Life Sciences

Technology Available for Licensing

DARTMOUTH
Technology Transfer

2004-0269

EXTENSIVE IP PORTFOLIO AVAILABLE FOR REVIEW

Leveraging PD-L3 and VISTA Antibodies to Address the Following Indications: Autoimmunity, Cancer, Viral Infection, and Inflammation

PRINCIPAL INVESTIGATOR: Dr. Randy Noelle, Emeritus Professor of Microbiology and Immunology

VIEW PUBLICATIONS

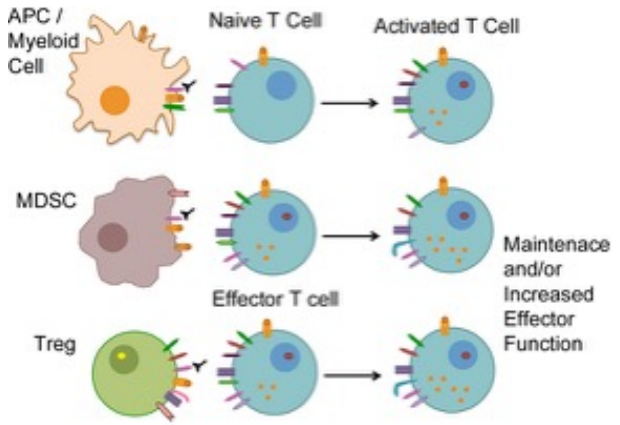
DESCRIPTION

- Autoimmune disorders, various cancers, inflammatory diseases, and viral infections affect the lives of many in the US and globally.
- Immunotherapies and anti-inflammatory drugs are utilized treat these conditions.
- V-domain Ig suppressor of T cell activation (VISTA) is an immune checkpoint molecule that is expressed on various immune cells.
- These technologies target VISTA, as well as PD-L3, for multiple indications such as autoimmune diseases, viruses, and various cancers.

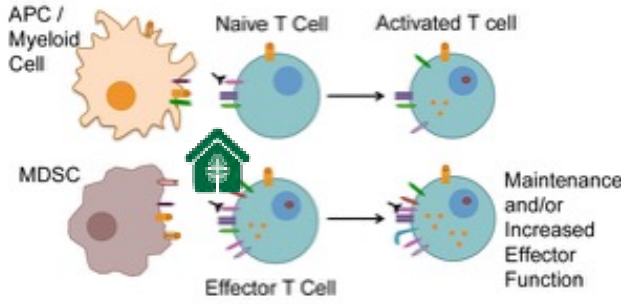
ADVANTAGES AND BENEFITS

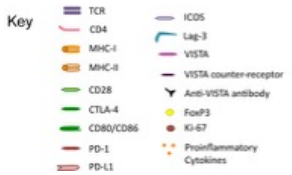
- Utilizing an anti-PD-L3 antibody results in enhanced T cell immune responses, strengthened anti-tumor immunity, and defense against viral infection.
- The use of PD-L3-Ig fusion proteins suppresses excessive immune activity to treat autoimmune disorders, and controls inflammation in various conditions.
- Leveraging a VISTA-Ig fusion protein results in immunosuppression.
- Harnessing anti-VISTA antibodies induces immunosuppression and treats ovarian cancer.
- The use of VISTA-IG treats inflammation in multiple sclerosis.
- Administering an anti-VISTA antibody alongside a PD-1 antagonist enhances antitumor immunity, and boosts CD8+ T cell responses in conditions other than cancer.
- Removing T cells, genetically modifying them to eliminate VISTA-mediated immune suppression, and reintroducing them strengthens antitumor activity.
- Removing T cells, genetically modifying them using siRNA to downregulate VISTA, PD-1, and/or PD-L1, then reintroducing them enhances immune responses against cancer.
- The combined use of a VISTA agonist and an iNOS/NO inhibitor restores B cell immunity in cancer and infectious disease.

VISTA as a Ligand



VISTA as a Receptor





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2014-0828

EXTENSIVE IP PORTFOLIO AVAILABLE FOR REVIEW

Deimmunized Lysostaphin is effective against multi-resistant S. aureus without inducing unwanted immune response

PRINCIPAL INVESTIGATOR: Dr. Karl Griswold, Professor of Engineering

VIEW PUBLICATION

INVENTION OVERVIEW

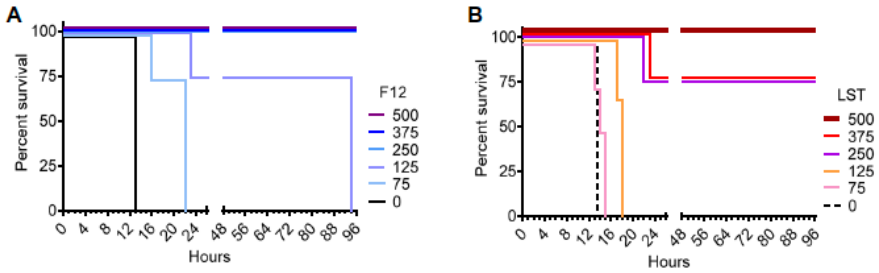
- Lysins are effective bacteriolytic enzymes against S. aureus and other drug-resistant bacteria but they suffer from immunogenic responses, especially upon repeat dosing.
- A directed evolution approach has been used to produce a deimmunized lysostaphin variant, F12.
- Immunological analysis with human PBMCs and human HLA transgenic mice provide preclinical evidence that the F12 variant achieved general evasion of human immune surveillance while maintaining efficacy against S. aureus.

EFFICACY

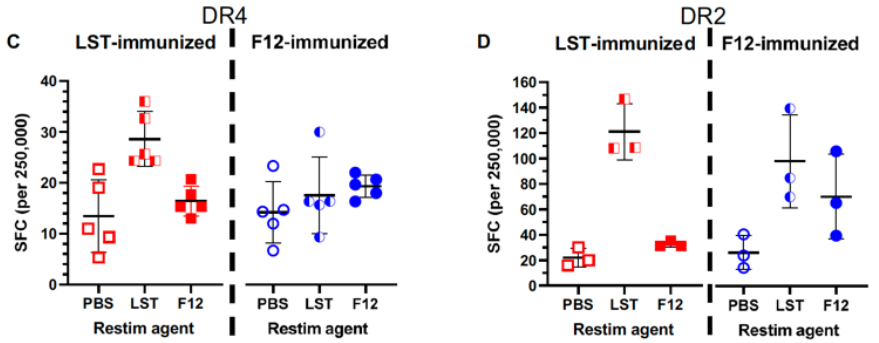
- F12 retains potent *in vitro* anti-staphyloccocal activity against MRSA, VRSA, LRSA and DRSA. *In vivo*, F12 rescued all mice and/or achieved significantly better protection (dose dependent) compared to non-deimmunized lysostaphin (LST) in an acute bacteremia study.
- F12 exhibited better minimum inhibitory concentration (MIC) potency than two clinical-stage anti-MRSA lysins: CF-301 (Aurobac/Boehringer Ingelheim) and SAL200 (iNtRON Biotechnology).
- F12 in combination with daptomycin reduced mortality in a rabbit endocarditis MRSA infection model to 0% compared to 14% for daptomycin and 20% for F12 monotherapy. The combination therapy eradicated MRSA from all target tissues while monotherapies were only marginally effective at reducing bacterial burden.

ADVANTAGES

- **F12 dampens human T cell activation:** A study of T-cell activation in a 17-donor human peripheral blood mononuclear cell (PBMC) assay showed highly effective dampening of the T cell response by F12 compared to LST.
- **F12 reduced immunogenicity *in vivo*:** Using SC injection and inhaled routes of delivery, studies showed reduced immunogenicity by one to two orders of magnitude for F12 compared to LST in two different human HLA transgenic mouse strains.
- **F12 evades established anti-LST immunity:** *Ex vivo* assays using (i) splenocytes harvested from HLA transgenic mice exposed to LST and (ii) human PBMCs expanded in the presence of LST showed F12 evades surveillance by helper T cells primed to recognize the LST protein. An in vivo HLA transgenic mouse preimmunization study showed that F12 is capable of rescuing mice from a lethal MRSA challenge despite preexisting anti-LST immunity.



F12 v. LST dose-response survival curves in murine bacteremia model (dose provided in micrograms per mouse)



Deimmunized lysostaphin variant, F12, shows reduced immune reaction in DR4 and DR2 mouse splenocytes following immunizations with LST and F12.

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Director for Industry Engagement

2017-1005

EXTENSIVE IP PORTFOLIO AVAILABLE FOR REVIEW

Portfolio of Novel Steroid-like Molecules for Oncology and Inflammatory Disorders

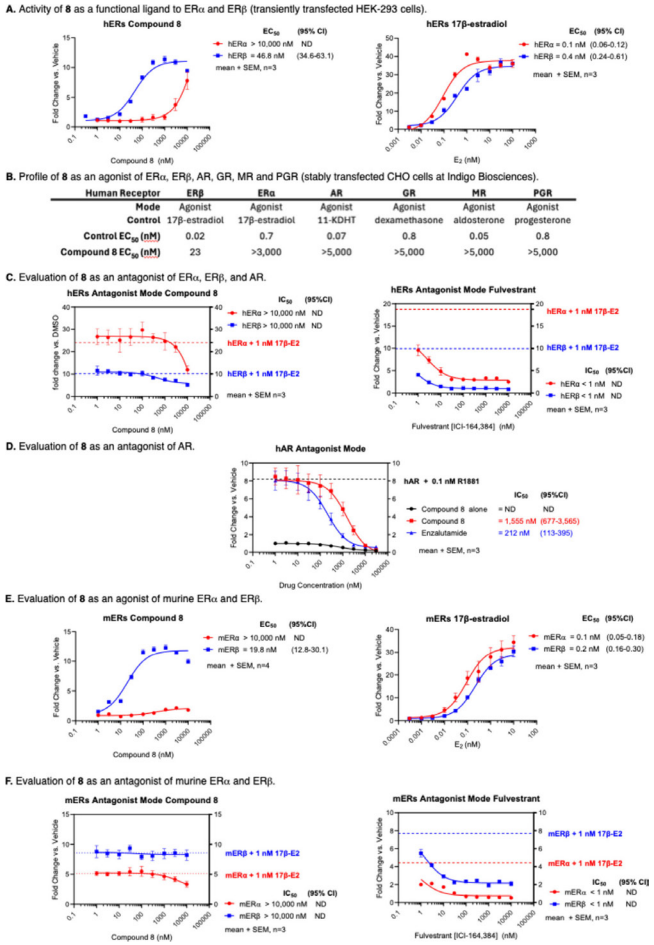
PRINCIPAL INVESTIGATOR: Dr. Glenn Micalizio, Professor of Chemistry

INVENTION OVERVIEW

- This portfolio introduces a wide variety of steroid-like novel compounds available for development including *glucocorticoid receptor modulators, estrogen receptor beta agonists, androgen receptor agonists, G protein-coupled receptors modulators, TLX nuclear receptor ligands, liver X receptor modulators and tetracyclic and pentacyclic triterpenoid compounds* that show high activity and/or selectivity against relevant targets.
- It also presents a **revolutionary chemical platform** for the design and synthesis of novel steroid-like molecules and fatty acid mimetics that overcome the limitations of traditional drug discovery.

ADVANTAGES

- **Simple and Efficient Synthesis:**
  The technology provides a **simple and efficient solution** for the enantioselective synthesis of functionalized steroid-like molecules, including the unnatural enantiomers ("*ent-steroids*"), enabling expedited drug discovery and efficient scale up and manufacturing.
- **Access to Novel Chemical Space:**
  The technology enables the synthesis of previously inaccessible steroid-like molecules, including unnatural enantiomers and diverse structural scaffolds, opening up unexplored regions of chemical space.
- **Enhanced Potency and Selectivity:**
  The technology allows for the intentional design of drugs with improved binding affinity and selectivity for nuclear receptors. For example, ALZ-201 demonstrates **10x** better binding affinity to the Androgen Receptor compared to Enzalutamide, and ERβ agonists have shown over **1600x** selectivity (ALZ-101).



Evaluation of 8 as a dual selective ERβ agonist and AR antagonist. Differences in human estrogen receptor (hER) 17β-estradiol (17β-E2) and 8 response between (A) and (B) are due to use of complementary assays systems (transiently transfected HEK-293 cells and stably transfected CHO cells, respectively; see the Supporting Information). (E) and (F) confirm potent and selective ERβ agonist activity is maintained against murine estrogen receptors (mERs) facilitating preclinical in vivo study. 95% confidence intervals (95% CI) for EC50 and IC50 estimates are provided where calculated. ND, not determined.

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2018-119

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US PATENT APPLICATION 16,639,836

Cellular Therapies for Fibrotic, Inflammatory and Autoimmune Disease

PRINCIPAL INVESTIGATORS: Patricia Pioli, Ph.D., Associate Professor, Department of Microbiology and Immunology | Michael Whitfield, Ph.D., Professor of Molecular and Systems Biology

DESCRIPTION

- Fibrotic diseases contribute to 20-25% of all deaths in the industrialized world, yet there are few effective treatments for fibrosis.
- Systemic Sclerosis (SSc) is a progressive, chronic, and ultimately, deadly fibrotic disease that lacks curative treatment.
- SSc is characterized by dermal and internal organ fibrosis, loss of subcutaneous fat, inflammation, and vasculopathy.
- CD206+ macrophages induce SSc fibroblast activation, and mediate pathology in multiple diseases.
- This invention leverages an Anti-CD206 Chimeric Antigen Receptor (CAR) T Cell to attack fibrosis.

ADVANTAGES AND BENEFITS:

- Anti-CD206 CAR-T cell therapy reduces dermal thickness in local delivery model and restores subcutaneous fat in systemic delivery model.
- Unique macrophage targeting therapy eliminates a key source of fibrotic activation and is the first CAR T cell treatment focused on the innate immune system for fibrotic disease.
- Target is supported by significant data, is mechanistic, and we can identify patients most likely to derive therapeutic benefit.
- Potential for a durable response and can be engineered to secrete anti-fibrotics.

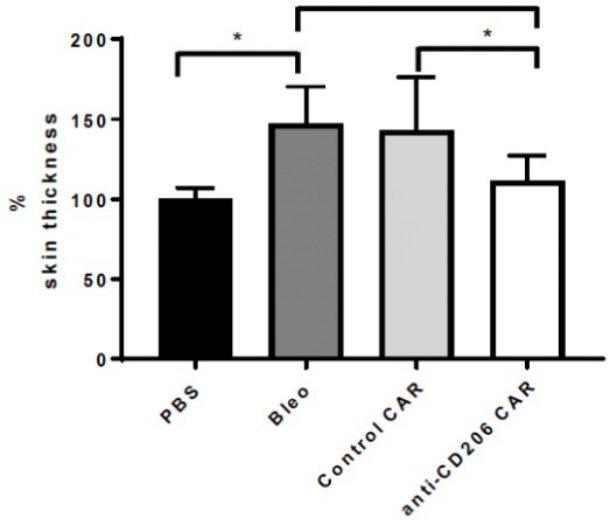

Figure 1: Local delivery of Anti-CD206 CAR-T Cells reduces dermal thickness compared to vehicle control and control CAR

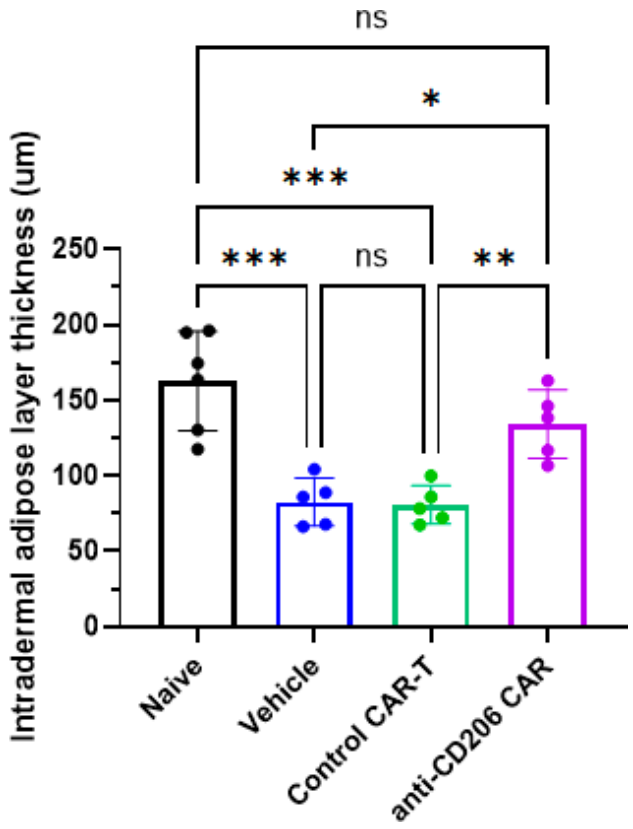

Figure 2: Systemic delivery of Anti-CD206 CAR-T Cells restores subcutaneous fat compared to vehicle control and control CAR.

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2020-014

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US PATENT APPLICATION 17/766,121

Handheld, Inexpensive, Side-by-side Transmission Probe

PRINCIPAL INVESTIGATOR: Paul M. Meaney, Professor of Engineering, Dartmouth
CO-INVENTORS: Timothy Raynolds, Lead Senior Systems Engineer, Dartmouth | Dr. Robin Augustine, Associate Professor of Electrical Engineering, Uppsala University

VIEW PUBLICATION

DESCRIPTION

- Critical to clinical diagnosis and monitoring of conditions such as lymphedema, edema and skin wound is an **accurate picture** of all the diseased and injured tissues.
- Current technologies such as commercial reflection-based dielectric probes include **inadequate penetration** for interrogating deeper tissues and **high sensitivity** to movement during measurements, rendering them less suitable for dynamic or point-of-care applications.
- This **handheld, inexpensive, side-by-side transmission dielectric probe** builds upon the principles of **oversized coaxial probes and transmission techniques**, combining deeper signal penetration with reduced susceptibility to artifacts and improved clinical usability.
- The probe operates using an **"open-circuit" coaxial interface**, where a signal fringes out from one open-circuit coax and is coupled to an adjacent receiving open-circuit coax, propagating through the intervening tissue for interrogation.

ADVANTAGES AND BENEFITS:

- **Enhanced penetration:** This technology achieves penetration depths of **several centimeters**, far surpassing the sub-millimeter range of existing probes.
- **Motion artifact reduction:** Its transmission-based design is far **less susceptible to cable motion artifacts** than current technologies.
- **Improved clinical applicability:** The **side-by-side layout mitigates multi-path signal corruption**, enhancing clinical versatility.
- **Broadband capability:** An "open-circuit" coaxial interface enables **very broad bandwidth** and rich spectral content for diagnosis at varying tissue depths.
- **Portability and cost:** The probe pairs with emerging **handheld Vector Network Analyzers (VNAs) operating up to 3 GHz for under $500**.
- Prototypes have been fabricated using **advanced CAD and metal 3D metal printing**, showing strong early promise. The design has evolved from earlier concepts, now potentially using **elliptical coaxes** to better confine fields and focus the interrogation zone.

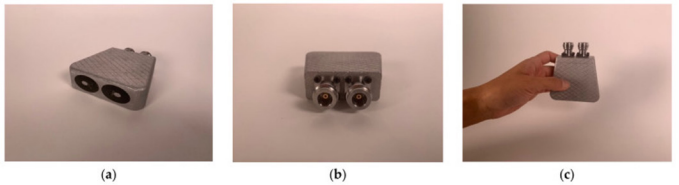

Figure. 1: Preliminary design of the probe.

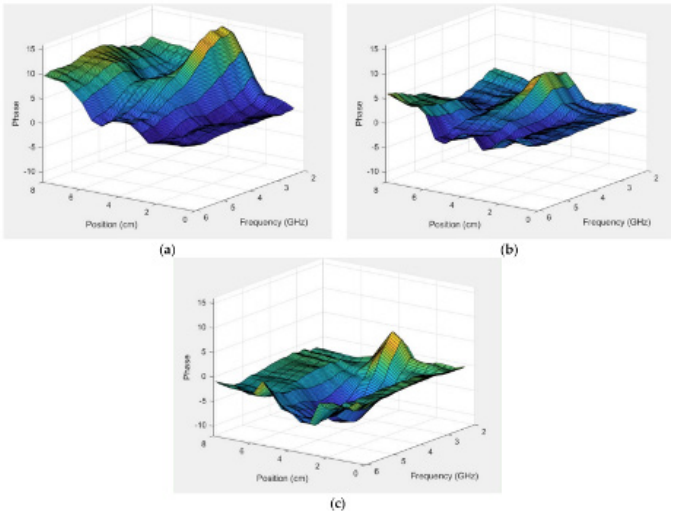

Figure. 2: Normalized phase plots as a function of horizontal position above muscle phantom for all frequencies: (a) 4.32, (b) 2.54, and (c) 1.78 cm diameter. The fat rod was clearly visible for a relatively large frequency range (2-4 GHz).

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2020-015

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US PATENT 12,116,579
US PATENT APPLICATION 18/440,756

Modulation of Fungal Oxygen Consumption via Expression of a Novel Gene Cluster

PRINCIPAL INVESTIGATOR: Dr. Robert A. Cramer, Professor of Microbiology and Immunology

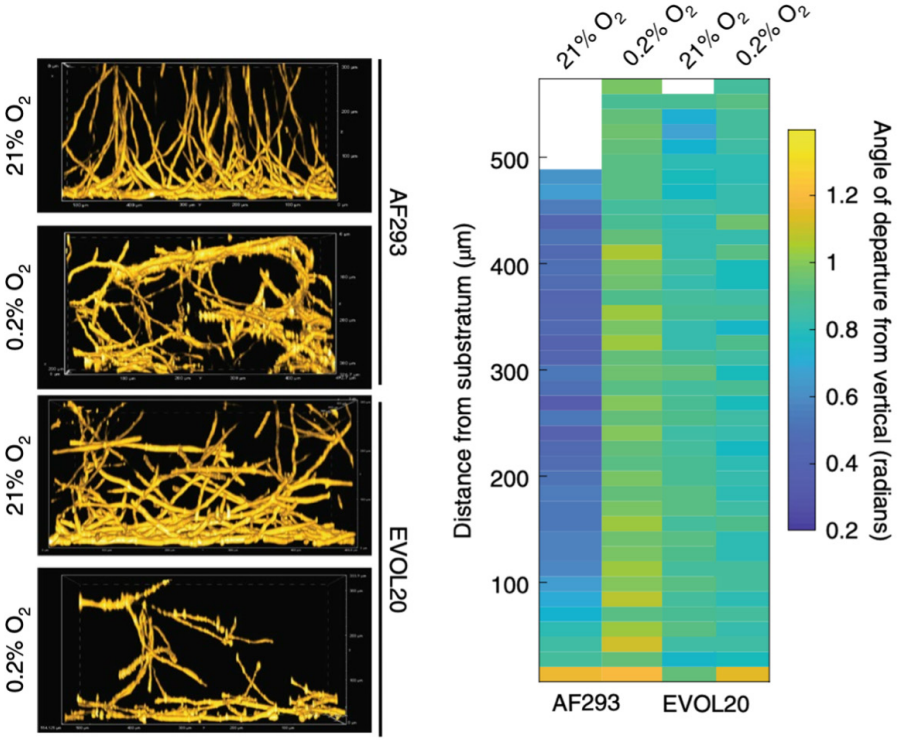
DESCRIPTION

The current industrial enzymes market relies heavily on fungal bioproduction via large-scale fermentation with a $10 billion market growing at 7% annually. Producing enzymes requires large, dense fungal cultures that demand proper aeration. Researchers at Dartmouth have identified **targeted genetic modifications in commercial fungal strains** that will improve characteristics beneficial for industrial fermentation, including reduced oxygen consumption and increased adherence. Either inserting the hypoxia responsive morphology factor A (*hrmA*) associated (HAC) cluster or making a specific mutation in the regulatory gene (*hrmA*, D304G) within the HAC is sufficient to produce the beneficial phenotypes in commercial fungal strains even if the cluster is already present in the strain but normally silenced.

ADVANTAGES AND BENEFITS

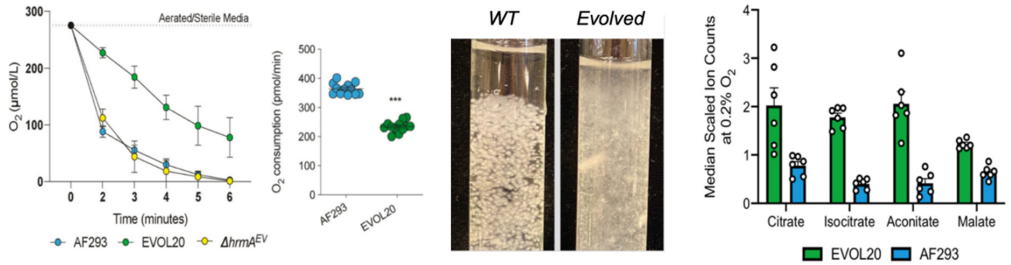
- **Reduced oxygen consumption:** Introducing the discovered gene cluster or a specific mutation into fungal strains can reduce 0_2 consumption by 50%.
- **Increased biomass:** The technology achieves decreased oxygen consumption while maintaining and even increasing the amount of biomass the fungus produces.
- **Reduced adherence:** Expression of the novel gene cluster or introduction of the A. fumigatus baf protein reduces fungal adherence to surfaces, which improves the fermentation process.
- **Improved fermentation:** The invention confers a diffuse mycelial morphology, which is a desirable trait in fungal biomanufacturing, unlike the adherent, biofilm-prone cultures that are problematic in large-scale fermentations.

VIEW PUBLICATION



[Top]: Comparison of mutant EVOL20's loose, non-pelleting mycelial network with wild-type AF293's dense pellets, showing a morphology that diffuse oxygen more efficiently.

Kowalski, C. H., Kerkaert, J. D., Liu, K. W., Bond, M. C., Hartmann, R., Nadell, C. D., Stajich, J. E., & Cramer, R. A. (2019). Fungal biofilm morphology impacts hypoxia fitness and disease progression. Nature microbiology, 4(12), 2430-2441. https://doi.org/10.1038/s41564-019-0558-7



[Left]: Mutated strains display significantly decreased oxygen consumption.

[Center]: Mutated strains exhibits diffuse mycelial morphology, a desirable trait in fungal biomanufacturing.

[Right]:Evolved strains increase secretion of industrially-relevant chemicals in hypoxia.

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2020-027

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PCT/US2021/014145
US PATENT APPLICATION US17/759,045

Immunologically Optimized Botulinum Toxin Light Chain Variants

PRINCIPAL INVESTIGATOR: Dr. Karl Griswold, Professor of Engineering

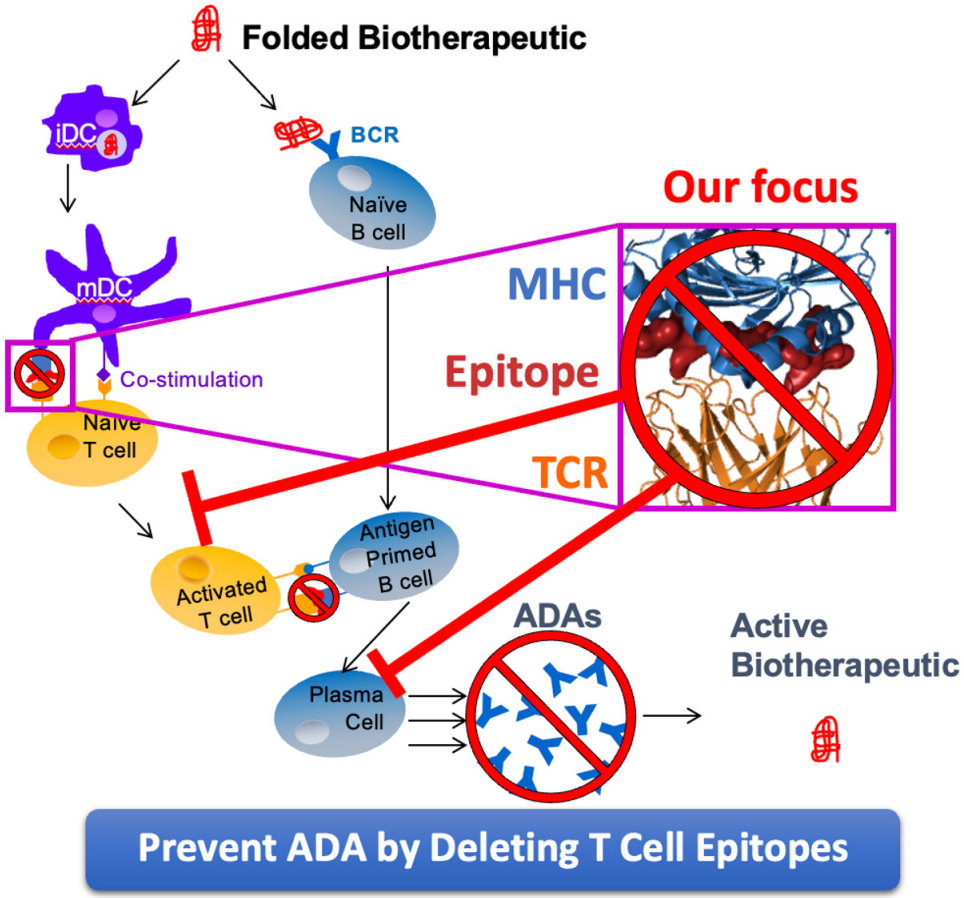
VIEW PUBLICATION

DESCRIPTION

- Botulinum neurotoxin serotype A (BoNT/A) is a biotherapeutic used for both cosmetics and for the treatment of diseases.
- BoNT/A, however, is immunogenic and its use can result in adverse immune responses resulting in various consequences.
- This technology leverages a computationally-driven design of deimmunized BoNT/A LC libraries.
- Using this approach, the immunogenicity of BoNT/A is overcome by preventing anti-drug antibodies (ADAs) via T cell epitope deletion.

ADVANTAGES AND BENEFITS

- This novel method for deimmunizing BoNT/A results in reduced immunogenicity of the botulinum toxin light chain or fragment.
- By utilizing computational protein library design coupled with ultra-high throughput screening, highly deimmunized yet highly active BoNT light chain variants are produced.
- Botulinum toxin has many therapeutic applications, and this mechanism has the potential to improve this drug's utility to improve patient outcomes.



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2020-047

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US PATENT 12,244,726

Amanuensis - A Healthcare Data System for Information Provenance

PRINCIPAL INVESTIGATOR: Dr. David F Kotz, Professor of Computer Science

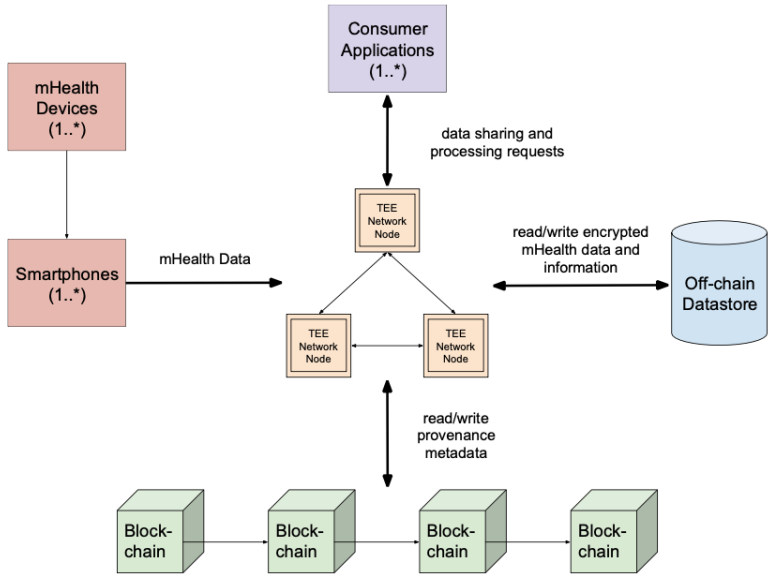
VIEW PUBLICATIONS

DESCRIPTION

- Many healthcare providers are recommending patients use mobile health (mHealth) devices because they **allow providers to monitor individuals' health outside of a clinical setting**. These devices tend to be managed by different organizations and implemented using different technologies, which makes creating a trusted and secure data sharing ecosystem difficult.
- **Current solutions face technological limitations** in ensuring **both data confidentiality during computation and verifiable information provenance** across disparate mHealth data silos.
- **Amanuensis** is a secure and integrated health data system designed to achieve information provenance for mobile health (mHealth) data. It leverages Blockchain and Trusted Execution Environment (TEE) technologies to establish a trusted and secure data sharing ecosystem.
- **The prototype implementation utilizes the VeChain Thor blockchain**, a public blockchain with a Proof-of-Authority consensus mechanism, and Intel Software Guard Extensions (SGX) for the TEE component, leveraging GrapheneSGX, a library OS that allows deploying unmodified applications within SGX enclaves. This demonstrates the practical feasibility of the Amanuensis concept using readily available technologies.

ADVANTAGES AND BENEFITS:

- **Enhanced security and trust:** Amanuensis establishes a consortium of participants who collectively verify data integrity and enforce access policies recorded on a blockchain, removing the need to trust a single entity for gatekeeping health data.
- **Confidential and verifiable:** This technology enables confidential computations on sensitive health data within TEEs, addressing the limitations of traditional blockchain-based smart contracts that expose data due to their transparency.
- **Scalability:** A prototype implementation using Intel SGX and VeChain Thor blockchain demonstrates the potential to support up to **14,256,000 mHealth data sources at $0.07 per data source per day**, showcasing its scalability and potential cost-effectiveness for managing large volumes of mHealth data.
- **Improved data provenance:** Amanuensis provides transparent and immutable data trails by recording provenance metadata on the blockchain, allowing data owners and consumers to verify the origin and history of mHealth data and derived information without accessing the raw data.



System Overview: A high-level depiction of the relationship between the different components of the Amanuensis system.

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2021-023

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US PATENT NO 18/359,373

IL-33 + IL-2 Cytokine Platform: Achieving CAR T Cell Efficacy Against Solid Cancers

PRINCIPAL INVESTIGATORS: Yina Huang, PhD, Professor of Microbiology & Immunology, Geisel School of Medicine at Dartmouth
Melanie Peck, Current Graduate Student, Dartmouth PhD Innovation Fellow | Rachel Brog, PhD, Former Graduate Student

VIEW PUBLICATION

INVENTION OVERVIEW

- In 2024 in the U.S. there were currently **16.4 million people** living with solid cancer in the U.S. and an estimated **1.6 million new solid cancer diagnoses**.
- There are **zero FDA-approved** CAR T cells for solid cancers.
- Current immunotherapies that fail patients in the clinic are unable to overcome the highly immunosuppressive tumor microenvironment (TME) and the heterogeneity of solid cancers.
- The IL-33 + IL-2 Cytokine Platform combines IL-33 and IL-2 to **safely, effectively, and durably** overcome the solid TME and activate new T cells to delay tumor growth.

FEATURES AND OPERATING PRINCIPLES

- The IL-33 + IL-2 CAR Platform is the **only immunotherapy to co-deliver Type I and Type II cytokines**.
- The IL-33 + IL-2 CAR Platform **activates** host immunity & **shifts** the TME from immune suppressive to stimulatory.

FEATURES / OPERATING PRINCIPLES (CONT.)

- The IL-33 + IL-2 CAR Platform is effective against multiple heterogenous tumors, independent of tumor type, target antigen, or CAR construct.
- The IL-33 + IL-2 CAR Platform generates persistent & durable antitumor immunity, promoting favorable CAR & host T cell memory phenotypes.

ADVANTAGES AND SCOPE

- The IL-33 + IL-2 CAR Platform:
  - **Overcomes** the key challenges to efficacy in solid tumors.
  - **Eliminates** the need for toxic co-treatments.
  - **Expands** patient eligibility.
  - Offers **diverse, flexible** product compatibility.
  - **Outperforms** other armoring strategies against solid tumors.

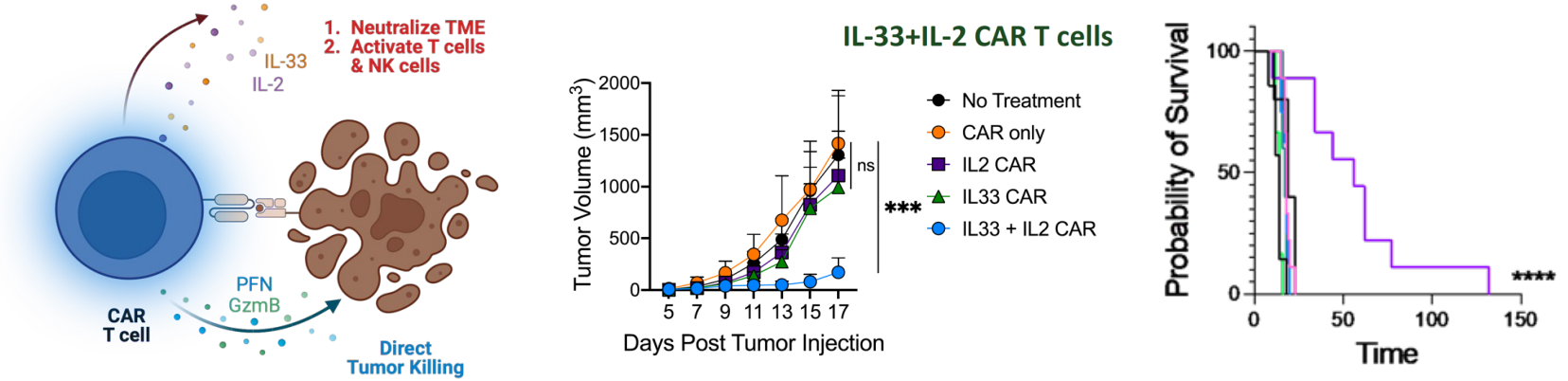

Figure 1: The delivery of IL-33 + IL-2 CAR T cells neutralizes the TME, activates T cells and NK cells, and enacts direct tumor killing. This results in decreased tumor volume and increased probability of survival as compared to no treatment control and CAR, IL2 CAR, and IL33 CAR alone.

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Dartmouth Health

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2021-026

AVAILABLE FOR LICENSE

US PATENT NO 11,771,323
US PATENT APPLICATION 18/229,086

Optical time-of-flight imaging methods and systems for surgical guidance and fluorescence depth estimation in tissue

PRINCIPAL INVESTIGATORS: Dr. Brian W. Pogue, Adjunct Professor of Engineering | Dr. Petr Brůža, Assistant Professor of Engineering

VIEW PUBLICATION

DESCRIPTION

- Critical information about the depth and shape of targets in florescence-guided surgery procedures is limited by the **one-millimeter visualization** barrier that hampers objectivity and utility.
- This invention introduces an **optical imaging system** that leverages time-of-flight data to precisely determine the depth and shape of fluorescence-tagged targets, such as tumor tissue, embedded within scattering media like healthy tissue.
- The technology addresses limitations in current surgical tumor guidance by **enabling subsurface imaging through diffuse radiation transport**.

ADVANTAGES AND BENEFITS:

- **Enhanced visualization:** The technology provides surgeons with crucial information about the depth and shape of fluorescent targets in vivo or ex vivo, offering guidance during procedures like fluorescence-guided surgery.
- **Improved accuracy:** By integrating multi-wavelength time-of-flight data, the invention calculates the target's surface topology, optical properties, and fluorophore depth, enhancing the precision of depth localization and shape evaluation.
- **Signal discrimination:** The technology reliably distinguishes the primary fluorescence signal from reflected secondary signals using time-of-flight information.

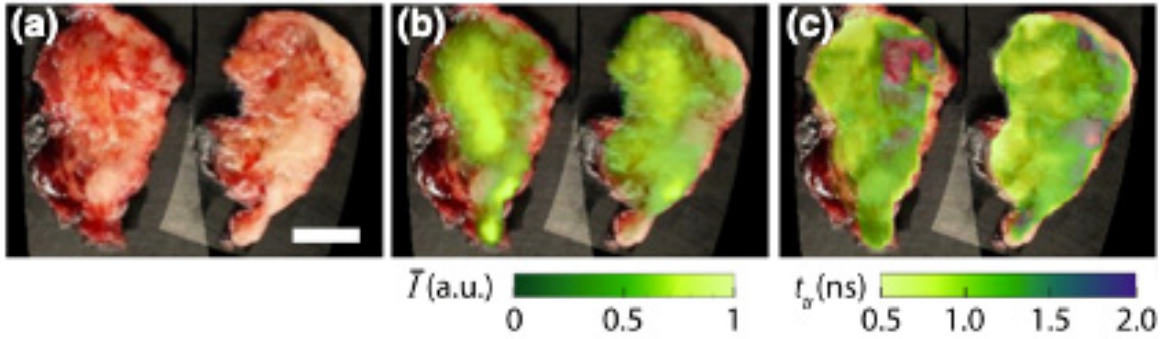

Figure 1: *In vivo* fluorescence LiDAR imaging of a resected head and neck tumour using time of flight data reveal picomolar ABY 029 fluorescence and map margins beneath the surface.

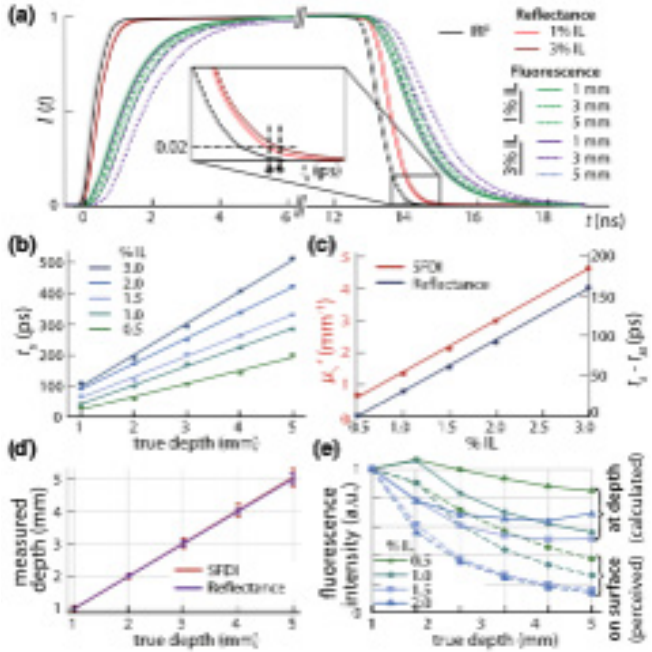

Figure 2: (a) shows depth dependent fluorescence/reflectance traces; (b) converts rising edge delay into a linear depth ruler; (c) retrieves tissue scattering and kernel width; (d) validates depth estimates within ≈0.3 mm across 1–5 mm; and (e) corrects surface measured intensity to the true subsurface fluorophore signal.

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2021-027

AVAILABLE FOR LICENSE

US PATENT APPLICATION 18/280,289

MR-Linac Compatible Daily Quality Assurance System and Methods Utilizing Cherenkov Imaging for Imaging-Radiation Isocenter Coincidence Measurement

PRINCIPAL INVESTIGATORS: Dr. Petr Brůža, Assistant Professor of Engineering | Dr. David J. Gladstone, Professor of Engineering and Professor of Medicine
Dr. Rongxiao Zhang, Assistant Professor/Clinical Physics | Daniel A. Alexander, PhD Graduate | Jacqueline M. Andreozz, PhD Graduate

VIEW PUBLICATION

DESCRIPTION

- The installation of magnetic resonance guided radiation therapy systems (MRgRT) has introduced the benefits of real-time magnetic resonance (MR) imaging to adaptive radiation therapy planning on a magnetic resonance guided linear accelerator (referred to as MR-Linac or MRI-Linac) platform. These benefits include superior soft tissue contrast compared to x-ray imaging and continuous imaging during treatment, enabling high positional accuracy and robust inter-fraction adjustments.
- However, the MR-Linac technology has more quality assurance (QA) procedure complications than with conventional accelerators **due to the magnetic environment's incompatibility with traditional detectors and the limited availability of onboard x-ray imaging**.
- Issues with **setup complexities, time-intensive procedures, and the need for specialized post-processing**, hinder current QA technologies' suitability for daily use.
- This invention **introduces a Cherenkov imaging-based system as a daily use MR-Linac QA systems**, specifically addressing the verification of mechanical-imaging-radiation isocenter coincidence.

ADVANTAGES AND BENEFITS:

- **Simplified measurement:** This system **allows for simplified and more efficient measurement of imaging-radiation isocenter coincidence** in therapeutic linear accelerators.
- **Near-real-time analysis:** The system **enables immediate analysis of results after localized data acquisition** via custom software, **avoiding time-consuming post-exposure readout**.
- **Comprehensive QA capability:** The phantom is **compatible with clinically available ionization chambers for machine output measurements**, allowing it to **perform all TG-142 dosimetric measurements for MR-Linac daily QA** in high precision.

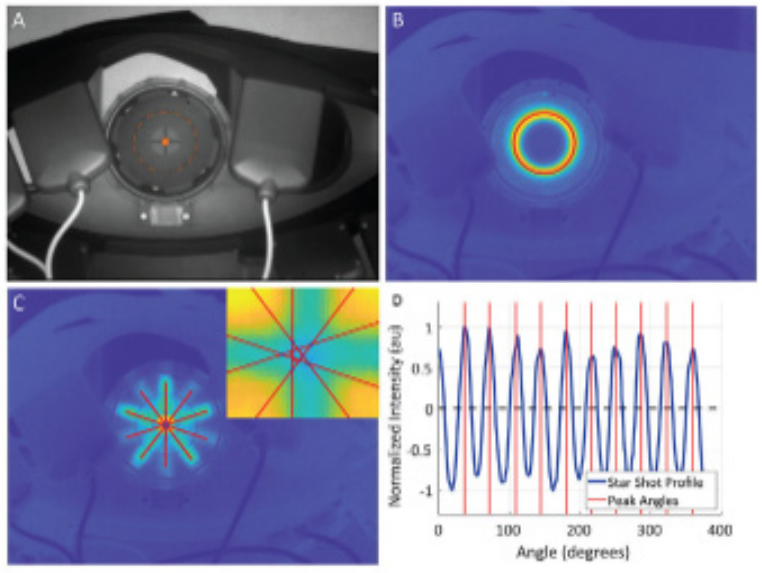

Figure 1: Results of the isocenter coincidence analysis from the custom software show that the isocenter coincidence is within the 2 mm TG-142 tolerance.

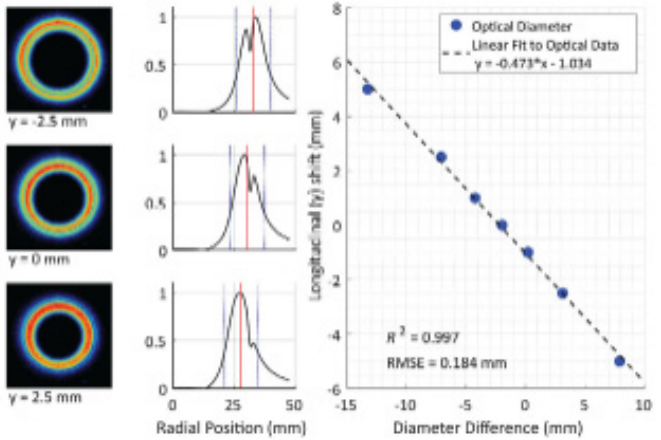

Figure 2: Results showing five deliberate couch shifts (-5 mm to +2.5 mm) that produces Cherenkov ring diameters that plot as a tight straight line (R^2 = 0.997, MSE = 0.184 mm).

DARTMOUTH Technology Transfer

Dartmouth Health

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2021-032

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US PROVISIONAL APPLICATION 63/744,007
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Barcoded-Antibody Library for *in vitro* Enhanced Fc Function Variance Screening

PRINCIPAL INVESTIGATOR: Dr. Jiwon Lee, Ralph and Marjorie Crump Assistant Professor of Engineering

INVENTION OVERVIEW

- This invention introduces a novel protein engineering platform that allows for efficient discovery of antibody drugs with **enhanced Fc functions** compared to manual screening.
- The platform enables high-throughput screening of soluble proteins by attaching cell-specific identifiers to both expressed proteins and their encoding nucleic acids.
- This overcomes existing limitations by enabling the screening of complex multi-chain proteins such as full-length antibodies without altering their natural format.

ADVANTAGES

- **Soluble Protein Screening:** The platform enables the screening of **soluble** proteins to directly interrogate Fc activities, solid tumor penetration and many existing *in vitro* assays in parallel, allowing for better evaluation of their properties before actually making the proteins.
- **High Efficiency and Precision:** Experiments confirmed **<0.1% incorrect identifiers** between antibodies and transcripts from single cells.

	Yeast / Phage Display	Mammalian Display	Site-Directed Mutagenesis	Dartmouth technology
High-Throughput	✓	✓		✓
Ease of Screening	✓	✓		✓
Human Antibody Format		✓	✓	✓
Screening Versatility				✓
Engineering with Particular Fab			✓	✓
In vitro / *in vivo* Screening				✓

More information is available on a confidential basis.

DARTMOUTH
Technology Transfer

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2021-049

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US PATENT APPLICATION 18/514,761

NEMO protein engineering for NMR and Structural Biology

PRINCIPAL INVESTIGATORS: Dr. Maria Pellegrini, Research Professor | Dr. Gevorg Grigoryan, Research Associate Professor of Computer Science

VIEW PUBLICATION

DESCRIPTION:

- This invention introduces novel variants of the natural NEMO protein to enable the development of new therapies targeting the NF- κB pathway in cancer. Existing technology could not utilize NMR and X-ray techniques effectively in the study of wild-type (WT) NEMO for drug discovery efforts. Current solutions faced significant limitations, as WT-NEMO exhibited conformational heterogeneity and line broadening in NMR spectra, hindering its use in NMR-based screening and structure determination. These modifications are specifically designed to achieve improved structural characteristics, enhanced stability and solubility, higher quality NMR spectra, and suitability for X-ray crystallography, all while maintaining crucial biological activity, such as IKK binding.

ADVANTAGES AND BENEFITS

- **Enables structural studies:** The modified NEMO proteins are suited for NMR and X-ray techniques, enabling structure determination of NEMO in both the apo-form and in complex with ligands/inhibitors, which was not achievable with WT-NEMO.
- **Improves NMR screening quality:** Mutant NEMO proteins like MP12 generate high-quality, well-dispersed NMR spectra, compared to the diffuse density spectra of WT-NEMO, thereby enabling effective NMR-based screening and lead validation.
- **Enhanced properties:** The modifications improve helical content, coiled-coil structure, dimerization propensity, and protein stability, reducing aggregation and conformational exchange compared to wild-type NEMO.
- **Enhanced drug discovery:** Improved properties facilitate structure-based rational design, screening, and validation of inhibitors targeting the NEMO-IKK interaction, accelerating the development of potential therapies.

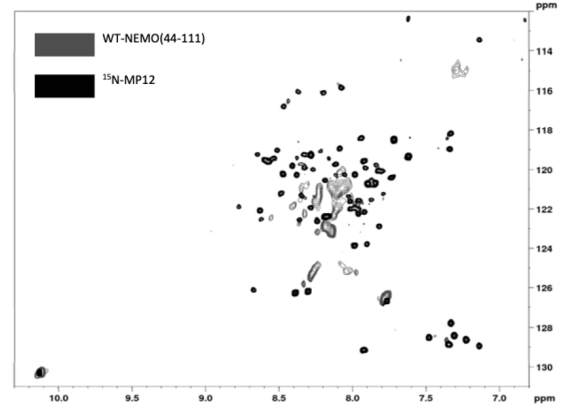

Figure 1: Comparison of wild-type NEMO(44-111) and the engineered ^{15}N-MP12 mutant

Source: WIPO Patent PCT/ US2022/072671

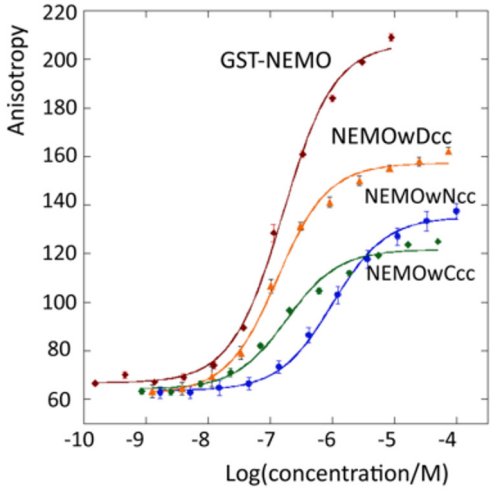

Figure 2: FA curves for direct binding of IKK βKK/RR to the engineered NEMO constructs and GST-NEMO(1–196), demonstrating structural stabilization of redesigned NEMO.

Guo, B., Audu, C. O., Cochran, J. C., Mierke, D. F., & Pellegrini, M. (2014). Protein engineering of the N-terminus of NEMO: Structure stabilization and rescue of IKKβ binding. *Biochemistry*, 53(43), 6776–6785. https://doi.org/10.1021/bi500861x

DARTMOUTH
Technology Transfer

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2022-019

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US PATENT NO 18/837,293

Methods To Predict Time Since CMV Infection

PRINCIPAL INVESTIGATOR: Dr. Margie Ackerman, Professor of Engineering

VIEW PUBLICATION

INVENTION OVERVIEW

- It is crucial to develop reliable systems and methods to both identify whether subjects have herpesvirus infections (primary or latent) and determine the time since the subject was exposed to or infected with a herpesvirus. This is especially important in subjects that are pregnant (vertical transmission).
- This novel method uses bodily fluid sample to detect a set of anti-virus antibody features of the subject and generate an input vector with this data.
- This method applies the input vector to a trained machine learning algorithm to classify the sample.
- This method also determines whether the subject is a suitable candidate for therapeutic intervention based on the classification.

FEATURES AND OPERATING PRINCIPLES

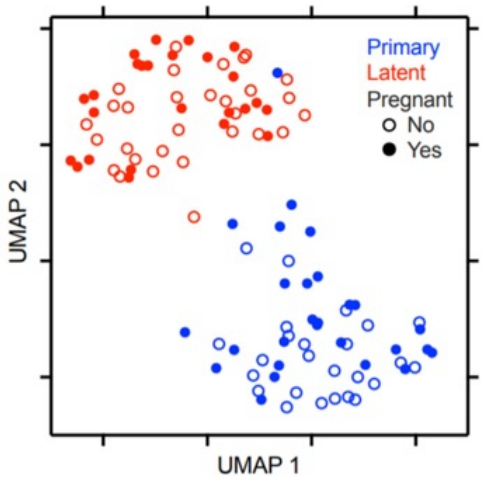
- A computer-implemented system identifies herpesvirus infections and exposures.
- The machine learning model classifies the subjects as having primary versus latent infections, and a less or more recent viral exposure.
  - ➤ The system recognizes anti-herpesvirus antibody features from subject samples.
- This system can be used in cases of cytomegalovirus (CMV), and assigns an importance measure to the detected anti-herpesvirus antibody features to determine therapeutic interventions (antiviral therapy).
  - ➤ This approach can also be used in a pregnant subject.

ADVANTAGES AND SCOPE

- The invention has the potential to identify important details of herpesvirus infections in an individual subject using the subject's bodily fluid sample in a machine learning platform.
- This approach can determine whether a subject is a candidate for therapeutic intervention, thus improving health outcomes.

Figure 1 [right]: Schematic shows workflow of this model.

1. Antibody features and activities are assessed.
2. A predictive model is built to identify important antibody feature.
3. Predictions and signatures are created and interpreted.



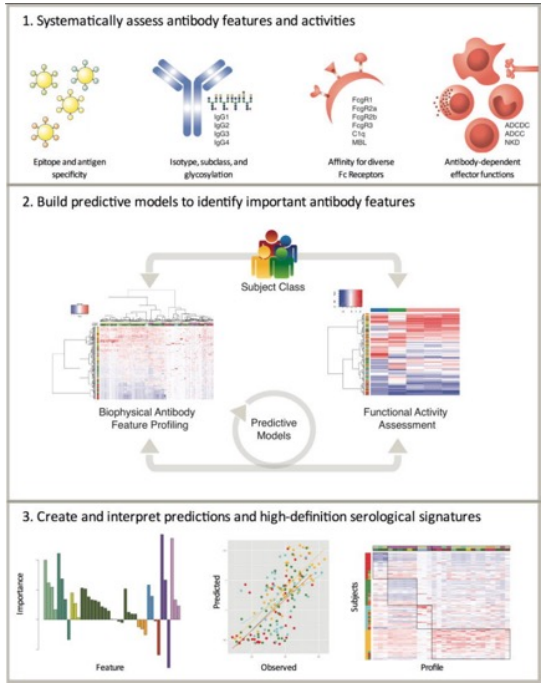


Figure 2 [left]: Data indicates that antibody profiles are highly distinct between primary and latent infection.

DARTMOUTH
Technology Transfer

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Director for Industry Engagement

2022-032

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PCT/US2019/055685

Compositions And Methods For Preventing Or Ameliorating Neonatal HSV Infection

PRINCIPAL INVESTIGATOR: Dr. Margie Ackerman, Professor of Engineering

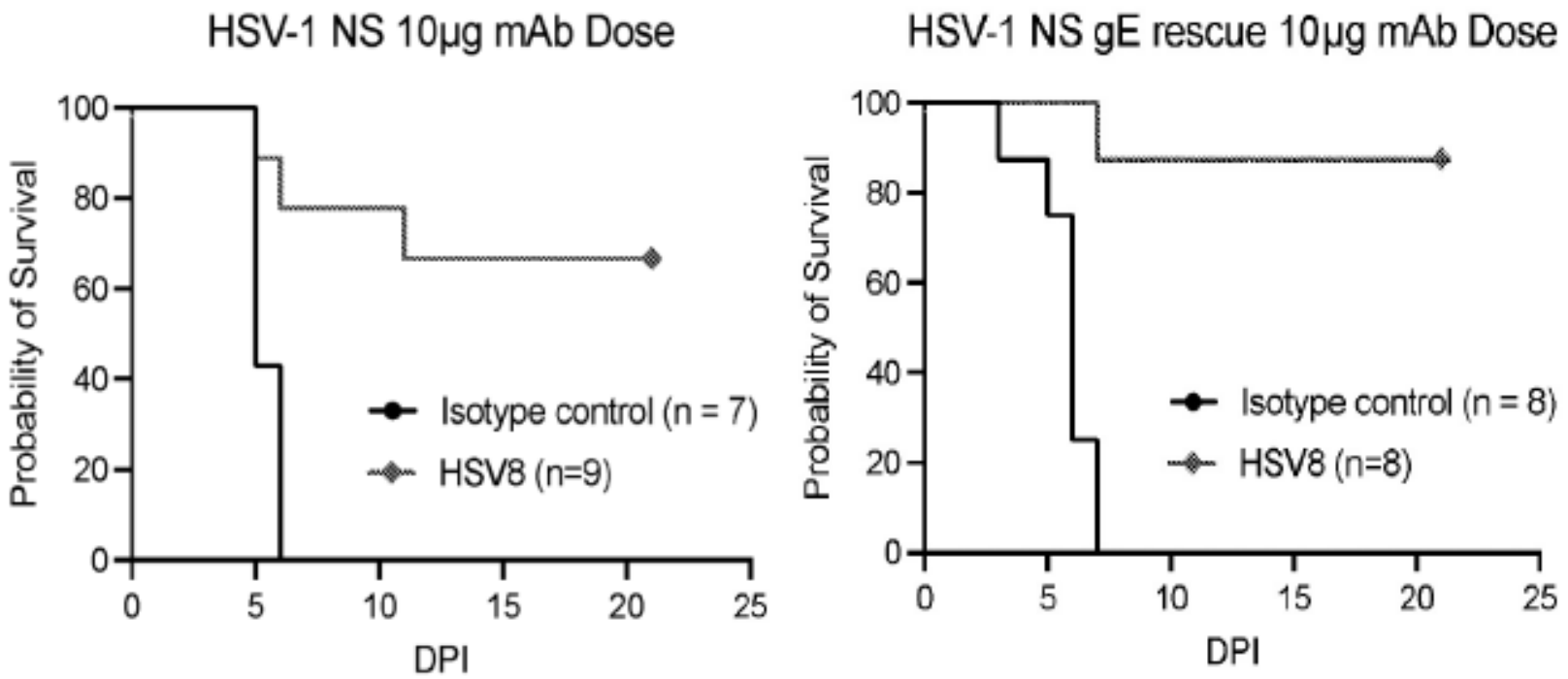
VIEW PUBLICATION

INVENTION OVERVIEW

- Neonates are at risk for herpesvirus (HSV) infection during birth or close contact with an infected individual.
- There are an estimated 14,000 annaul cases of neonatal HSV (nHSV) globally.
- nHSV infections often result in significant morbidity and mortality.
- Current antiviral drug therapy does not adequately ameliorate the effects of nHSV, highlighting a need for improved clinical interventions for neonates with HSV infections.
- This invention treats pregnant mothers or neonates with an anti-HSV antibody to reduce mortality and morbidity associated with nHSV.

FEATURES AND ADVANTAGES

- This invention engineers an anti-HSV antibody that comprises an Fc region with >1 modification or mutation.
- The anti-HSV antibody is administered to a maternal subject that is pregnant or likely to become pregnant, or to a neonate infected with HSV or at risk to be infected with HSV.
- Mouse studies demonstrate that this delivery of anti-HSV antibody results in ameliorated or prevented nHSV.



Data indicates treatment with anti-HSV antibody results in significantly increased probability of survival as compared to isotype control.

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2022-036

EXTENSIVE IP PORTFOLIO AVAILABLE FOR REVIEW

Methylation Cytometry DNA-based Cell Typing Technology for Advanced Immune and Cell Type Profiling

PRINCIPAL INVESTIGATOR: Brock Christensen, Ph.D, Professor of Epidemiology | Lucas Salas, MD, PhD, MPH, Assistant Professor of Epidemiology

VIEW PUBLICATION

INVENTION OVERVIEW

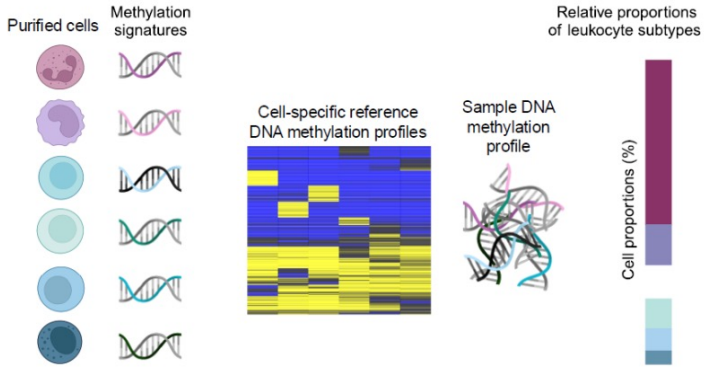
- Routine evaluation of patient immune and cell type status has many applications in **precision medicine**.
- Methylation Cytometry (MC) is a DNA-based immune cell profiling technology that allows **frequent, accurate, and direct** insights into immune system responses.
- MC **leverages stable epigenetic marks** on DNA called DNA methylation that define cell identity and uses the binary nature of un/methylation as a signal that is directly proportional to the number of cells.
- The technology portfolio includes cell typing approaches and accompanying software that **enable objective, standardized immune and other cell type profiling**.

LOOKING FOR

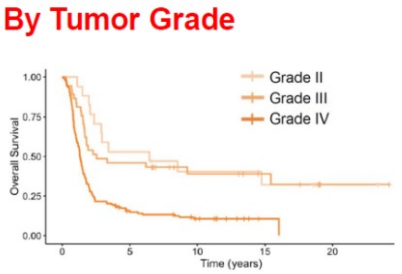
- Collaborations around clinical precision medicine applications, including outside of immune profiling. Support and management for platform start-up.

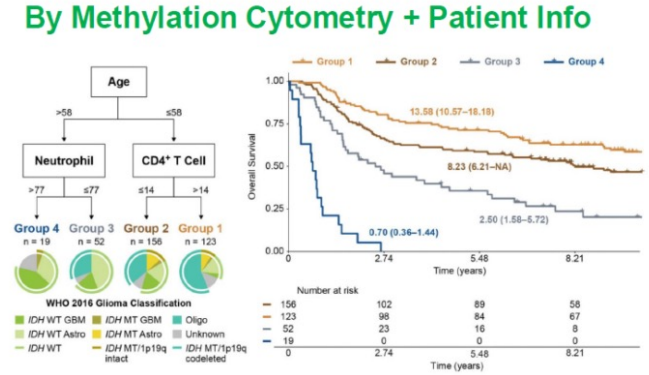
ADVANTAGES

- Offers **advanced, scalable profiling** across diverse biospecimens.
- Can use stable, **easy to acquire samples** (including in-home collection of blood).
- Can **accurately quantify** even low prevalence cell types in peripheral blood, tumor samples, and other specimen types.
- Uses existing instrumentation.
- Can provide **highly accurate quantification** of 12+ cell types and return >50 profile variables.
- **Broad applications** including:
  - evaluation of response to therapy
  - clinical trial eligibility criteria
  - determining patient prognosis
  - response to vaccines



Methylation Cytometry DNA-based cell typing technology simplifies immune profiling





Precision oncology applications of methylation cytometry – improved brain tumor prognostics

DARTMOUTH
Technology Transfer

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2022-043

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US PATENT APPLICATION 18/521,285

A Method to Diagnosis Infants and Children with CF at Risk for Respiratory Infections Using Stool Composition Data

PRINCIPAL INVESTIGATORS: Dr. George A. O'Toole, Professor of Microbiology & Immunology
Juliette Madan, MD, Associate Professor, Pediatrics, Epidemiology, Quantitative Biomedical Data Science

VIEW PUBLICATIONS

DESCRIPTION

Gut microbiota dysbiosis in cystic fibrosis (CF) patients can alter a host's inflammatory status, showing distinct microbial compositions between children with low versus high intestinal inflammation, which affects lung disease risk. Traditional diagnostic methods often involve uncomfortable oropharyngeal sampling or respiratory lavage. This invention introduces **machine learning-based diagnostic tool for identifying CF patients at high risk for upper respiratory infections (URIs) or systemic inflammation**. The system employs random forest machine learning models trained on stool microbiota data to classify patients' risk. Once identified, a clinician has a broad range of **therapeutic interventions to address the risk**, including altering the intestinal microbiome through bacterial compositions (e.g., Bifidobacterium, Bacteroides), probiotics, prebiotics, fecal microbiota transplantation (FMT), or conventional treatments such as antibiotics, anti-inflammatory medications, and CFTR modulators.

ADVANTAGES AND BENEFITS

- **Non-invasive diagnosis:** This invention uses **stool compositional data** from easily collected diaper samples to **accurately identify children most likely to experience respiratory events**, replacing uncomfortable and invasive sampling methods.
- **High predictive accuracy:** The machine learning model **predicts high upper respiratory infection frequency (URIfreq) with only 16% error** and **high neutrophil-to-lymphocyte ratio (NLR), a marker for systemic inflammation, with 27% error**.
- **Actionable insights:** By identifying specific gut microbiota profiles associated with negative health outcomes, this technology **provides physicians with crucial understanding to determine the need for therapeutic interventions**.

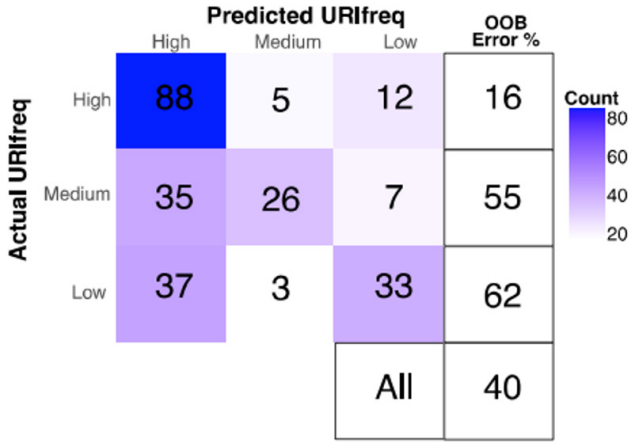

Figure 1 [top]: Predicted vs Actual URI with the OOB estimate of error rates for predicting age from stool microbiota being 40%.

Source: Valls, R. A., Hampton, T. H., Price, C. E., Barrack, K. E., O'Toole, G. A., Coker, M. O., & Madan, J. C. (2022). Predicting clinical outcomes in infants with cystic fibrosis from stool microbiota using random forest algorithms [Preprint]. bioRxiv. https://doi.org/10.1101/2022.08.06.503028

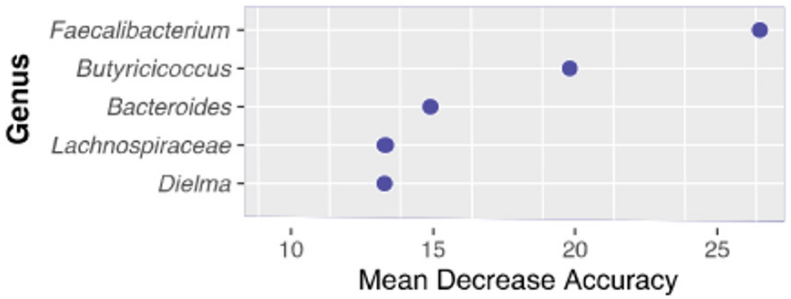

Figure 2: [left]: Model identified *Faecalibacterium*, *Butyricicoccus*, and *Bacteroides* as the top genera driving prediction.

Source: Valls, R. A., Hampton, T. H., Price, C. E., Barrack, K. E., O'Toole, G. A., Coker, M. O., & Madan, J. C. (2022). Predicting clinical outcomes in infants with cystic fibrosis from stool microbiota using random forest algorithms [Preprint]. bioRxiv. https://doi.org/10.1101/2022.08.06.503028

DARTMOUTH Technology Transfer

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2023-003

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PCT APPLICATION PCT/US2024/030955
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Discovery and Development of Novel Small Molecules with Antifungal Properties

PRINCIPAL INVESTIGATOR: Dr. Robert A. Cramer, Professor of Microbiology and Immunology

VIEW PUBLICATION

DESCRIPTION

Antifungal drug discovery against molds has lagged other pathogens due to their complex multicellular lifestyles. Currently, pathogenic filamentous fungi are exceedingly difficult to treat due to resistance to all three main classes of contemporary antifungals and rising drug resistance in susceptible strains. Researchers at Dartmouth have identified novel compounds and methods for treating fungal infections through a high-throughput screening platform specifically designed to find small molecules synergistic with fluconazole and/or those with preferential activity under low oxygen conditions, leveraging a sensitive luminescence-based reporter assay. Preliminary data from testing suggests some of these compounds may act through the SrbA-dependent hypoxia response pathway, a known virulence factor and regulator of azole resistance, representing a potentially novel mechanism of action.

ADVANTAGES AND BENEFITS

- **Targeting difficult infections:** The proposed compounds specifically addressed infections caused by Aspergillus species, including azole-resistant strains which are particularly challenging.
- **Enhanced efficacy:** The identified compounds inhibit fungal growth more effectively, including with lower concentrations of antifungal agents, and specifically potentiate antifungal agents like azoles, demonstrating synergy and increased efficacy against drug-resistant strains.
- **Hypoxia-specific activity:** The invention identifies molecules with preferential activity under low oxygen (hypoxic) conditions, which mimics the microenvironment found at the site of established infections and in biofilms, thereby targeting a crucial resistance mechanism.

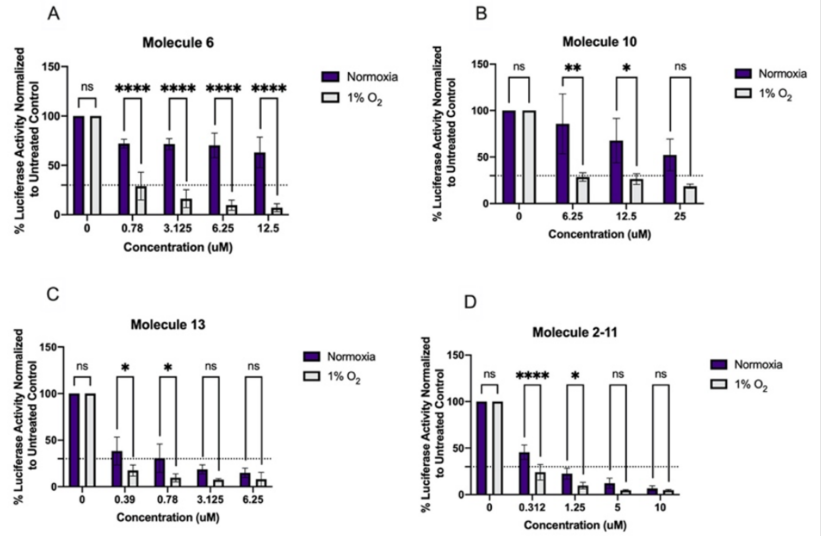

Figure 1 [top]: Example of novel small molecules that significantly reduce A. fumigatus growth under hypoxic (1% oxygen) conditions.

Source: Sophia patent application: [Invention 2023-003] R33 Transition Narrative_FINALSUBMIT_113020.pdf

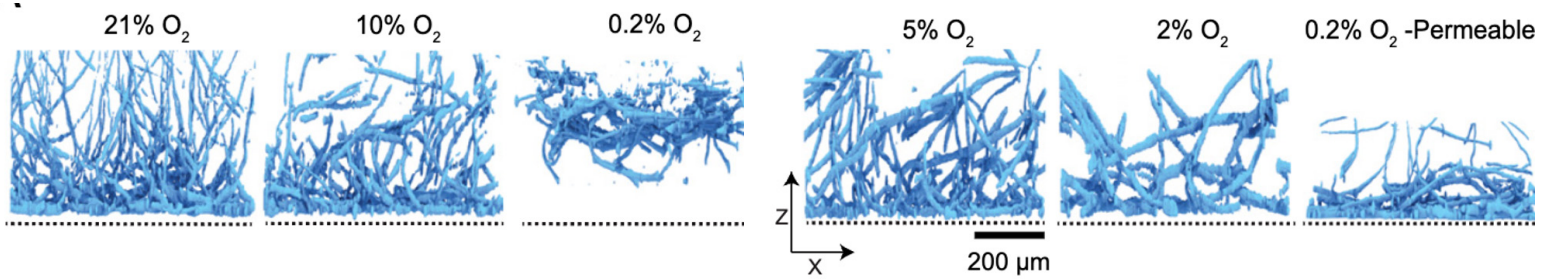

Figure 2 [left]: 3D renderings of A. fumigatus biofilms under varying oxygen levels, revealing how oxygen availability shapes fungal growth and drives antifungal resistance.

Source: C.H. Kowalski, K.A. Morelli, D. Schultz, C.D. Nadell, & R.A. Cramer, Fungal biofilm architecture produces hypoxic microenvironments that drive antifungal resistance, Proc. Natl. Acad. Sci. U.S.A. 117 (36) 22473-22483, https://doi.org/10.1073/pnas.2003700117 (2020).

DARTMOUTH
Technology Transfer

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2023-039

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US APPLICATION 18/784,881
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GyroGel: Redefining Bone Oncological Reconstruction

PRINCIPAL INVESTIGATOR: Dr. Katie Hixon, Assistant Professor of Engineering, Clinical Assistant Professor of Orthopaedics, Thayer School of Engineering)
GRADUATE STUDENTS: Peter Bertone | Levi Olevsky

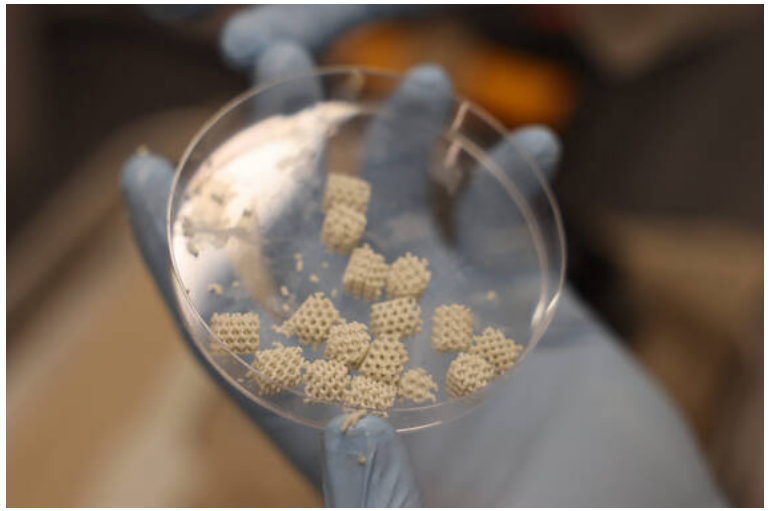
DESCRIPTION

The treatment of bone disorders caused by infection, trauma, or tumor-resection, are currently reliant on surgical interventions that may fracture or otherwise degrade over time through bone resorption. Solutions such as bone cement may cause an exothermic reaction, resulting in burns to healthy cells. While synthetic bone fillers and synthetic bone grafts are made from materials which can be effective in promoting bone growth, they are not tunable or customizable.

This invention utilizes both cryogels and 3D printing in combination resulting in a bone graft scaffold highlighting the advantages of both materials: high porosity and cellular infiltration of cryogels and customization and mechanical strength of 3D printing. The bone graft scaffold produced by the combination of two scaffold fabrication methods creates a composite bone graft scaffold with high porosity to ensure healthy cellular growth, while increasing mechanical durability to applied loads by the surrounding in vivo tissues.

ADVANTAGES AND BENEFITS:

- Better patient outcomes than traditional bone grafts
  - Significantly less invasive
  - Decreased recovery time
  - Less physical deformation
  - Estimated to be half the price of current surgical intervention



DARTMOUTH
Technology Transfer

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2024-005

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PCT APPLICATION PCT/US2024/055735
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Creation of Anti-Canine PD-1 Monoclonal Antibodies to Treat Cancer

PRINCIPAL INVESTIGATORS: Hugo Arias-Pulido, Senior Research Scientist, Microbiology & Immunology | Dr. Randolph J. Noelle, Emeritus Professor of Microbiology & Immunology

VIEW PUBLICATION

DESCRIPTION

- **HugPet9** is a novel antibody for detecting or treating canine cancers, alone or in combination therapies. The invention includes antibodies or antibody fragments binding to canine PD-1, comprising the same CDRs as HugPet9 (77A6H9) or 77A6H7, or possessing at least 98–99% sequence identity in their VH and VL polypeptides to these antibodies. These antibodies or fragments can be engineered to include various Fc regions (murine, human, feline, canine, optionally canine IgGA, IgGB, IgGC, or IgGD) and framework regions (canine or murine). The invention extends to nucleic acids encoding these antibodies, expression vectors designed to express them, and recombinant cells (including mammalian cells like CHO, BHK, COS, Hela, HEK; yeast; fungal; plant; insect; or bacterial cells) capable of producing the antibodies.

ADVANTAGES AND BENEFITS

- **Binding Specificity:** HugPet9 binds specifically to canine peripheral blood mononuclear cells (PBMCs) and different canine tumor tissues expressing PD-1 protein.
- **Diagnostic Specificity:** HugPet9 provides clear and specific detection of PD-1 protein levels in archival canine paraffin-embedded tissues, unlike a commercial antibody (JC053) which shows non-specific staining of multiple cell types in the same tissues.
- **Demonstrated Safety and Efficacy:** Intratumoral (IT) HugPet9 immunotherapy showed safety in a proof-of-concept trial and preclinical studies for canine mammary cancer patients, resulting in observed partial responses in one dog and stable disease in two dogs in a small cohort.
- **Reduced Toxicity:** The IT administration route for HugPet9 is estimated to require significantly lower doses (e.g., 2 mg total for a 4-week course vs. potentially 4–60 mg for systemic administration).

Figure 1A

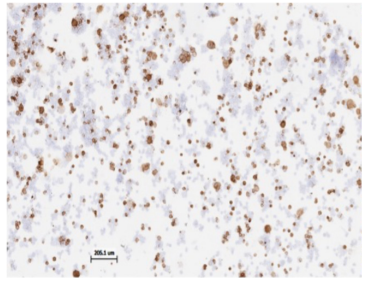

Figure 1B

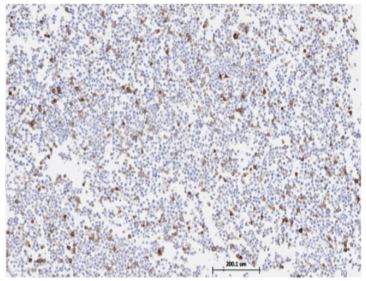

Figure 1: Detection of HugPet9 in 293T cells. The 293T cells were transfected with canine PD-1, expanded and used to detect PD-1 levels in these cells by immunocytochemistry (A) or in embedded in paraffin by standard IHC with HugPet9 (B). The two formats reflect fresh-frozen tissues and archival paraffin-embedded samples, respectively.

Figure 2A

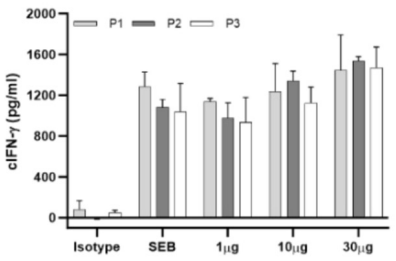

Figure 2B

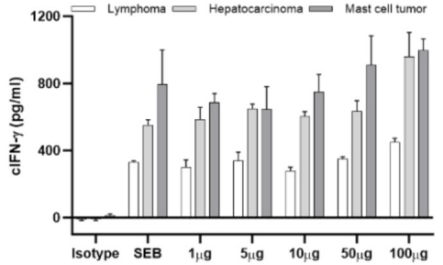

Figure 2: Effect of HugPet9 on IFN-g expression in PMBCs from healthy and cancer dogs. Canine PMBCs from healthy (left) and cancer-bearing dogs (right) were activated with an isotype IgG1 antibody (isotype), staphylococcal enterotoxin B (SEB, 50ng/ml) and SEB plus HugPet9 at the doses indicated in the x-axis. The IFN-g levels are indicated in the y-axis.

Figures from Sophia's patent application (filename: 1143252.007213 Fig 1-18A-C)
https://dartmouth.wellspringsoftware.net/kms/patent/detail/4714/

DARTMOUTH
Technology Transfer

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2024-009

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Method and composition for conferring abiotic stress resistance on plants by modulating activity of an F-box protein family

PRINCIPAL INVESTIGATORS: Dr. G. Eric Schaller, Professor of Biological Sciences
CO-INVENTORS: Dr. Sitwat Aman, Dartmouth College | Dr. Joseph J. Kieber, University of North Carolina

INVENTION OVERVIEW

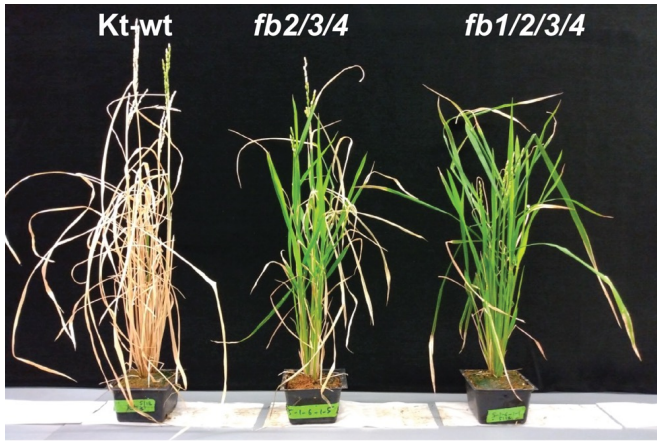
- This invention enhances abiotic stress resistance in plants by reducing the activity of an F-box protein family by altering the gene expression.
- Current molecular approaches to combat abiotic stress often involve transgenic expression of stress regulators, leading to genetically modified organisms (GMOs), which are subject to regulations that can limit commercial potential.
- There is a need for non-GMO methods that provide effective and long-lasting abiotic stress resistance, along with a more targeted approach for exogenous treatments.

LOOKING FOR

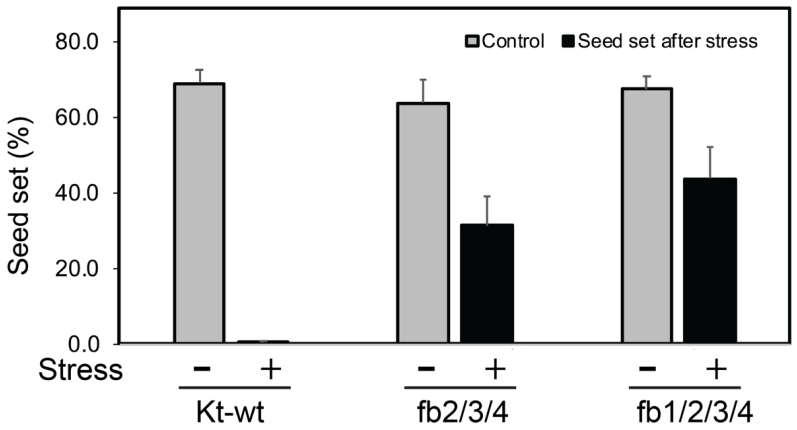
- Licensing opportunities and collaborations around testing and using the technology for drought improvement of crops and turf grass, as well as in developing chemical approaches to target and reduce expression of this F-box protein family.

ADVANTAGES

- **Non-GMO method**: This invention uses CRISPR-Cas9 editing of the F-box family to reduce their expression and confer drought resistance.
- **Improved drought resistance**: Reducing the expression levels of the F-box proteins in rice leads to drought resistance through delayed leaf senescence and improved seed set under drought conditions.
- **Broader stress resistance**: Due to overlaps in plant response mechanisms, this method also provided resistance to other abiotic stresses, including salt stress, high and low temperatures, and heavy metal stress.



Shoots of drought-stressed wild type (wt) and fb mutants following the withholding of water for 5 days and after 14 days of recovery period. Drought stress resulted in extensive leaf senescence for the wild type, but damage was mitigated in the fb mutants, where the leaves remained green.



Drought-stress result in a >99% decrease in seed set per panicle compared to 51% and 35% decreases in seed set for **fb mutants**.

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Technology Transfer

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2024-010

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Method for Inducing Aneuploidy and/or Chromosomal Instability in Human or Non-Human Primate Pluripotent Stem Cells

PRINCIPAL INVESTIGATOR: Kristine M. Godek, Ph.D., Principal Research Scientist, Geisel School of Medicine at Dartmouth

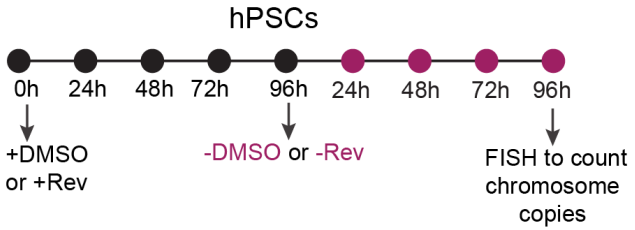
VIEW PUBLICATIONS

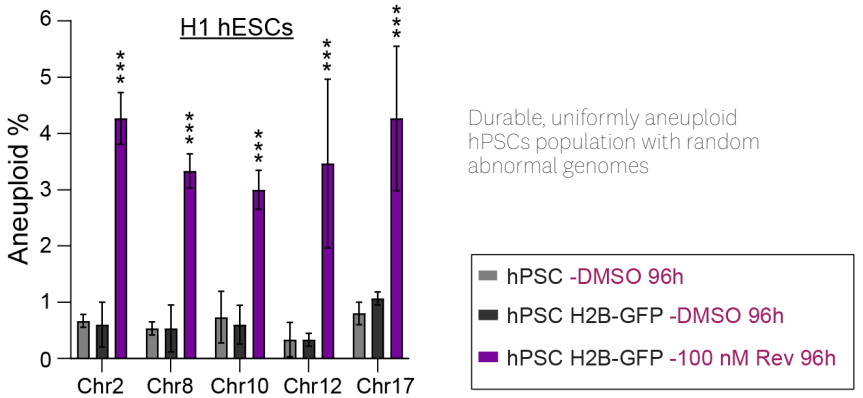
INVENTION OVERVIEW

- Aneuploidy is associated with a variety of human conditions and diseases including, but not limited to, **cancer, congenital birth defects, infertility, aging, and rare diseases**.
- In cancers, 90% of solid tumors and 75% of hematological malignancies are estimated to be aneuploid, making aneuploidy a **near universal feature of cancers**.
- **New and improved methods** and compositions for use in identifying genes and pathways that cause aneuploidy and/or CIN and which contribute to their pathological consequences are sorely needed.

LOOKING FOR

- Industry therapeutic development collaboration, especially in areas outside of oncology and platform start-up development and support.

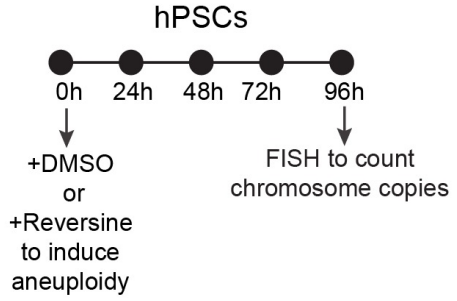




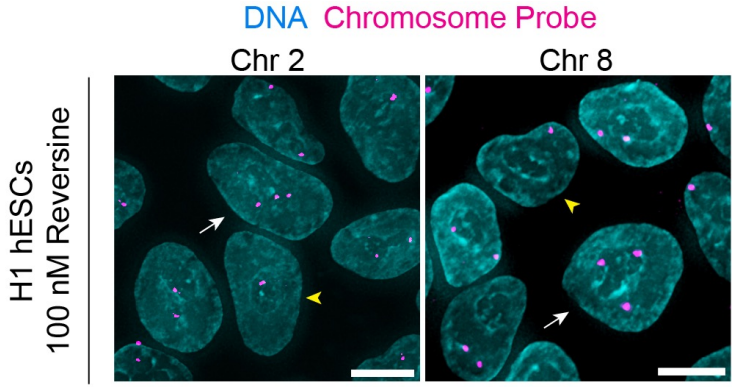
Durable, uniformly aneuploid hPSCs population with random abnormal genomes

ADVANTAGES

- This technology generates a **durable, uniformly aneuploid** human pluripotent stem cell (hPSCs) population with random abnormal genomes.
- Requires **no genetic modification or transformation of the cells**, controlling the type of mutations to aneuploid.
- Easily generated and the uniformity allows **matched normal vs aneuploid** comparisons.



Ya et al, bioRxiv. 2024.



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2024-029

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US PROVISIONAL APPLICATION 63/730,661
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Inhibition of Oligosaccharyltransferase (OST) as Therapy for Prion Disease

PRINCIPAL INVESTIGATOR: Dr. Surachai Supattapone, Professor of Biochemistry and Cell Biology

DESCRIPTON

Prion diseases are fatal neurodegenerative diseases caused by the misfolding of the prion protein PrPC, leading to severe neurological dysfunction. Currently, no approved treatments exist for prion diseases, and non-toxic drug treatments show limited efficacy lifespan in animal models. They also face challenges such as strain-dependent activity and administration at late clinical stages. Researchers at Dartmouth have shown that administering an oligosaccharyltransferase (OST) complex inhibitor which blocks N-glycosylation of PrPC and its cell surface expression, inhibits the replication of disease-causing PrPSc.

ADVANTAGES AND BENEFITS

- **Targeted mechanism:** The method directly targets the cell surface expression of PrPC and inhibits the replication of disease-causing PrPSc by inhibiting the attachment of the glycosylphosphatidylinositol anchor to PrPC and/or its attachment to the outer surface of the plasma membrane.
- **Broad strain efficacy:** OST complex inhibition of PrPC, achieved complete removal of PrPSc from cells infected with three or four different types (strains) of prions in laboratory testing.
- **Significant PrPC reduction:** Treatment effectively lowers PrPC levels on the surface of cells by over 50%.
- **Superior cellular outcomes:** OST complex inhibition demonstrates the unique capability to fully cure cells infected with every prion strain tested, a significant advantage over previously tested N-glycosylation inhibitors that exhibited strain-dependent results.

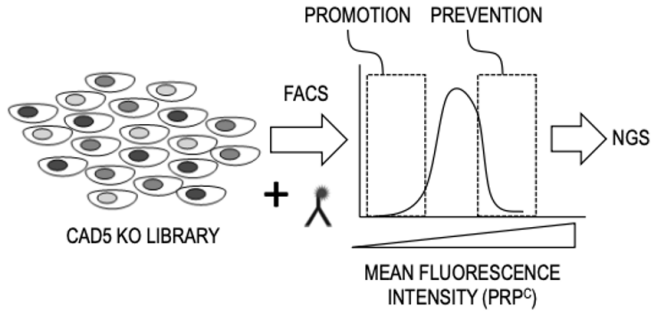

Figure 1: Schematic of the CAD5 knockout (KO) library screening process to identify genes involved in the surface expression of PrPC.

Source: USPTO 63/730,661 (Filed 12/11/2024)

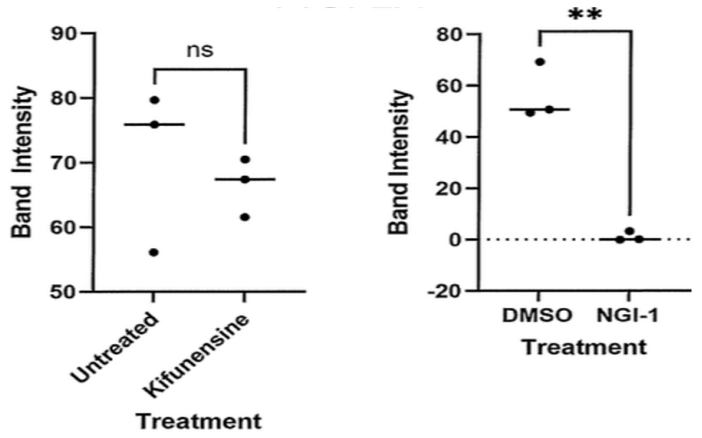

Figure 2: Comparison of untreated cells and cells treated with kifunensine (Fig. 2B), and comparison of cells treated with DMSO and NGI-1 (Fig. 2C)

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US PROVISIONAL APPLICATION 63/753,628
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Evolved Bacteroides Strains for Use as a probiotic in Cystic Fibrosis and Inflammatory Bowel Disease

PRINCIPAL INVESTIGATOR: Dr. George A. O'Toole, Professor of Microbiology & Immunology

DESCRIPTION

While life changing the new cystic fibrosis (CF) therapeutics have demonstrated little to no positive impact on the CF gut, whose altered intestinal microbiome can lead to nutritional deficiencies and an increasing burden of linked obesity. The gut conditions of these patients, such as excess mucus, increased fat content, acidic pH, and heightened inflammation are not amendable to modification with standard probiotics either. Through evolutionary development using a serial adjusted cell culture media, a set of evolved strains that can survive the CF and other guts altered by inflammation was identified and shown to be viable in the gut and still producing the anti-inflammatory factors. Compositions containing these evolved bacteria can be formulated as nutraceutical or pharmaceutical products for oral or nasogastric administration, and are envisioned for use in subjects with low abundance of target bacteria like Phocaeicola and Bacteroides, including pediatric CF patients as young as 0 days old, potentially in conjunction with existing CF therapies.

ADVANTAGES AND BENEFITS

- **Increased viability in CF and inflamed GI tract:** Evolved bacterial cells exhibit significantly higher viability in CF-like gastrointestinal conditions.
- **Retained immunomodulatory function:** The evolved strains continue to produce short-chain fatty acids (SCFAs) at levels comparable to the ancestral bacterial strain, which is a key compound known to drive anti-inflammatory effects and modulate inflammation.
- **Effective colonization:** The evolved bacterial cells have demonstrated the capability to colonize the GI tract in mammalian CF models at levels similar to ancestral strains, providing similar immunomodulatory effects.
- **Wide commercial potential:** This technology possesses potential for other inflammatory gut conditions such as inflammatory bowel disease (IBD), ulcerative colitis, and Crohn's disease.
- **Non-engineered development:** These evolved strains were not genetically engineered but arose naturally through adaptive evolution in a laboratory medium designed to mimic the inflamed CF gut.

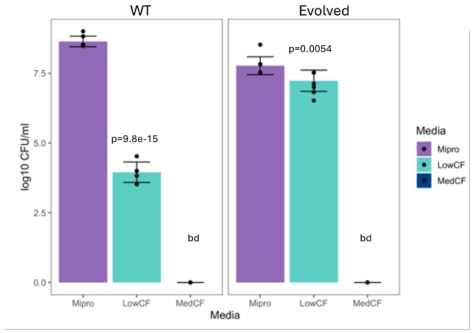

Figure 1: The evolved strains maintain viability in LowCF-MiPro, showing less than 0.5 log10 CFU/ml decrease, in contrast to the wild-type strain's >4 log10 CFU/ml drop, showing that the evolution of P. vulgatus strains are capable of surviving CF-like gut environments.

Source: Patent manuscript

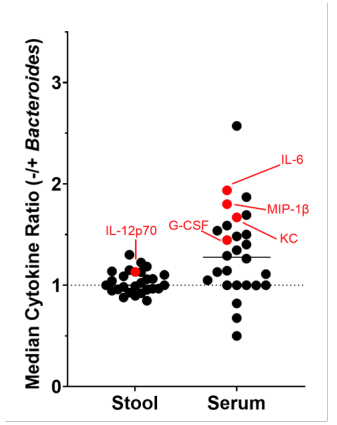

Figure 2: Fold-change in 32 cytokines across stool, serum, and intestinal tissue, showing that without Bacteroides pro-inflammatory signals rise systemically and locally, showing its crucial role in dampening CF-associated inflammation.

Source: Price, C. E., Valls, R. A., Ramsey, A. R., Loeven, N. A., Jones, J. T., Barrack, K. E., Schwartzman, J. D., Royce, D. B., Cramer, R. A., Madan, J. C., Ross, B. D., Bliska, J., & O'Toole, G. A. (2024). Intestinal Bacteroides modulates inflammation, systemic cytokines, and microbial ecology via propionate in a mouse model of cystic fibrosis. mBio, 15(2), e0314423. https://doi.org/10.1128/mbio.03144-23

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2025-021

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US PATENT APPLICATION 63/777,912

Lymph Node (LN) Resident Memory (Trm) Cells for the Treatment of Cancer

PRINCIPAL INVESTIGATOR: Mary Jo Turk, Professor of Microbiology and Immunology

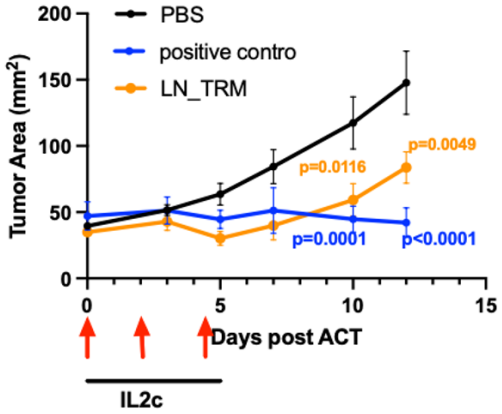
VIEW PUBLICATION

DESCRIPTION

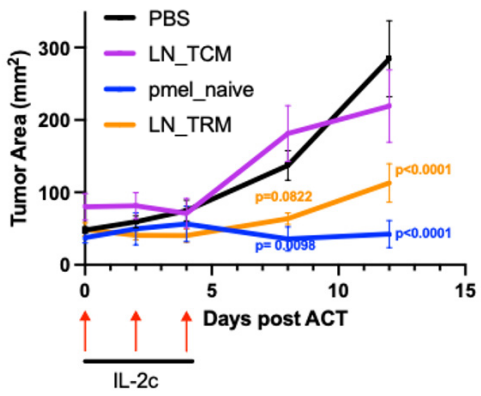
- CD8+ tissue-resident memory (Trm) cells are essential to the immune responses against cancer and can be identified by surface expression of specific proteins.
- The Turk lab determined that a Trm population resides in tumor draining lymph nodes (TDLNs) and often has specificity for tumor-expressed antigens.
- This innovative approach sorts LN Trm cells using cell-surface markers to selectively capture and expand this functional, tumor antigen-specific population of cells for immunotherapy.

ADVANTAGES AND BENEFITS

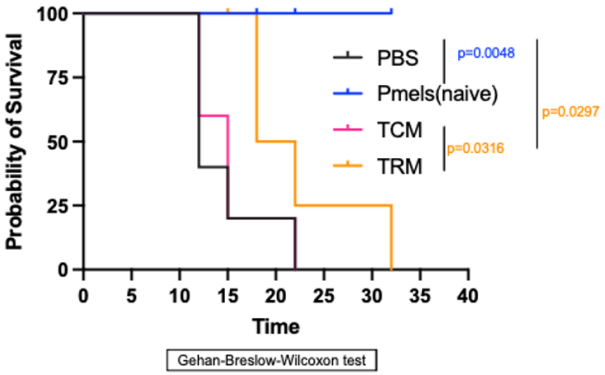
- The field has utilized TDLN-derived CD8 T cells for adoptive immunotherapy, but this method is limited due to lack of tumor antigen specificity.
- This method allows for the selection of cells that harbor tumor antigen specificity to overcome this challenge.
- Preliminary data shows that these cells can be cultured ex vivo and transferred into mice (B16F10-KVP model) to restrain growth of established melanoma tumors.



LN Trm cells mediate significant tumor growth inhibition in mice bearings established B16 melanomas. Mice were transferred with no cells, 20,000 LN Trm cells, or 1.5x10⁶ pmel cells (positive control) and treated. Error bars depict SEM of n=7 mice per group for PBS and positive control and n=4 for LN_TRM group. Statistical significance was calculated by 2-way ANOVA.



Second study demonstrating significant tumor growth inhibition with 20,000 LN Trm cells. B16F10-KVP tumor bearing mice were treated with PBS, LN TRM, TCM or naïve pmels . LN TRM demonstrate significant tumor growth inhibition and improved survival in mice bearing B16F10 KVP tumors. Error bars depict SEM of N=5 mice per group. Statistical significance was calculated by 2-way ANOVA.



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2025-022

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US PROVISIONAL APPLICATION 63/770,185
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MIST: Mucosal-Associated Invariant T (MAIT) Cell Induced Skin Therapy

PRINCIPAL INVESTIGATORS: Sladjana Skopelja-Gardner, Assistant Professor of Microbiology & Immunology, Geisel School of Medicine at Dartmouth
Dorothea Barton, MD, Associate Professor of Dermatology | Grace Crossland, MD/PhD Student

INVENTION OVERVIEW

- The patient burden for Systemic Lupus Erythematosus (SLE) and Cutaneous LE (CLE) is high, affecting **~1 million people in the U.S. and 3.5 million people globally**.
- There are no FDA-approved targeted topical therapies to treat CLE. Further, current treatment paradigms include systemic drugs that are not designed for skin disease.
- Inflamed lupus skin typically has low immune-suppressing cells, high inflammatory and tissue-damaging proteins, and low tissue-healing MAIT cells.
- MIST leverages MAIT cells to promote skin healing and suppress inflammation.

FEATURES AND OPERATING PRINCIPLES

- MIST uses a MAIT specific activator to activate MAIT cells to locally expand Treg in lupus skin, resulting in higher immune suppressing Treg, lower inflammatory and tissue-damaging protein, and increased tissue-healing mediators.
- This novel approach uses liposomal reformulation to stabilize an unstable metabolite that expands MAIT cells, for topical use in lupus skin disease.

ADVANTAGES AND SCOPE

- Topical expansion of MAIT cells **heals lupus skin lesion**.
  - ➤ Treatment results in **complete and durable** local response, **decreased** skin inflammation, and **no adverse effects** with long-term exposure.
- MIST offers a novel approach to CLE/SLE skin disease, which currently lacks an FDA-approved topical therapy.
- MIST offers an alternative approach to current treatment paradigms, which all rely on immunosuppressants (systemic) or steroids (weak), and include major side effects.
- There are currently only two topical candidates in early development, and neither are cell-specific.
- The Total Addressable Market (TAM) is ~$3 billion in the U.S. and ~12 billion globally.
- The Serviceable Available Market (SAM) is ~$1.8 billion in the U.S. and ~6 billion globally.
- The Serviceable Obtainable Market (SOM) is ~$1 billion in the U.S. and ~3 billion globally.

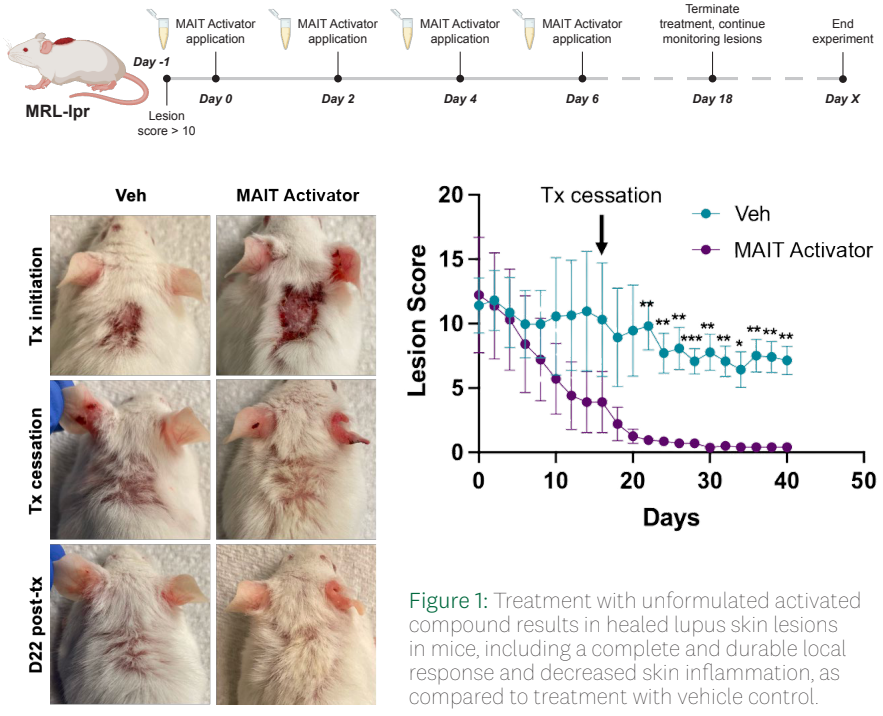

Figure 1: Treatment with unformulated activated compound results in healed lupus skin lesions in mice, including a complete and durable local response and decreased skin inflammation, as compared to treatment with vehicle control.

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2025-025

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US PROVISIONAL APPLICATION 63/760,153
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Methods for Enhancing T Cell-Based Adoptive Cell Therapy Products with Small Molecule Combinations

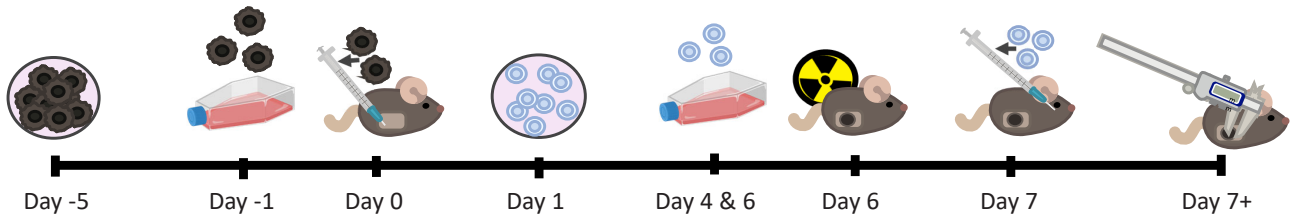
PRINCIPAL INVESTIGATORS: Edward Usherwood, Ph.D., Professor of Microbiology and Immunology | Danielle Douglas, Graduate student, Geisel College of Medicine

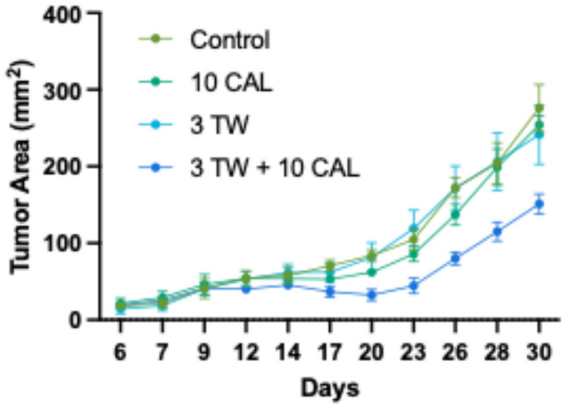
DESCRIPTION

- Adoptive T cell therapy (ACT) has shown promise in certain cancer treatments, but its use remains limited due to the suppressive microenvironments and poor persistence of transferred T cells.
- Promoting a stem cell memory T cell (TSCM) phenotype in T cells prior to transfer is a promising strategy to improve ACT outcomes.
- This technology introduces a novel composition and method to improve ACT by treating the cells with a combination of pathway inhibitors and activators. Specifically, it utilizes a PI3K-AKT-mTOR pathway inhibitor, coupled with either a Wnt/β-catenin pathway activator or an acetyl-CoA synthesis inhibitor.
- Tested combinations significantly reduced tumor burden in a B16-OVA model compared to single treatments.

ADVANTAGES AND BENEFITS

- Enhances the efficacy of cell therapies through targeted pathway modulation.
- Addresses common challenges in cell therapy, including cell exhaustion and limited persistence.
- Flexible composition, allowing for various modality implementations including small molecules, siRNA, and antibodies.
- Potentially increases the in vivo persistence of therapeutic cells, reducing the need for repeated dosing.
- Development of more efficient and durable cell-based therapeutic products could expand use for a range of diseases requiring an immune response.





P values by two-way ANOVA

3TW+ 10CAL compared to:	Control	10CAL	3TW
Day 23	$p \leq 0.05$		$p \leq 0.01$
Day 26	$p \leq 0.001$		$p \leq 0.001$
Day 28	$p \leq 0.001$	$p \leq 0.01$	$p \leq 0.001$
Day 30	$p \leq 0.0001$	$p \leq 0.0001$	$p \leq 0.001$

Figure 1: Only CAL + TW Reduced Tumor Burden

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