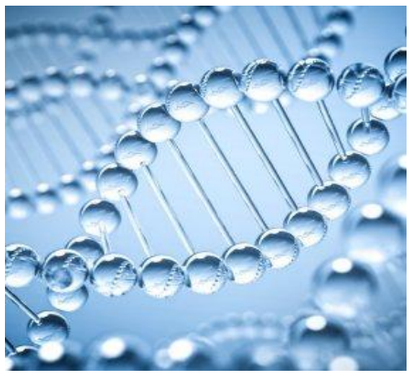
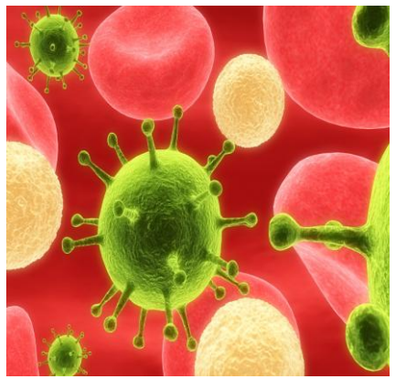
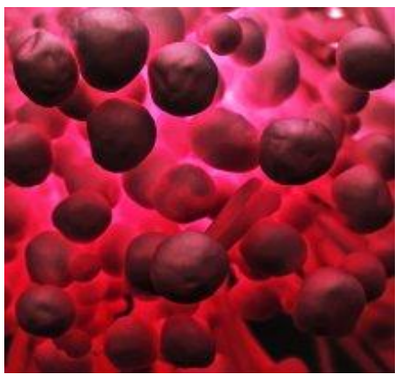
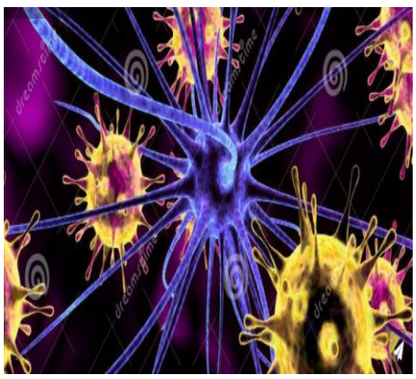
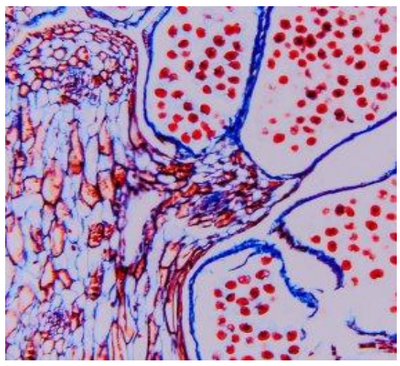
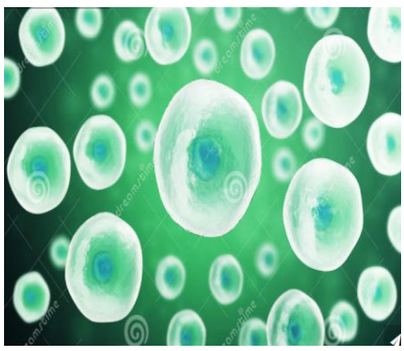







Commonwealth Health Research Board (CHRB)

Fiscal Year 2026 Annual Report








Commonwealth Health Research Board [CHRB]
Fiscal Year 2026 Annual Report

Introduction:

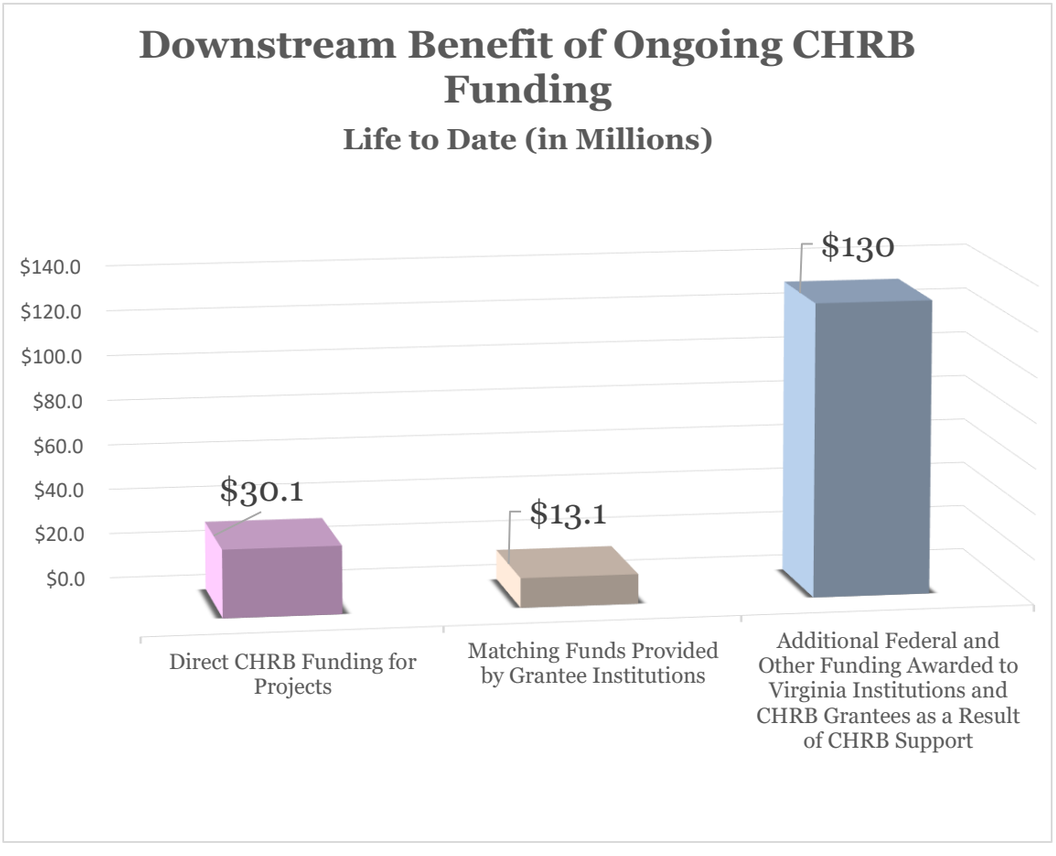
The Commonwealth Health Research Board (CHRB or Board) Fiscal Year 2026 Annual Report includes information about the CHRB 2026/2027 grant award process that occurred from July 1, 2025 – June 30, 2026. At the May 7, 2026 CHRB Board Meeting, the Board voted to award eleven new grants.

Goals, Purposes and Accomplishments of the Commonwealth Health Research Board (CHRB)

The CHRB was created by ***Virginia Code* §32.1-162.23** to provide financial support—in the form of grants, donations, or other assistance— for research efforts having the potential of maximizing human health benefits for the citizens of the Commonwealth. Research efforts eligible for support by the Board may include traditional medical and biomedical research relating to the causes and cures of diseases, as well as research related to health services and the delivery of health care.

Downstream Benefits of Ongoing CHRB Funding:

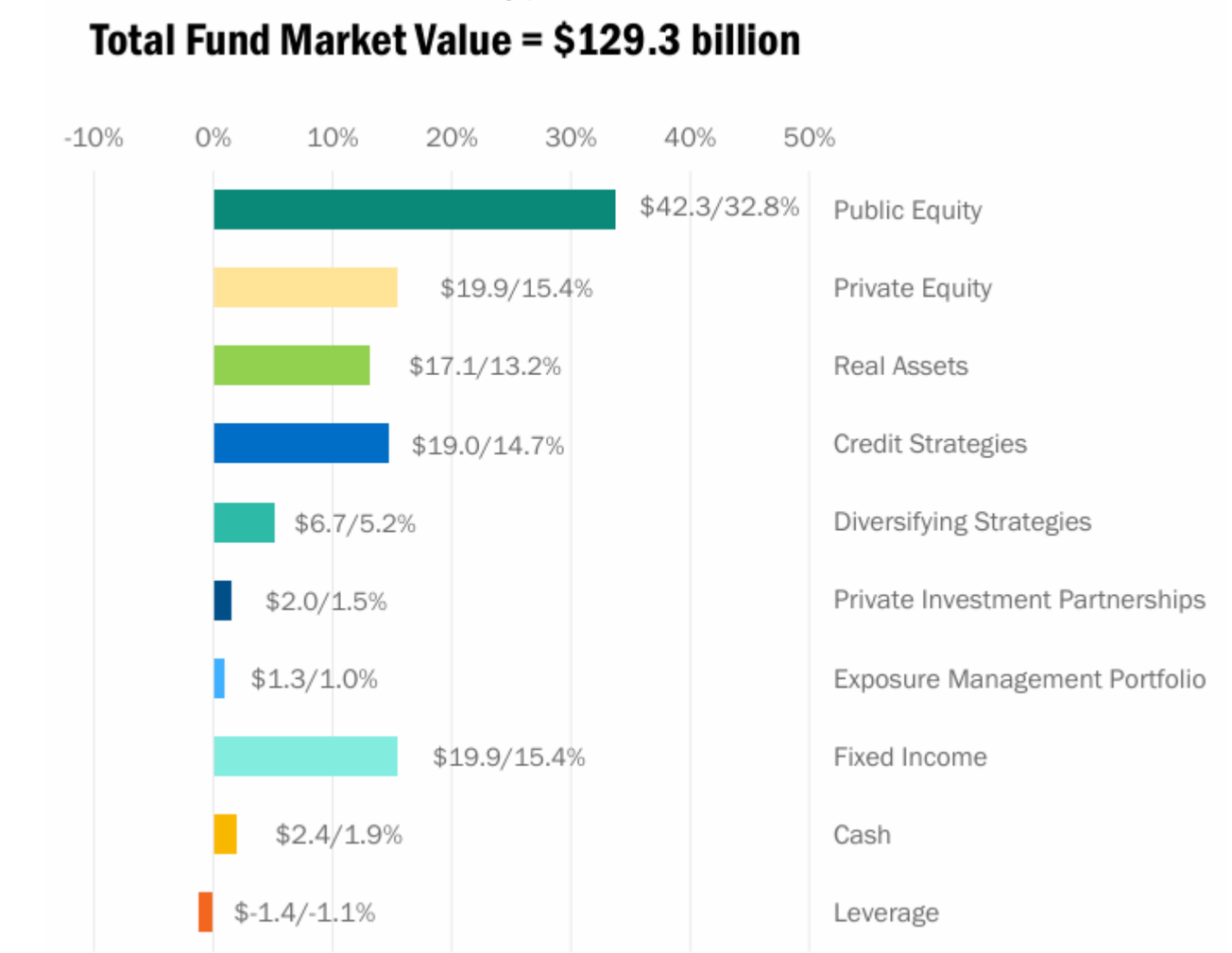
In accordance with ***Virginia Code* §32.1-162.24,** the Board encourages collaborative research efforts among two or more institutions or organizations, gives priority to those research efforts where Board support can be leveraged to foster contributions from federal agencies or other entities, and supports both new research efforts and the expansion or continuation of existing research efforts. CHRB grant recipients — for grant awards life-to-date — have leveraged over **$130** million in additional private and federal grant funds to further their research studies. CHRB funds provide a vital conduit for Virginia scientists with nascent innovations by providing seed grants to generate the early data necessary to provide proof of concept for new ideas and then be competitive for NIH and next level grants.



Commonwealth Health Research Fund [CHRF]

***Virginia Code* § 51.1-124.36** delegates the authority to invest and manage the assets of the Commonwealth Health Research Fund (CHRF) to the Virginia Retirement System (VRS). Assets of the CHRF are pooled with the **$129.3** billion VRS investment fund (as of March 31, 2026); however, the provision requires the VRS to maintain a separate accounting for the CHRF assets. The estimated value of the CHRF as of March 31, 2026, before year end income accruals, was almost **$54.9** million, per the Virginia Retirement System Finance Division Commonwealth Health Research Fund Activity Report.

VRS current Asset allocation as of March 31, 2026:



Source: https://www.varetire.org/media/members/pdf/investments/quarterly-reports/investments-quarterly-report-03-31-26.pdf

The Department of Accounts serves as the fiscal agent for the CHRB through a Memorandum of Understanding. Audits are conducted every two years by the Auditor of Public Accounts.

Commonwealth Health Research Board [CHRB]
Fiscal Year 2026 Annual Report

Executive Summary of 2026/2027 Grant Process:

Institution/ Organization Identification #	Institution/Organization	Concept Papers Received	Full Proposals Reviewed	Presentations to the Board	Grant Awards
204	The College of William and Mary	4	0	0	0
207	University of Virginia	12	4	2	2
208	Virginia Polytechnic Institute and State University	12	5	2	2
221	Old Dominion University Research Foundation (now includes EVMS)	12	1	0	0
236	Virginia Commonwealth University	11	3	2	2
242	Christopher Newport University	1	0	0	0
247	George Mason University	11	1	1	1
268	Virginia Institute of Marine Science	1	1	1	1
307	University of Richmond	1	0	0	0
335	Hampton University	3	1	0	0
804	Carilion Medical Center	3	1	1	1
811	Richmond Institute for Veterans Research (formerly McGuire Research Institute)	3	2	2	2
	Total	**74**	**19**	**11**	**11**

Commonwealth Health Research Board [CHRB]
Fiscal Year 2026 Annual Report

CHRB Current and Historical Funding

Since its inception, the CHRB has made **341** grant awards totaling approximately **$30.1 million** in grant funding to institutions of higher education and other not-for-profit or nonprofit organizations that conduct health, or health-related research in Virginia. When the required 33% matching funds are added to the CHRB funded amount, the cumulative funding totals approximately **$43.2 million** for health research in Virginia.

Grant Year	Total Grant Awards	# New Grant Awards	# Ongoing Grant Awards	CHRB Grant Awards	Grantee Matching Funds	Total Project Funds
1999	9	9	0	$597,377	$272,041	$869,418
2000	11	11	0	$717,442	$305,309	$1,022,751
2001	13	13	0	$825,590	$344,954	$1,170,544
2002	12	12	0	$718,382	$344,603	$1,062,985
2003	8	8	0	$509,806	$199,999	$709,805
2004	14	10	4	$868,514	$367,202	$1,235,716
2005	10	6	4	$755,436	$305,909	$1,061,345
2006	12	8	4	$954,058	$451,983	$1,406,041
2007	12	7	5	$1,105,585	$512,493	$1,618,078
2008	12	8	4	$1,102,030	$446,400	$1,548,430
2009	8	2	6	$727,615	$310,338	$1,037,953
2010	9	7	2	$775,105	$312,808	$1,087,913
2011	11	5	6	$1,061,644	$397,212	$1,458,856
2012	8	6	2	$799,746	$327,186	$1,126,932
2013	8	5	3	$746,688	$372,766	$1,119,454
2014	11	6	5	$1,017,500	$558,485	$1,575,985
2015	13	7	6	$1,213,983	$645,285	$1,859,268
2016	11	6	5	$1,077,444	$526,569	$1,604,013
2017	11	6	5	$1,019,696	$445,311	$1,465,007
2018	13	8	5	$1,251,185	$577,194	$1,828,379
2019	14	8	6	$1,399,997	$583,883	$1,983,880
2020	16	8	8	$1,517,067	$700,610	$2,217,677
2021	14	8	6	$1,400,000	$653,582	$2,053,582
2022	15	9	6	$1,500,000	$615,728	$2,115,728
2023	16	8	8	$1,541,750	$616,835	$2,158,585
2024	15	7	8	$1,431,175	$571,103	$2,002,278
2025	16	9	7	$1,598,501	$576,855	$2,175,356
2026	19	11	8	$1,900,000	$721,723	$2,621,723
Cumulative Total	**341**	**218**	**123**	**$30,133,316**	**$13,064,366**	**$43,197,682**

Commonwealth Health Research Board [CHRB]
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Comparison of Grant Award Success Rates (based upon a five-year average)

Step 1: Concept Paper to Step 2: Submission of a Full Proposal	**Step 2:** Submission of a Full Proposal to Step 3: Presentation of the Full Proposal to the Board	**Step 3:** Presentation of Full Proposal to the Board to receiving a CHRB Grant Award
40%	50%	76%

Success rate from the submission of a Concept Paper to CHRB Grant Award = 15%

Grants Cycle	Step 1: Concept Papers submitted	Step 2: Full Proposals submitted	% Success Full Proposals	Step 3: Full Proposals Presented	% Success Present	New Grant Awards	% Success Awards	From Step 1 to Awards
2026/2027	74	19	26%	11	58%	11	100%	15%
2025/2026	58	24	41%	13	54%	9	69%	16%
2024/2025	64	29	45%	10	34%	7	70%	11%
2023/2024	48	21	44%	12	57%	8	67%	17%
2022/2023	49	24	49%	12	50%	9	75%	18%
Cumulative 5-year Total	293	117	40%	58	50%	44	76%	15%
Cumulative 5-year Average	59	23	40%	12	50%	9	76%	15%

Please note: This chart excludes two-year grant awards that are approved for Year 2 funding.

Commonwealth Health Research Board [CHRB]
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CHRB Grant Awards and Funded Types or Categories of Research

The chart below provides statistics concerning the number of CHRB Grant Awards funded by type or category of research, from 1999 to 2026.

Key Codes	Disease/Research Area	1999 to 2026 Grant Awards	1999 to 2026 Grant Awards in CHRB Dollars
AG	Aging and Diseases of the Aging	6	$710,675
BD	Behavioral Disorders	7	$734,039
BV	Bacterial and Viral Diseases and Treatments	34	$5,674,681
CA	Cancer and Cancer Treatment	47	$6,256,520
CB	Cartilage and Bone	7	$976,078
CV	Cardiovascular Disease	16	$2,026,209
DI	Diabetes	12	$1,480,685
DM	Drug Metabolism	4	$525,900
DA	Drug Addiction and Alcoholism	1	$83,350
EE	Eye and Ear Diseases	5	$678,925
GI	Gastrointestinal Diseases	4	$448,274
GE	Genetics	0	$0
HS	Health Services Research	3	$181,126
HE	Hematology	6	$520,983
KD	Kidney Disease	5	$640,927
LD	Lung Disease	10	$1,484,083
ME	Metabolism	9	$916,082
ND	Neurological Disorders	23	$4,069,104
WH	Women's Health	10	$1,271,820
PD	Psychiatric Diseases	2	$278,382
WO	Wound Healing	1	$76,373
ZZ	Other	6	$1,099,100
	Total	**218**	**$30,133,316**

A one-year or two-year grant award is still considered one grant award for purposes of categorizing disease/research areas.

Commonwealth Health Research Board (CHRB) 2026/2027 Grant Awards

Planned Second-year funding for Two-Year Grant Awards

Principal Investigator	Submitting Institution/ Organization	Grant Award $	Recipient Matching $	Total Project $	Grant Title
Huan Bao, Ph.D.	University of Virginia	$ 100,000	$ 33,000	$ 133,000	Developing Primedisc to characterize tau pathology in Alzheimer's disease
Rishi Drolia, Ph.D.	Old Dominion University Research Foundation	$ 100,000	$ 33,000	$ 133,000	Receptor-Targeted Probiotic Therapy: Engineering Lactobacillus Strains for Enhanced Adhesion and Biofilm Formation in IBD Treatment
Mohammad Fallahi-Sichani, Ph.D.	UVA	$ 100,000	$ 33,000	$ 133,000	Multiparameter Analysis of Tumor Cell State Interplay with Stroma to Predict Metastasis Risk in Melanoma Patients
Marissa Howard, Ph.D.	George Mason University	$ 100,000	$ 33,000	$ 133,000	Personalized therapy sickle cell nephropathy using urine PINK1 markers of glomeruli mitochondria podcyte damage
Nadine Kabbani, Ph.D.	GMU	$ 100,000	$ 33,000	$ 133,000	Proteomic and Neuroimmune Signatures of Chemotherapy-Induced Peripheral Neuropathy in Breast Cancer
Qinglian Liu, Ph.D.	Virginia Commonwealth University	$ 100,000	$ 33,000	$ 133,000	Next-generation fungicidals for the selective targeting of fungal Hsp110s
Ji Ma, Ph.D.	University of Virginia	$ 100,000	$ 33,000	$ 133,000	The Metallic Sponge: eliminating follow-up surgeries and accelerating healing in upper extremity bony fracture through hybrid bioresorbable fracture fixation
Alexander Neuwelt, M.D.	RIVR	$ 100,000	$ 33,000	$ 133,000	High dose propacetamol with fomepizole rescue as a cancer stem cell-targeting strategy for the treatment of advanced malignancies
Alia Marie Iqbal O'Meara, M.D.	Virginia Commonwealth University	$ 100,000	$ 33,000	$ 133,000	Age-dependent Effects of ICU Sedation on Brain Metabolism: A Noninvasive Diagnostic Approach in Pediatric and Adult Rats
Yuchin Albert Pan, Ph.D.	VT	$ 100,000	$ 33,000	$ 133,000	Transcriptional Adaptation as a Novel Mechanism for TSC Pathogenesis and Treatment
John Ryan, Ph.D.	VCU	$ 100,000	$ 79,877	$ 179,877	A New Therapeutic Intervention for Eczema: Targeting Protein Isoprenylation
Daniel Rodriguez-Agudo, Ph.D.	RIVR	$ 100,000	$ 33,000	$ 133,000	StarD5's role in cholesterol reverse transport and atherosclerosis.

(continued next page)

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Principal Investigator	Submitting Institution/ Organization	Grant Award $	Recipient Matching $	Total Project $	Grant Title
Birgit Scharf, Ph.D.	VT	$ 100,000	$ 45,750	$ 145,750	Flagella-dependent bacteriophages for Salmonella therapy
Aashit Shah, M.D.	CMC	$ 100,000	$ 48,696	$ 148,696	Toward Identifying Novel Antiepileptic Drugs: A Brain-Wide Neural Dynamic Intracranial EEG (iEEG) Investigation
Dong Sun, M.D., Ph.D.	Virginia Commonwealth University	$ 100,000	$ 33,000	$ 133,000	Traumatic brain injury-induced activation of NLRP3 inflammasome as the link to the development of Alzheimer's disease
Xuewei Wang, Ph.D.	VCU	$ 100,000	$ 33,000	$ 133,000	Nitric Oxide–Releasing Inflation Solution to Combat Catheter-Associated Urinary Tract Infections (CAUTI)
Andrew Wargo, Ph.D.	VIMS	$ 100,000	$ 52,400	$ 152,400	Development of Rapid Surveillance for Foodborne Pathogens in the Virginia Oyster Industry
Baoxing Xu, Ph.D.	University of Virginia	$ 100,000	$ 33,000	$ 133,000	A force sensor integrated smart retractor for anterior cervical discectomy and fusion (ACDF) surgeries
Stephanie Zuo, M.D.	UVA	$ 100,000	$ 33,000	$ 133,000	Quasi-Experimental Risk Quantification of Overactive Bladder Medications in Nursing Home Residents
		$1,900,000	**$721,723**	**$2,621,723**	

2026/2027 Grant Award Project Summaries

The Commonwealth Health Research Board (CHRB) has awarded **$1,900,000** in grants to 19 medical and health researchers in Virginia. Of this amount, **$1,100,000** represents grants to eleven medical and health researchers for new 2026 Grant Awards and **$800,000** represents continued second-year funding for eight grant awards initially approved in July 2025.

Huan Bao, Ph.D., The Rector & Visitors of the University of Virginia
Developing Primedisc to characterize tau pathology in Alzheimer's disease

Project Summary: The accumulation of tau proteins is a key factor driving neurodegeneration in Alzheimer's disease (AD), leading to cognitive decline and memory loss. Despite significant advances in understanding tau pathology, how tau aggregation perturbs cellular homeostasis remains elusive. Our team has demonstrated that smaller tau oligomers (O-tau) exhibit higher toxicity compared to other tau aggregates, significantly contributing to AD pathology. These O-tau forms compromise cellular integrity by disrupting the nuclear membrane and impairing the translocation of RNA/RNA binding proteins (RBP) as well as translation and protein synthesis. However, the underlying mechanism is poorly understood due to the difficulty in probing the membrane interactome of O-tau using detergents that completely disrupt biological membranes. To tackle this challenge, we recently engineered a novel system for detergent-free isolation of O-tau with native cell membranes into nanodiscs, bypassing a critical limitation of detergent-mediated reconstitution in current approaches. In conjunction with robust high-throughput proteomic, lipidomic and genetic tools, the proposed study seeks to develop a powerful platform for comprehensively profiling the interactome of membrane surface with detergent-free nanodiscs (Primedisc), thereby providing an enabling technology to dissect the molecular mechanism of tau pathology and various human diseases. Moreover, we will further validate and explore the therapeutic potential of O-tau interactome in patient-derived brain organoids and mouse models of AD. By investigating the direct interactions and consequences of O-tau with RNA, proteins, and lipids, the outcome of this study will bridge critical gaps in our understanding of tauopathies, advancing potential therapeutic strategies for AD and related neurodegenerative diseases.

Rishi Drolia, Ph.D., Old Dominion University Research Foundation
Receptor-Targeted Probiotic Therapy: Engineering Lactobacillus Strains for Enhanced Adhesion and Biofilm Formation in IBD Treatment

Project Summary: Inflammatory bowel disease (IBD), including ulcerative colitis and Crohn's disease, is primarily caused by a disruption in gut microbial populations and an abnormal immune response. Current treatments, such as surgery or immunotherapy, are often invasive, expensive, and provide only temporary relief. Therefore, there is a *critical need* for non-invasive therapies with minimal side effects. Probiotics, beneficial bacteria in the gut, have been tested as a potential treatment for IBD. However, conventional probiotics are often ineffective because they are adapted to healthy gut environments and struggle to colonize the inflamed gut during dysbiosis.

This proposal *aims* to develop a Bioengineered *Lactobacillus* Probiotic (*BLP*) that targets inflamed intestinal tissue. The BLP is designed to adhere and form biofilms to inflamed epithelial cells via receptors that are overexpressed in IBD patients, promoting mucus secretion, improving gut barrier integrity, and modulating the immune system. Preliminary data from a dextran sulfate sodium (DSS)-induced IBD mouse model showed that the BLP restored body weight, improved fecal consistency, reduced blood leakage, and suppressed inflammation.

In the first aim, we will assess the therapeutic efficacy of BLP in a mouse model of colitis and evaluate the expression of target receptors in human IBD tissue samples. In the second aim, we will explore the molecular mechanisms underlying BLP's effects on immune modulation and gut restoration. This *innovative* approach could *significantly* revolutionize IBD treatment by offering a non-invasive, personalized therapy that avoids surgery and immunosuppressive drugs, with the potential for at-home use.

Mohammad Fallahi Sichani, Ph.D., The Rector and Visitors of the University of Virginia
Multiparameter Analysis of Tumor Cell State Interplay with Stroma to Predict Metastasis Risk in Melanoma Patients

Project Summary: Melanoma, the deadliest skin cancer, remains a clinical challenge with >100,000 new cases in the USA in 2024, and 250 deaths in Virginia. While early-stage melanoma is curable, survival falls to 30-50% once metastasis occurs, highlighting the need to define mechanisms driving early dissemination. A key challenge is that melanomas are highly heterogeneous, including switchable cell states that coexist within the same tumor and differ in their capacity to grow, invade, and spread. Our recent work identified a network of interacting transcription factors as key regulators of melanoma cell state heterogeneity. A balance among these factors predicts cell states at single-cell resolution, and perturbing this balance reprograms them. Their

spatial heterogeneity within the tumor microenvironment (TME) further suggests regulation by stromal interactions that may promote tumor plasticity and metastatic competence. However, how the TME governs these dynamics and initiates metastasis-driving transitions remains unclear. This project will test the hypothesis that stromal features regulate melanoma cell state heterogeneity to shape pro-metastatic phenotypes. We will analyze tumors from >100 patients with and without sentinel lymph node metastasis using highly-multiplexed imaging and spatially resolved single-cell analysis. By mapping melanoma cells and their neighbors (including immune cells, fibroblasts, and vasculature), we will identify transcription factor patterns linked to invasive states and metastatic risk. Integrating these spatial datasets with patient-level variables through machine learning, we will define signatures predictive of metastasis across cellular, tissue, and patient scales. These studies will yield mechanistic insights, biomarkers, and therapeutic targets to improve prediction and prevention of metastatic melanoma.

Marissa Howard, Ph.D., George Mason University
Personalized therapy sickle cell nephropathy using urine PINK1 markers of glomeruli mitochondria podcyte damage

Project Summary: Children with sickle cell disease (SCD), a genetic disorder of red blood cells (Rbcs), causes terrible bouts of pain when the Rbcs contort into a sickle shape and block small blood vessels. Whenever these bouts occur in the kidney, the filtration system of the kidneys are damaged. This damage accumulates with each SCD crisis. Kidney damage is severe in 30% of SCD patients and doubles the mortality. We have discovered a new way to detect early damage of kidney cells, and we have a strategy to rescue some of this damage during a crisis event. Uniquely, we analyze the actual damaged mitochondria, the power houses of the cell, that are crippled by lack of oxygen. We measure these damaged mitochondria shed by the kidney in a few mL of urine. In this study, we will apply this discovery to a banked cohort of retrospective and an IRB-approved, longitudinal prospective cohort of 700 SCD children before and after kidney crises with the aim to develop an early warning system for the onset of kidney damage, so that early therapy can be instituted. In parallel, we will develop an in vitro model to test our proven drug strategies to rescue the specific cells that are damaged in the kidney. The study leverages the proteomics expertise from Mason, our urinary biomarker expert at ODU and the SCD clinic at Children's National Hospital. The goal is to reduce the high rate of mortality caused by Sickle Cell kidney failure for SCD children.

Nadine Kabbani, Ph.D., George Mason University
Proteomic and Neuroimmune Signatures of Chemotherapy-Induced Peripheral Neuropathy in Breast Cancer

Project Summary: Chemotherapy-induced peripheral neuropathy (CIPN) is a common and serious side effect of cancer treatment that causes pain, numbness, and tingling in the hands and feet. These symptoms can persist after treatment ends and often force patients to reduce or stop life-saving chemotherapy. Despite its high prevalence, particularly in breast cancer patients treated with the chemotherapy drug paclitaxel, there are currently no approved therapies to prevent or treat CIPN.

The purpose of this study is to understand how chemotherapy causes nerve damage in the context of cancer and to identify molecular targets that could lead to better treatments for CIPN. Importantly, most prior studies have examined chemotherapy effects in healthy animals, even though patients receive these drugs while living with cancer. This project addresses that gap by studying CIPN in a tumor-bearing breast cancer model that more closely reflects the clinical situation.

Using mice with breast tumors treated with paclitaxel, the study will combine behavioral testing to measure pain and sensory sensitivity with molecular analyses of in neural centers of pain processing. Studies will reveal protein changes associated with nerve injury and inflammation and link these biological alterations to behavioral symptoms.

The expected outcomes of this research are a better understanding of how cancer and chemotherapy interact to worsen nerve damage and the identification of specific molecular pathways that drive CIPN. These findings are poised to uncover new, actionable targets for developing therapies to prevent or treat chemotherapy-related nerve pain, ultimately improving quality of life for cancer patients and survivors.

Qinglian Liu, Ph.D., Virginia Commonwealth University
Next-generation fungicidals for the selective targeting of fungal HSP110s

Project Summary: As one of the leading causes of hospital-acquired infections, the fungal pathogen *Candida* can cause bloodstream infections with mortality rates above 40%, especially in patients with AIDS, cancers or organ transplants. However, treatment for *Candida* infections is limited to a small number of antifungal drugs and is further complicated by the dramatic rise in drug resistance, particularly for the newly

discovered *Candida auris*, which the CDC designated as an urgent antimicrobial resistance threat in 2023. New treatment options are urgently needed.

Heat Shock proteins 110 kDa (Hsp110s) in *Candida* are essential for the infection process. We have identified a novel inhibitor for *Candida* Hsp110s, which efficiently inhibits and kills *Candida* with limited toxicity in human cells. These original findings provide proof-of-principle evidence supporting *Candida* Hsp110s as targets for the development of new and efficient antifungal drugs.

The overall objective of this proposal is to develop novel, potent, and selective antifungals based on this inhibitor by targeting Hsp110s. Support from the CHRB will accelerate the development of these novel agents and enhance the likelihood of finding a clinical candidate that will benefit patients in Virginia and beyond. Our team, composed of professors, graduate students, and undergraduates, has led the way in the discovery of these first-in-class fungicidal agents. Funding for this application will provide further research opportunities to current and future students and help us secure federal funding in the future.

Ji Ma, Ph.D., The Rector & Visitors of the University of Virginia
The Metallic Sponge: eliminating follow-up surgeries and accelerating healing in upper extremity bony fracture through hybrid bioresorbable fracture fixation

Project Summary: This project aims to create a bioresorbable orthopedic fixation technology that eliminates the need for removal surgery following fracture healing of wrist and fingers while accelerating healing. These removal surgeries are costly, often painful for the patient, and further add to the long recovery time for these procedures. The system is built upon a composite of biodegradable magnesium alloy and a permanent titanium scaffold created through metal additive manufacturing. As magnesium dissolves from interactions with the body, the space left behind is backfilled with the growing bone, and the implant is converted from a fixation device to a bone tissue scaffold. We aim to develop and provide evidence for proof-of-concept for the fixation system and test the hypothesis that resorbable fixation can provide improved mechanical performance and accelerate healing in a rat femur model. The bioresorption and time-dependent mechanical properties of the hybrid composite will be studied. We will also identify the technology transfer and regulatory pathways of the product and conduct interviews with surgeons, hospital officials, and regulatory experts to reduce the time and risk of bringing the technology to hospitals and surgical centers.

Alexander Neuwelt, M.D., Richmond Institute for Veterans Research
High dose propacetamol with fomepizole rescue as a cancer stem cell-targeting strategy for the treatment of advanced malignancies

Project Summary: Actaminophen (AAP, Tylenol) is the most commonly used drug ingredient in America. CYP2E1-mediated metabolism is a minor metabolic pathway that is closely linked to AAP toxicity but is not involved in anti cancer efficacy. Our group has shown that using concurrent fomepizole-based rescue to block CYP2E1 mediated toxicity, we can dose-escalate AAP 100-fold without liver toxicity. At these high doses, AAP has anti cancer stem cell activity that is mediated by blockade of STAT3. However, the administration of high dose AAP faces both logistical hurdles as well as financial/patent protection limitations given the wide use and availability of AAP. To overcome these challenges, we use propacetamol (PAP), an ester-based water-soluble pro-drug of AAP that is not currently approved in Europe or the US, thus presenting a barrier to generic competition. PAP is >10-fold more water soluble than AAP and as a result can be dissolved at high doses in low volumes that are more practical to administer. Furthermore, PAP turns out to have enhanced anti-cancer activity in vivo relative to AAP, likely explained by 2-3-fold higher cellular permeability relative to AAP. We have submitted a patent on the use of both high dose AAP (March 2023) and separately on water-soluble pro drugs of AAP (June 2025) in combination with CYP2E1 inhibition. In the present proposal, we study whether PAP has anti-cancer stem cell activity via inhibition of STAT3 (Specific Aim #1). We will additionally evaluate PAP in combination with standard chemotherapy agents and determine if potential synergism is mediated by STAT3 (Aim 2).

Alia Marie Iqbal O'Meara, M.D., Virginia Commonwealth University
Age-dependent Effects of ICU Sedation on Brain Metabolism: A Noninvasive Diagnostic Approach in Pediatric and Adult Rats

Project Summary: In the intensive care unit (ICU), delirium is a sign of impaired brain function, characterized by confusion and an inability to think clearly. It is associated with an increased risk of death, medical complications, prolonged hospital stays, and even disability after discharge. Delirium is especially common in ICU patients who receive opioid pain relievers and benzodiazepine sedatives. Recent studies show that children under the age of 5 years are at an increased risk, suggesting that the developing brain is more vulnerable to these drugs. The reasons for this vulnerability are not well understood, highlighting an understudied area in pediatric ICU care that makes it difficult to prevent or treat delirium in young children. One possibility is that sedation compromises the elevated metabolic rate that is necessary for early

brain development. The goal of this project is to determine how sedation affects brain chemistry and metabolism in young versus adult rats, using a noninvasive brain imaging technique called magnetic resonance spectroscopy (MRS). MRS measures important brain messaging chemicals and markers of metabolism without the need for surgery or other invasive procedures. Understanding how sedation affects brain chemistry and metabolism at different life stages will guide the development of more effective treatments to reduce the impact of ICU delirium in both children and adults. MRS can be easily incorporated into regular magnetic resonance imaging (MRI), and findings could quickly translate into clinical research and practice, ultimately improving outcomes and healthcare utilization for ICU patients of all ages.

Yuchin Albert Pan, Ph.D., Virginia Polytechnic Institute and State University
Transcriptional Adaptation as a Novel Mechanism for TSC Pathogenesis and Treatment

Project Summary: Study Purpose: This research proposal explores a novel strategy for treating genetic brain disorders by utilizing a recently discovered biological mechanism known as transcriptional adaptation (TA). The goal is to determine whether TA can compensate for defective genes responsible for conditions like Tuberous Sclerosis Complex (TSC), a rare genetic disorder that affects the brain and other organs.

Research Approach: Our team will use zebrafish as the model organism due to their genetic and neurological similarities to humans and their suitability for genetic studies. We will engineer zebrafish with mutations that mimic TSC and then investigate whether activating TA can boost the expression of genes that alleviate disease symptoms. In Aim 1, we will compare zebrafish with and without the ability to activate TA, identifying which genes are upregulated in response to TA. In Aim 2, we will use advanced imaging and genetic tools to assess whether TA ameliorates key TSC symptoms such as abnormal brain development and seizures.

Outcome and Impact: If successful, the study will demonstrate the potential for TA as a new therapeutic avenue for TSC and other hard-to-treat genetic disorders. This approach could complement or overcome the limitations of current gene therapy techniques.

Daniel Rodriguez Agudo, Ph.D., Richmond Institute for Veterans Research
StarD5's role in cholesterol reverse transport and atherosclerosis

Project Summary: The metabolic conditions that lead to the accumulation of cholesterol and its toxic metabolites (oxysterols) in macrophages initiate and drive endothelial inflammation and atherogenesis (1, 2). StarD5 is a macrophage intracellular transport protein able to transfer cholesterol from the ER to the plasma membrane (PM), limiting cholesterol accumulation, its metabolites formation and their deposition in the endothelium. Our studies have shown overexpression of StarD5 increases cholesterol delivery to the acceptor protein ApoA1, of HDL; suggesting an unappreciated rate limiting therapeutic means to increase 'reverse cholesterol transport' (RCT) to prevent endothelial accumulation. Additionally, StarD5 binds the toxic oxysterol 25-hydroxycholesterol, with its likely similar transfer yet to be determined. In liver, overexpression of StarD5 reduces cholesterol/oxysterol accumulation and increases their secretion; while its absence leads to increased cholesterol accumulation and the formation/accumulation of oxysterols in hepatocytes that drive inflammation, and subsequent fibrosis (3). Interestingly, StarD5 and the cholesterol/oxysterol pathways exist within macrophages (Figure 1), and their role in the macrophage could be similar to that in liver. We propose studies in macrophages isolated from wild type (C57BL/6;WT) and StarD5-/- mice, and focused feeding studies in several mouse models to study development and regression of the atherosclerotic plaque. Specific goal: determine the connection of StarD5 to macrophage RCT, oxysterol metabolism, and the developing atherosclerotic plaque; pursing a unique translational role.

John Ryan, Ph.D., Virginia Commonwealth University
A New Therapeutic Intervention for Eczema: Targeting Protein Isoprenylaation

Project Summary: Purpose: Eczema is a chronic allergic skin condition characterized by inflammation and near-constant itching. It affects >7% of the US population1, including at least 800,000 Virginians. One-third of eczema patients have disease that is only partly controlled2. Among these >10M Americans, more than half report itch and skin pain lasting at least 12 hours/day that is poorly controlled by medication1. Our project will use clinically relevant models of eczema to test the hypothesis that targeting protein prenylation is a new way of treating the disease.

Methods: We will test the novel drug FGTI-2734 for its effects in two mouse models of eczema. FGTI-2734 inhibits protein prenylation, a cell signaling pathway that promotes inflammation and has not been targeted in eczema. The drug is the intellectual property of Dr. Said Sebti (VCU). We will employ two models because when combined, they offer a full view of acute and chronic disease. We will also test the importance of

KRAS, a candidate protein inhibited by FGTI-2734. Knockout (KO) mice lacking KRAS in mast cells or eosinophils will be tested for resistance to eczema.

Populations: This is a pre-clinical study using mouse models.

Expected Outcomes:
1. We will determine if FGTI-2734 reduces eczema pathology in mouse models.
2. We will determine if KRAS expression in mast cells or eosinophils promotes eczema.
3. We will obtain data supporting a 5-year NIH grant application.
4. We will seek a novel use patent for FGTI-2734.

Birgit Scharf, Ph.D., Virginia Polytechnic Institute and State University
Flagella-dependent bacteriophages for Salmonella therapy

Project Summary: Multi-drug resistance (MDR) represents a major obstacle to the antibiotic treatment of pathogenic bacterial infections, necessitating the development of new antibacterial agents. Using bacteriophages (the viruses of bacteria) is an emerging alternative to combat bacterial infections and food contaminations. The studies outlined in this proposal will explore and characterize the dynamic interactions between clinically relevant Salmonella serovars and a distinct family of bacteriophages. The χ(Chi) phage family is uniquely valuable as an antibacterial therapeutic because its receptor, the rotating flagellum, is vital for the pathogen to move within the host. A common strategy of bacteria to resist phage infection is the deletion of the phage receptor, which would render Salmonella avirulent to the χ phage family. Due to this evolutionary tradeoff, flagella-dependent phages have an exclusive edge over other types of phages as therapeutics. However, they are currently not being used in phage therapy.

The objective of this proposal is to characterize and uncover the χ phage family infection process. We will define the phage machinery interacting with the host flagellum using molecular biochemistry, cryo-electron and fluorescence microscopy. We will employ natural co-evolution between the χ phage family and a range of Salmonella serovars to expand their host spectrum and gain valuable information about specificity determinants. We will assess the efficiency of the χ phage family in Galleria mellonella (wax moth) larvae as non-mammalian infection model. The proposed approaches will close knowledge gaps, which is necessary for a safe and effective expansion of phage therapy approaches to treat human disease.

Aashit Shah, M.D., Carilion Medical Center
oward Identifying Novel Antiepileptic Drugs: A Brain-Wide Neural Dynamic Intracranial EEG (iEEG) Investigation

Project Summary: Epilepsy is the fourth most common neurological disorder in the world. It is marked by recurring seizures— bursts of atypical electrical activity in the brain that can lead to involuntary changes in behavior, such as body movements, and changes in mental faculties, such as state of awareness. Approximately 1.2% of the US population suffers from epilepsy with approximately 1 million suffering from uncontrolled epilepsy, often due to the ineffectiveness of antiepileptic drugs or anti-seizure medications (ASMs). Uncontrolled seizures significantly impact quality of life by preventing individuals from being able to perform important daily activities like driving. Therefore, the pressing need for better ASMs is evident.

For treatment purposes, individuals with epilepsy often undergo invasive monitoring of brain activity to identify the focus of their epileptic seizures. While they are monitored, patients receive various types of ASMs. This monitoring provides unique data about human brain activity—data that provides a level of physiologic detail normally available only in animal studies. These data will allow the proposed work to investigate the impact of ASMs on brain activity at a fine spatial scale and in deep brain structures.

We will identify neural dynamics that all ASMs induce across brain regions as well as those that differentiate the various classes of ASMs, thus identifying network or region-specific actions that may be critical to the effectiveness of ASMs. We expect that these investigations will provide a foundation for the development of more precisely targeted and effective medications for epilepsy, with fewer unwanted side effects.

Dong Sun, M.D., Ph.D., Virginia Commonwealth University
Traumatic brain injury-induced activation of NLRP3 inflammasome as the link to the development of Alzheimer's disease

Project Summary: Extensive epidemiological evidences have demonstrated that traumatic brain injury (TBI) is a significant risk factor for the development of Alzheimer's disease (AD) and related dementia (ADRD). Thus far, the mechanisms by which TBI promotes AD/ADRD remain unknown, TBI resulted long-lasting abnormal innate immune response likely plays critical role. Recently, inflammasomes have been

identified as the critical platform regulating the innate immune response. Among the known inflammasomes, the NLRP3 inflammasome is involved in many neurological diseases including TBI and AD. However, whether abnormal activation of NLRP3 inflammasome can act as a mechanistic crosslink between these two pathologies is not completely understood. We **hypothesize** that TBI-triggered activation of NLRP3 inflammasome and downstream abnormal immune response is the key factor responsible for potentiating onset and severity of AD. We will test this hypothesis in two aims. **Aim 1**, we will assess TBI-induced changes of NLRP3 inflammasome pathways and immune/inflammatory response in the triple transgenic AD (3xTg) mice using a moderate/severe TBI model that is closely associated to AD/ADRD. The results of this aim will comprehensively ascertain TBI-induced changes in NLRP3 pathways and immune responses with and without AD predisposition, and understand how TBI and AD interact. In **Aim 2**, we will use a novel 3xTg/NLRP3-/- mice and a pharmacological approach to establish the significance of TBI-induced activation of NLRP3 in post-TBI AD development. The results will define the interaction of TBI and AD particularly the role of NLRP3 in between, and ascertain that NLRP3 is a viable therapeutic target for TBI and AD.

Xuewei Wang, Ph.D., Virginia Commonwealth University
Nitric Oxide–Releasing Inflation Solution to Combat Catheter-Associated Urinary Tract Infections (CAUTI)

Project Summary: Catheter-associated urinary tract infection (CAUTI) is one of the most common healthcare-associated infections, with more than 100,000 cases annually in U.S. hospitals and long-term care facilities. CAUTI increases morbidity and healthcare costs by causing recurrent urinary tract infections, catheter blockage and encrustation, and, potentially progressing to life-threatening complications such as pyelonephritis, bacteremia, and sepsis. Despite decades of research and the development of urinary catheters coated or impregnated with antimicrobial agents, the real-world clinical impact of antimicrobial catheters has been very limited. A key reason is that these drugs are applied only to the catheter tubing rather than the balloon, leaving the bladder site unprotected. In this project, we aim to develop a novel inflation solution that releases nitric oxide (NO), a natural, broad-spectrum antimicrobial agent. Unlike antibiotics, NO readily permeates the hydrophobic balloon wall, diffuses into the bladder, and forms an antimicrobial barrier that prevents bacterial growth in urine and halts progression to the kidneys and bloodstream. Our formulations, based on low-toxicity prodrugs and unique excipients, are engineered to release NO at precisely controlled concentrations within the therapeutic window, with tunable durations tailored for different catheterization periods. We will evaluate the efficacy and safety of NO-releasing catheter balloons in both an in vitro bladder model and a rabbit model. If successful, this technology will significantly reduce the incidence of CAUTI and its complications. The pathway toward commercialization and clinical adoption is highly feasible, as this strategy does not require any modification of existing Foley catheter designs.

Andrew Wargo, Ph.D., Virginia Institute of Marine Science
Development of Rapid Surveillance for Foodborne Pathogens in the Virginia Oyster Industry

Project Summary: Consumption of raw oysters is a leading source of foodborne illnesses. Three of the pathogens transmitted by oysters of high concern to human health in Virginia include Vibrio parahaemolyticus, norovirus G2, and hepatitis A virus. Characterized by gastrointestinal illness, these pathogens can become life threatening in some cases. Current approved detection methods for foodborne pathogens in oysters are often labor intensive and have limited sensitivity. This hinders wide-scale surveillance and risk assessment in the Commonwealth. Implementation of new high-throughput human pathogen diagnostics are needed to meet the demands of the state's rapidly expanding raw half-shell oyster industry. Novel digital PCR technologies have emerged, with proven higher throughput, sensitivity, and pathogen load enumeration in systems such as SARS-CoV-2. We propose to adapt these technologies for the detection and quantification of oyster pathogens of high concern to human health in Virginia, with the following aims:

Aim 1: Development of rapid detection methods for Vibrio parahaemolyticus
Aim 2: Validation of rapid detection methods for norovirus G2 and hepatitis A virus
Aim 3: Implementation of human pathogen detection methods through oyster surveillance

This work will establish the framework for improved real-time surveillance and risk assessment of human foodborne illness associated with oyster consumption in Virginia. We anticipate developing methods with 10 100 times increased throughput and sensitivity compared to currently approved methods. This approach can be readily adapted to other foodborne pathogens of concern. Advancements from this proposal will enhance public health while supporting the sustainable growth of aquaculture throughout the Commonwealth and beyond.

Baoxing Xu, Ph.D., The Rector & Visitors of the University of Virginia

A force sensor integrated smart retractor for anterior cervical discectomy and fusion (ACDF) surgeries

Project Summary: Swallowing difficulty (dysphagia) affects up to 83% of patients after undergoing Anterior Cervical Discectomy and Fusion (ACDF) surgery. Patients may need tube feeding for nutrients intake and even die due to aspiration pneumonia. It is often caused by damage to the esophageal and nearby tissues and nerves during surgery because too much force is applied by surgical retractors to hold tissue aside. Currently, surgeons rely on their experience to estimate the amount of force applied, and there is no tool that can monitor it directly during surgery and offer a feedback for control. We propose to develop a smart surgical retractor. It includes a highly sensitive soft force sensor capable of measuring the force in real time. This sensor would be integrated into the retractors surgeons already use, giving them instant feedback and helping prevent tissue damage that leads to dysphagia. The sensor will be made using advanced 3D printing technology and will be highly sensitive to changes in force thanks to its lattice structures based porous design. The overall goal is to create a retractor that makes surgeries safer by providing precise control over the force applied during the procedure. This project will go through three stages of testing including in vitro test to prove the effectiveness of this smart retractor. The team's complimentary expertise and early research data ensures the success of conducting this project.

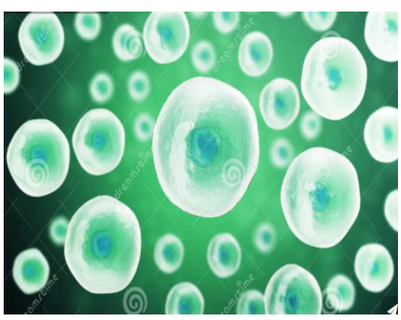
Stephanie Zuo, M.D., The Rector & Visitors of the University of Virginia

Quasi-Experimental Risk Quantification of Overactive Bladder Medications in Nursing Home Residents

Project Summary: There are over 1.3 million older adults in Virginia, each with a 50-60% risk of entering a nursing home (NH) during their lifetime. Once a person enters a NH, the primary goal is to improve function and return to the community. Yet, certain common medical decisions made in the NH, such as the choice of medication to treat overactive bladder (OAB), may unknowingly cause significant harm.

OAB is a highly treatable condition that affects up to 65% of NH residents. There are two main classes of OAB medications: anticholinergics and beta-3 agonists. While both are effective for improving symptoms, anticholinergics negatively impact cognitive function and may increase risk of falls and fractures. Yet, anticholinergics are still used in 75% of residents with an OAB diagnosis. Beta-3 agonists may be safer, but robust evidence is lacking, especially in NH residents, who are more prone to medication-related side effects.

Our proposed research leverages a unique, national database of >3 million NH residents (Long-Term Care Data Cooperative) to compare the 1-year incidence of falls, fractures, and delirium in NH residents who were newly prescribed anticholinergic versus beta-3 agonists. We will employ a quasi-experimental study design to estimate causal impacts in NH residents exposed to at least 30 days of an OAB medication. This novel, rich database enables us to draw conclusions that are credible in a setting where large randomized trials are infeasible. Our results will inform best practices in NH OAB care with significant implications for patient safety and healthcare system costs.



Commonwealth Health Research Board [CHRB]
Fiscal Year 2026 Annual Report

Commonwealth Health Research Funds available for 2026/2027 Grant Awards

Pursuant to ***Virginia Code* §32.1-162.28(E)**, (CHRF) Grant funding is calculated by an amount not to exceed six percent of the moving average of the market value of the CHRF calculated over the previous five years on a one-year delayed basis, net of any administrative fee assessed pursuant to subsection **E of § 51.1-124.36**.

Commonwealth Health Research Board [CHRB] Financials

Supporting documentation for CHRB Annual Report and ACFR Reporting

Funds available for 2026.2027 Grant Awards

Calendar Year		Market Value as of 12/31/xx	
January 1 - December 31, 2020	Year 1	$43,250,731.05	Source: VRS Finance Division Activity Report through December 31, 2020
January 1 - December 31, 2021	Year 2	$49,523,068.01	Source: VRS Finance Division Activity Report through December 31, 2021
January 1 - December 31, 2022	Year 3	$45,217,004.36	Source: VRS Finance Division Activity Report through December 31, 2022
January 1 - December 31, 2023	Year 4	$47,924,262.66	Source: VRS Finance Division Activity Report through December 31, 2023
January 1 - December 31, 2024	Year 5	$50,331,421.28	Source: VRS Finance Division Activity Report through December 31, 2024
	Total	$236,246,487.36	
	Average Market Value	$47,249,297.47	
Example: Funds available for 2026 grants based on 6% of the average market value (upper limit)	6.00%	$2,834,958	

Commonwealth Health Research Board [CHRB]
Fiscal Year 2026 Annual Report

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