AWARD NUMBER: W81XWH-18-1-0296

TITLE: High-Throughput TCR Repertoire-Based Platforms for Antigen-Specific Cancer Immunotherapy

PRINCIPAL INVESTIGATOR: Brandon DeKosky

CONTRACTING ORGANIZATION: The University of Kansas Center for Research, Inc.

REPORT DATE: August 2021

TYPE OF REPORT: Annual Report

PREPARED FOR: U.S. Army Medical Research and Materiel Command
Fort Detrick, Maryland 21702-5012

DISTRIBUTION STATEMENT: Approved for Public Release;
Distribution Unlimited

REPORT DOCUMENTATION PAGE

Form Approved
OMB No. 0704-0188

1. REPORT DATE	2. REPORT TYPE	3. DATES COVERED
AUGUST 2021	Annual	08/01/2020 - 07/31/2021

4. TITLE AND SUBTITLE

High-Throughput TCR Repertoire-Based Platforms for Antigen-Specific Cancer Immunotherapy

5a. CONTRACT NUMBER

5b. GRANT NUMBER
W81XWH-18-1-0296

5c. PROGRAM ELEMENT NUMBER

6. AUTHOR(S)

Brandon DeKosky

E-Mail: dekosky@ku.edu

5d. PROJECT NUMBER

5e. TASK NUMBER

5f. WORK UNIT NUMBER

7. PERFORMING ORGANIZATION NAME(S) AND ADDRESS(ES)

The University of Kansas Center for Research, Inc.
2385 Irving Hill Road
Lawrence, KS 66045-7552

8. PERFORMING ORGANIZATION REPORT NUMBER

9. SPONSORING / MONITORING AGENCY NAME(S) AND ADDRESS(ES)

U.S. Army Medical Research and Materiel Command
Fort Detrick, Maryland 21702-5012

10. SPONSOR/MONITOR'S ACRONYM(S)

11. SPONSOR/MONITOR'S REPORT NUMBER(S)

12. DISTRIBUTION / AVAILABILITY STATEMENT

Approved for Public Release; Distribution Unlimited

13. SUPPLEMENTARY NOTES

14. ABSTRACT

We seek to develop new platform technologies that will help us to better understand why and how immune-based cancer treatments are effective, and to apply that fundamental knowledge to develop rapid, targeted cancer therapeutics and improve cancer care. Modern immune-based therapies have shown tremendous success for treating many different kinds of cancers, and T cells play a critical role in these treatments because they have a unique ability to specifically target and selectively destroy tumor cells. However, T cells are difficult to analyze in the laboratory because each T cell has multiple unique genes, and thus each T cell must be studied one cell at a time. In the prior reporting period, we have made progress toward establishing these new systems using both control TCRs and with patient immune libraries. We are excited to apply these technologies to understand the mechanistic features of cancer-specific T cell targeting, and apply that information to develop more precise and effective cancer therapeutics in future reporting periods.

15. SUBJECT TERMS

Key words or phrases identifying major concepts in the report

T cell receptor; single-cell analysis; T cell screening, Next-generation sequencing; renal cell carcinoma

16. SECURITY CLASSIFICATION OF:			17. LIMITATION OF ABSTRACT	18. NUMBER OF PAGES	19a. NAME OF RESPONSIBLE PERSON
a. REPORT	b. ABSTRACT	c. THIS PAGE			USAMRMC
U	U	U	UU	23	19b. TELEPHONE NUMBER *(include area code)*

Table of Contents

1. **INTRODUCTION:** We seek to develop new platform technologies that will help us to better understand why and how immune-based cancer treatments are effective, and to apply that fundamental knowledge to develop rapid, targeted cancer therapeutics and improve cancer care. Modern immune-based therapies have shown tremendous success for treating many different kinds of cancers, and T cells play a critical role in these treatments because they have a unique ability to specifically target and selectively destroy tumor cells. However, T cells are difficult to analyze in the laboratory because each T cell has multiple unique genes, and thus each T cell must be studied one cell at a time. This study will overcome these barriers and develop new ways to analyze T cell responses for millions of cells at once, allowing us to understand anti-cancer T cell responses at a much broader scale than is currently possible. We will apply these technologies to understand the mechanistic features of cancer-specific T cell targeting, and apply that information to develop more precise and effective cancer therapeutics.

2. **KEYWORDS:** T cell receptor; single-cell analysis; T cell screening, Next-generation sequencing; renal cell carcinoma

3. **ACCOMPLISHMENTS:**

- **What were the major goals of the project?**
  - Specific Aim 1
    - Major Task 1: Develop TCRα:β cloning platforms for transducing patient naïve T cells
    - Major Task 2: Sort repertoires cloned into naïve T cells for activation by primary RCC tumor cell samples.
    - Major Task 3: Perform analysis and cloning of anti-tumor TCR responses using melanoma tumor samples.
  - Specific Aim 2
    - Major Task 1: Develop a workflow for cloning linked TCRα:β genes into TCR surface display expression vectors.
    - Major Task 2: Validate sort strategies using small numbers of known antigen-specific TCRs.
    - Major Task 3: Clone and transduce a large library from lymphoma patients for TCR panning, and quantify library size and efficiency. Sort against lymphoma BCR neoantigens to validate anti-cancer TCR sorting capabilities.

- **What was accomplished under these goals?**

1) Major activities

Our laboratory has made steady progress on this CDMRP project, and the lab has continued to produce data at a rapid pace. We developed and validated our single-cell emulsion devices for single T cell analysis, and we are submitting two research manuscripts related to T cell response analysis. We have established computational pipelines for analyzing TCR NGS data, and we also submitted a research methods article to share these advances with the broader community. We have established the experimental, bioinformatic, and collaborative infrastructure necessary to implement these projects, and have completed substantial data acquisition and analysis for our studies in anti-cancer TCR research.

We have one postdoc, one technician, and one graduate student who have focused on this project, in addition to help from other undergraduate and postdoctoral students. We implemented our bioinformatic scripts for data analysis and optimized yield of our custom single-cell workflows and developing methods for simpler single cell

analysis. We completed optimization of library preparation strategies and have been applying our techniques for live cell co-culture for anti-cancer TCR identification.

One major publication from this work has been submitted related to the development and application of natively paired T cell receptor functional screening pipelines (Aim 1 Task 1, Aim 2 Major Tasks 1 and 2), with another two manuscripts in preparation for submission soon. We also have anlayzed our first RCC patient samples (Aim 1 Task 2), with several libraries showing positive data for anti-cancer TCR screening.

2) Specific Objectives

We refined our experimental methods for large-scale processing of T cell samples and library screening, and we have applied them to perform high-throughput functional analysis of natively paired alpha:beta T cell receptors in a variety of settings. We established our system for *in vitro* T cell stimulation as part of Valpha:Vbeta sequencing, and we are drafting a paper based on these methods and also for the establishment of live cell co-culture methods for identifying anti-cancer T cells. We developed a robust TCR library cloning and expression system, whereby we introduce silent and conservative mutations at the alpha and beta constant regions and leader regions, to allow for massively parallel cloning of natively paired and physically linked alpha:beta amplicons derived from single T cells. We validated our approach to dissect fine affinity features that will compare not just TCR affinity, but the on-rate and off-rate of T cells to peptide:MHC targets, as described in a paper with anticipated submission in September 2021. We also applied these unique technologies for analyzing cell-based TCR activation using live cell co-culture using a samples from multiple RCC patients for anti-cancer TCR discovery, in collaboration with the Godwin laboratory at the University of Kansas Medical Center.

We advanced our technologies for rapid computational profiling of TCR immune responses, including several techniques for TCR response analysis in a recently submitted paper. We have been applying our methods for rapid interpretation of T cell receptor NGS data, including for the identification of antigen-specific TCRs. We finalized pipelines for compiling and interpreting TCR prevalence after various library screening conditions, as reported in a collaborative methods article that is currently under review.

Our major current objectives are to publish the current version of the TCR library generation and screening protocols (Aim 1 Task 1, Aim 2 Tasks 1 and 2) in a series of publications, of which the first two have been submitted and the next three studies will require another 12 months until final publication. We have applied this technology in parallel to identify the anti-cancer TCRs in several RCC patients (Aim 1 Task 2), which is the current major objective that we are now focused on and generating strong data. Finally, once these pipelines are fully established with RCC patient samples, we will apply them for analysis of melanoma tumor samples (Aim 1 Task 3) and for lymphoma samples (Aim 2 Task 3). For an unrelated project, we also submitted a manuscript related to the computational prediction of T cell epitopes, which we may be able to use to help understand the neoantigen targets of the anti-cancer TCRs that we identify in our lymphoma TCR sample analysis.

3) Significant Results

We achieved major progress using our single cell platforms and strategies for advancing the bioinformatic analysis of these datasets to interpret immune function. Experimentally, in a different project we developed a new technology for precise interrogation of NGS datasets for immune receptor function, which was published in the *Proceedings of the National Academy of Sciences* (Madan & Zhang et al, PNAS 2021), and we have applied these technologies for the NGS-based analysis of T cell receptor affinity and specificity in a paper that will be submitted in September 2021.

We have also made major advances in workflows for high-throughput paired functional analysis of natively paired alpha:beta T cell receptor genes (Aim 1 Task 1, Aim 2 Tasks 1 & 2). We have applied our primer set and cloning strategy for the amplification of human T cell receptors and display on lentivirally transduced mammalian T cells (**Figure 1, Figure 2**), and we are now using it with human T cell receptor libraries.

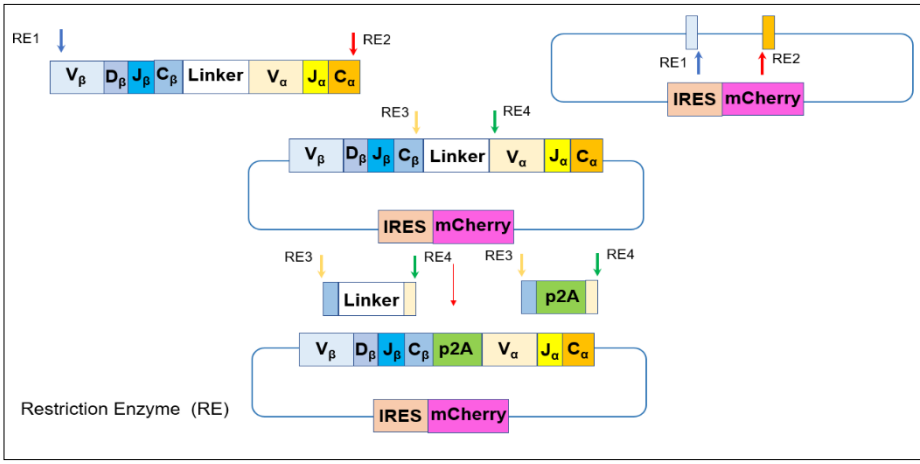

Figure 1: *Cloning strategy for display of our linked Valpha:Vbeta TCR genes. Two unique restriction enzymes at the outside and inside of the linked TCR gene amplicon are used to clone the amplicon into display plasmids. A p2a sequence is cloned into the center to allow for separate expression of alpha and beta chains, while an IRES and mCherry sequence is used to quantify TCR transcription. Surface staining for TCR constant region genes is used to determine surface TCR expression.*

We fully developed our sequencing and cloning workflow, and we have sequenced and displayed several human TCR repertoires (as shown in **Figure 3**). We applied the T cell repertoires for the discovery of antigen-specific TCR genes, and we identified some enriched cell populations after p:MHC staining and screening that contain multiple antigen-specific TCRs of varying affinities. We are preparing these results for publication and we anticipate to send out the manuscript in September.

We shifted our focus onto library screening assays and live-cell killing and activation assays for the identification of cancer cell-specific TCRs in the past year. We are preparing a publication related to cell-based activation screening methods, which we anticipate to submit around December 2021. We are also finalizing experiments for anti-RCC T cell immune responses, and we hope to prepare that work for publication soon.

On the bioinformatic side, we have been applying new workflows to analyze T cell receptors and to track their prevalence across screening rounds, following cell sorting for either live-cell activation (e.g. against co-culture cancer cells) or peptide:MHC staining directly. We have used these methods to analyze the diversity of cloned natively paired alpha:beta chains, confirming the accuracy of our native T cell pairing workflows (to be reported in the Sept 2021 submission). We also applied them for the analysis of antigen-specific T cell receptors from sorted TCR libraries (**Figure 3**). We successfully applied NGS for screening affinity of pMHCs directly, with positive results.

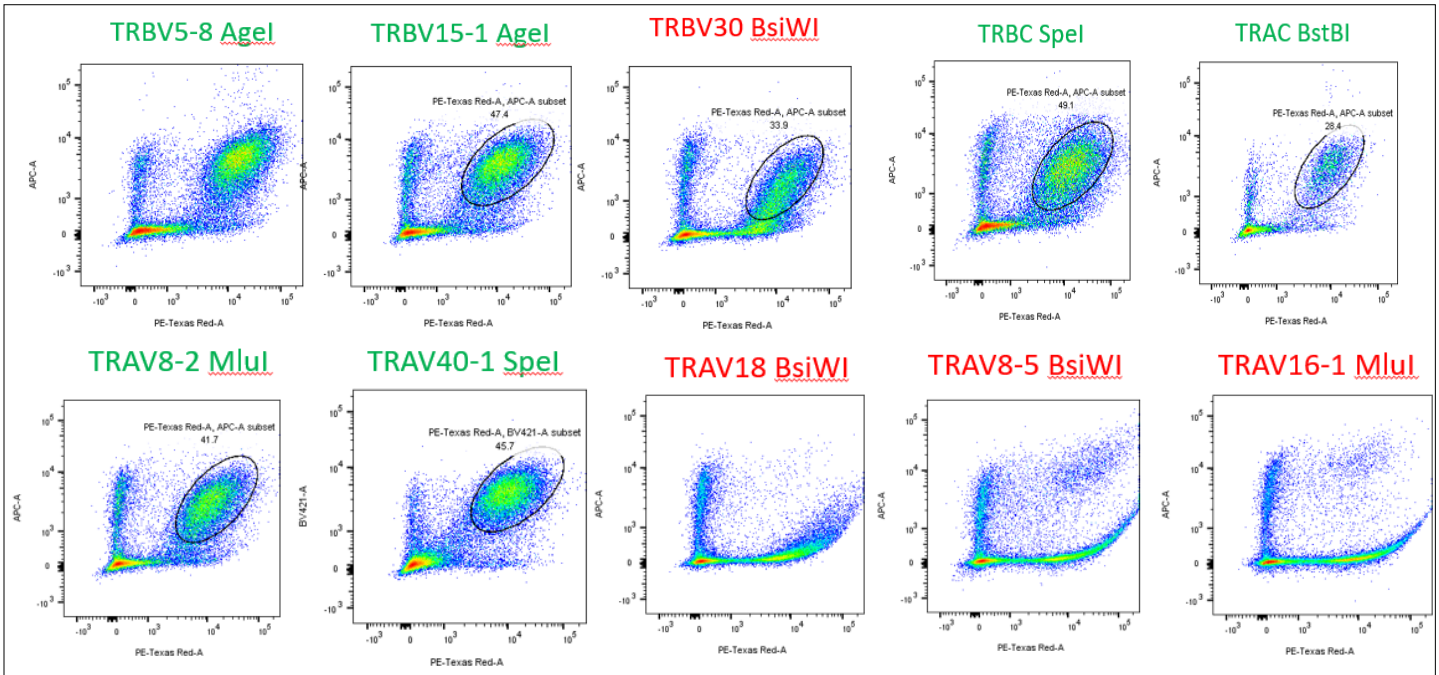

Figure 2: *A small panel of the restriction enzymes and leader peptides (for TRAV/TRBV) that we tested for allowing proper TCR display, using JRT3 cells displaying a known anti-HIV positive control antibody. mCherry expression is shown on the x-axis, while HIV peptide p:MHC binding is shown on the y axis. By performing this analysis individually, we were able to determine a set of mutations that allowed for proper TCR display (successful restriction enzymes for use in our cloning scheme are shown in green).*

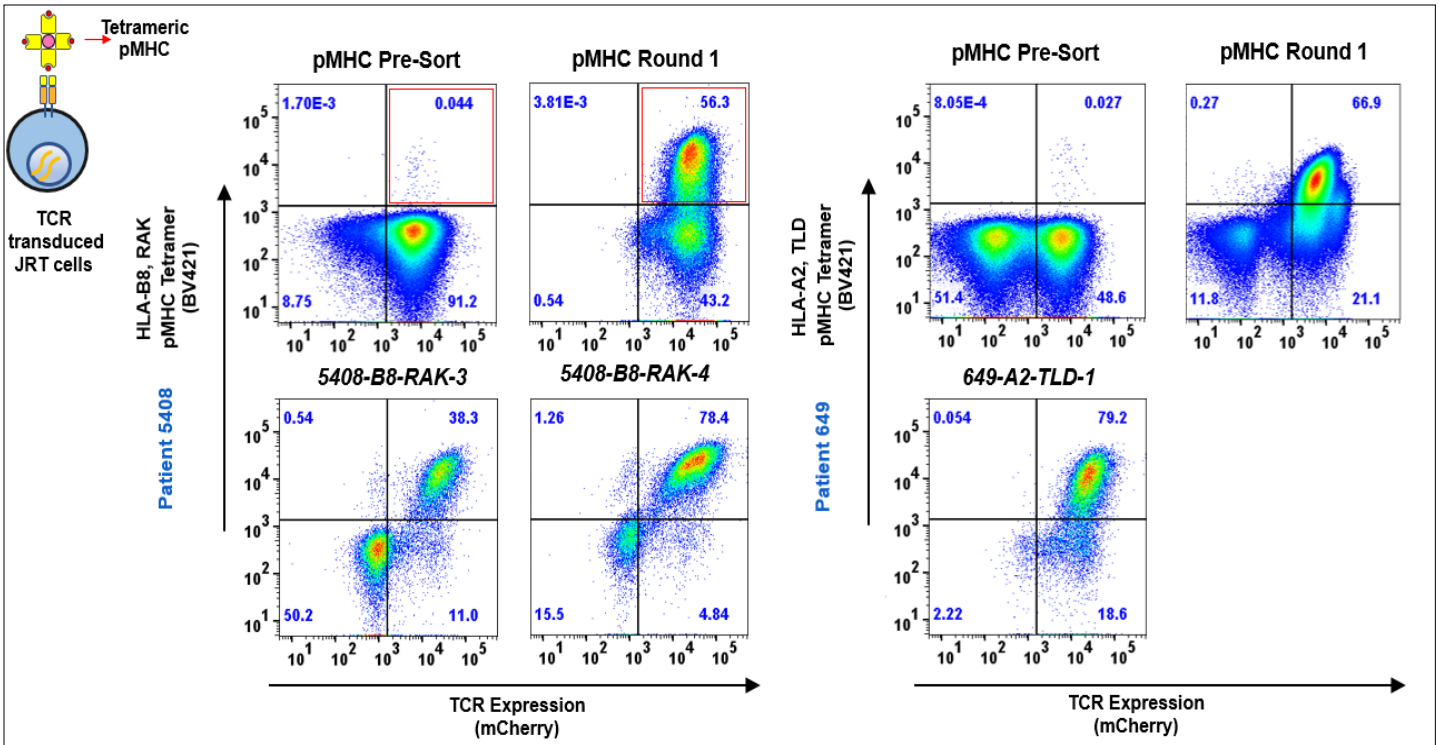

Figure 3: *Analysis of infectious mononucleosis patient samples for anti-EBV peptides as validation of our screening workflows. These data demonstrate the effective screening of immortalized TCR libraries from human patients using soluble peptide:MHC fluorescent screening antigens.*

We also established the platforms for detecting live cell activation in co-culture cell systems (**Figure 4**). We have applied these technologies for the screening of for anti-RCC patient libraries from our collaborator, Dr. Andrew Godwin, and his team at the KU Medical Center (**Figure 5**).

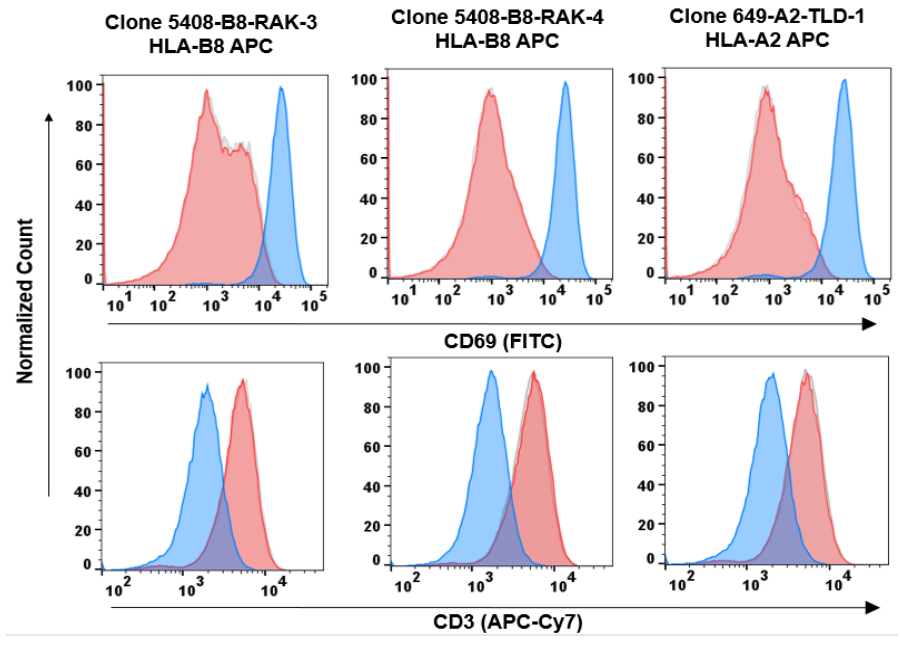

Figure 4: *Activation-based screening of T cell receptor libraries for antigen-specific T cell receptors. Antigen-specific T cell clones that we discovered using our single-cell TCR screening workflow were incubated with antigen-presenting cells (APCs) either with a targeted peptide pulse (blue), without any peptide pulse (red), or with a mismatched peptide (gray). These data show that activation-specific changes can be detected using the CD69 and CD3 fluorescent markers, for robust transduced library sorting. We will apply these methods for screening anti-cancer T cell libraries in the coming reporting period.*

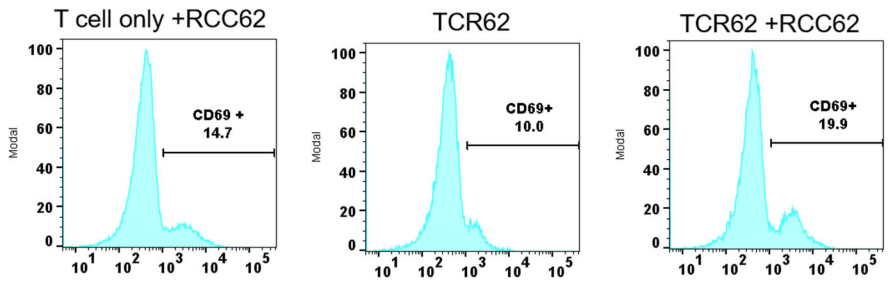

Figure 5: *Activation-based screening of human T cell repertoires against personalized cancer cell immune responses. TCR genes were captures from tumor-infiltrating lymphocytes and cloned into lentiviral display in human T cells. In parallel ("TCR62"). In parallel, patient-matched tumor cells were co-cultured with the cloned T cell libraries ("RCC62"). T cell activation was measured using the CD69 marker (x-axis). These data demonstrate higher responses in patient-matched T cell libraries co-cultured with cancer patient cells, presenting a new method to identify highly specific T cell responses against cancer cells.*

4) Key Outcomes or Other Achievements

We have achieved major progress on our research goals. In the next reporting period, we will continue to make public presentations about these exciting new platforms and submit our findings for publication to additional peer-reviewed journals. We look forward to isolating human anti-cancer T cells in the coming reporting period and evaluating their ability to target cancer cells *in vitro*.

- **What opportunities for training and professional development has the project provided?**

This project has provided training for postdoctoral researchers Andrew Chung, Matias Gutierrez, and Bharat Madan, and for technician Nicoleen Boyle. Andrew has been our project lead for advancing methods and techniques for T cell receptor analysis of anti-cancer immunity. Matias has assisted Andrew and also helped to develop new bioinformatic techniques, and Bharat Madan helped develop those bioinformatic methods as well. Nicoleen has been assisting with the cloning and sample analysis of TCR libraries.

This project provided for the training and professional development of graduate student Ahmed Fahad, who has developed computational approaches for the rapid interrogation and analysis of TCR display functional data, and has also made major contributions to the live-cell sorting protocols of these experiments. We have also trained undergraduate students Mattison Sills, and research technicians John Zhou and Shauna Moore who worked under the supervision of Dr. Andrew Chung with TCR transduction experiments.

- **How were the results disseminated to communities of interest?**

Conference presentations related to this work:

- *Model Informed Drug Development (MIDD) Symposium*, US Food and Drug Administration, Bethesda, MD (via Webinar, June 2021)
- *The Protein Engineering Summit (PEGS-Boston)*, Boston, MA (via Webinar, May 2021)
- *Millipore-Sigma Single Cell Analysis Symposium,* via Webinar (Apr 2021)
- *Immunogenicity Summit, Cambridge Health International*, Washington, DC (Webinar, Oct 2020)
- *Computational Drug Discovery & Development for Biologics*, Boston, MA (changed to Webinar, Oct 2020)
- *The Protein Engineering Summit (*PEGS-Boston*)*, Boston, MA (changed to Webinar, Sep 2020)

Academic seminar presentations related to this work:

- *Department of Chemical Engineering, Massachusetts Institute of Technology / Ragon Institute of MIT/MGH/Harvard,* Boston, MA (virtual visit, Mar 2021)

- *Department of Biomedical Engineering, The University of Texas at Austin,* Austin, TX (virtual visit, Feb 2021)
- *Center for Vaccines and Immunology, The University of Georgia,* Athens, GA (virtual visit, Dec 2020)
- *Biological Standards Working Group, Adaptive Immune Receptor Repertoire Community* (Dec 2020)
- *Research in Progress Seminar Series, KU Medical Center,* Kansas City, KS (Aug 2020)

- **What do you plan to do during the next reporting period to accomplish the goals?**

We will continue to advance both experimental work and prepare multiple additional publications in the coming year. We are have screened anti-peptide:MHC TCR libraries from four different RCC clinical samples and achieved positive resultsour experimental and bioinformatic parameters for T cell receptor analysis. We anticipate that these works will contribute to a publication on high-throughput TCR screening that will be sent out in 2021. We are continuing to perform experimental sample analysis from Dr. Godwin's clinical samples for anti-cancer TCR discovery in a variety of settings. Future studies will also investigate the use of PDX mouse models for evaluation of the protective effects of the anti-cancer TCRs that we discover.

In parallel with our experimental advances we are also continuing to optimize our methods for computational interrogation of immune datasets. Once the data is obtained from our current TCR screening and the manuscript submitted for publication, we will generate automated scripts for simplified processing of experimental data based on those optimized parameters. We have prepared one bioinformatics-focused paper on quality control of TCR repertoire analysis of screened libraries in the past year, and we plan to prepare another paper focused on antigen-specific TCR repertoire analysis.

4. IMPACT:

- **What was the impact on the development of the principal discipline(s) of the project?**
  - The advances we have made in the previous reporting period have enabled the large-scale interrogation of T cell receptors for anti-cancer immune responses. This will greatly impact future studies on T cell responses against cancer neoantigens, and may lead to new personalized and targeted cancer therapeutics.
- **What was the impact on other disciplines?**
  - Our initial progress in T cell receptor screening technologies will also enable the analysis of viral infections and autoimmunity in other fields.
- **What was the impact on technology transfer?**
  - Nothing to report
- **What was the impact on society beyond science and technology?**
  - Nothing to report

5. CHANGES/PROBLEMS:

- **Changes in approach and reasons for change**
  - There are no significant changes to objective or scope
- **Actual or anticipated problems or delays and actions or plans to resolve them**
  - We had continuing delays due to COVID-19 disrupting research facilities access in the current fiscal year, and from one of our lab members being away on maternity leave. We mostly resolved COVID-19 barriers and have fully resumed efforts on this project. We have also experienced another slight delay with the Sleeping Beauty transposon/transposase system, as the Sleeping Beauty system appears to have somewhat low efficiency compared to lentiviral transduction methods. Thus, we have

optimized our systems using lentiviral transduction (as in currently used cell-based therapies), and will adapt our systems to targeted genomic insertion systems at a later date.

- **Changes that had a significant impact on expenditures**
  - Nothing to report
- **Significant changes in use or care of human subjects, vertebrate animals, biohazards, and/or select agents**
  - Nothing to report
- **Significant changes in use or care of human subjects**
- **Significant changes in use or care of vertebrate animals.**
- **Significant changes in use of biohazards and/or select agents**

6. PRODUCTS:

- **Publications, conference papers, and presentations**
  - **Journal publications.**

    Chung C-Y, Gutiérrez-González M, López Acevedo SN, Fahad AS, DeKosky BJ, "The AIRR Community Guide to Quality Control: Chain Pairing Precision and Monitoring of Cross-Sample Contamination," *Submitted to Methods in Molecular Biology*, May 2021

  - **Books or other non-periodical, one-time publications.** Nothing to report
  - **Other publications, conference papers, and presentations.**

Conference presentations related to this work:

- *Model Informed Drug Development (MIDD) Symposium*, US Food and Drug Administration, Bethesda, MD (via Webinar, June 2021)
- *The Protein Engineering Summit (PEGS-Boston)*, Boston, MA (via Webinar, May 2021)
- *Millipore-Sigma Single Cell Analysis Symposium,* via Webinar (Apr 2021)
- *Immunogenicity Summit, Cambridge Health International*, Washington, DC (Webinar, Oct 2020)
- *Computational Drug Discovery & Development for Biologics*, Boston, MA (changed to Webinar, Oct 2020)
- *The Protein Engineering Summit (*PEGS-Boston*)*, Boston, MA (changed to Webinar, Sep 2020)

Academic seminar presentations related to this work:

- *Department of Chemical Engineering, Massachusetts Institute of Technology / Ragon Institute of MIT/MGH/Harvard,* Boston, MA (virtual visit, Mar 2021)
- *Department of Biomedical Engineering, The University of Texas at Austin,* Austin, TX (virtual visit, Feb 2021)
- *Center for Vaccines and Immunology, The University of Georgia,* Athens, GA (virtual visit, Dec 2020)
- *Biological Standards Working Group, Adaptive Immune Receptor Repertoire Community* (Dec 2020)
- *Research in Progress Seminar Series, KU Medical Center,* Kansas City, KS (Aug 2020)

- **Website(s) or other Internet site(s)**
  - Nothing to report

- **Technologies or techniques**
  - We have established new techniques for cloning T cell receptors, and we are in the process of applying those technologies for anti-cancer TCR discovery.
- **Inventions, patent applications, and/or licenses**
  - Nothing to report
- **Other Products**
  - Nothing to report

7. PARTICIPANTS & OTHER COLLABORATING ORGANIZATIONS:

- **What individuals have worked on the project?**

Name:	Brandon DeKosky
Project Role:	PI
Researcher Identifier (e.g. ORCID ID):	BDEKOSKY
Nearest person month worked:	0.12 calendar months
Contribution to Project:	Scientific lead, coordinate with collaborators, and directly supervise lab staff
Funding Support:	none

Name:	Cheng Yu (Andrew) Chung
Project Role:	Post Doc
Researcher Identifier (e.g. ORCID ID):	
Nearest person month worked:	6.6 calendar months
Contribution to Project:	Lead experiment design and laboratory data collection for TCR screening.
Funding Support:	none

Name:	Matias Fernando Gutierrez
Project Role:	Post Doc
Researcher Identifier (e.g. ORCID ID):	
Nearest person month worked:	0.25 calendar months
Contribution to Project:	Assist with laboratory data collection for TCR screening.
Funding Support:	none

Name:	Nicoleen Boyle
Project Role:	Assistant Researcher
Researcher Identifier (e.g. ORCID ID):	
Nearest person month worked:	9.0 calendar months
Contribution to Project:	Assist with laboratory data collection for TCR screening.
Funding Support:	none

- **Has there been a change in the active other support of the PD/PI(s) or senior/key personnel since the last reporting period?**

Previous/Current/Pending Support

DeKosky, Brandon – University of Kansas
nine ended; three new

PREVIOUS

Title:	A New Experimental Platform to Analyze anti-gB Antibodies in Human B Cells
Effort:	1%
Supporting Agency:	NIH
Grants Officer:	Emily Tran, 301-451-7280, trane@mail.nih.gov
Performance Period:	01/11/2016 – 04/30/2018
Funding Amount	
Project Goals:	The goals was to establish a new pipeline to understand the comprehensive features of antibody-based immune protection from HCMV in human subjects in an effort to develop new therapeutics and design effective HCMV vaccines.
Specific Aims:	Aim 1: Establish an experimental platform for rapid discovery of human antibodies targeting the HCMV neutralization-sensitive glycoprotein B cell surface receptor. Aim 2: Develop a high-throughput robotic HCMV neutralization assay and apply it to discover HCMV-neutralizing antibodies.
Overlap:	none

Title:	New platforms for rapid and personalized TCR-based cancer immunotherapy
Effort:	2%
Supporting Agency:	NIH/University of Kansas Medical Center Research Institute, Inc. flowthru
Grants Officer:	240-276-5600, ncicenters-r@mail.nih.gov
Performance Period:	02/01/2018 – 01/31/2019
Funding Amount	
Project Goals:	The goal was to leverage high-throughput techniques to accelerate tumor-specific cancer treatment and to develop new personalized cancer therapeutics.
Specific Aims:	Aim 1: Develop a platform for rapid isolation of antigen-specific TCR repertoires as personalized, targeted cancer therapies for solid tumors. Aim 2: Develop a paired TCRα:β library display platform for rapid neoantigen-specific TCR library isolation and screening *in vitro.*
Overlap:	none

Title:	New technologies to analyze T cell responses to Epstein-Barr virus
Effort:	2%
Supporting Agency:	NIH/University of Kansas Medical Center Research Institute, Inc. flowthru
Grants Officer:	Christy Leake, 301-594-7706, Christy.leake@nih.gov
Performance Period:	05/01/2018 – 04/30/2019
Funding Amount	
Project Goals:	The goal was to establish new technologies and generate the research environment needed to analyze cellular development of T cell receptor (TCR) responses to Epstein-Barr virus (EBV) in transplant settings.
Specific Aims:	Aim 1: Establish a paired TCR alpha:beta library display platform to analyze T cell repertoire development in EBV-naïve transplant patients and EBV seropositive healthy donor controls. Aim 2: Establish technologies to express anti-EBV TCRs in naïve human T cells for PTLD therapies.
Overlap:	none
Title:	Antibody response to protein drugs
Effort:	1%

Supporting Agency:	US-Israel Binational Science Foundation
Grants Officer:	Dr. Wine Yariv, 913-582-8239, bsf@bsf.org.il
Performance Period:	10/01/2018 – 09/30/2020
Funding Amount	
Project Goals:	The goal was to develop and apply a suite of new technologies for high-throughput analysis of anti-drug antibodies in human patients.
Specific Aims:	Aim 1: To establish a reliable, accurate and sensitive immunoassay for detecting all serum ADA while keeping a low background signal, two main factors are considered pivotal during the development of the immunoassay: i) retaining functionality of the MAb-F(ab')2 so that ADA epitopes are preserved, and ii) high purity of the MAb-F(ab')2 with no traces of Fc or undigested IgG that may contribute to the background level when using anti-Fc labeled antibody in the detection phase.
Overlap:	none

Title:	Columbia University's proposed response to the new coronavirus outbreak
Effort:	1%
Supporting Agency:	Jack Ma Foundation/Columbia University flowthru
Grants Officer:	Grants-office@columbia.edu
Performance Period:	04/15/2020 – 10/14/2020
Funding Amount	
Project Goals:	The goal was to investigate a range of different biotechnology solutions to interrupt the global COVID-19 pandemic.
Specific Aims:	Aim 1: Generate natively paired immortalized yeast display antibody libraries from convalescent coronavirus patients for use in analyzing the human response to coronaviruses. Aim 2: Perform high-throughput yeast display screening of natively paired antibody yeast display libraries and prepare those libraries for NGS analysis to enable deconvolution of genetic and functional anticoronavirus antibody molecular features. Aim 3: Perform bioinformatic analysis of NGS data to rapidly identify and discover new anti-coronavirus antibodies and enable antibody generation and recombinant antibody performance analysis. Aim 4: Evaluate key molecular features of humoral immune responses to coronavirus antigens via analysis of immune response data, and collaboratively apply those insights for the design of new pan-coronavirus vaccines and therapeutics.
Overlap:	none

Title:	COVID-19 Fast Grant
Effort:	1%
Supporting Agency:	Mercatus Center
Grants Officer:	Tyler Cowen, fastgrantscovid19@gmail.com
Performance Period:	04/15/2020 – 10/14/2020
Funding Amount	
Project Goals:	The goal was to rapidly identify protective SARS-CoV-2 neutralizing monoclonal antibodies and generate new biologic drugs as powerful medical countermeasures.
Specific Aims:	Aim 1: Mine immune responses in individuals who recovered from COVID-19 and to identify the antibody molecules they carry, and translate those antibodies into drugs for disease prevention and treatment.
Overlap:	none

Title:	Mining natively paired macaque antibodies for Marburg virus protective antibodies
Effort:	1%
Supporting Agency:	Integrated Biotherapeutics, Inc / SBIR NIH flowthru
Grants Officer:	Vandhana Khurana, 240-669-2966, khuranav@niaid.nih.gov
Performance Period:	04/01/2019 – 03/31/2021
Funding Amount	

Project Goals:	The goal is to discover new protective antibodies against Marburg virus from immunized rhesus macaques.
Specific Aims:	n/a
Overlap:	none

Title:	Bridge Proposal: Droplet-based single B and T cell receptor screening for multi-parameter adaptive immune monitoring
Effort:	4.17%
Supporting Agency:	NIH /KU Medical Center Research Institute, Inc. flow thru
Grants Officer:	Heita Chapman, 913-588-7170, hcchapman@kumc.edu
Performance Period:	10/01/2020 – 04/30/2021
Funding Amount	
Project Goals:	The goal is to develop innovative cell-based assays that mine human immunity with molecular detail, and to accelerate progress in human immune research and drug discovery.
Specific Aims:	Aim 1: Develop new natively paired BCR heavy:light screening technologies for repertoire-scale functional molecular analyses of B cell immune responses.
Overlap:	none

Title:	T cell responses shared among triple negative breast cancer patients
Effort:	0.5%
Supporting Agency:	NIH /University of Colorado, Denver Flowthru
Grants Officer:	Mutema Nyankale, 240-276-5987, nyankalem@mail.nih.gov
Performance Period:	09/01/2018 – 08/31/2021
Funding Amount	
Project Goals:	The goal is to develop new technologies to identify TCRs targeting triple negative breast cancer cells.
Specific Aims:	Aim 1: To identify T cell *Receptors* of shared memory T cells from the *Blood* of *TNBC* survivors. Aim 2: To determine longitudinal changes in the memory T cell repertoire that correlate with a *Pathologic* complete response after treatment.
Overlap:	none

Title:	Antibody display libraries for precision screening of antibody immune responses to SARS-CoV-2
Effort:	12.5%
Supporting Agency:	NIH
Grants Officer:	Becky Miller, 301-594-9979, becky.miller2@nih.gov
Performance Period:	09/01/2020 – 08/31/2021
Funding Amount	
Project Goals:	The goal is to determine the antibody-based immune features in COVID-19 patients to accelerate the development of new medical interventions. SARS-CoV-2 causes asymptomatic or mild disease in many individuals, demonstrating that an effective human immune response can fully prevent disease.
Specific Aims:	Aim 1: Map antibody responses to broad SARS-CoV-2 proteins and epitopes in mild vs. severe cases to identify molecular immune correlates of COVID-19 disease severity. Aim 2: Apply a yeast display screening strategy to emulate the low pH endosomal environment and directly identify potent antibodies that prevent viral fusion.
Overlap:	none

Title:	Development and application of antibody optimization technologies to improve public health
Effort:	2%
Supporting Agency:	NIH/Leidos Biomedical flow thru
Grants Officer:	Joshua Wynne
Performance Period:	10/25/2017 – 08/30/2021

Funding Amount	
Project Goals:	The goal is to apply recent advances for in vitro antibody screening to optimize antibodies with high importance for advancing public health.
Specific Aims:	n/a
Overlap:	none

CURRENT

Title:	Comprehensive analysis of human adaptive immune receptors to elucidate correlates of Epstein-Barr virus disease suppression
Effort:	50%
Supporting Agency:	NIH
Grants Officer:	Gabriel Hidalgo, 301-827-4630, gabriel.hidalgo@nih.gov
Performance Period:	09/19/2016 – 08/31/2022
Funding Amount	
Project Goals:	The goal is to apply new high-throughput immune profiling techniques to elucidate the features of effective Epstein-Barr virus (EBV) immune control.
Specific Aims:	Aim 1: Gain a comprehensive understanding of B-cell responses to EBV infection in clinical cohorts. Aim 2: Gain a comprehensive understanding of T-cell responses to EBV infection in clinical cohorts. Aim 3: Develop a machine-learning analytical workflow to rapidly identify immune correlates from high dimensional immune profiling data.
Overlap:	none

Title:	High-throughput TCR repertoire-based platforms for antigen-specific cancer immunotherapy
Effort:	3%
Supporting Agency:	DoD
Grants Officer:	Jamie Shortall, 301-619-2393, Jamie.a.shortall.civ@mail.mil
Performance Period:	08/01/2018 – 07/31/2022
Funding Amount	
Project Goals:	The goal is to develop new technologies to advance antigen specific cancer therapies.
Specific Aims:	Aim 1: Develop a platform for rapid isolation of antigen-specific TCR repertoires as personalized, targeted cancer therapies for solid tumors. Aim 2: Develop a paired TCRα:β library display platform for rapid neoantigen-specific TCR library isolation and screening *in vitro.*
Overlap:	none

Title:	The influence of evolutionary landscapes on protective antibody development 1000967
Effort:	8%
Supporting Agency:	NIH/University of Colorado flow thru
Grants Officer:	Laura Pone, 240-669-2951, laura.pone@nih.gov
Performance Period:	09/01/2018 – 12/31/2023
Funding Amount	
Project Goals:	The goal is to provide a new, powerful method to map and manipulate rules of in vivo antibody affinity maturation to develop vaccines against refractory pathogens of high interest to public health including Influenza, Dengue, and HIV.
Specific Aims:	Aim 1: To determine *ontogeny* from germ line to mature human antibodies for two heterosubtypic HA stem binders. Aim 2: To determine *ontogeny* from germ line to mature human antibodies for four heterosubtypic and subtype- specific HA head binders. Aim 3: To determine the number of evolutionary trajectories from a representative germline Ab.
Overlap:	none

Title:	Comprehensive molecular and functional analyses of anti-HIV-1 broadly neutralizing antibody repertoires
Effort:	3%
Supporting Agency:	NIH
Grants Officer:	Chernay Rogers, 240-669-2992, Chernay.Rogers@nih.gov
Performance Period:	12/01/2018 – 11/30/2021
Funding Amount	
Project Goals:	The goal is to establish several technologies to comprehensively determine HIV-1 protective antibody responses and for enhanced understanding of HIV-1 protective antibodies.
Specific Aims:	Aim 1: Establish and validate technologies for epitope-specific characterization of anti-HIV antibody repertoires. Apply these technologies for bNAb discovery from HIV-1 patients. Aim 2: Develop a system for direct bNAb discovery from CAPRISA cohorts by directly identifying antibodies with broad affinity to many HIV strains. Aim 3: Establish a platform for rapid mammalian IgG secretion of antibody libraries to enable direct neutralization screening of anti-HIV-1 immune repertoires.
Overlap:	none

Title:	Probing antigen specificity and response of autoimmune B cells in Neuromyelitis Optica
Effort:	4%
Supporting Agency:	NIH
Grants Officer:	Jason Lundgren, 240-669-2973, jason.lundgren@nih.gov
Performance Period:	01/11/2019 – 12/31/2021
Funding Amount	
Project Goals:	The goal is to develop new technologies for immune response analysis and treatment of Neuromyelitis Optica.
Specific Aims:	Aim 1: Determine the molecular features of the anti-AQP4 antibody repertoire in NMO patients during active stages of NMO disease. Aim 2: Develop a set of AQP4 probes for capturing AQP4-specific B cells as targeted cell therapies.
Overlap:	none

Title:	Improved T Cell Receptor Screening for Rapid Personalized Cancer Treatments
Effort:	1%
Supporting Agency:	University of Kansas Medical Center, Cancer Center
Grants Officer:	Mario Medina, spa@kumc.edu
Performance Period:	03/01/2021 – 02/28/2022
Funding Amount	
Project Goals:	The goal is to establish a new strategy for rapid manufacturing of personalized T cell receptor alpha and beta (TCRα:β) anti-tumor immune molecules.
Specific Aims:	Aim 1: Develop optimized methods to rapidly identify potent anti-tumor TCRs in an ex vivo human model of renal cell carcinoma. Aim 2: Develop optimized methods to rapidly identify potent anti-tumor TCRs in an ex vivo humanized mouse model of human colon cancer.
Overlap:	none

Title:	Molecular analysis of antibody responses associated with COVID-19 respiratory distress
Effort:	4.17%
Supporting Agency:	American Lung Association
Grants Officer:	Alexandra Sierra, 312-940-7916, Alexandra.sierra@lung.org
Performance Period:	07/01/2020 – 06/30/2022
Funding Amount	
Project Goals:	The goal is to reveal basic and applied insights related to the role of antibody-based protection against SARS-CoV-2 lung injury and help accelerate new medical interventions to suppress the global COVID-19 pandemic.

Specific Aims:	Aim 1: Discover lead candidate antibody drugs that block ACE2 receptor interactions and neutralize via S protein binding, reducing SARS-CoV-2's ability to infect lung tissue. Aim 2: Map antibody responses to broad SARS-CoV-2 proteins and epitopes in mild vs. vs. severe cases to identify molecular immune correlates of COVID-19 respiratory distress.
Overlap:	none

Title:	K-INBRE: Molecular identification and precise therapeutic targeting of anti-insulin B cells in Type I diabetes
Effort:	1%
Supporting Agency:	University of Kansas Medical Center/NIH flowthru
Grants Officer:	Mario Medina, spa@kumc.edu
Performance Period:	05/01/2021 – 04/30/2022
Funding Amount	
Project Goals:	The goal is to develop a suite of technologies to identify Type 1 Diabetes (T1D)-associated autoimmune B cells and develop new T1D therapeutics that precisely target those B cells for inactivation or destruction.
Specific Aims:	Aim 1: Determine the molecular features of the anti-insulin, anti-proinsulin, and anti-pre-proinsulin antibody repertoire in Type 1 Diabetes patients at the initial stages of T1D onset.
Overlap:	none

PENDING

Title:	Droplet-based single B and T cell receptor screening for multi-parameter adaptive immune monitoring
Effort:	25%
Supporting Agency:	NIH
Grants Officer:	
Performance Period:	07/01/2021 – 06/30/2026
Funding Amount	
Project Goals:	The goal is to establish a suite of technologies that maximize the information collected from cell samples and enable new approaches in antibody and T cell receptor drug discovery.
Specific Aims:	Aim 1: Develop new natively paired BCR heavy:light screening technologies for repertoire-scale functional molecular analyses of B cell immune responses. Aim 2: Establish natively paired TCRα:β gene sequencing and screening for repertoire-scale T cell functional analysis of human clinical samples. Aim 3: Apply a commercially available single-cell platform to link BCR/TCR immune receptor function to single-cell transcriptomes in adaptive immune cells.
Overlap:	none

Title:	A rapid throughput platform for COVID-19 B cell epitope identification and characterization of antibody repertoires in Convalescent Plasma
Effort:	10%
Supporting Agency:	NIH/New York University School of Medicine flow thru
Grants Officer:	
Performance Period:	07/01/2021 – 06/30/2026
Funding Amount	
Project Goals:	The goal is to synthesize and express antibody genes and/or deliver new antibody sequences to the Silverman laboratory for DNA synthesis, expression in HEK293 cells, IgG purification, and use in phage display serum library panning.
Specific Aims:	Aim 1: Isolate new anti-COVID-19 antibodies against broad SARS-CoV-2 protein targets to aid the study of serological immune features in the course of clinical disease. Aim 2: Immortalize COVID-19 patient libraries into yeast display vectors for high-throughput screening.
Overlap:	none

Title:	New high-throughput assays for direct protein drug discovery and engineering
Effort:	25%
Supporting Agency:	Moore Foundation
Grants Officer:	
Performance Period:	08/01/2021 – 07/31/2024
Funding Amount	
Project Goals:	The goal is to validate performance with a collection of known antiviral antibodies (including antibodies targeting SARS-CoV-2, HIV-1, and yellow fever virus) as key controls to quantify success.
Specific Aims:	Aim 1: Optimize the cell line needed for assay implementation at a very large scale Aim 2: Finalize droplet reactor manipulations for high-throughput protein drug screening.
Overlap:	none

Title:	T Cell Receptor Screening for Rapid and Personalized Cancer Therapeutics
Effort:	5%
Supporting Agency:	Midwest Biomedical Accelerator Consortium (MBArC)/NIH
Grants Officer:	
Performance Period:	08/01/2021 – 07/31/2022
Funding Amount	
Project Goals:	The goal is to develop a rapid and practical solution for personalized TCR therapeutics on a clinically relevant scale.
Specific Aims:	Aim 1: Discover potent cancer-killing TCRs from a humanized mouse cancer model. Aim 2: Demonstrate efficacy of personalized anti-cancer treatments in a humanized mouse cancer model. Aim 3: Demonstrate personalized anti-cancer TCR efficacy using ex vivo human tissue.
Overlap:	none

Title:	Antigen-specific apheresis device for treating and monitoring Neuromyelitis Optica
Effort:	3%
Supporting Agency:	NIH
Grants Officer:	
Performance Period:	07/01/2021 – 06/30/2023
Funding Amount	
Project Goals:	The goal is to develop a new device to selectively filter autoreactive cells from circulation for targeted treatment and monitoring autoimmune diseases.
Specific Aims:	Aim 1: Prototype an antigen-specific apheresis device for NMO cell capture. Aim 2: Evaluate the antigen-specific apheresis device for capturing AQP4-specific B cells.
Overlap:	none

Previous/Current/Pending Support

Ellington, Andrew - University of Texas at Austin
Three ended; two new

PREVIOUS
1541244 (Simmel; Germany) 08/01/2015 – 07/31/2018 0.24 CAL
ERASynBio
ERASynBio: A Unified Nucleic Acid Computation System for Organisms
Major Goals: To generate dCas9 and T7 RNA polymerase variants that can be used as parts in the UNACS system for cellular programming.

DBI-0939454 (Ellington;Wichman) 08/01/2016 – 07/31/2018 0.12 CAL
NSF/Michigan State
Rapid analysis of parasite dynamics and evolution in arthropod populations

Major Goals: To create a point of contact diagnostic to monitor arboviral diseases and to better understand the evolutionary dynamics of these diseases.

R43NS105463 (Hall) 04/01/2018 – 09/30/2018 0.12 CAL
NIH
Development of a Unified Information Rich Test for CNBP and DMPK to Improve Assessment of Myotonic Dystrophy Type 1 and 2
Major Goals: To develop a comprehensive molecular diagnostic test for Myotonic Dystrophy Type 1 and 2.

HDTRA1-16-1-0001 (Anslyn) 10/28/2015 – 10/27/2018 0.12 CAL
DoD-DTRA
Rapid, Selective, and Sensitive Sensors for Nerve Agents
Major Goals: To create a series of colorimetric, fluorescent, and chemiluminescent detection methods for nerve agents using oximes as the relative moiety.

Unknown (Arimoto) 11/01/2017 – 10/31/2018 0.12 CAL
Military Infectious Diseases Research Program
Evaluation of novel assay for field-deployable molecular diagnostic platform for rapid identification of mosquitoes, pathogens, and insecticide resistance status for military vector control operations
Major Goals: To evaluate the LAMP-OSD assay for use in rapid vector identification, pathogen detection, and insecticide resistance detection and conduct an in depth assessment of the potential utility of this tool in military vector control operations and identify improvements for optimum field readiness.

SOMNOGHP (Ellington) 03/01/2016 – 11/30/2018 0.12 CAL
Templeton Foundation
Balancing reactivity and replicability with phosphorothiorates
Major Goals: To develop a short replicator that relies on foldback priming and use this replicator and its accompanying replication mechanism as a ‘breadboard’ to examine origins problems.

F-1654 (Ellington) 06/01/2016 – 05/31/2019 0.12 CAL
Welch Foundation
Kinetic and structural characterization of the first error-correcting reverse transcriptase
Major Goals: To determine important residues and perform kinetic analyses for the error-correcting function of an evolved reverse transcriptase.

W911-NF-17-2-0091 (Davies) 05/11/2017 – 09/09/2019 0.0 CAL
Army Research Labs
Synthetic assembly of bacterial communities
Major Goals: To produce of peptide and protein materials that contain non- standard amino acids that can improve the biophysical properties of the materials.

227 (Ellington) 08/01/2017 – 11/27/2019 0.12 CAL
Ajinomoto
0.12 cal.mo.
Metabolic engineering of E. coli for high-level production of L-DOPA
Major Goals: Use directed evolution to create E. coli strains that can produce large amounts of enantiomerically pure L-DOPA.

I-Corps (Ellington) 06/15/2019 – 11/30/2019 0.12 CAL
National Science Foundation
Structure Based Machine Learning Aided Protein Engineering
Major Goals: To evaluate the market potential of structure based machine learning algorithms for protein design

300439 (Ellington) 04/30/2018 – 03/31/2020 0.12 CAL
Asuragen

Development of a unified information-rich test for CNBP and DMPK to improve assessment of Myotonic Dystrophy Type 1 and 2
Major Goals: Production, purification and quality control of enzymes, and for providing enzymes to Asuragen.

HR001117S002-IA-FP-008 (Barrick) 07/01/2017 – 05/30/2020 0.6 CAL
DARPA
AEPHID: Aphid Endosymbionts for Plant Host Immunization and Defense
Major Goals: To engineer therapeutic viruses to be carried by aphid vectors into plant hosts in order to protect them from pathogens and deliver beneficial traits.

(Beacon) 08/01/2019 – 07/31/2020 0.12 CAL
NSF
Evolution of synthetic plant viruses
Major Goals: To create and observe the evolution of a fully synthetic plant virus to study how synthetic biological entities interface with hosts.

HR00111820048 (Ellington) 04/1/2019 – 09/30/20206 1.0 CAL
DARPA
Sensor Plants that Communicate via High Amplification Volatile Organic Channels
Major Goals: To develop sensor plants that communicate via volatile organic channels

UTAP-EXPL/NTec/0015/2017(Peterson) 11/05/2018 – 11/04/2020 0.12 CAL
Portuguese Science and Technology Foundation
International Collaboratory for Emerging Technologies-CoLab
Major Goals: DREAM seeks to use the actual lines of research of the national and international groups involved (which already have a strong background in the development of nanosystems), deepening it to develop a novel vehicle-ligand with antiviral and antitumoral effect in precancerous cells infected by HPV.

W911-NF-17-2-0091 (Ellington) 09/10/2019 – 06/29/2021 0.1 CAL
Army Research Labs
Synthetic assembly of bacterial communities
Major Goals: To produce of peptide and protein materials that contain non- standard amino acids that can improve the biophysical properties of the materials.

CURRENT
W81XWH-18-1-0296 (DeKosky; Ellington) 8/01/2018 – 07/31/2022 0.12 CAL
DOD
High-throughput TCR repertoire-based platforms for antigen-specific cancer immunotherapy
Major Goals: The goal is to develop new technologies to advance antigen specific cancer therapies.

HDTRA1-20-1-0011 (Ellington) 06/17/2020 – 06/16/2024 0.12 CAL
DTRA
A structure-based machine learning framework to engineer antibody stability maturation and affinity
Major Goals: To use a neural network to predict potential mutations for the creation of more stable antibodies with greater affinity for their target.

R01EB027202 (Ellington) 03/15/2020 – 11/30/2023 0.6 CAL
NIH
Directed evolution of polymerases that can read and write extremely long sequences
Major Goals: To generate long read DNA polymerases that should prove capable of generating PCR amplicons > 100 kb in length, with few errors.

17-NAI8_2-0026 (Johnson) 07/01/2018 – 06/30/2023 0.02 CAL
NASA
Agnostic biosignatures of extant life

Major Goals: To refine definitions of the fundamental characteristics of life and optimize measurement strategies in the search for agnostic biomarkers.

R01EB026533 (Ellington) 05/04/2019 – 01/31/2023 0.6 CAL
NIH
Synthetic biology for controlled release
Major Goals: To develop gut bacteria that can produce the amino acid L-DOPA, which is a known treatment for Parkinson's disease, and determining if the bacterial factories can provide benefit to a Parkinson's mouse model.

R21AT010777 (Ellington) 09/15/2019 – 08/31/2022 0.24 CAL
NIH
Synthetic biology for the chemogenetic manipulation of pain pathways
Major Goals: To evolve individual variants of CB2 that can interact with high affinity with the cannabinoids b-caryophyllene, cannabidiol (CBD), and other minor cannabinoids prove the utility of these compounds and their evolved receptors with isolated neurons and directly in a mouse model for pain.

UTA18-000656 (Ellington) 09/02/2018 – 08/31/2022 0.1 CAL
Promega
Screening for reduced stutter polymerases
Major Goals: To develop a thermally-stable DNA amplification system with enhanced fidelity for amplifying STRs.

(Ellington) 11/01/2020 – 08/31/2022 0.12 CAL
Pine Trees Health, Inc.
Optimization of reverse transcription for LAMP-OSD for the detection of SARS-CoV-2

(Ellington) 08/01/2020 – 08/31/2022 0.24 CAL
Homodeus, Inc.
COVID: Adapting LAMP to lateral flow assays

FA9550-14-1-0089 (Alper) 08/15/2014 – 08/14/2022 0.6 CAL
DoD-Air Force Research Laboratory
Theory-based Construction of Synthetic Circuit Robustness through a Parts to Circuit Approach Focusing on Environmental and Evolutionary Robustness

R01GM124141 (Finkelstein) 09/15/2017 – 06/30/2022 0.36 CAL
NIH
Mechanism, specificity, and design of CRISPR RNA-mediated gene regulation
Major Goals: To mechanistically dissect a newly discovered family of RNA-guided nucleases.

F-1654 (Ellington) 06/01/2019 – 05/31/2022 0.12 CAL
Welch Foundation
A Neural Network for Polymerase Engineering
Major Goals: To determine important residues and perform kinetic analyses for the error-correcting function of an evolved reverse transcriptase.

W911NF1610372 (Ellington; Jewett) 06/01/2016 – 04/20/2022 0.12 CAL
Army Research Office
Engineering the translation apparatus for synthesis of electronically active sequence-defined polymers
Major Goals: To establish a framework to design and synthesize polymers of defined length and sequence that are comprised solely of non-natural monomers.

NNX15AF46G (Ellington) 02/17/2015 – 02/16/2022 2.4 CAL
NASA
Expanded Alphabets for Constructing Evolutionary Machines
Major Goals: To identify nucleic acid molecules that could have evolved in alien environments.

HDTRA1-18-1-0030 (Co-PI) 03/22/2018 – 02/28/2022 0.6 CAL
DTRA
Immunization with transition state analogues
Major Goals: To create a series of transition state antibodies for the neutralization of nerve agents.

090165-16882 (Ellington, Co-I) 10/01/2019 – 01/28/2022 0.12 CAL
University of Illinois Urbana-Champaign/DARPA
Native DNA-Based Data Storage and Computing
Major Goals: Development of tools and methods for DNA information storage, based on increasing the scale of so-called "DNA punch cards." One aspect of this project will be to develop higher throughput methods for the preparation, execution, and analysis of punch cards, using chemical modifications and high-throughput sequencing approaches.

GT10481(Ellington; Anslyn) 01/01/2018 – 12/31/2022 0.6 CAL
HHMI
Accelerating Professional Development for Undergraduate Science Majors
Major Goals: To establish a unique training experience for undergraduate and graduate chemistry and biochemistry majors, aimed at creating the next generation of both scientist-leaders and scientist-entrepreneurs.

UTA18-000856 (Ellington) 07/15/2018 – 12/31/2021 0.12 CAL
ExxonMobil
Systems and Synthetic Biology Approaches to Plastic Degradation
Major Goals: To provide a better path towards engineering the degradation and biotransformation of plastics.

R21AI135576 (Ellington) 04/01/2017 – 11/30/2021 0.6 CAL
NIH
Rapid, cellphone-based POC detection of Borrelia species in field-caught ticks
Major Goals: To develop a point-of-care test to identify tick species and the presence of Borrelia

R21AI143407 (DeKosky; Ellington) 12/01/2018 – 11/30/2021 0.24 CAL
University of Kansas/NIH flowthru
Comprehensive molecular and functional analyses of anti-HIV antibody repertoires
Major Goals: To establish several technologies to comprehensively determine HIV-1 protective antibody responses and for enhanced understanding of HIV-1 protective antibodies.

2027169 (Ellington, Co-PI) 04/01/2020 – 10/31/2021 0.24 CAL
NSF
RAPID: Development of Rapid POC SARS-2019-nCoV LAMP-OSD Assay System
Major Goals: To develop a low cost easy to use point of care test platform for SARS-2019-nCoV virus responsible for COVID-19.

RGP0015-2017 (Ellington) 11/01/2017 – 10/31/2021 0.36 CAL
Human Frontiers Science Program
Rebuilding and reimagining the last common ancestor, a ribo-organism
Major Goals: To create a form of life that is a ribo-organism whose genetic code is read by ribozymes.

PENDING
(Ellington) 01/01/2022 – 01/01/2024 0.24 CAL
BioMADE
Distributed manufacturing for antigen for serological testing & countermeasures

(Ellington) 09/01/2021 – 08/31/2025 0.26 CAL
NSF
EFRI E3P Preliminary Proposal: Biodegrading environmental plastics using engineered and bio-prospected microbes and

(Ellington) 08/01/2021 – 07/31/2024 0.24 CAL
NSF

- **What other organizations were involved as partners?**
  - **Organization Name:** The University of Kansas Medical Center
  - **Location of Organization:** Kansas City, KS
  - **Partner's contribution to the projec**t
    - **Collaboration**: Discussion and analysis of workflows for anti-cancer TCR screening (with PI Andrew Godwin, Mentor); sharing of reagents, protocols, and clinical samples
    - **Personnel exchanges** Personnel travel between laboratories to discuss and facilitate collaboration.
    - **Other.**
  - **Organization Name:** The University of Texas at Austin
  - **Location of Organization:** Austin, TX
  - **Partner's contribution to the projec**t
    - **Collaboration**: Production and sharing of custom enzyme reagents, and advice/guidance connected with the use of those enzymes for single-cell genetic analysis.
    - **Personnel exchanges** N/A
    - **Other**

8. SPECIAL REPORTING REQUIREMENTS:

- **COLLABORATIVE AWARDS:** n/a
- **QUAD CHARTS:** n/a

9. APPENDICES: n/a