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): November 17, 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 ☒

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 November 17, 2021, Kiromic BioPharma, Inc. (“the Company”) presented slides at the Cell Immunotherapies for Solid Tumors 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 November 17, 2021, of Kiromic BioPharma, Inc.
104	Cover Page Interactive Data File (embedded within the Inline XBRL document).

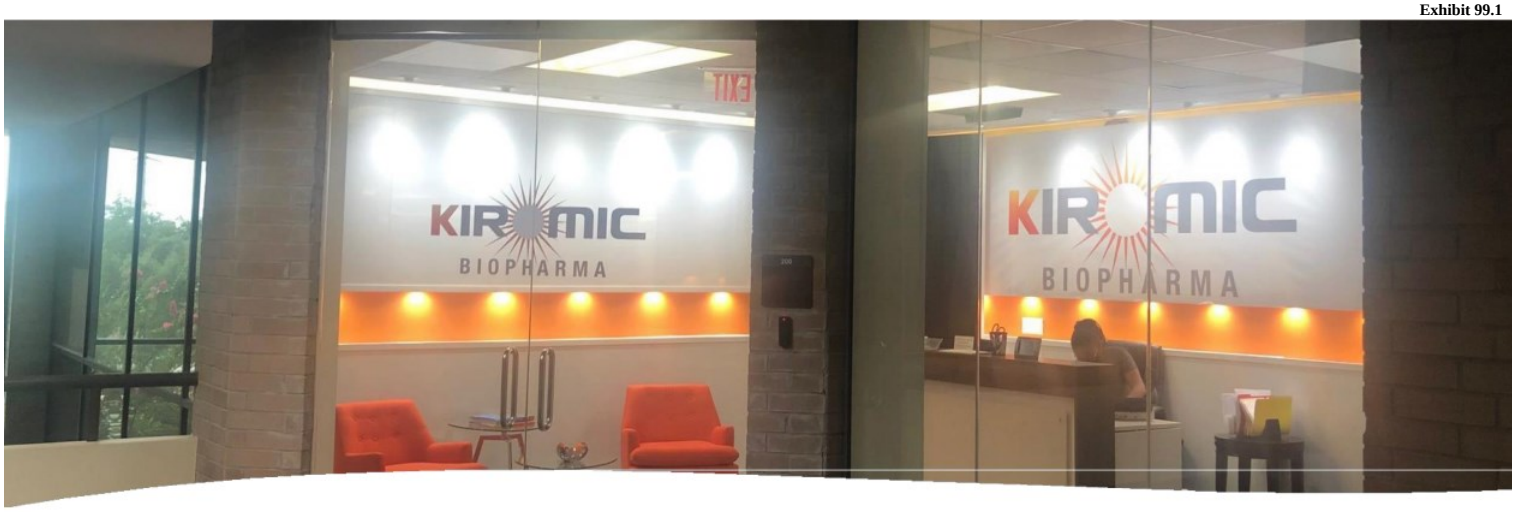
SIGNATURES

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: November 19, 2021

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



Bioinformatics to Identify Optimal Solid Tumor Targets and Improve Antigen Selection

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

Forward Looking Statements

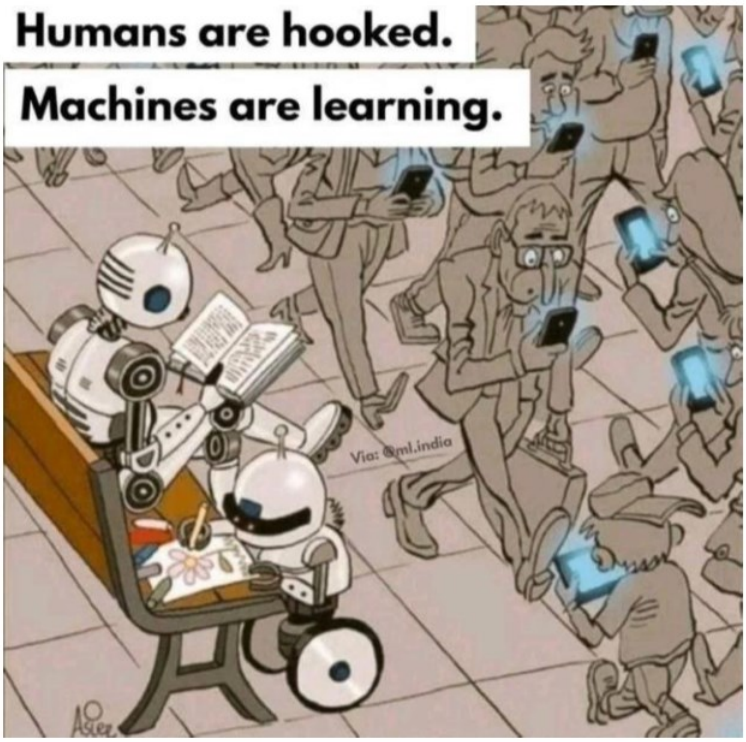
This press release contains forward-looking statements that involve substantial risks and uncertainties. We make such forward-looking statements pursuan the safe harbor provisions of the U.S. Private Securities Litigation Reform Act, Section 21E of the Securities Exchange Act of 1934, as amended, and other fed securities laws. All statements other than statements of historical facts are forward-looking statements. These statements relate to future events or to our fut financial performance and involve known and unknown risks, uncertainties and other factors that may cause our actual results, levels of activity, performance achievements to be materially different from any future results, levels of activity, performance or achievements expressed or implied by these forward-look statements. Forward-looking statements include, but are not limited to, statements about: Our goals and strategies; our future business development, finan condition and results of operations; expected changes in our revenue, costs or expenditures; growth of and competition trends in our industry; our expectati regarding demand for, and market acceptance of, our products; our expectations regarding our relationships with investors, institutional funding partners other parties we collaborate with; fluctuations in general economic and business conditions in the markets in which we operate; including those fluctuati caused by COVID-19; and relevant government policies and regulations relating to our industry.

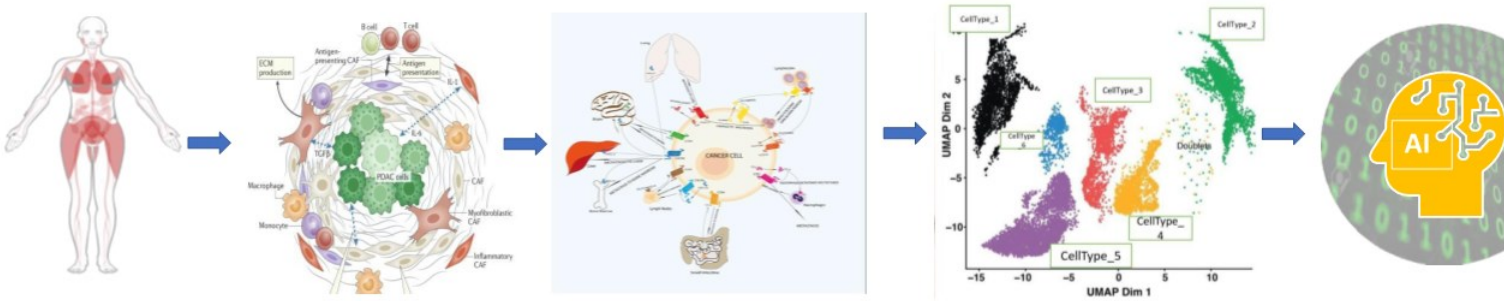
In some cases, you can identify forward-looking statements by terms such as "may," "could," "will," "should," "would," "expect," "plan," "intend," "anticipate," "belie "estimate," "predict," "potential," "project" or "continue" or the negative of these terms or other comparable terminology. These statements are only predictions. should not place undue reliance on forward-looking statements because they involve known and unknown risks, uncertainties and other factors, which are some cases, beyond our control and which could materially affect results. Factors that may cause actual results to differ materially from current expectati include, among other things, those listed under the heading "Risk Factors" included in our Registration Statement on Form S-1 (file no. 333-257427) , originally filed with the Securities and Exchange Commission (SEC) on June 25, 2021, and elsewhere in this press release. If one or more of these risks uncertainties occur, or if our underlying assumptions prove to be incorrect, actual events or results may vary significantly from those implied or projected by forward-looking statements. No forward-looking statement is a guarantee of future performance.

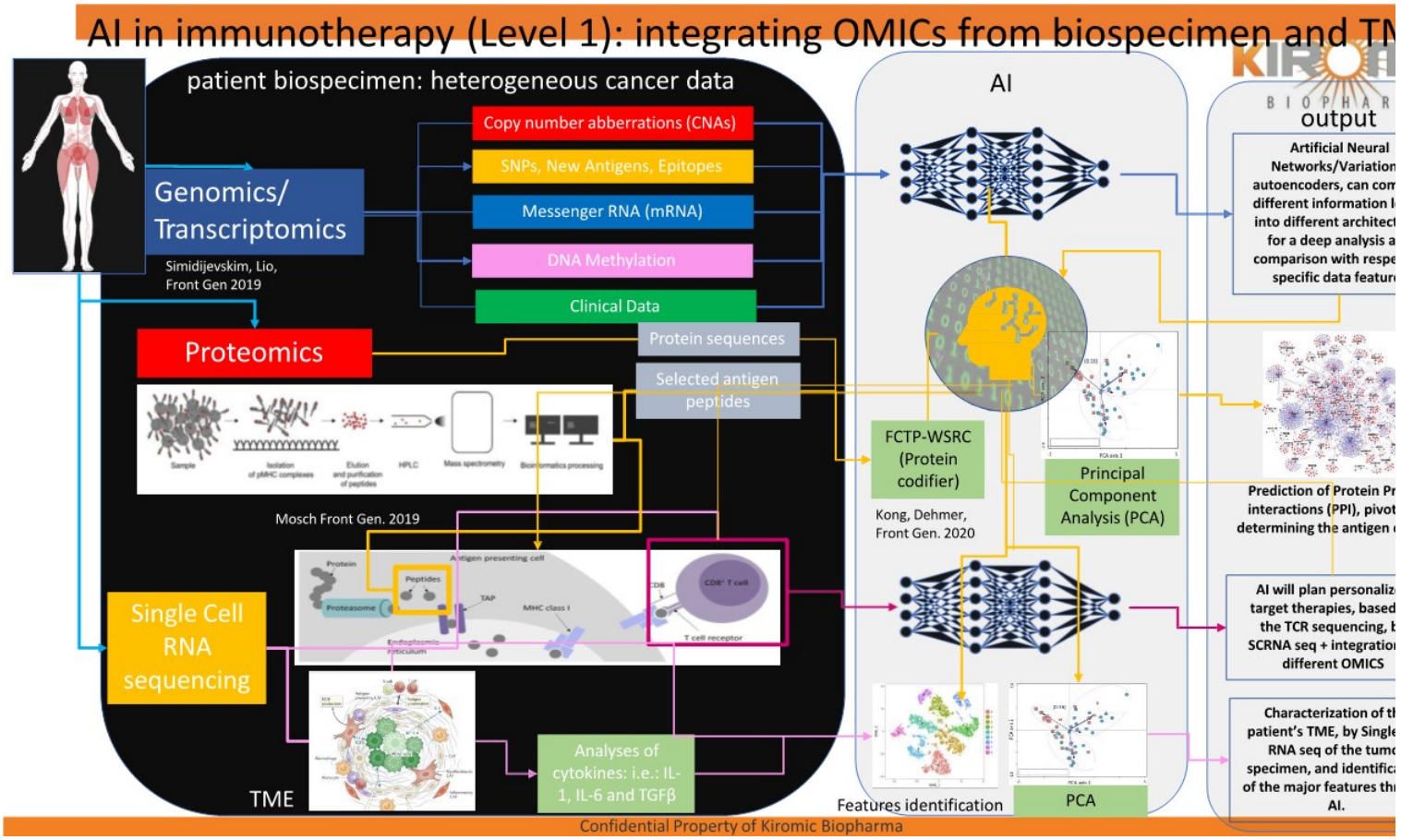
The forward-looking statements made in this report relate only to events or information as of the date on which the statements are made in this report. Exc as expressly required by the federal securities laws, there is no undertaking to publicly update or revise any forward-looking statements, whether as a resul new information, future events, changed circumstances or any other reason.

Outline

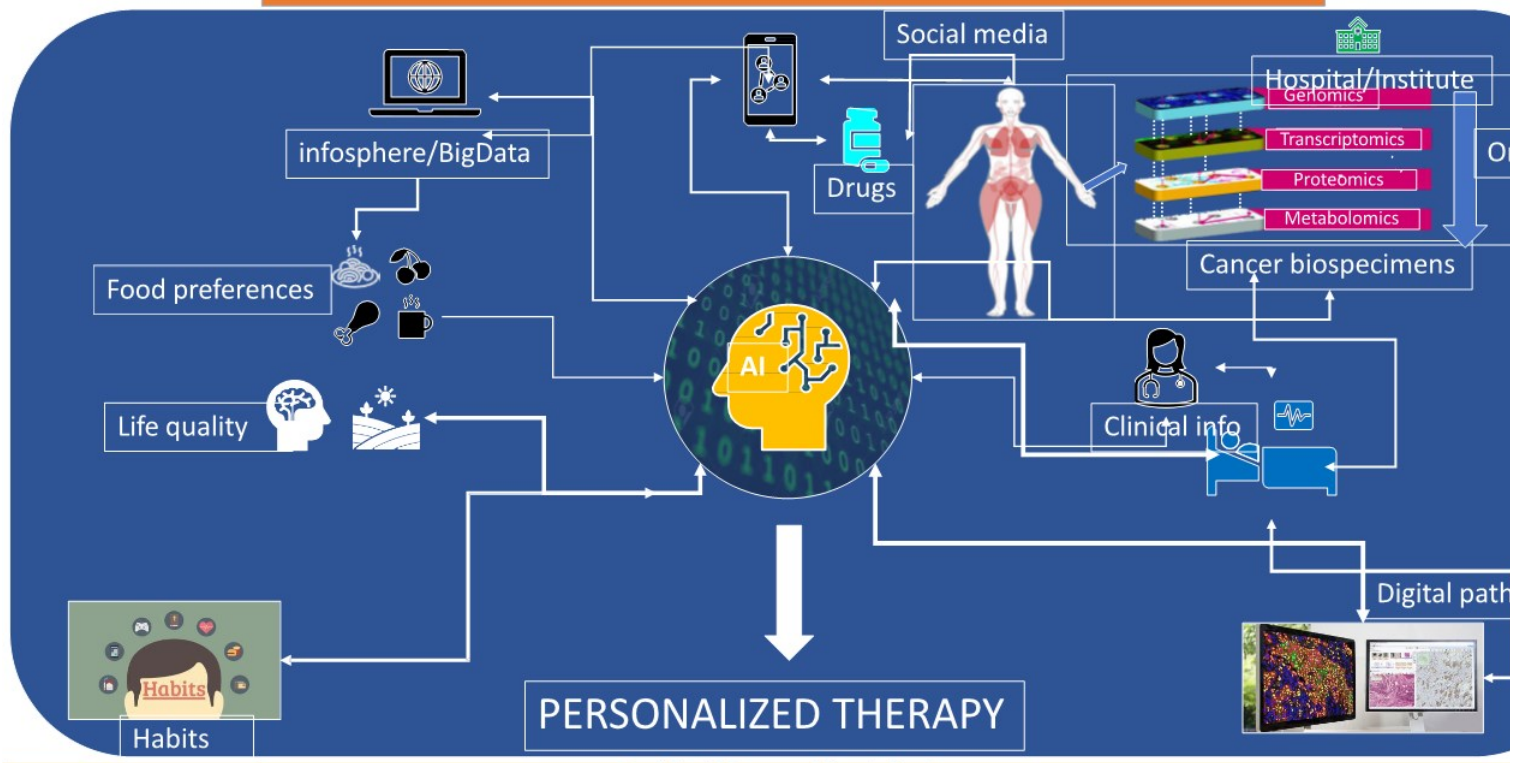
1. **AI**
2. **Discuss what is the Cd19 equivalent in solid tumor (Isomeso)**
3. **Review the clinical potential of HER2, MAC3,, Mage3, Mage 4**
4. **Best in Class bioinformatics platforms to identify safe targets**

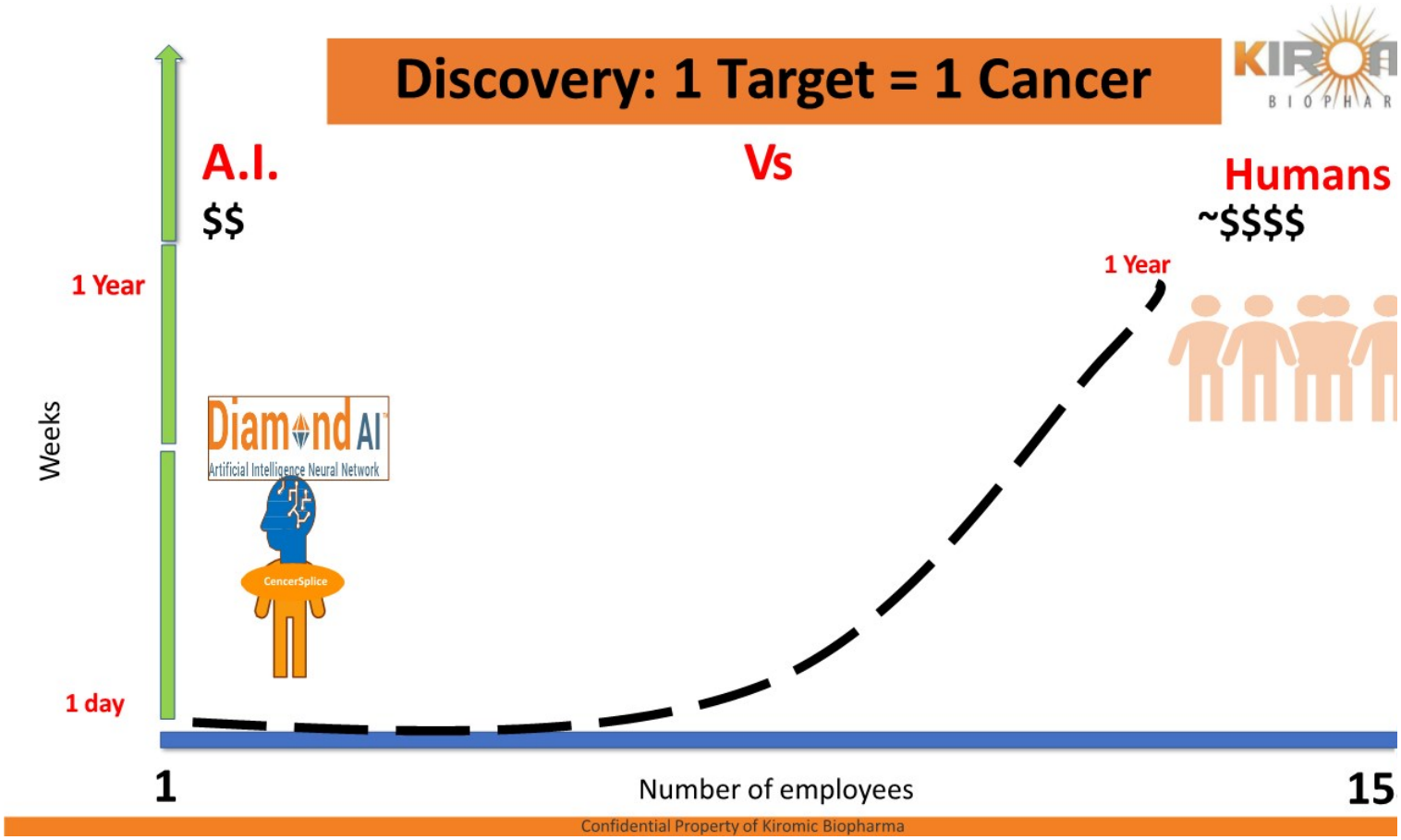



B cell
T cell
Antigen-presenting CAF
ECM production
Antigen presentation
IL1
IL6
TGFβ
PDAC cells
Macrophage
Monocyte
CAF
Myofibroblastic CAF
Inflammatory CAF
CANCER CELL
CellType_1
CellType_2
CellType_3
CellType_4
CellType_5
Doublets
UMAP Dim 1
UMAP Dim 2
AI


AI in immunotherapy (Level 1): integrating OMICs from biospecimen and TM
patient biospecimen: heterogeneous cancer data
Genomics/ Transcriptomics
Simidijevskim, Lio, Front Gen 2019
Copy number abberrations (CNAs)
SNPs, New Antigens, Epitopes
Messenger RNA (mRNA)
DNA Methylation
Clinical Data
Proteomics
Protein sequences
Selected antigen peptides
Mosch Front Gen. 2019
Single Cell RNA sequencing
TME
Analyses of cytokines: i.e.: IL-1, IL-6 and TGFβ
AI
FCTP-WSRC (Protein codifier)
Kong, Dehmer, Front Gen. 2020
Principal Component Analysis (PCA)
Features identification
PCA
output
Artificial Neural Networks/Variation
autoencoders, can com
different information
into different architect
for a deep analysis a
comparison with respe
specific data feature
Prediction of Protein Pr
interactions (PPI), pivot
determining the antigen
AI will plan personaliz
target therapies, based
the TCR sequencing, b
SCRNA seq + integratio
different OMICS
Characterization of th
patient's TME, by Single
RNA seq of the tumo
specimen, and identifica
of the major features th
AI.
Confidential Property of Kiromic Biopharma

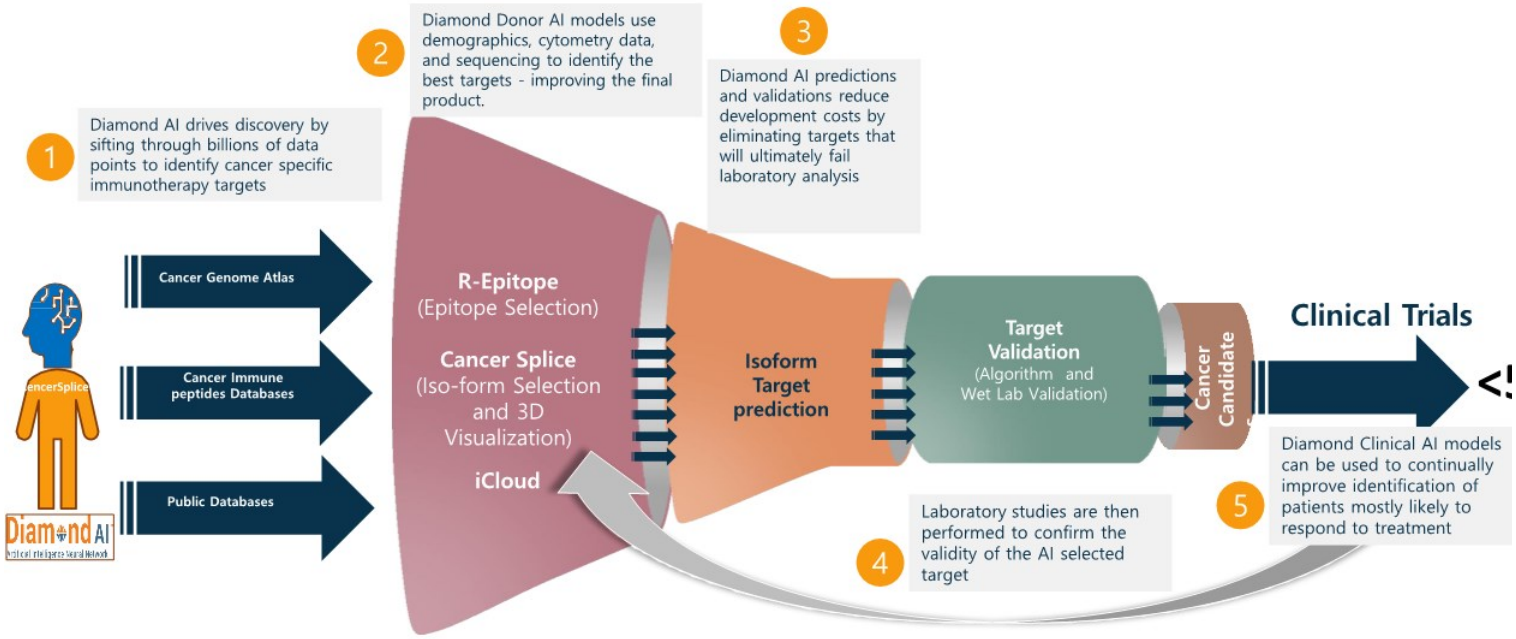
AI in immunotherapy (Level 2)



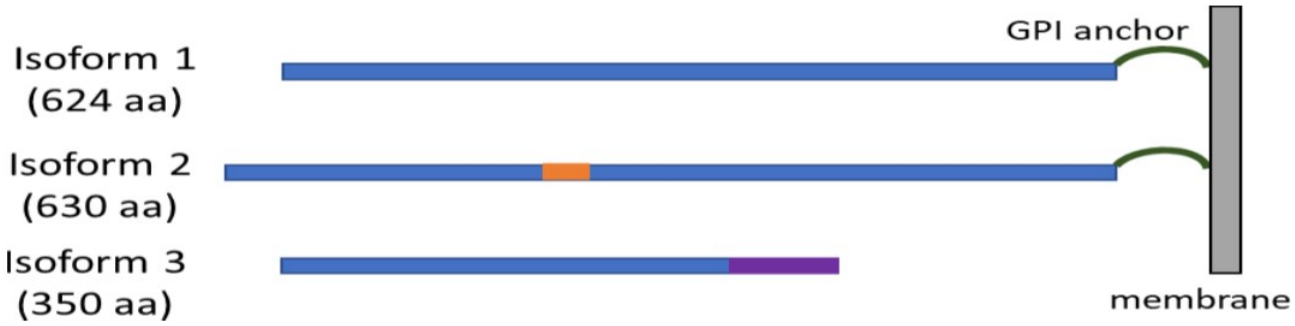

Discovery: 1 Target = 1 Cancer
A.I.
Vs
Humans
$$
~$$$$
1 Year
1 Year
Weeks
Diamond AI
Artificial Intelligence Neural Network
CencerSplice
1 day
1
Number of employees
15
Confidential Property of Kiromic Biopharma

The Difference - Diamond AI™ Target Discovery Engine

Diamond™ A.I. target discovery engine powers innovation, speeds development and reduces costs



- 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 hi 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 2021

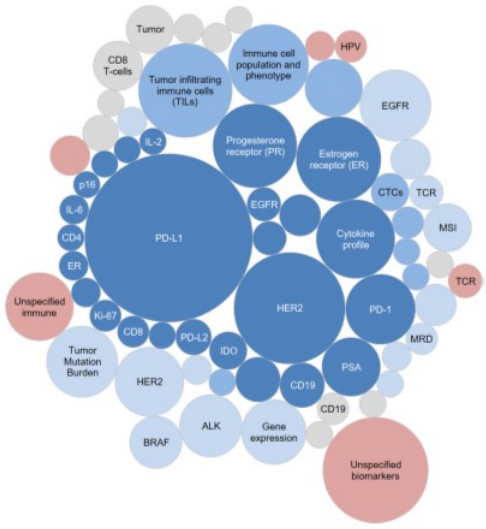


Cancer biomarker landscape

- Large, heterogeneous with various method of administration landscape

Tumor heterogeneity	• Different cancers have different targetable antigens and express them at different levels • Not all tumor cells in a tumor mass are positive for the same target • This leads to different cancer biomarker
Biomarker antigens have a variety of method of administration	• The therapeutic approach needs to be tailored to the [tumor] localisation of the target • The main cancer biomarkers used in the clinical practice are still dominated by PD-1, Her2, PSA, CD19, and hormone receptors • This limits the number of targetable indications and the general applicability of related immunotherapies
Discovery platform needed to identify the variety of biomarker antigens	• **Past approaches do not target most of the cancer indications and do not show the expected clinical efficacy** • Most single-analyte biomarkers have been generated and studied because of a pre-conceived biological association between them and the associated disease • Time consuming approach

Various biomarker method of administration



Biomarker discovery platform landscape Oncology & Other Diseases

Patient and tumor specific expression profile

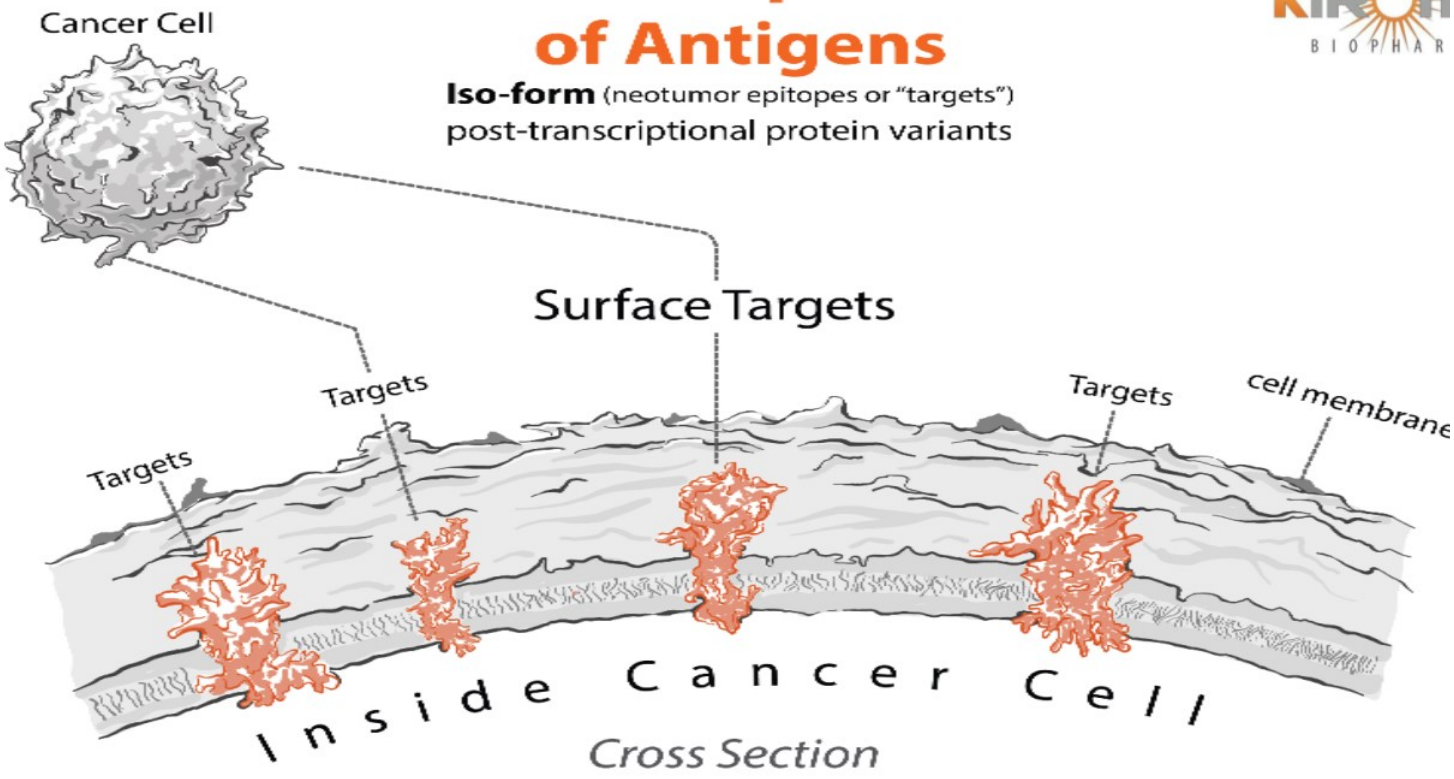
Patient's medical history will be factored in to:

1. Maximize drug potency
2. Minimize harmful side effects

- A myriad of open access and proprietary database are at Kiromic's disposal
- "Kiromic only" training set and library

Surface Expression of Antigens

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



Kiromic Diamond AI engine identified a “tumor-specific” MSLN isoform

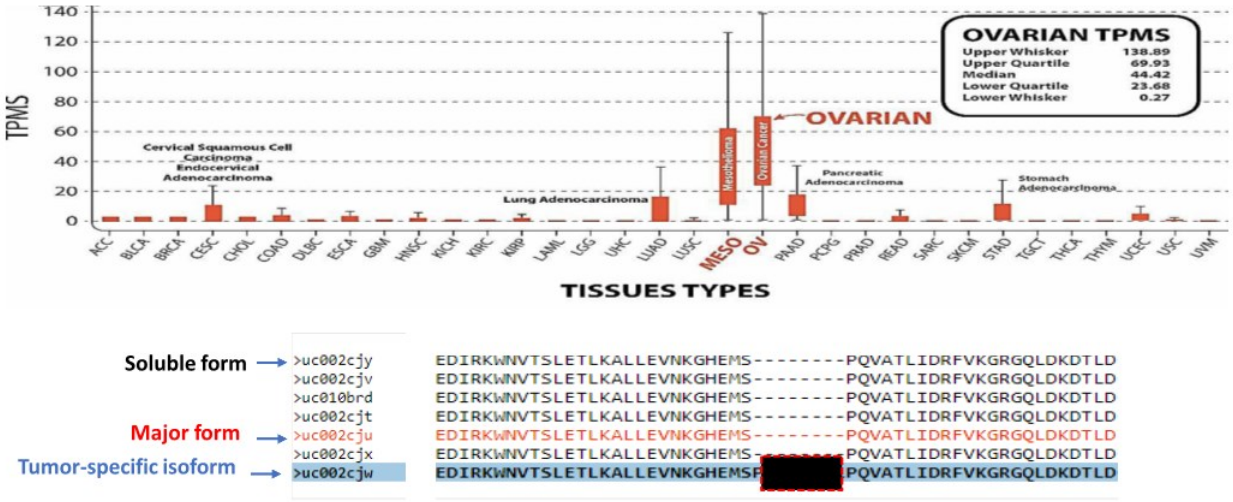
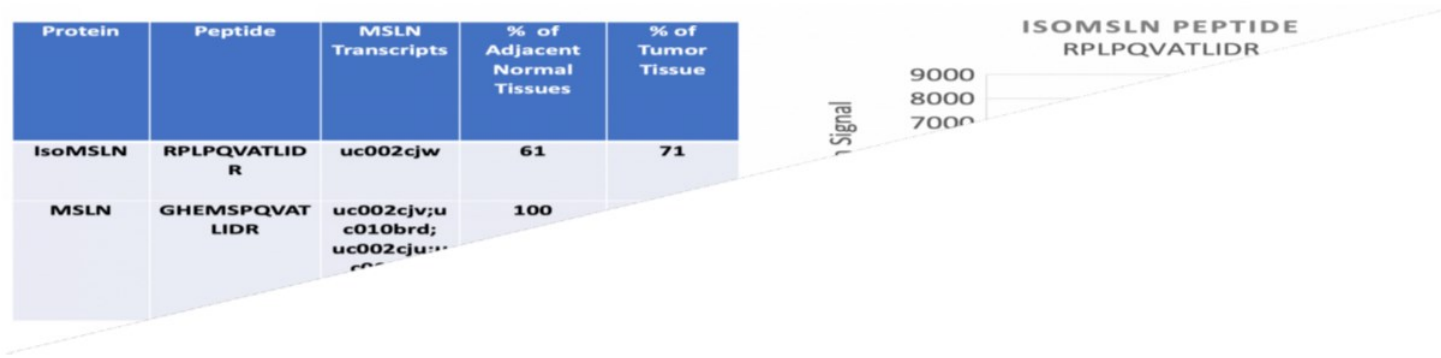


Figure. Bioinformatic analysis for the detection of cancer-associated isoforms. A) cancer tissues distribution of the IsoMSLN transcripts per million reads (TPM) values is presented, showing the greatest upregulation in ovarian cancer (OC) followed by malignant pleural mesothelioma (MPM). B) Multi sequence 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

Proteomics

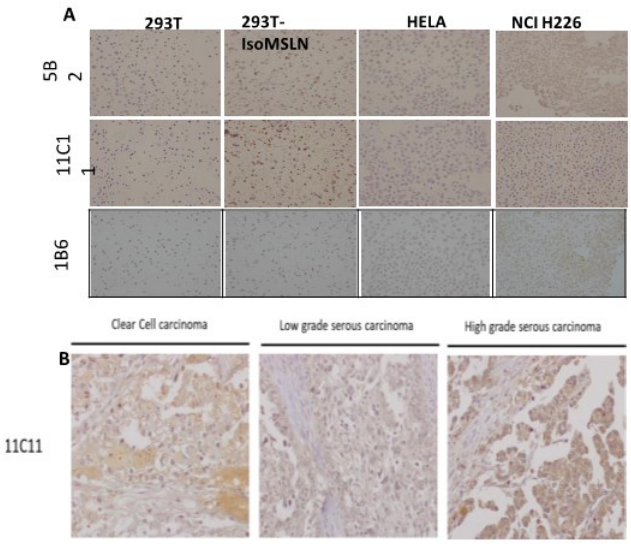
Protein	Peptide	MSLN Transcripts	% of Adjacent Normal Tissues	% of Tumor Tissue
IsoMSLN	RPLPQVATLIDR	uc002cjw	61	71
MSLN	GHEMSPQVATLIDR	uc002cjv;uc010brd;uc002cju…	100	



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*

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.

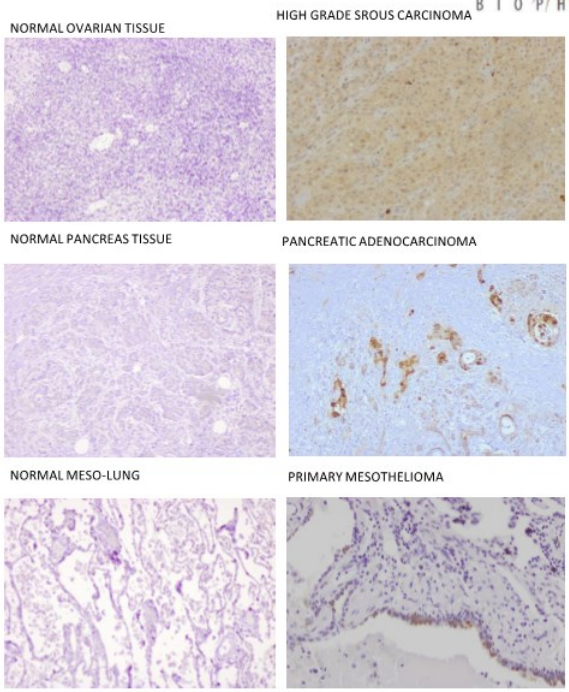


Figure. Histopathology staining of tumor cell line and primary tumor tissue array by anti-IsoMSLN-specific antibodies. A) Validation of anti-IsoMSLN antibodies for IHC staining in Lenti-X 293T cells with or without IsoMSLN expression. Anti- pan-MSLN antibody (5B2) is used as positive control. Tumor cells 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

The MAC antigen family: MAC-1

The ITGAM gene (MAC-1) encodes the integrin alpha M chain.

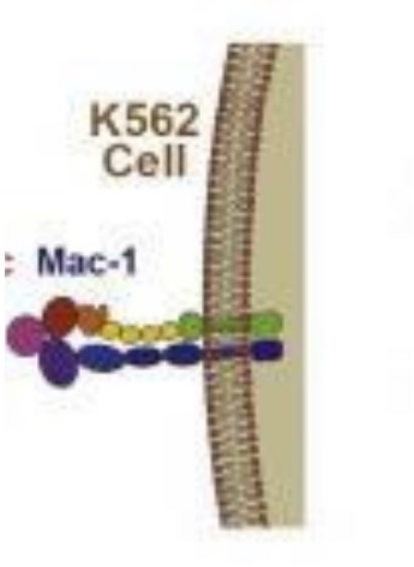
Integrins are heterodimeric integral membrane proteins composed of an alpha chain and a beta chain.

This I-domain containing alpha integrin combines with the beta 2 chain (ITGB2) to form a leukocyte-specific integrin referred to as macrophage receptor 1 ('Mac-1'), or inactivated-C3b (iC3b) receptor 3 ('CR3').

The alpha M beta 2 integrin is important in the adherence of neutrophils and monocytes to stimulated endothelium, and also in the phagocytosis of complement coated particles.

Multiple transcript variants encoding different isoforms have been found for this gene.

ITGAM Facilitates transmigration of leukocytes across vascular endothelia, intercellular adhesion



Cancers 2021, 13, 77. https://doi.org/10.3390/ cancers13010077
https://www.ncbi.nlm.nih.gov/gene/3684

The MAC antigen family: MAC-3

- Lysosome-associated membrane protein 2 (LAMP2), called also **MAC-3** or CD107b (Cluster of Differentiation 107b one of the lysosome-associated membrane glycoproteins. This glycoprotein provides selectins with carbohydr ligands. It may play a role in tumor cell metastasis.

- It may also function in the protection, maintenance, and adhesion of the lysosome.

- Alternative splicing of the gene produces three variants - LAMP-2A, LAMP-2B and LAMP-2C.[5] LAMP-2A is t receptor for chaperone-mediated autophagy.

- LAMP-2B is associated with Danon disease.

- **Alternative antigens trafficking use lysosome-associated membrane protein 1 (LAMP) domain to enhance vaccine efficacy against HER2 and other model antigens in both in vitro and in vivo studies.**

- Inclusion of LAMP protein in plasmid vaccines effectively trafficked antigens to endo-lysosomal compartments, resulting in **enhanced major histocompatibility complex (MHC) class I and II presentation.**

- *Chang MH, Karageorgos LE, Meikle PJ (2003). "CD107a (LAMP-1) and CD107b (LAMP-2)". Journal of Biological Regulators and Homeostatic Agents.* ***16*** *(2): 147–51. PMID 12144129*

- *Journal for ImmunoTherapy of Cancer 2020;8:e000258. doi: 10.1136/jitc-2019-000258*

Identification of MAC-1 (ITGAM) in pancreatic adenocarcinoma stroma (PAC)

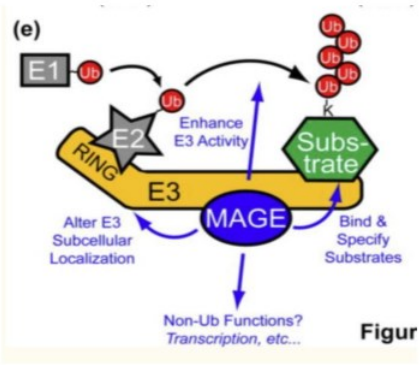
Moffitt et al. identified two different stromal subtypes, normal and activated based on different genes expression. The first subtype is characterized by high expression of genes that are associated with macrophages, such as integrins (ITGAM) and chemokine (C-C motif) ligand (CCL) 13/18. (*Nature Genetics* **volume 47**, pages1168–1178 (2015)

Despite the fact that pancreatic cancer is a non-immunogenic cancer, a robust amount of infiltrate immunogenic cells, such as tumor-associated macrophages (TAMs), myeloid derived suppressor cells (MDSCs) and neutrophils, has been identified (https://doi.org/10.1177/1758835918816281)

https://doi.org/10.1016/j.ctrv.2020.102016

The MAGE family

- The **Melanoma Antigen Gene (MAGE)** protein family is a large, highly conserved group of proteins that share a common MAGE homology domain.
- Many MAGE proteins are restricted in expression to reproductive tissues but are aberrantly expressed in a **wide-variety of cancer types.**
- Originally discovered as antigens on tumor cells and developed as cancer immunotherapy targets, recent literature suggests a more prominent role for **MAGEs in driving tumorigenesis**.
- They are of particular interest for cancer immunotherapy because of their strict tumoral specificity and because they are shared by many tumors.



Figur

Summary of known biochemical and cellular functions of MAGEs: altering the subcellular localikzation of E3, binding ubiquinated substrates, and/or processing non-Ub functions, like transcription

Curr Opin Cell Biol. 2015 Dec; 37: 1–8. doi: 10.1016/j.ceb.2015.08.002

Antigenic peptide **EADPTGHSY** encoded by **MAGE-A1** and known to be presented by HLA-A1 is currently being used in therapeutic vaccination trials.

Literature has reported that a cytotoxic T-lymphocyte (CTL) clone, which is restricted by HLA-B35, recognizes the same peptide and, importantly, lyses HLA-B35 tumor cells expressing MAGE-A1. This peptide can be presented to CTL by both HLA-B*3501 and HLA-B*3503 molecules, which are expressed by approximately 19% of Caucasians.

These results infer that the current clinical use of peptide EADPTGHSY can now be extended to HLA-B35 patients.

MAGE-3.A1 peptide vaccine may stimulate the immune system to mount a cytotoxic T-cell (CTL) response against tumor cells expressing MAGE-3, resulting in tumor cell lysis. MAGE-3, a tumor-associated antigen (TAA), **is overexpressed by a variety of cancer cell types**.

Luiten RM et al: Tissue Antigens 2000 Jul;56(1):77-81. doi: 10.1034/j.1399-0039.2000.560110.x

MAGE-3.A1 in melanoma immunotherapy

A cancer vaccine comprising synthetic peptides derived from human melanoma antigen A1 (MAGE-A1), human melanoma antigen A3 (MAGE-A3) and cancer-testis antigen NY-ESO-1, was developed.

The vaccine has potential immunostimulating and antineoplastic activities.

Upon administration, MAGE-A1/MAGE-A3/NY-ESO-1 peptides vaccine may stimulate the immune system to mount a cytotoxic T-cell (CTL) response against tumor cells expressing MAGE-A1, MAGE-A3 and NY-ESO-1, resulting in tumor cell lysis. The MAGE-A1, MAGE-A3, and NY-ESO-1 tumor-associated antigens (TAAS) are overexpressed by a variety of cancer cell types.

The MAGE-3.A1 peptide used is **EVDPIGHLY**

Int J Cancer. 1999 Jan 18;80(2):219-30.
doi: 10.1002/(sici)1097-0215(19990118)80:2<219::aid-ijc10>3.0.co;2-s

Thank you