UNITED STATES
SECURITIES AND EXCHANGE COMMISSION

Washington, DC 20549

FORM 8-K

CURRENT REPORT

Pursuant to Section 13 or 15(d) of the Securities Exchange Act of 1934

Date of Report (Date of earliest event reported): July 29, 2021

KIROMIC BIOPHARMA, INC.

(Exact name of registrant as specified in its charter)

Delaware	**001-39619**	**46-4762913**
(State or other jurisdiction of incorporation)	(Commission File Number)	(IRS Employer Identification No.)

7707 Fannin, Suite 140
Houston, TX, 77054
(Address of principal executive offices) (Zip Code)

Registrant's telephone number, including area code **(832) 968-4888**

Check the appropriate box below if the Form 8-K filing is intended to simultaneously satisfy the filing obligation of the registrant under any of the following provisions (see General Instruction A.2. below):

[ ] Written communications pursuant to Rule 425 under the Securities Act (17 CFR 230.425)
[ ] Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12)
[ ] Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b))
[ ] Pre-commencement communications pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13e-4(c))

Securities registered pursuant to Section 12(b) of the Act:

Title of Each Class	**Trading Symbol(s)**	**Name of Each Exchange on Which Registered**
Common Stock, $0.001 par value	KRBP	The Nasdaq Stock Market LLC

Indicate by check mark whether the registrant is an emerging growth company as defined in Rule 405 of the Securities Act of 1933 (§230.405 of this chapter) or Rule 12b-2 of the Securities Exchange Act of 1934 (§240.12b-2 of this chapter).

Emerging growth company [X]

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act. [ ]

Item 8.01. Other Events.

On July 29, 2021, Kiromic BioPharma, Inc. (“the Company”) presented slides at the Gamma Delta T-Cell Summit. A copy of the slides is furnished as Exhibit 99.1 to this Current Report on Form 8-K.

Item 9.01 Financial Statements and Exhibit

(d) Exhibits.

The following exhibit is filed with this Current Report on Form 8-K:

Exhibit Number	Description
99.1	Slide Presentation, dated July 29, 2021, of Kiromic BioPharma, Inc.

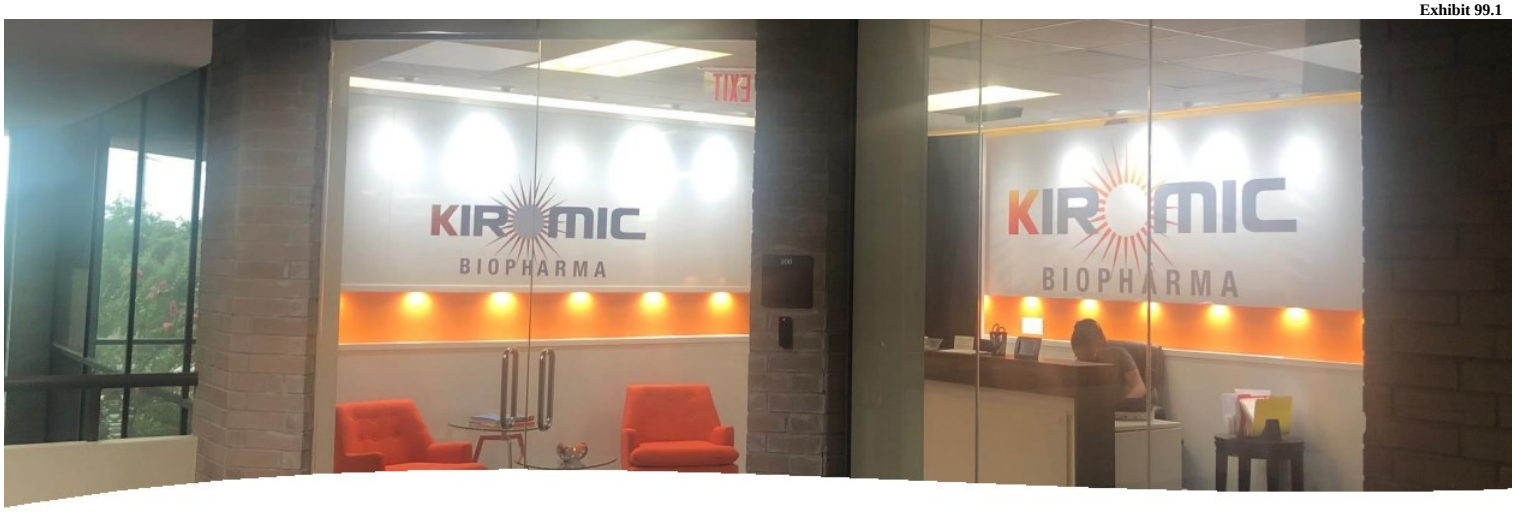
SIGNATURES

Pursuant to the requirements of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned hereunto duly authorized.

Kiromic BioPharma, Inc.

Date: August 4, 2021

By: */s/ Maurizio Chiriva Internati*
Maurizio Chiriva Internati
Chief Executive Officer



Allogenic Off the Shelf CAR T Cell Therapy

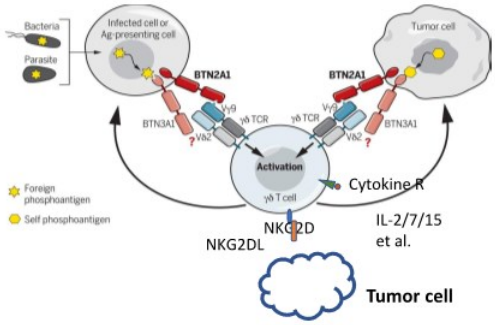
Maurizio Chiriva Internati,DBSc, PhDs
CEO and President, Kiromic BioPharma
Associate Professor,
The University of Texas, MD Anderson Cancer Center
Houston, Texas

mchiriva@kiromic.com

Outline

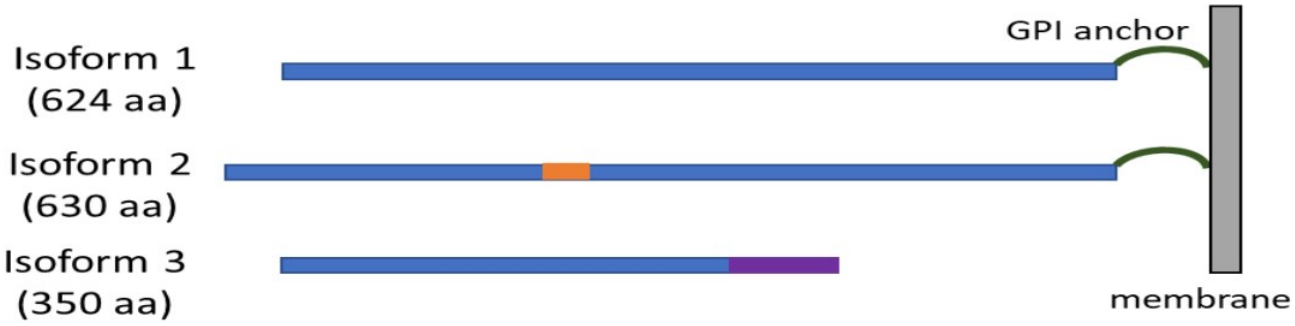
1. **To validate if MSLN isoform 2 (IsoMSLN) is specifically expressed on human tumors.**

2. **To generate CAR-modified γδ-T cells targeting IsoMeso-expressing tumors.**



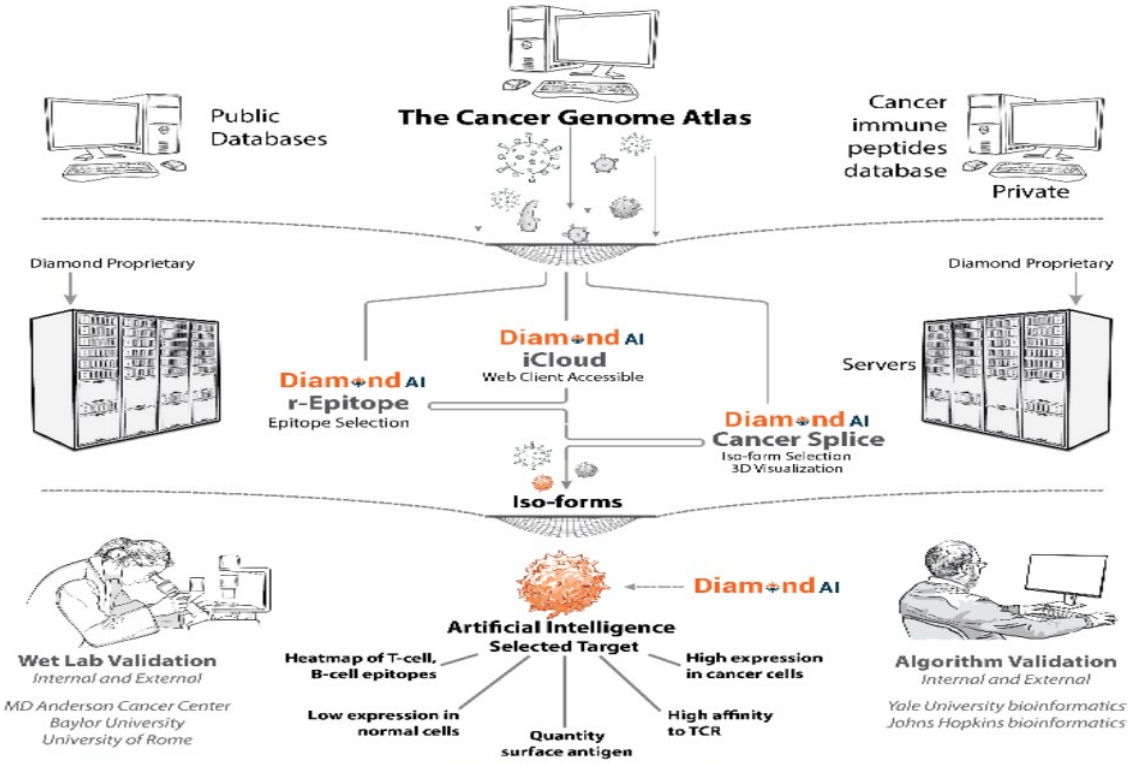
Modified from Science. 2020 Feb 7;367(6478).

- Mesothelin is a GPI-anchored cell surface glycoprotein that is overexpressed in abo 30% of solid tumors. Given its limited expression in normal mesothelial cells and hig expression in the majority of mesothelioma, ovarian and pancreatic cancers, mesotheli directed therapy has been intensively studied in preclinical and clinical settings.
- ***Based on our proprietary diamond AI platform, we found MSLN isoform 2 ("IsoMSLN is specifically expressed in mesothelioma, ovarian cancers and pancreatic cancer.*** AACR 202



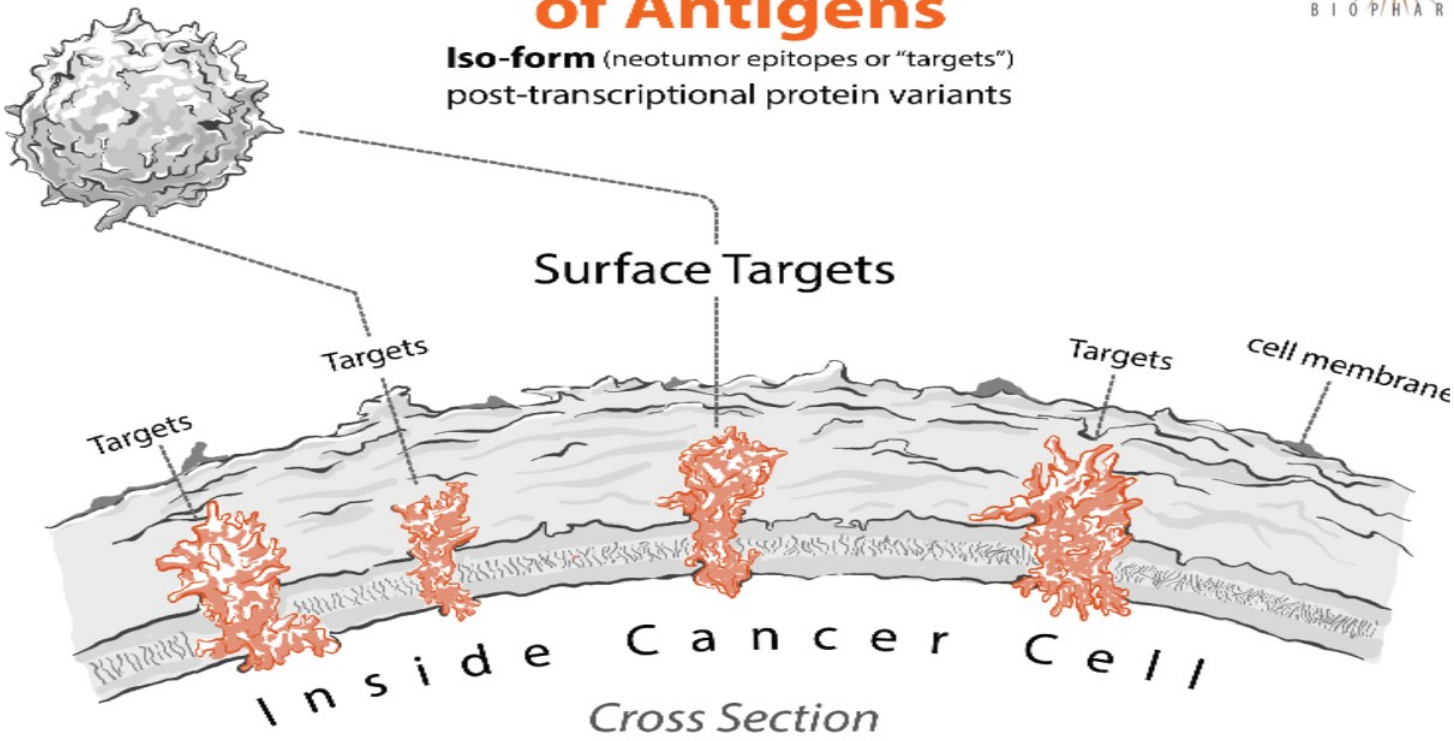
How Diamond Works

+1,000,000,000 data points



Surface Expression of Antigens

Iso-form (neotumor epitopes or "targets")
post-transcriptional protein variants



Steps to Validate The Target Iso-MSLN™

1. ***AI Diamond predication***
2. *Proteomics validation*
3. *Anti-MSLN isoform 2 (IsoMSLN)-specific antibodies were generated through hybridoma technology and screened via ELISA-based assays to IsoMSLN-specific peptides and flow cytometry-based binding to 293T cells that overexpress IsoMSLN protein.*
4. *IHC using formalin fixed paraffin embedded (FFPE) tissue tested in 10 patients EOC*
5. *Construction of CAR construct based on the sequence of anti-IsoMSLN antibodies.*
6. *Generate anti-IsoMSLN-specific CAR γδ-T cells and perform T cell cytotoxicity assays against Hela cells overexpressing IsoMSLN.*

Kiromic Diamond AI engine identified a "tumor-specific" MSLN isoform

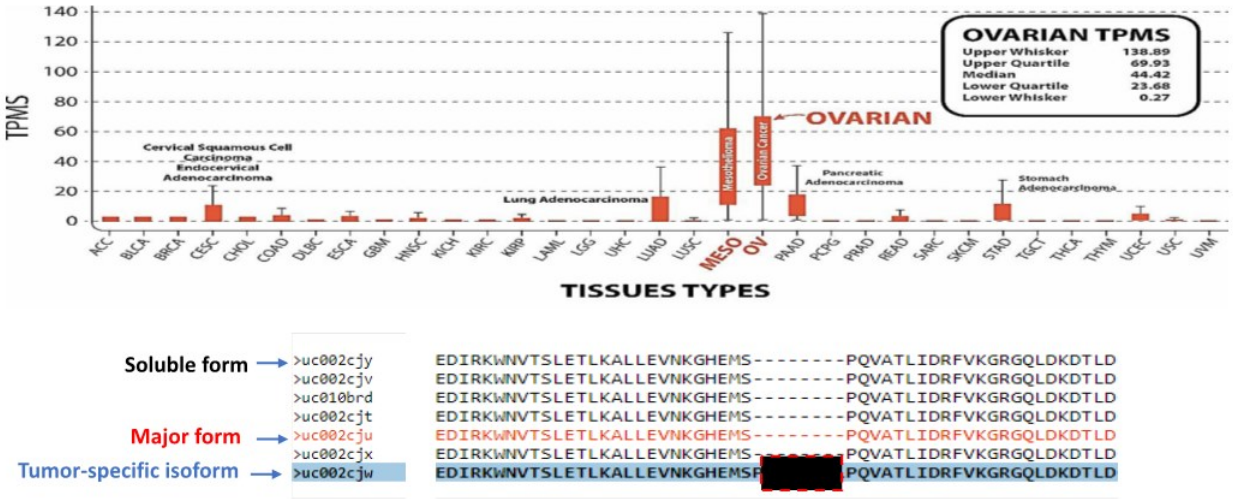


Figure. Bioinformatic analysis for the detection of cancer-associated isoforms. A) cancer tissues distribution of the IsoMSLN transcripts per million reads (TPM) values is presented, showing the greatest upregulation in ovarian cancer (OC) followed by malignant pleural mesothelioma (MPM). B) Multi sequence alignment of the transcript variants protein products. Red sequence= canonical form, blue highlighted sequence= cancer-associated isoform, black sequences= protein products of minor transcripts with low TPM values. AACR 2021

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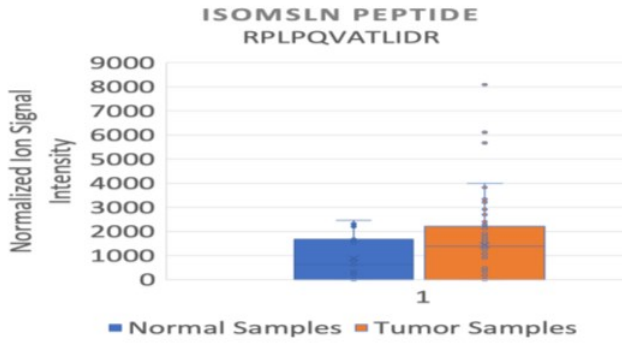
Proteomics

Protein	Peptide	MSLN Transcripts	% of Adjacent Normal Tissues	% of Tumor Tissue
IsoMSLN	RPLPQVATLIDR	uc002cjw	61	71
MSLN	GHEMSPQVATLIDR	uc002cjv;uc010brd;uc002cju;uc002cjy	100	100



This study analyzed the proteomics of OV tissue samples from a cohort of 109 OV cancer patients, with 100 % Serous Adenocarcinoma histological subtype, 81% of tumors of grade 3, and 64% tumor stage IIIC and 15% stage IV.
A total of 77,108 unique peptide sequences were identified at the false discovery rates indicated above (based on forward/decoy database searching); 220 peptide sequences were matched to splice variant predictions from SpliceDi.

Figure. The peptide *is a fragment of the unique peptide of ISOMSLN was detected in 71% of OV tumor samples and in 61% of adjacent normal samples. The peptide GHEMSPQVATLIDR, which is not found in IsoMSLN but it is found in all the protein translated from to the other MSLN transcripts, was also detected. This peptide was found in 100 % of normal and 100% of tumor samples. The box plots illustrates the distribution of RPLPQVATLIDR, the IsoMSLN peptide, in tumor samples and adjacent normal.* *AACR 2021*

Steps to Validate The Target Iso-MSLN™

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Results – IsoMSLN is localized on the cell surface

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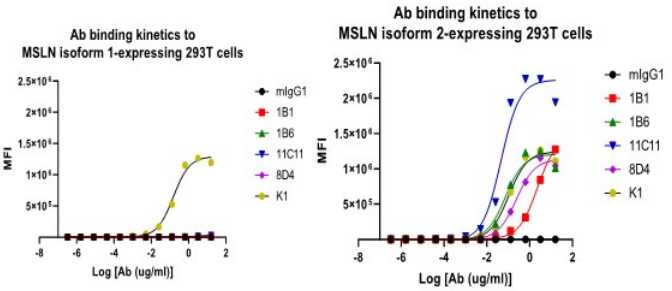

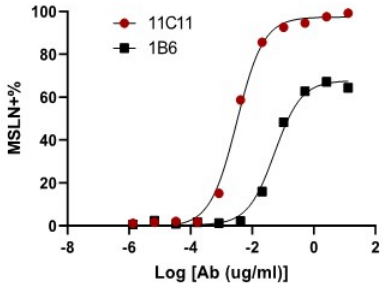

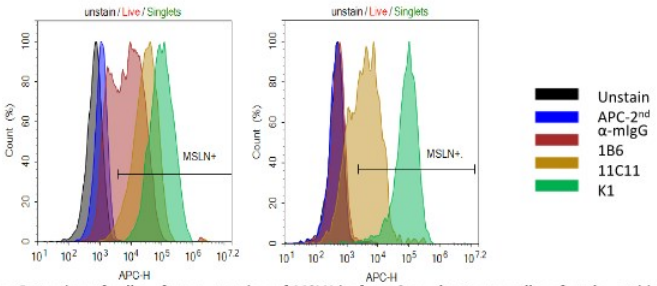

Anti-MSLN mAb clone #	EC50 to bind MSLN (µg/ml)		Notes
	Isoform 1	Isoform 2	
K1	0.152	0.106	Commercial
1B1	No binding	2.308	In-house
1B6	No binding	0.073	In-house
11C11	6.879*	0.046	In-house
8D4	No binding	0.238	In-house

Figure. Detection of cell surface expression of MSLN isoform 2 on the tumor cell surface by anti-isoMSLN-specific antibodies. A). The binding curve of different MSLN antibody clones in MSLN isoform 1 or isoform 2-overexpressing HEK293T cells. HEk293T cells were transiently expressed with MSLN isoform 1 or 2, as indicated; 48 h after transfection, the cells were harvested and stained for different anti-IsoMSLN antibodies, or with the anti-pan-MSLN Ab, clone K1, or with mIgG1 isotype control. MSLN-expressing cells were gated based on EGFP expression (linked to the C-terminus of MSLN by T2A self-cleaving peptide). The antibody binding MFI is plotted as a function of the antibody concentration. B) Flow cytometry staining of NCI H226 (IsoMSLN+) and HeLa (IsoMSLN-) tumor cell lines with different anti-MSLN antibody clones. C) Binding curve of anti-IsoMSLN antibody clones in NCI H226 cells. The percentage of positive events is plotted as a function of the antibody concentration. D) EC50 of anti-MSLN mAb clones to different MSLN isoforms. AACR 2021

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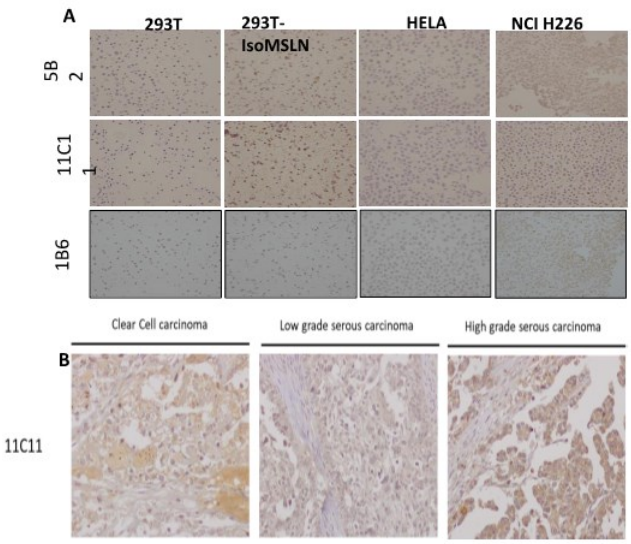
5. ***IHC using formalin fixed paraffin embedded (FFPE) tissue tested in patients EOC, other solid tumors***
6. *Construction of CAR construct based on the sequence of anti-IsoMSLN antibodies.*
7. *Generate anti-IsoMSLN-specific CAR γδ-T cells and perform T cell cytotoxicity assays against Hela cells overexpressing IsoMSLN.*

Results – IsoMSLN is protein is expressed in Solid tumors tissues



We selected the 11C11 antibody clone for further development, due to its specificity of IsoMSLN and higher affinity compared to the 1B6 clone.

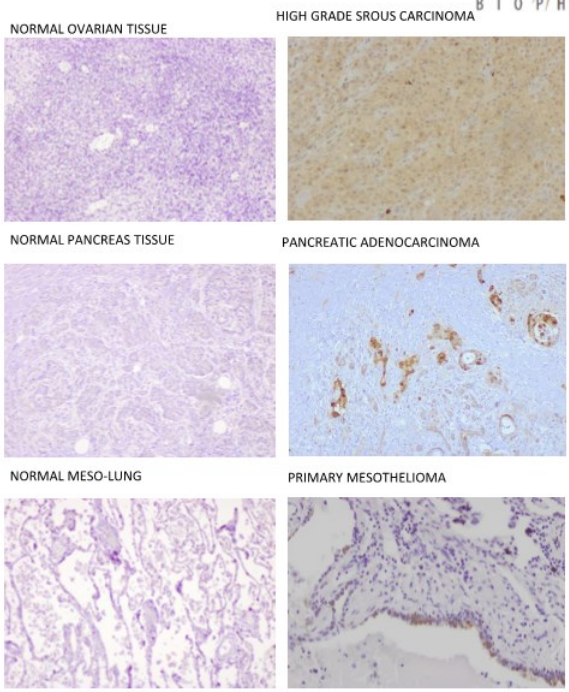


Figure. Histopathology staining of tumor cell line and primary tumor tissue array by anti-IsoMSLN-specific antibodies. A) Validation of anti-IsoMSLN antibodies for IHC staining in Lenti-X 293T cells with or without IsoMSLN expression. Anti-pan-MSLN antibody (5B2) is used as positive control. Tumor cells from cell culture were harvested and embed in HistoGel (Thermo Scientific). **B**) anti-IsoMSLN antibody IHC staining in primary tissues (50x magnification) from ovarian cancer tissue section. **C**) anti-IsoMSLN antibody IHC staining in primary tissues (50x magnification) from ovarian cancer tissue, pancreatic adenocarcinoma tissue, primary mesothelioma tissue. **D**) Summary table of the IHC findings. AACR2021

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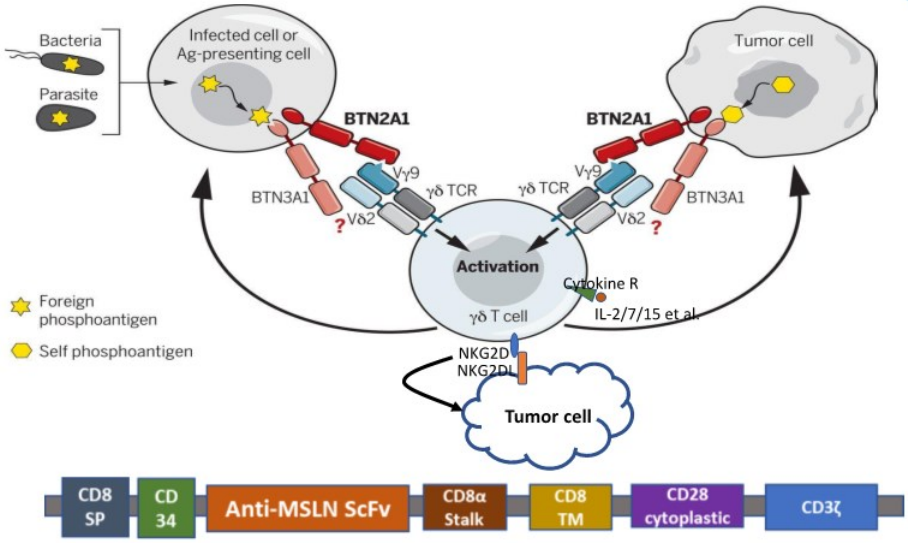
Mechanism of γδ-T cell activation & CAR construct

Modified from Science. 2020 Feb 7;367(647



Signal 1: TCR

Signal 2: Costimulatory receptors (CD28, CD27 et al)

Signal 3: Cytokine receptor (IL-2, I IL-7 et al)

Signal 4: NKR (e.g., NKG2D)

Signal 5: Inhibitory receptor (PD-1 BTLA4)

Signal 6: TLRs (TLR1/2/3/5/6)

Figure . Schematic of the anti-IsoMSLN CAR construct. The CAR constructs is composed of a CD8 membrane signal peptide (CD8 SP), a CD34 tag for flow-cytometric detection of the CA using an antiCD34 antibody (CD34), the murine monoclonal antibody-derived ScFv (VH-VL, anti-MSLN ScFV), the CD8a stalk region, the CD8 transmembrane domain, the CD28 cytoplasmatic and the CD3z cytoplasmatic domain (CD3z).

In-house development of γδ-T cell expansion Procedure

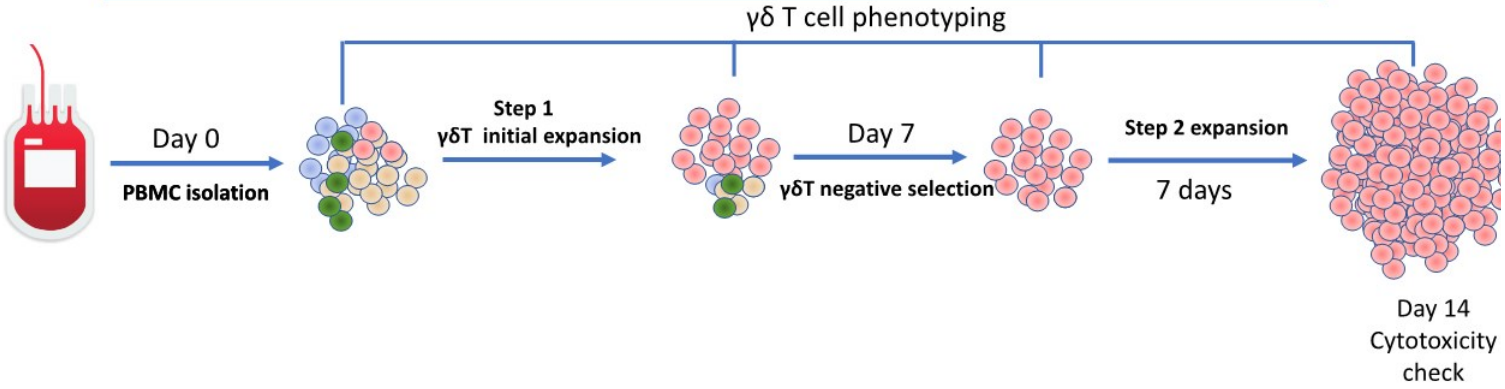


Figure. Manufacturing of anti-IsoMSLN CAR gdT cells. AACR 2021

Results – CAR gdT cells PD, PK, toxicity, and persistence *in vivo*

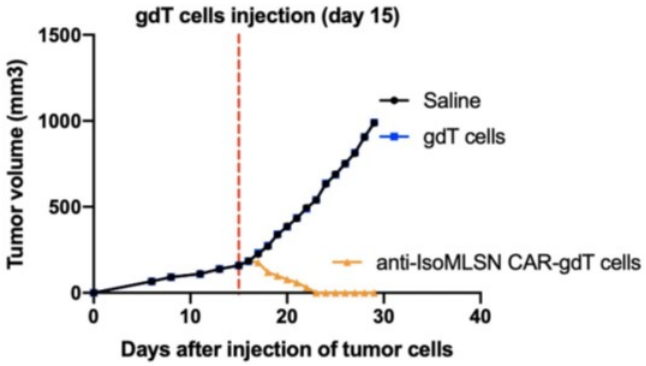


Figure 7. In vivo efficacy of CAR gdT cells. We tested *the in vivo* efficacy and tolerability of a high dose of gdT cell in Nude mice sub-cutaneously implanted with the IsoMSLN+ cell line, NCI-H226. 15 days after tumor cell implantation, mice with comparable tumor volumes were then divided into 3 groups (n=10 mice/group): i) injected with gdT cells, ii) injected with CAR gdT cells, iii) injected with saline solution. Group 4 consisted of tumor-free, untreated mice (n=5). Tumor volumes and mice weight were measured daily for an additional 30 days. The dotted vertical line indicates the day when the gdT cells were administered. Graphs show the average values out of 10 mice (Saline, gdT cells, CAR gdT cells), or 5 mice (tumor-free), +/- 95% C.I.

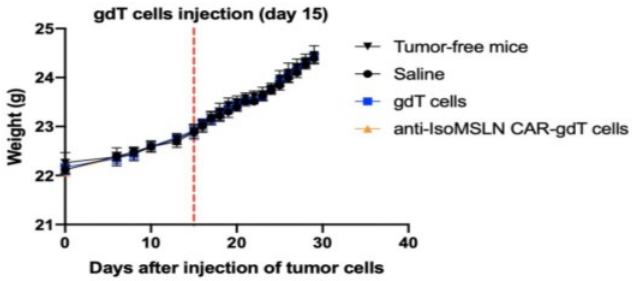


Figure 8. Animal body weight and general health. No adverse reactions were observed over the course of the study in the tumor-bearing mice treated with CAR- expressing human gamma delta T cells. Adverse reactions that were monitored included presence of labored breathing, ruffled fur, reduced appetite, lethargy, or hunched posture. Furthermore, the mice treated with CAR- expressing human gamma delta T cells did not experience any weight loss over the course of the study. Non-tumor bearing mice were also included as a healthy animal control. The dotted vertical line indicates the day when the gdT cells were administered. Graphs show the average values out of 10 mice (Saline, gdT cells, CAR gdT cells), or 5 mice (tumor-free), +/- 95% C.I.

AACR 2021

Results – CAR gdT cells PD, PK, toxicity, and persistence *in vivo*

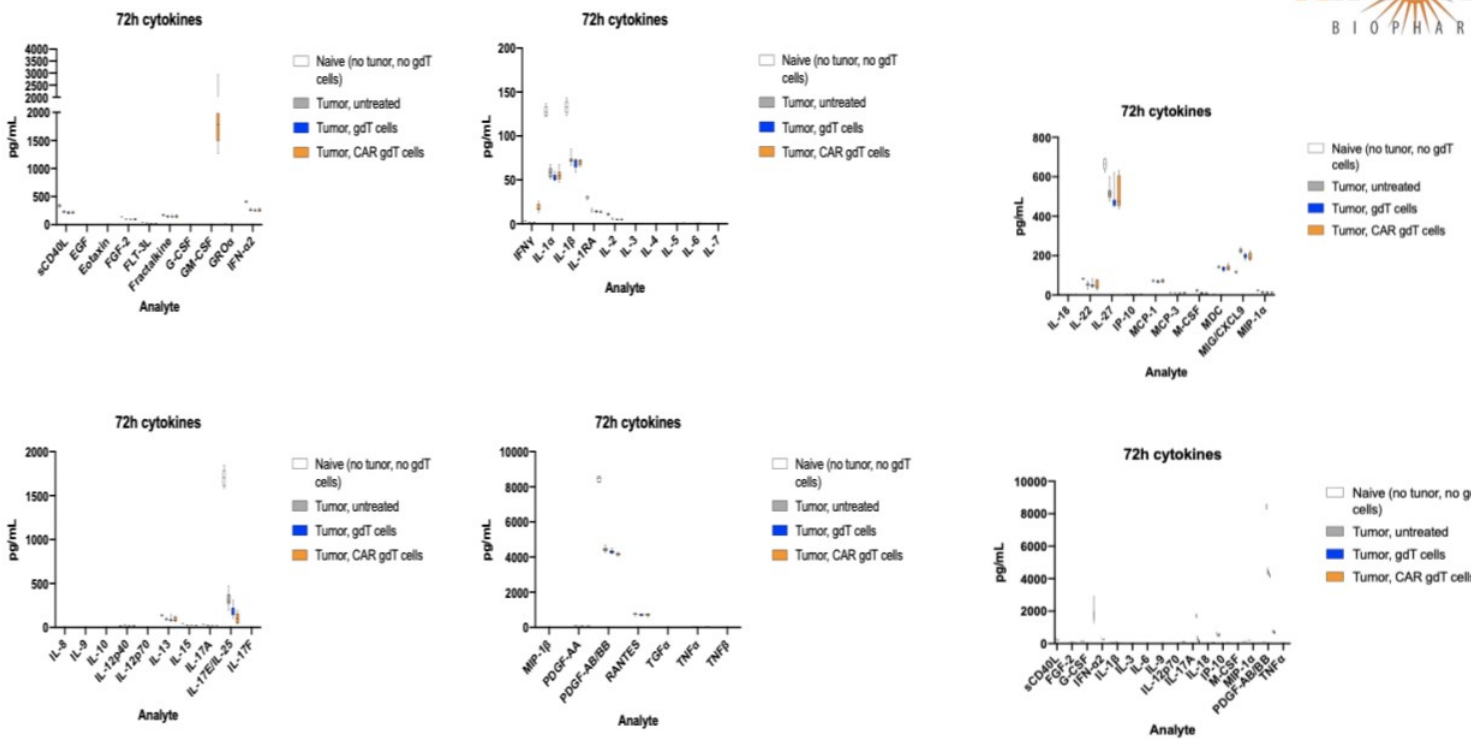


Figure 9. Inflammatory cytokines in mice. The cytokines in panel were not significantly different in CAR gdT treated mice compared with untreated or non-transduced gdT cells treated mic

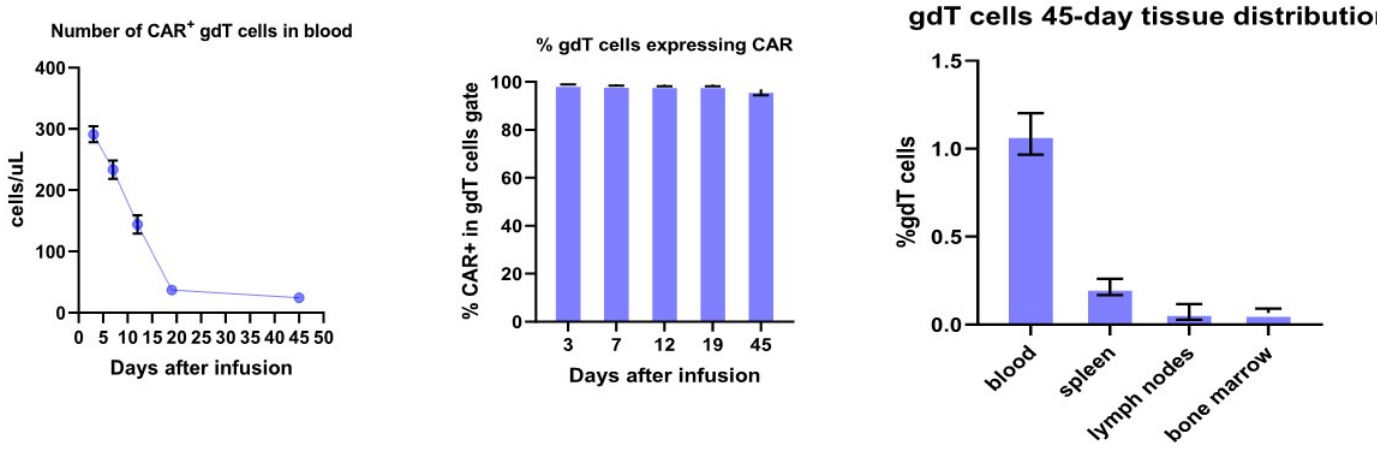


Figure 10. Pharmacokinetics. A) The peak number of CAR gdT cells in the blood was three days after injection. This peak T cell number correlates with the timing of when the tumor burden began to shrink. B) The gdT cells in the blood retained surface expression of the CAR.
C) 45 days after T cell injection, there were very low numbers of gdT cells in the blood, lymph nodes, and bone marrow.
AACR 2021

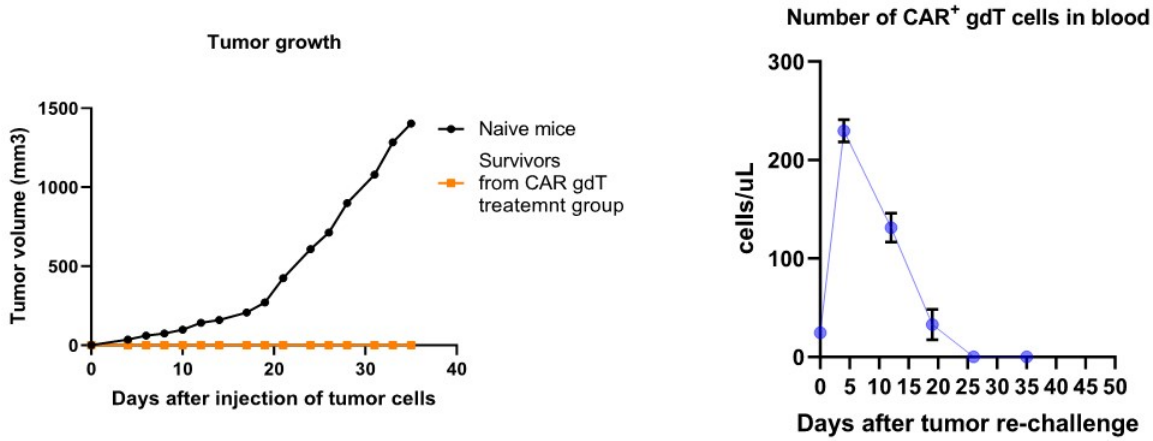


Figure 10. 5.1. Persistency of gdT cells in vivo measured by tumor re-challenging experiments. 45 days after the CAR gdT cells infusion, 5 mice from the CAR gdT cells treatment group, and 5 mice from the tumor-free group (naïve mice) were injected with NCI-H226 cells, following the same protocol of the first tumor injection. Tumor volume and mice weight was measured as indicated above, while blood was drawn for the measurement of circulating CAR gdT cells. A peak in the number of circulating CAR gdT cells was observed 5 days after the re-challenge with tumor cells, which corresponds to the first day when tumors become palpable in naïve mice. AACR2021

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Conclusions

1) IsoMSLN in a tumor-specific target in solid malignancies such as ovarian cancer pancreatic adenocarcinoma tissue cancer and primary mesothelioma.
2) Anti-IsoMSLN CAR gdT cells are a specific and potent off-the-shelf tumor therapy.
3) The selected dose of 5 million cells/mouse in a single i.v. injection is safe and effective in controlling tumor growth with a 100% response rate without any alteration of the serum cytokine profile, indicating low CRS risk.
4) Pharmacokinetic and pharmacodynamics data shows that the engineered cells persist for at least 45 days after injection.
5) CAR gdT cells persist *in vivo* and show the ability to completely reject a second tumor injection, indicating that anti-IsoMSLN CAR gdT therapy may prevent tumor recurrence.

Thank you