIT cell cytotoxicity is specific to cells expressing HER2

- No cytotoxicity observed on cancer cells devoid of the RTK.

BiXAb® -mediated Cytotoxicity assay



Freshly prepared CD8 population or PBMCs. CT-26 cancer cell lines +/- expression of RTK were co-cultured with CD8s or PBMCs and BiXAb® s at an E:T ratio of 10:1 or 2:1 respectively for 18 hrs at. Cell lysis measured by Chromium release assay. Assays run in triplicate



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The BiXAb® specifically activate MAIT cells to kill cancer cells and does not induce cytokine release syndrome like other CD3+ TCE do

The BiXAb® specifically activate MAIT cells and NOT other T-cells including Tregs

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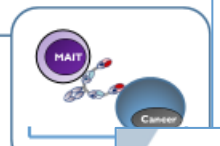
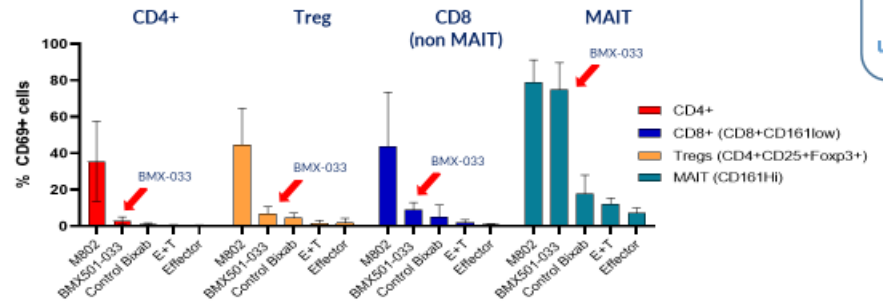
- BiXAb® **does not** activate CD4+ or CD8+ non MAIT subsets
- BiXAb® **does not** activate Tregs
- M802 (clinical TCE) targeting the epsilon chain of the TCR activates all T cell subsets including Tregs



T-cell subset activation: BiXAb vs CD3 engager (M802)



Freshly prepared PBMCs population. OVCAR3 cancer cell line co-cultured with PBMCs and BiXAb® s / comparator molecule at 0.1nM for 18 hrs. T cell activation measure by CD69 by FACS gated on MAIT population (CD161Hi), CD8+non MAIT (CD161Low/med), CD4+ T cells, Tregs (CD4+CD25+FoxP3+). Mean of 4 donors, M802: clinical PhI/II CD3 x HER2 drug

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Dramatic reduction in cytokine response of a MAIT engager compared to a classical TCE

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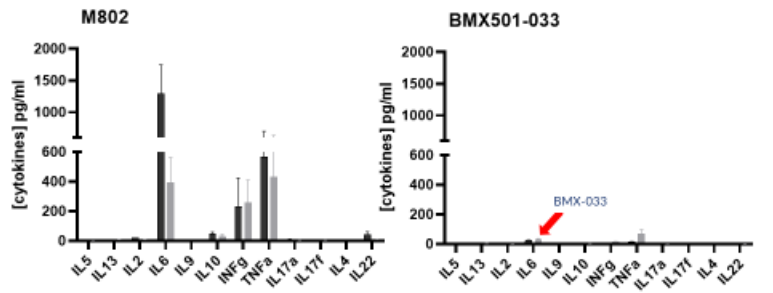
- Cytokine profile and magnitude from MAIT-cell or T-cell redirection in a PMBC mixture demonstrates **dramatically reduced cytokine production** with the MAIT engager

Quantitation of cytokines released by PBMCs redirection



Freshly prepared PBMCs population. OVCAR3 cancer cell line co-cultured with effector cells and BiXAb® s (1 nM) at E:T ratio of 5:1 for 43 hrs. Cytokines measured by LegendPlex TH kit (data in duplicate). Two donors shown, M802: clinical PhI/II CD3 x HER2 drug

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Preliminary conclusions: BiXAb-MAIT engagers can become a game-changer in cancer immunotherapy

BiXAb-MAIT engagers will change the paradigm of immunotherapy treatment and dramatically improve overall survival, safety and quality of life of cancer patients:

- **increased efficacy on solid tumors**, with as a consequence and **expected improvement on overall survival**
- significantly **improved therapeutic window** in the **treatment of solid tumors**
- safer therapy with **reduced side effects** compared to other therapies, including immunotherapies, with **potential concomitant use of chemotherapeutic agents**
- **simple treatment administration**
- **improved quality of life** of cancer patients and families

Biomunex' innovative immunotherapy may profoundly change clinical practice, providing oncologists and patients with therapeutics that may dramatically improve treatment of advanced and metastatic cancer patients, by majorly increasing efficacy and safety of cancer treatments