JOHNS HOPKINS UNIVERSITY

Startups and Technologies

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TECHNOLOGY VENTURES

STARTUPS

OPHTHALMOLOGY

COVE THERAPEUTICS

Niren Shah

JOHNS HOPKINS UNIVERSITY

Stage of Dev	Capital Received	Raising Total	IP Status
Seed > Series A	$7.25M	$65M	Patented

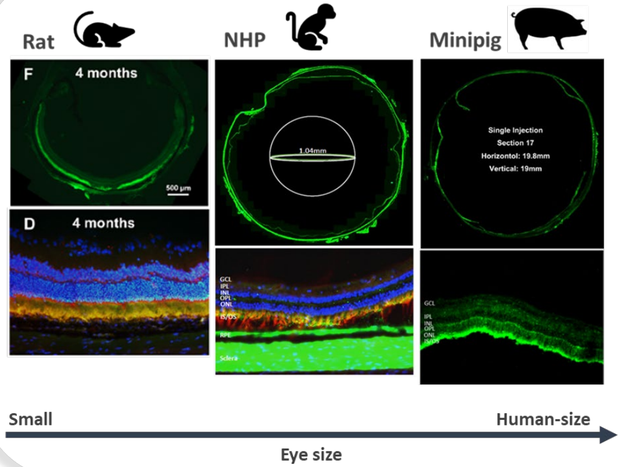
CURRENTLY RAISING

Value Proposition

- Cove is raising a Series A to advance CVTX407 (Stargardt) through Phase 1/2 and CVTX409 (Geographic Atrophy) through Phase 1.
- Next evolution in delivery using a non-viral, polymeric nanoparticle platform (INPUT) to overcome limitations in genetic medicine such as tropism, redosing, large genes, safety, and manufacturing.
- CVTX407 for Stargardt has demonstrated proof-of-concept in the KO animal model, showing a reduction in A2E, and robust gene expression with an expected IND in 2H26
- CVTX409 for Geographic Atrophy demonstrated proof-of-concept in a CNV model, showing a sustained reduction in neovascularization with an expected IND in 2H26

Background and Team

- Viruses and LNPs have key issues Cove intends to solve.
- Taysha (IPO exit), Spark (acquired), Biogen, PTC Therapeutics, NPS Pharma (acquired), Novartis, and significant involvement from ex-AveXis as investors/board/advisor

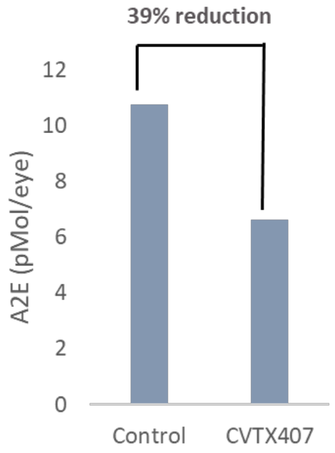


Pan-retinal expression seen in all species tested

Single suprachoroidal dose leads to expression of retina at the equator, anterior, and posterior sections

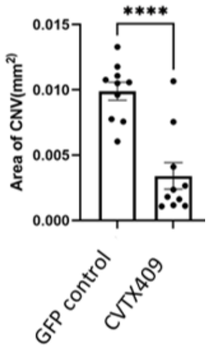
CVTX407 for Stargardt

A2E reduction after 6 months



CVTX409 for Dry AMD/GA

CNV reduction after 4 weeks



NEURODEGENERATION
SYNDEO LIFE

Al Hawkins

Phillip Wong, PhD

JOHNS HOPKINS UNIVERSITY

Stage of Dev	Funding	IP Status
NewCo	Federal Grants	Patents Pending

Value Proposition

- Global rescue of TDP-43 loss-of-function resulting in restoration of splicing quality control and prevention of cell death
- Novel biomarker to detect loss of TDP-43 function, enabling patient stratification and measurement of target engagement

Background

- TDP-43 functions in the nucleus to suppress cryptic splicing events and incorporation of cryptic exons.
- Loss of TDP-43 function result in incorporation of premature stop codons, global mRNA degradation, abnormal protein production, and cellular dysfunction and death
- Delivery of gene therapy restores TDP-43 function, preventing neuronal loss and significantly prolonging survival in a murine model of ALS

Updates

- Initiating manufacturing at CDMO
- Seeking dilutive and non-dilutive funding to support IND enabling studies

Syndeo Foundational Technologies

AAV-CTR Therapeutic

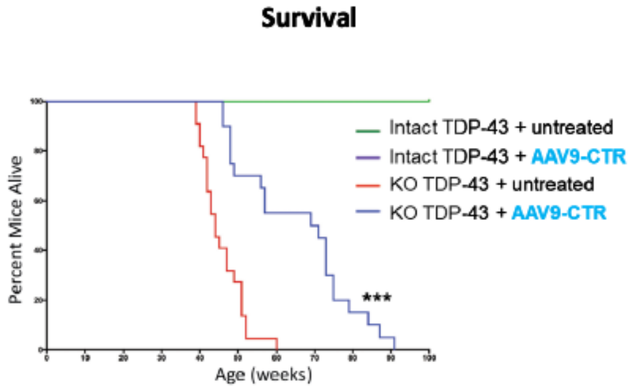
CTR: Chimeric TDP-43/RAVER1

Restore TDP-43 Function

TDP-43 Biomarker

Detect Loss of TDP-43 Function

AAV-CTR Rescues TDP-43 Expression and Prolongs Survival



70% of Motor Neurons Protected

CANCER VACCINES
ADVENTRIS PHARMACEUTICALS

Jen Herbach

Mark Yarchoan, MD

JOHNS HOPKINS UNIVERSITY

Stage of Dev	Funding	IP Status
Seed	$12M Seed	Licensed

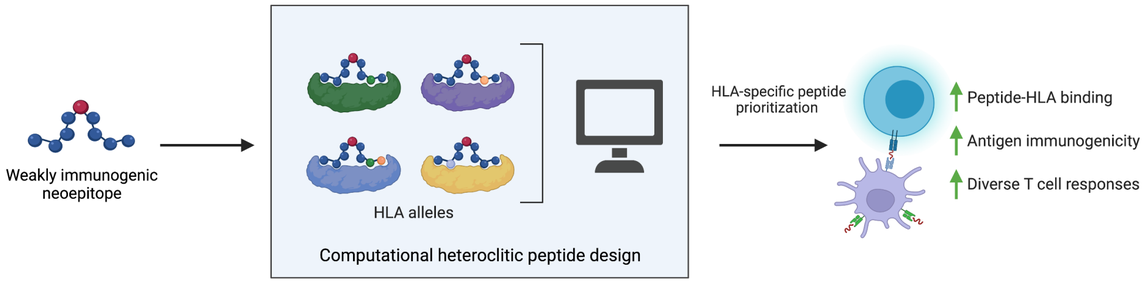
Value Proposition

- Adventris' vaccine platform enables us to make "off the shelf" cancer vaccines targeting the most common oncogenes, for the treatment and prevention of cancer

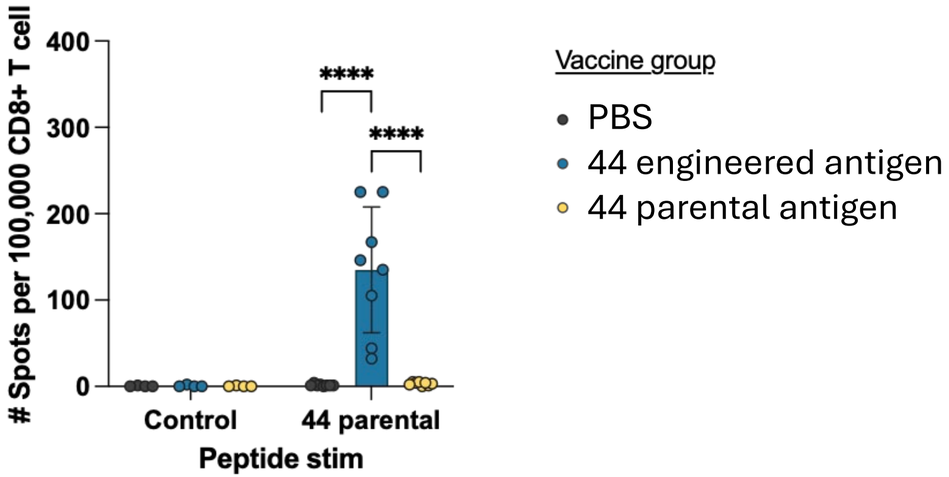
Background

- A small number of oncogenes cause the majority of human cancers.
- Mutant KRAS, our first vaccine target, is implicated in ~30% of all cancers.
- Oncogenes are the ideal cancer vaccine target and result in tumor-specific neoantigens that can be selectively targeted by the immune system.
- However, their lack of immunogenicity has prevented successful targeting to date.
- Adventris' antigen engineering platform drives stronger immunity against tumor-specific neoantigens creating safe and more effective vaccines.

First & Best in Class Antigen Engineering Platform



Engineered Antigens Drive More Potent Immunized Responses than the Native Peptides *In Vivo*



RETINAL DISEASE

AGNOS THERAPEUTICS

Mandeep Singh, MD

Robert Johnston, PhD

Euguene De Juan, MD

JOHNS HOPKINS UNIVERSITY

Stage of Dev	Raising Total	IP Status
Seed	$10M	Patent Pending

CURRENTLY RAISING

Value Proposition

- Mutation-agnostic and modifiable cell therapy method for cytoplasmic protein replacement for retinal diseases.
- Designed for transfer into photoreceptor cells as therapy for retinal diseases with potential applications across rare diseases.

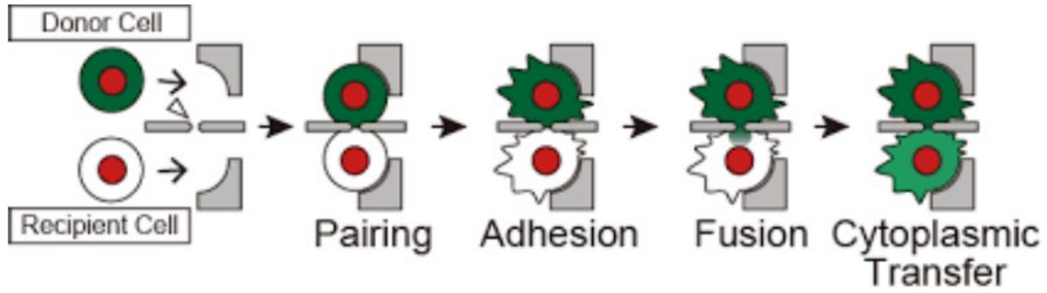
Background

- Over 2 million people worldwide are affected by inherited retinal diseases, but only 1% of patients are served by a single FDA approved drug
- Inherited retinal diseases show greatest diversity with causative mutations in over 300 genes
- Current treatments are not mutation agnostic, rendering single gene treatments impractical and unaffordable.

Updates

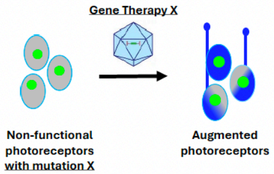
- Lead candidate (AGN-001) mechanism has been independently verified by multiple labs
- Pursuing IND-enabling trials for device safety in pig model

Cytoplasmic Transfer Can Transfer Wild-Type Proteins into Diseased Photoreceptor Cells

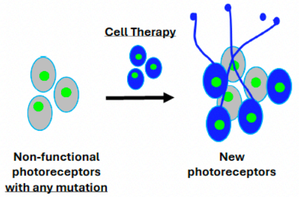


Agnos' Lead Candidate, AGN-001, is Mutation Agnostic and Does Not Require New Synapse Formation

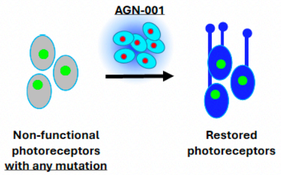
Gene Therapies are limited to addressing only a single known gene mutation to restore function



Cell Therapies are limited by the need to mature and form new synapses to restore function



Agnos overcomes these limits as a gene agnostic therapy that does not require new synapses



Kalargyrou et al. (2021) *EMBO Rep*

DIABETES
EMC2 BIO

Scott Carmer

JOHNS HOPKINS UNIVERSITY

Stage of Dev	Capital Received	Raising Total	IP Status
Seed	$500K	$3.5M	Patented

CURRENTLY RAISING

Value Proposition

- A nanoparticle-based delivery system designed to target therapeutic cargo specifically to β cells
- Translates immune-evasive mechanisms from tumor cells to β cells by modulating similar immune-protective gene pathways

Background

- Gene networks that modulate immune-protective pathways are not unique to β-cells, and using non-specific therapies is not clinically feasible
- Current moieties to target therapeutics to T1D disease-related cells (autoimmune cells and pancreatic β cells) lack specificity required for clinical translation
- The ability to target specific disease-related cells enables development of potentially curative immune-therapies in T1D

Updates

- Lead EMC2 LNPs demonstrate significantly greater pancreas-specific distribution and gene transfection vs Moderna control LNP in healthy mice

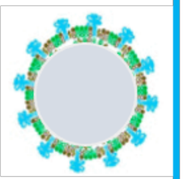
Innovation and Design Concepts of the β cell-targeting LNP Delivery System

Targeting Design 1: β cell-specific binding

- β cell-specific target: DPP6 cell-surface protein
- Target-specific binding moiety: 4hD29 camelid nanobody

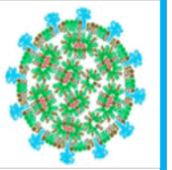
Targeting Design 2: Cell-specific LNP design

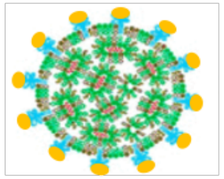
- Optimized for biodistribution to pancreas
- Optimized for preferential uptake and gene transfection in β cells



Therapeutic Concept: Target gene pathways that modulate cross-talk between autoimmune cell and β cell

- siRNA to induce immune-protective mechanisms
- mRNA to dampen metabolic stress mechanisms





***β*-cell targeting LNP with RNA cargo**

DIGITAL HEALTH, DIAGNOSTIC

CURIE DX

Therese Canares, MD

Rashmi Sachan

Johns Hopkins University

Stage of Dev	Funding	IP Status
Seed	$900K	Two patents pending

Value Proposition

- Increase telehealth practice revenue by making the patient experience so delightful they keep coming back with smartphone image disease prediction: Labcorp for your Phone

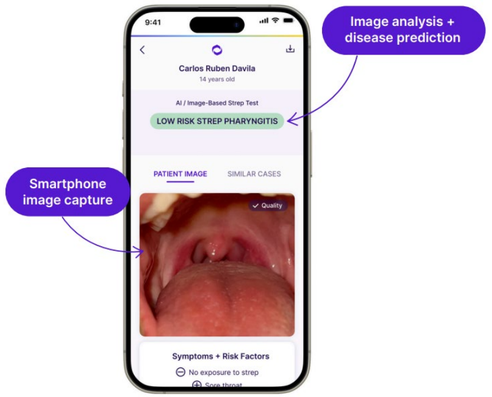
Background

- B2B SaaS- software platform enables disease prediction from a smartphone
- Target market is chief medical officers at telehealth practices
- Starting with strep throat, UTI, 5+ other diseases in the pipeline
- Leverages AI/Computer vision + medical images

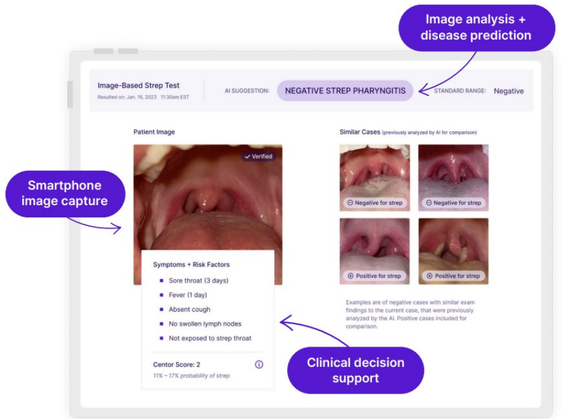
Updates

- Partnerships with national urgent care chain, JHU, Brown University
- Paid pilot booked with a telehealth practice
- Go to Market: Direct sales, with $2M in the sales pipeline
- App launched in the iOS app store
- Awarded $600k non-dilutive (NSF, Microsoft)
- Raising $1.3M
  - $400k of $1.3M preseed in the bank (TEDCO, Angels) as of May 2024

Instantly Predict Disease with a Photo and Sync with Telehealth Physician



(Patient mobile view)



(Clinician desktop view)

PRE-CO

CANCER THERAPEUTICS

BISPECIFIC ANTIBODIES FOR METASTASIS

Jamie Spangler, PhD

JOHNS HOPKINS UNIVERSITY

Stage of Dev	Funding	IP Status
Technology	Grants	Patent Pending

Value Proposition

- Multifunctional antibody that specifically targets and blocks tumor metastasis as a novel cancer therapeutic.

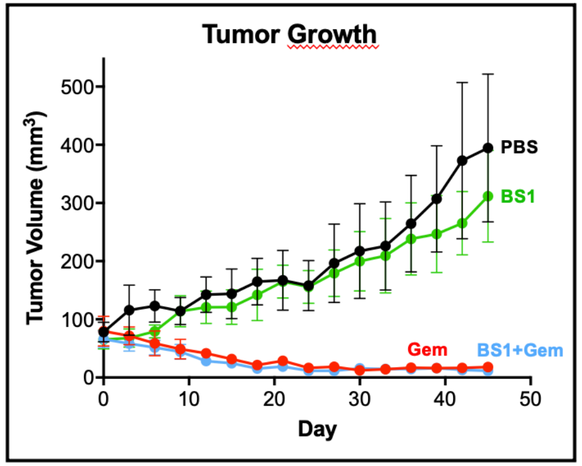
Background

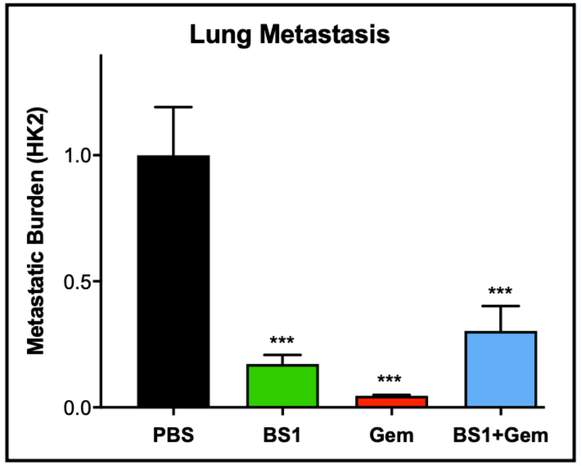
- Metastasis accounts for 90% of deaths from solid tumors.
- Cell migration driven by IL-6/IL-8 signaling promotes metastatic spread in cancer.
- Novel bispecific antibodies block metastasis better than combination therapy with enhanced potency, increased specificity, reduced drug resistance, and single-molecule format.

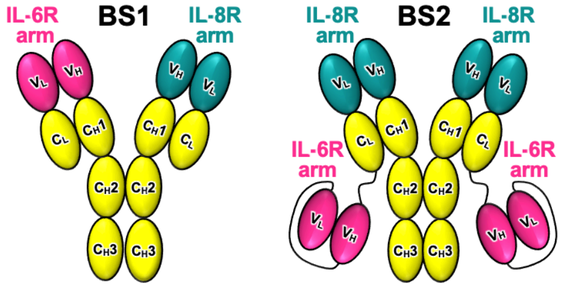
Updates

- Completed pre-clinical efficacy studies in mice, alone and in combination therapy regimens.

Bispecific Antibodies Complement Standard of Care in Inhibiting Breast Cancer Tumor Growth and Metastasis







Advantages of Bispecific Antibodies

- ✓ Enhanced affinity and potency
- ✓ Increased specificity
- ✓ Reduced drug resistance
- ✓ Single-drug therapy

AUTOIMMUNE DISEASES

BISPECIFIC AUTOANTIGEN-T CELL ENGAGERS (BAITE)

Maximilian Konig, MD

JOHNS HOPKINS UNIVERSITY

Stage of Dev	Funding	IP Status
Technology	$4M	Patent Filed

Value Proposition

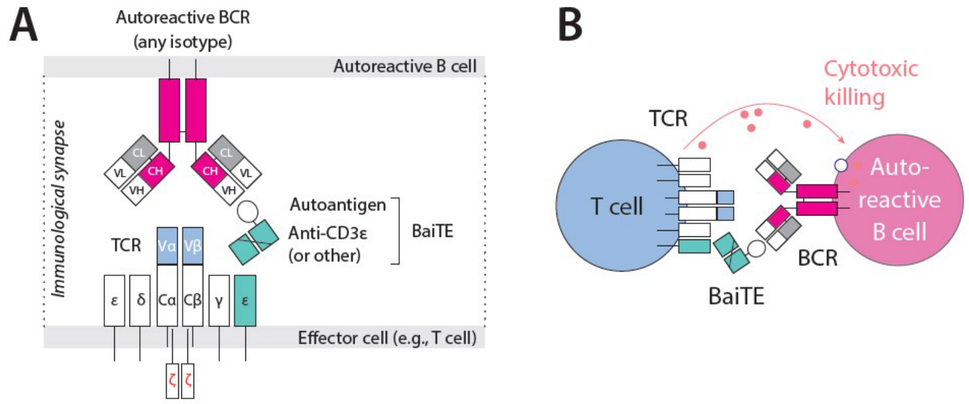
- First-in-class precision immunotherapies for autoimmune diseases
- Selective depletion of autoreactive B cells with wide applicability across autoimmune and rheumatic diseases (e.g., antiphospholipid syndrome, lupus, rheumatoid arthritis)
- Normal immune cells are spared, eliminating risk of infection
- Treatment of mild disease or even preclinical autoimmunity possible
- Off-the-shelf, no need for conditioning, and maximally scalable

Background

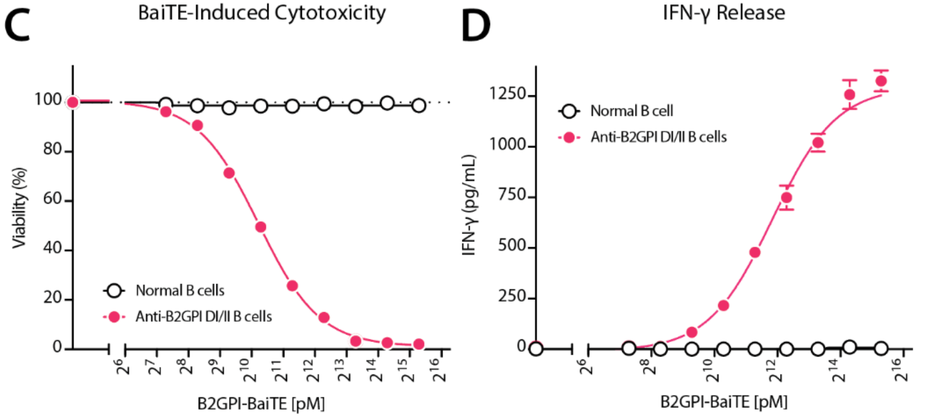
- A protein-based immunotherapeutic platform technology that redirects T cells to induce deep depletion of autoreactive B cells
- Optimized for potency and engineered to eliminate off-target binding

Updates

- Funded through Lupus Research Alliance (Innovation Award)
- Part of a growing portfolio of cellular and antibody-based precision immunotherapy platforms: BaiTE, CATCR-T, TCR-targeted bispecific antibodies for B cell- and T cell-mediated autoimmune diseases



A: BaiTEs are disease-tailored precision immunotherapies designed to redirect T cells to selectively eliminate autoreactive B cells, while sparing all other B cells. **B:** BaiTEs induce immune synapse formation and deep depletion of the polyclonal autoreactive B cell pool via T cells. BaiTEs are off-the-shelf precision therapies and can be administered at scale.



C: B2GPI-BaiTE induces depletion of autoreactive, anti-B2GPI Ramos B cells (pink) in a dose-dependent manner, without causing depletion of Ramos B cells with irrelevant BCRs (normal, back circles). **D:** Interferon-ɣ (IFN-ɣ) secretion by T cells incubated with BaiTE is only observed in the presence of target B cells (pink), but not normal B cells.

AUTOIMMUNE DISEASES

CHIMERIC AUTOANTIGEN-T CELL RECEPTOR (CATCR-T)

Maximilian Konig, MD

JOHNS HOPKINS UNIVERSITY

Stage of Dev	Funding	IP Status
Seed	$100K	Patented

Value Proposition

- Selective targeting of B cells expressing a specific autoantibody with wide applicability across autoimmune diseases (e.g. multiple sclerosis (MS), antiphospholipid syndrome (APLS)) and B cell lymphomas
- Likely fewer adverse effects than current therapies due to improved targeting

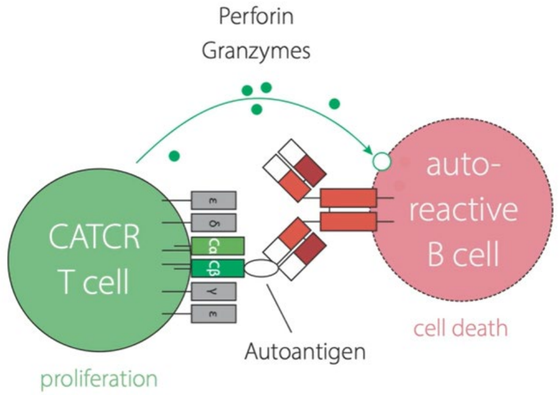
Background

- CRISPR-mediated introduction of engineered T cell receptors (TCRs) designed to target an autoantibody
- *In vitro* proof of concept demonstrated with autoreactive B cells associated with MS, APLS, and other conditions

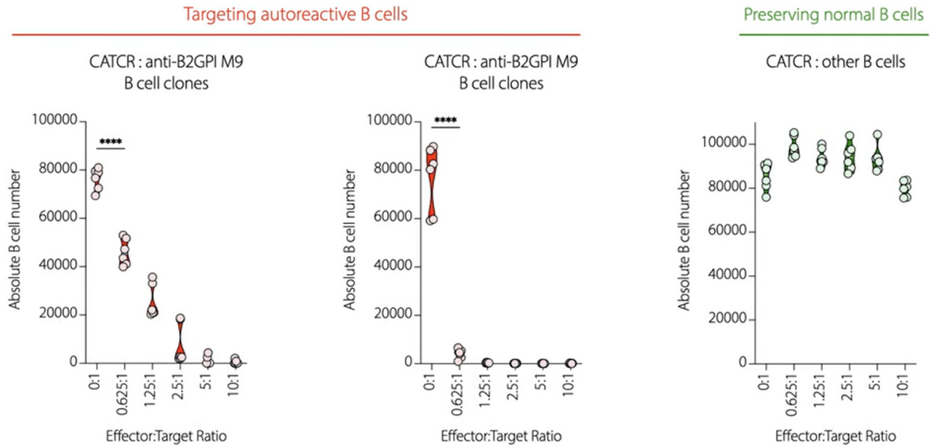
Updates

- Recipient of the 2023 Biscotti award.
- Focus on finalizing constructs to move forward with *in vivo* testing.

CATCRs Reprogram T Cells to Selectively Kill Autoreactive B Cells Approach



In Vitro Killing of Autoreactive B Cells that Drive APLS



B2GPi = Beta-2-Glycoprotein I – Target of autoreactive antibodies in APS

CARDIOLOGY
IDENTIFYING CARDIOPROTECTIVE CAMKII INHIBITORS

Marc Anderson, MD, PhD

Betsy Luczak, PhD

JOHNS HOPKINS UNIVERSITY

Target	Modality	IP Status
CAMKII	Small Molecule	-

Value Proposition

- Novel screening platform allowed for in vivo CAMKII inhibition and identification of ruxolitinib as a potent inhibitor with poor BBB permeability.

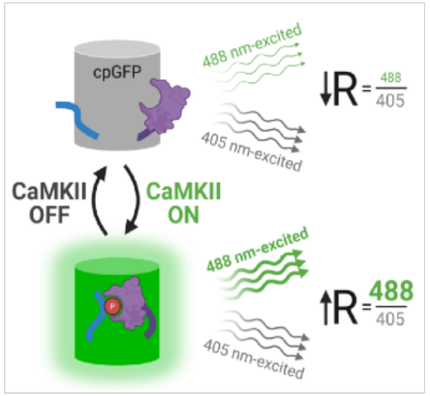
Background

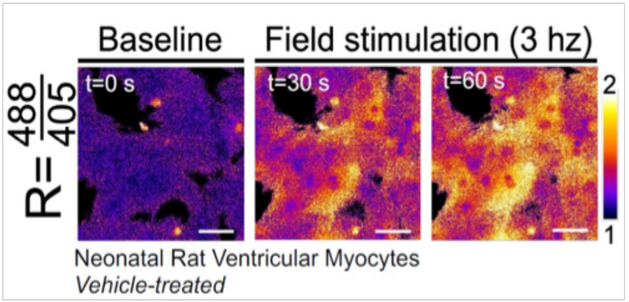
- CAMKII is a highly validated driver of cardiac diseases and arrhythmias.
- Previous development of inhibitors has been hampered by poorly designed assays to monitor inhibition and BBB permeability of inhibitors identified and inhibition of CAMKII within the CNS.
- Characterization of in vitro and in vivo activity of ruxolitinib in multiple murine models revealed potential therapeutic benefit.

Updates

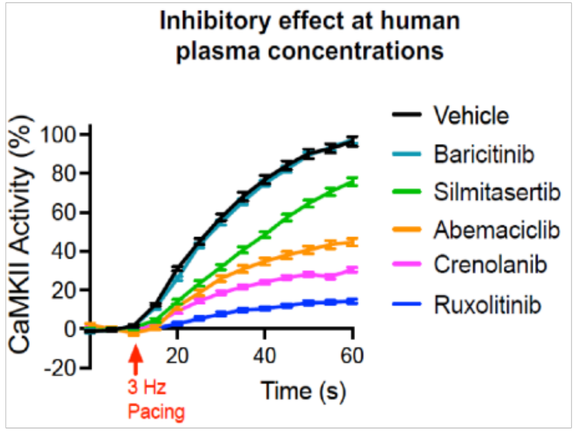
- Evaluating pharmacophore screening to identify novel molecular entities with lack or reduced JAK inhibition.
- Additional screening of novel compound library to identify novel hits.

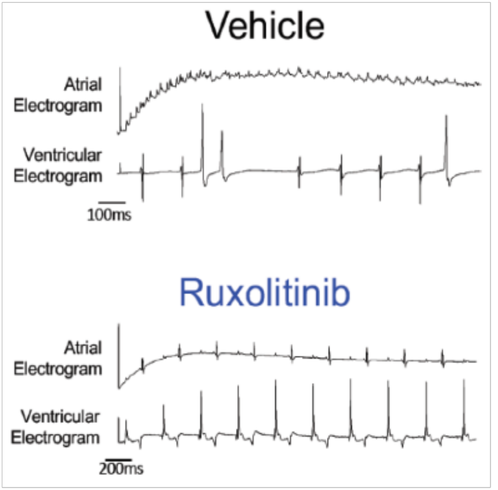
Design & Testing of CAMKII Cellular Reporter System





Identification of Ruxolitinib as a Potent CAMKII Inhibitor





Reyes et al. (2023) *Science Translational Medicine*

IMMUNOTHERAPY
LIPID NANOPARTICLES TARGETING TUMOR-SPECIFIC CD4+ T-CELLS FOR IN SITU CAR T-CELL GENERATION (C16388)

Jonatha Schneck, MD, PhD

Hai-Quan Mao, PhD

JOHNS HOPKINS UNIVERSITY

Target	Modality	IP Status
Tumor Specific CD4+ T -Cells	Lipid Nanoparticles	Patent Pending

Value Proposition

- Magnetic nanoparticle-based artificial antigen presenting cells (aAPCs) to enrich and expand antigen-specific T-cells

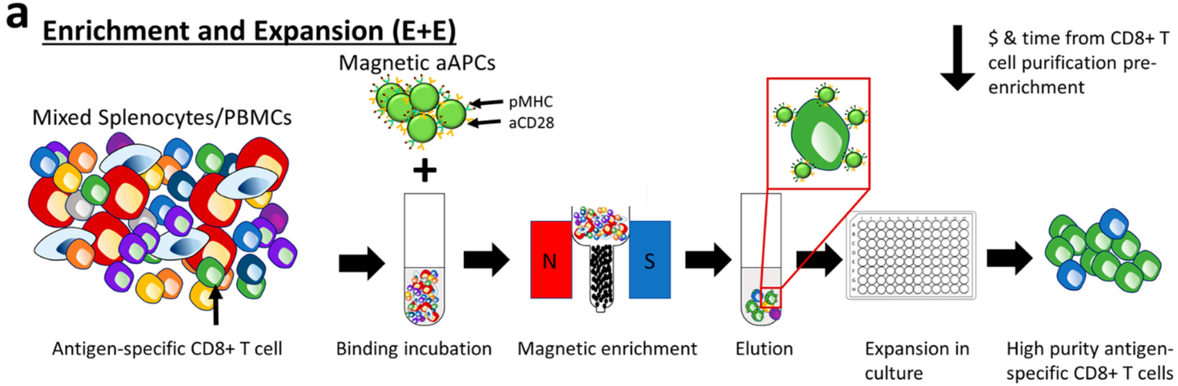
Background

- Identification and expansion of antigen specific T-cells is challenging, low-throughput, and complex.
- Easy to adopt high-throughput workflow allows for identification and analysis of antigen-specific T-cell responses by non-specialists.
- Artificial antigen-specific T-cells allow for expansion with co-stimulatory molecules.

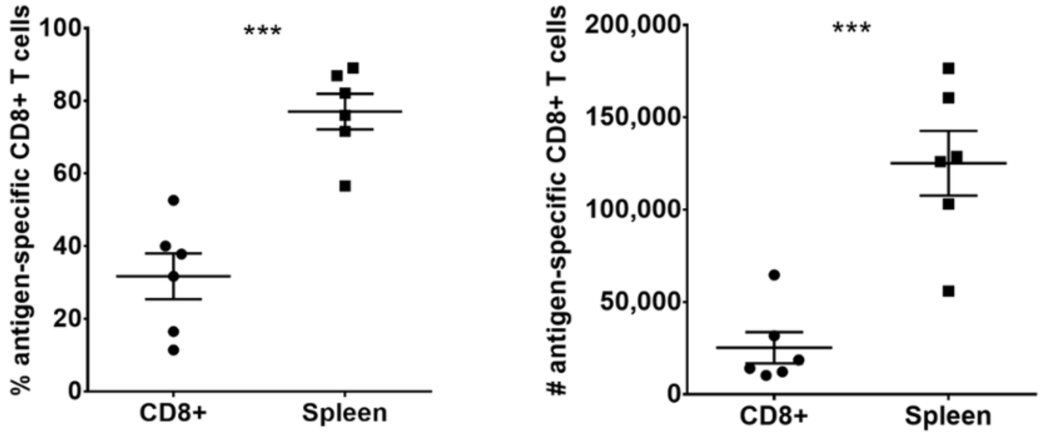
Updates

- Awarded $100K Thalheimer translational funding grant
- Preparing application for MII Ph 1?

aAPC-Mediated Antigen-Specific T-Cell Expansion Workflow



Expansion of Unpurified Splenic CD8+ T-Cells After 7-Days of aAPC Culture



Hickey et al. (2020) *Nano Letters*.

NEUROLOGY
MIF NUCLEASE INHIBITORS FOR NEUROLOGICAL DISORDERS

Ted Dawson, MD, PhD

Johns Hopkins University

Valina Dawson, PhD

Target	Modality	IP Status
MIF nuclease	Small molecule	IP Filed and Granted

Value Proposition

- Inhibition of nuclease offers neuroprotective strategy across several models of neurodegeneration.

Background

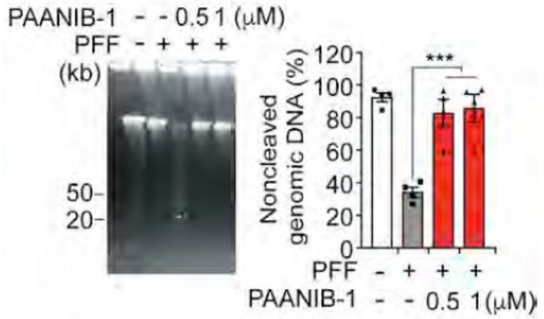
- Macrophage migration inhibitory factor (MIF) is a PARP-1 dependent AIF-associated nuclease that leads to DNA fragmentation and promotes pro-inflammatory cytokines.
- Depletion or inhibition of MIF nuclease activity inhibits neurotoxicity following glutamate excitotoxicity, focal stroke, alpha-synucleinopathy (a-syn), and other neurodegenerative models.
- Inhibitor PAANIB-1 has been identified.

Updates as of 1/16/24

- Optimization of inhibitor and additional characterization on-going.

TH = Tyrosine hydroxylase a marker for dopamine neurons; SNpc DA = substantia nigra pars compacta dopaminergic neurons

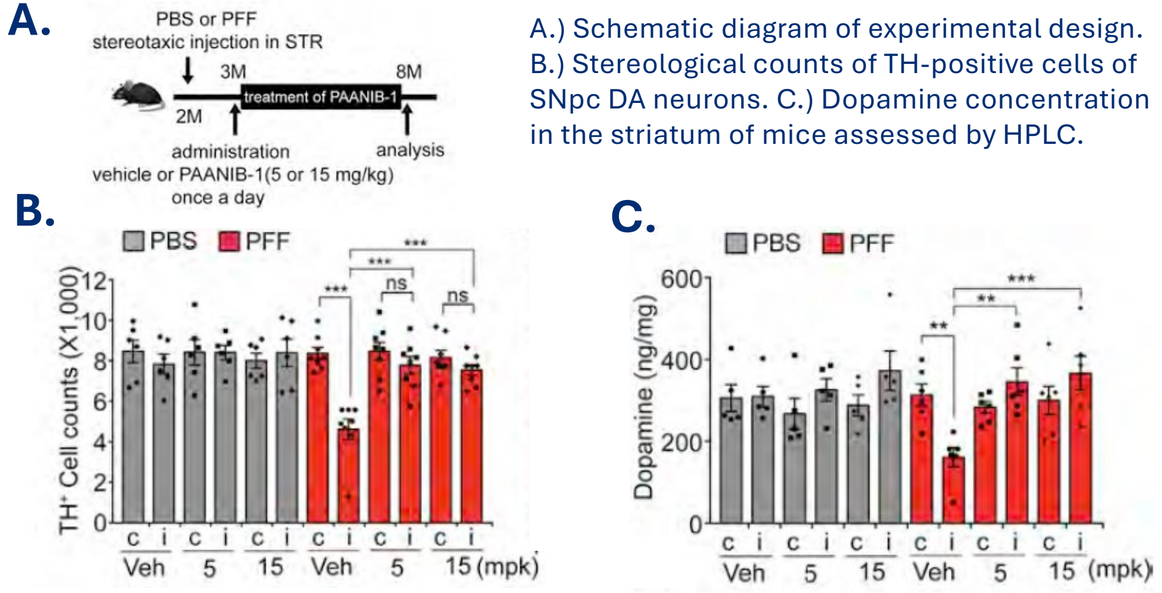
PAANIB-1 Inhibits α-Syn Induced DNA Fragmentation



Pulse-field gel electrophoresis of α-syn-PFF-induced DNA cleavage in mouse cortical neurons treated with PAANIB-1

PFF = pre-formed fibrils of a-syn

PAANIB-1 Protects PD-Related Neurodegeneration *In Vivo*



A.) Schematic diagram of experimental design. B.) Stereological counts of TH-positive cells of SNpc DA neurons. C.) Dopamine concentration in the striatum of mice assessed by HPLC.

Park et al. (2022) *Cell*

NEUROLOGY
MGGPRX1

Xinzhong Dong, PhD

Johns Hopkins University

Target	Modality	IP Status
MrgX1	Small molecule	Filed

Value Proposition

- Effectively attenuates persistent, and spontaneous pain without causing opioid-like side effects and abuse potential.
- Target is expressed in DRG neurons, eliminating the possibility of off-site related side effects seen in opioid-based analgesics.

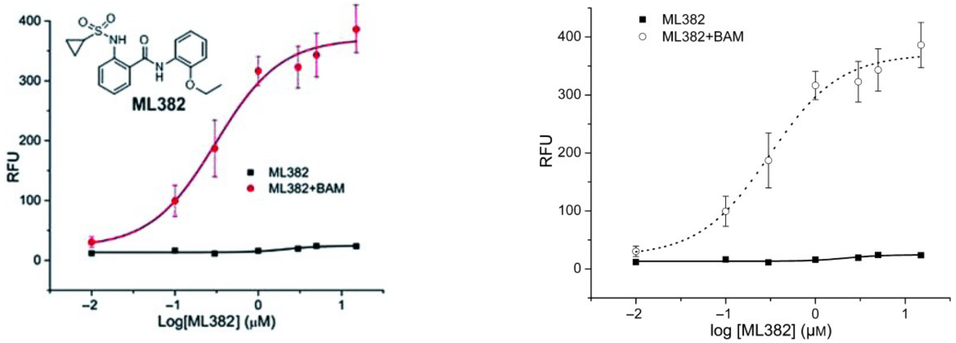
Background

- Mrgx1 is a G-protein coupled receptor involved in perception or sensation of pain.
- MrgX1 activated in the spinal cord inhibits pain similar to morphine, without an itch side effect.
- ML382 is a beneficial tool compound, needs to be optimized.

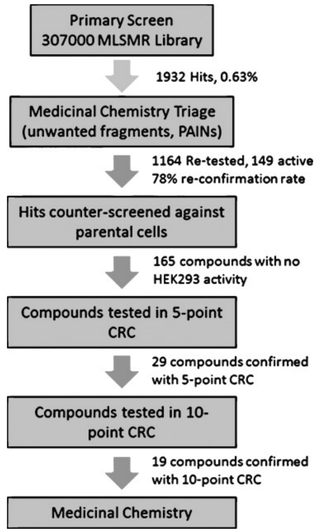
Updates as of 1/16/24

- Working on strategy to file more IP.

Pharmacological Profile of ML382 on MrgX1 – Expressing HEK293 Cells



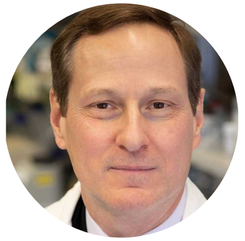
Flowchart of the Screening Paradigm for MrgX1 PAM



Wen et al. (2014) *Discovery and Characterization*

ONCOLOGY

NONSENSE MEDIATED DECAY INHIBITORS



Ken Kinzler, PhD

Nick Wyhs

JOHNS HOPKINS UNIVERSITY

Target	Modality	IP Status
SMG1	Small Molecule	-

Value Proposition

- Lead target SMG1 inhibitor, KVS0001, was developed through rational design and is bioavailable, safe, and efficacious in mouse cancer models.

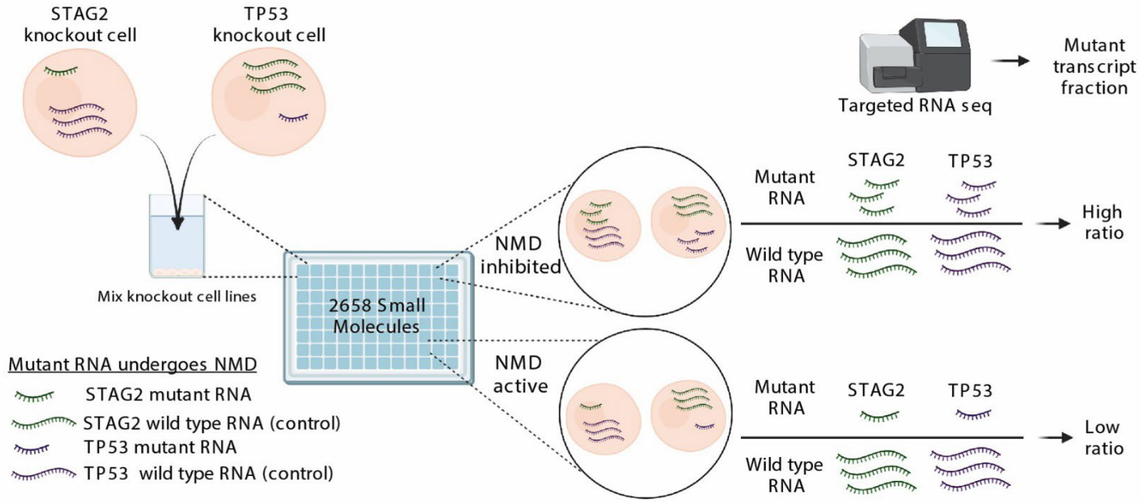
Background

- Non-sense mediated decay (NMD) is a surveillance pathway which destroys mutant RNA transcripts before translation.
- In disease states, such as cancer, clinical symptoms are more profound when mutations undergo NMD
- NMD proteins serve as a potential target for inhibition to reduce protein suppression and cure these disease through NMD inhibition.

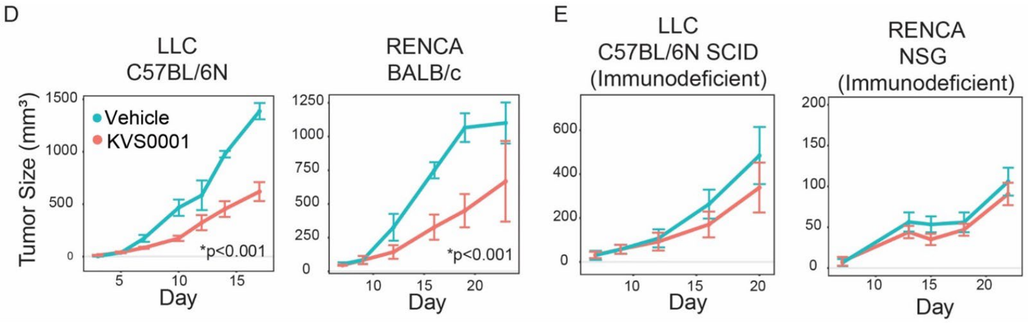
Updates

- Toxicity and specificity studies are ongoing.

High Throughput Screening Assesses for NMD Inhibition



Lead Candidate Demonstrates Tumor Size Reduction in High Mutational Burden Cancers



HAPLOINSUFFICIENCY DISORDERS

RNA BOOSTER TECHNOLOGY

Jeff Coller, PhD

JOHNS HOPKINS UNIVERSITY

Target	Modality	IP Status
TBD	Oligonucleotide	-

Value Proposition

- Mutation agnostic technology to increase expression of normal mRNA.
- Utilizing modified oligonucleotides to increase stability and translation of endogenous mRNA.

Background

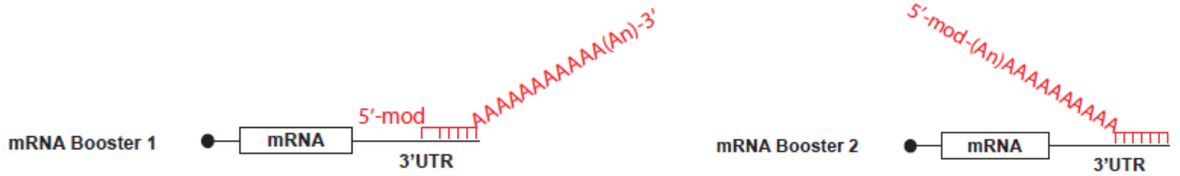
- Therapeutic strategy for haploinsufficiency disorders typically relies on gene product restoration to preserve function.
- Proof of concept demonstrated *in vitro* with multiple mRNA targets including MeCP2, CTNNB1, PURA, and SYNGAP1.
- *In vivo* activity demonstrated with MeCP2 in the liver and SYNGAP1 in the brain.

Updates as of 6/20/24

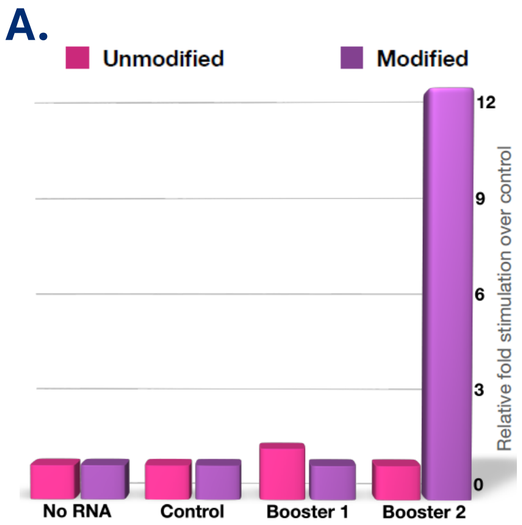
- Continuing to make progress in refining booster size and sequence for multiple targets with additional *in vitro* and *in vivo* data

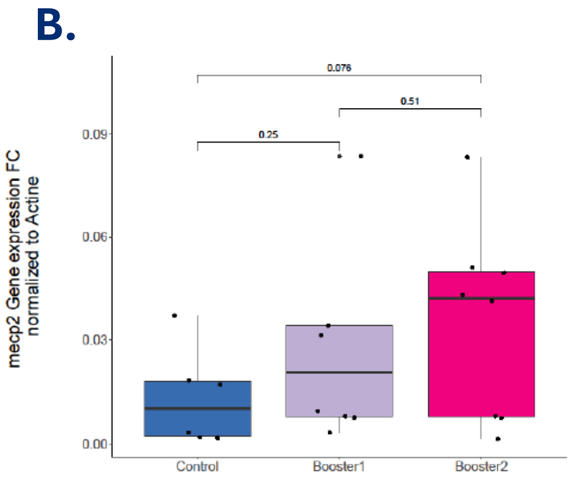
MeCP2 = methyl CpG binding protein 2; CTNNB1 = beta-cantenin; PURA = Pur-alpha ; SYNGAP1 = synaptic Ras-GAP 1

Design of Two Initial RNA Boosters Developed



Evaluation of RNA Booster For MeCP2





A.) RNA was transfected into HEK cells and then incubated for 24 hours B.) MeCP2 mRNA and protein levels in mouse liver injected with control and booster RNA. RNA was mixed with LNP and tail vein injected. Each mouse was dosed with 25mg RNA.

ONCOLOGY

VR-CAR T CELLS FOR SOLID TUMORS

Denis Wirtz, PhD

JOHNS HOPKINS UNIVERSITY

Target	Modality	IP Status
TBD	Cell therapy	Patent Pending

Value Proposition

- Identification and leverage of "velocity receptors", cytokine receptors that increase CAR-T cell motility and infiltration of solid tumors.
- Expression of velocity receptors (VR) on CAR T cells result in increased infiltration in tissue and tumor-killing activity.

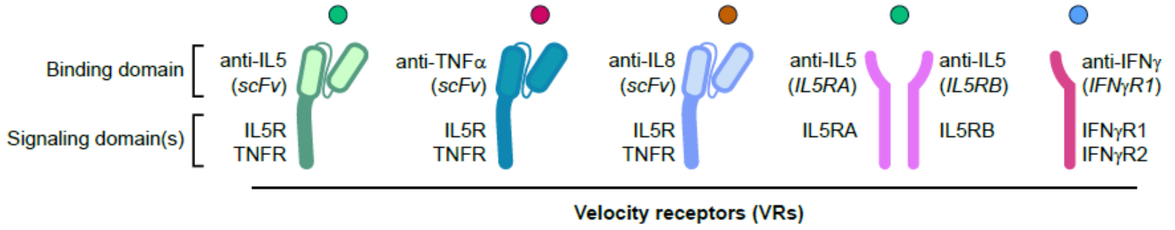
Background

- Solid tumors present an accessibility challenge for cancer therapeutics such as CAR-T cells.
- Engineering of CAR-T cells to increase efficacy (tumor infiltration and killing).
- Extensive *in vitro* data in 3D organoid models demonstrate improved CAR-T cell motility in presence of VRs.
- Proof of concept demonstrated with mesothelin CAR T cells (M5CAR) with and without VRs.

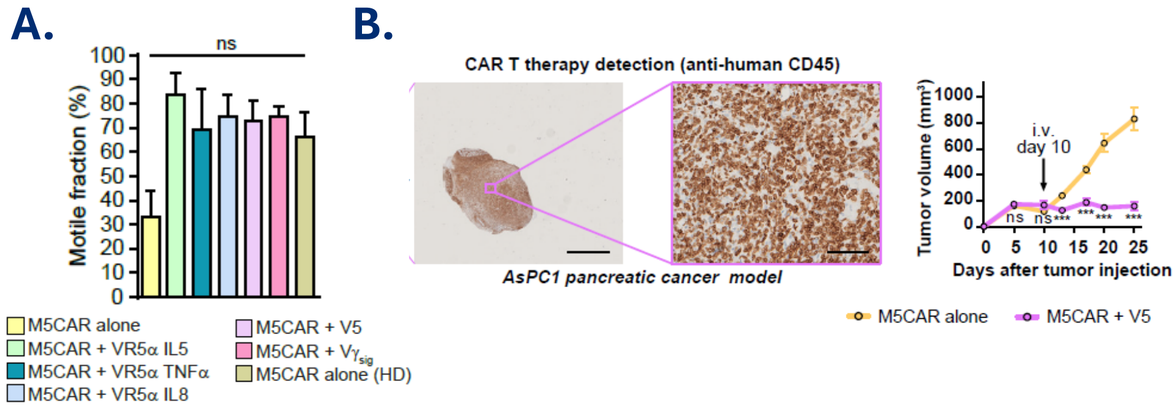
Updates as of 1/16/24

- Identifying additional CARs and optimizing VR constructs to support candidate selection.

Design of Velocity Receptor Constructs



In Vitro & *In Vivo* Activity of VR-CAR T Cells



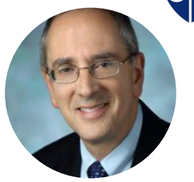
A.) M5CAR or VR-M5CAR T cells at low density were encapsulated in a 3D collagen gel for 48 hrs and the migration and motility measured. B.) Pancreatic cancer tumor cell line AsPC1 were engrafted into NSG mice and treated with M5CAR or V5-M5CAR at Day 10. Tumor volume and CAR T infiltration evaluated.

Johnston et al. (2023) *bioRxiv* (preprint)

ONCOLOGY

NOVEL ONCOLOGY TARGETS FROM THE NEXUS OF AUTOIMMUNITY AND CANCER

Andrew Ewald, PhD



Antony Rosen, MD

JOHNS HOPKINS UNIVERSITY

Target	Modality	IP Status
Target X	Antibody	Patent Pending

Value Proposition

- Target X, identified using our autoimmune patient sera platform, is uniquely expressed on the surface of various tumor cells, while remaining undetected on healthy cells.

Background

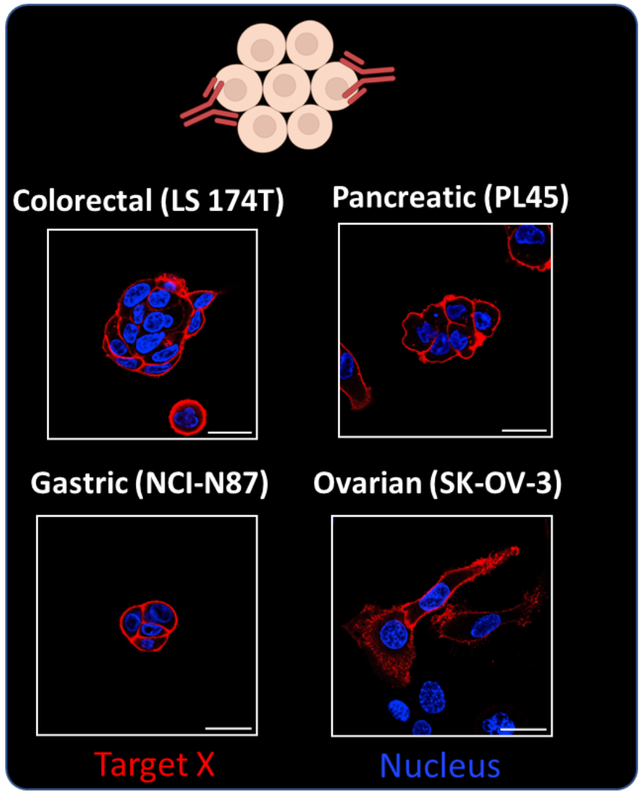
- Similar cell stresses observed in both cancer and autoimmunity can induce the surface expression of novel antigens, signaling to the immune system that something is wrong.
- We can co-opt this connection to identify novel targets on cancer cells and design new therapeutics.

Updates

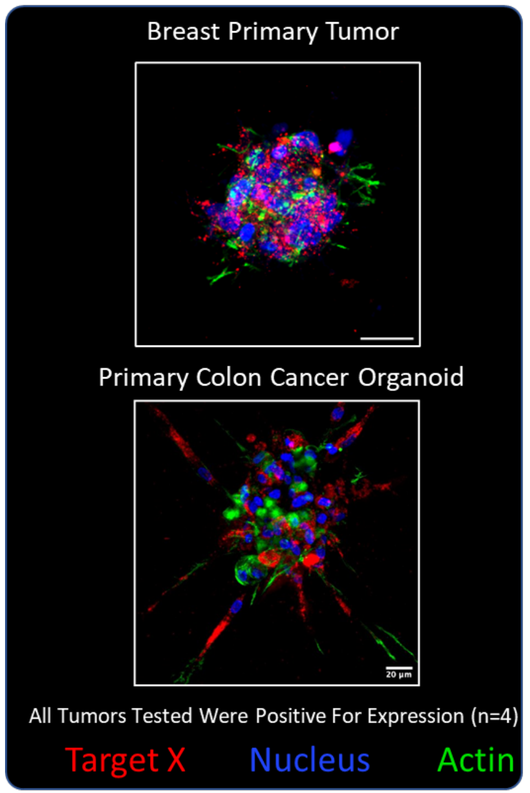
- Additional potential targets identified to enable future pipeline growth.
- Looking for investment to support lead identification, initiate IND-enabling studies, and expand target discovery platform.

Target X has been extensively evaluated on multiple human cell lines, and patient tumor samples

Cancer Cell Lines



Patient Tumors



Commercial Antibody Against Target X Demonstrates Therapeutic Potential in Multiple Assays (Data Not Shown)