Autism Research Program

Congressionally Directed Medical Research Programs

CDMRP

Department of Defense

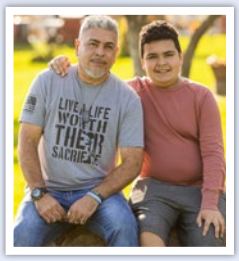
U.S. Army Medical Research and Development Command

Vision:

Improve the lives of individuals with ASD now

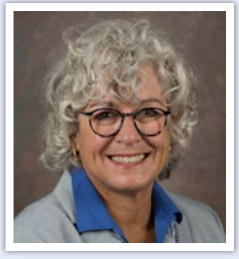
Mission:

Promote innovative research that advances the understanding of ASD and leads to improved outcomes for Service Members, their families, and the American public



"It is disheartening to see how many families struggle daily when they lack resources, [and experience a] scarcity of medical services, support, or information. As a parent, I find the ARP valuable because it not only involves parents and their input, but the fusion of the scientific community and ASD families."

Juan Dipini, *FY21 Consumer Peer Reviewer*



"It has been an honor to serve on the ARP for the last 14 years. The panel is a true collaboration of researchers and persons with ASD and their family members. This collaboration has enabled funding of the best research aimed at the vision of improving the lives individuals with ASD now."

Diane Chugani, Ph.D., *FY21-22 Programmatic Panel Chair*

Congressionally Directed Medical Research Programs

Autism Research Program

Background and History

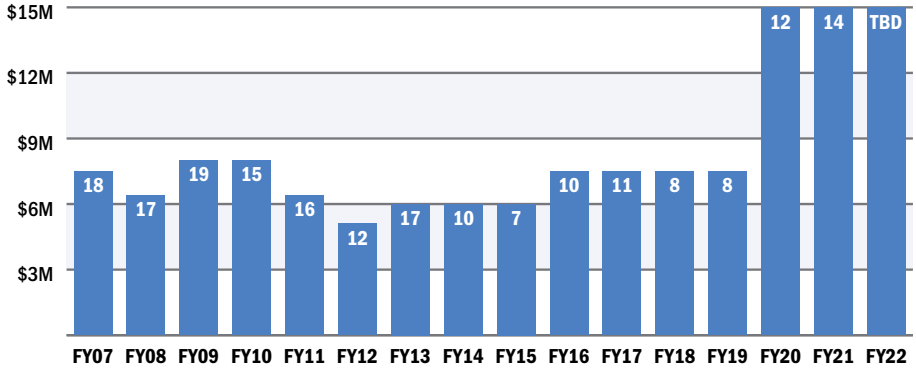
The office of the Congressionally Directed Medical Research Programs (CDMRP) was created in 1992 from a powerful grassroots effort led by the breast cancer advocacy community that resulted in a congressional appropriation of funds for breast cancer research. This initiated a unique partnership among the public, Congress, and the military. Since that time, Congress has added additional research programs and topics. Funds for the CDMRP are added to the Department of Defense (DOD) budget, in which support for individual programs, such as the Autism Research Program (ARP), is allocated via specific guidance from Congress. Since its inception in fiscal year 2007 (FY07) and on through FY22, appropriations totaling $134.4 million have been directed to the ARP by the Peer-Reviewed Autism Research congressional appropriation.

Autism Spectrum Disorder (ASD) encompasses a wide range of complex developmental disorders characterized by mild to severe challenges in social, emotional, and communication abilities. Additionally, many individuals living with ASD are afflicted with co-occurring conditions (e.g., anxiety, gastrointestinal [GI] issues, sleep disorders, and aggression) that are not well understood. The causes of ASD are unknown; however, progress is being made on several fronts, and the answers related to autism are expected to be, like the disorder itself, multifaceted.

Recent reports by the Centers for Disease Control and Prevention indicated the prevalence of ASD may be as high as 1 in 44.[1] Furthermore, ASD was found to be four times more common in males than females.[1] The cost of caring for Americans with ASD reached $268 billion in 2015 and could rise to $461 billion by 2025.[2]

The ARP focuses on improving the lives of those living with ASD by funding innovative and highly impactful research. Through the program's Areas of Interest, the ARP has placed emphasis on research that assists ASD individuals in their transition to adulthood, as well as research aimed at improving healthcare delivery to adults with ASD. The ARP also focuses on ways to improve diagnosis, treatment, and co-occurring conditions to enhance the quality of life for those with autism and their families.

ARP Appropriations and Number of Awards



[1] CDC Morbidity and Mortality Weekly Report - Maenner et al. 2021. *Surveillance Summaries.* 70(11);1–16)
[2] Leigh, JP and Du J. 2015. Brief Report: Forecasting the Economic Burden of Autism in 2015 and 2025 in the United States. 2015. *J Autism Dev Disord.* 45;4135–4139. https://doi.org/10.1007/s10803-015-2521-7.

Research Portfolio

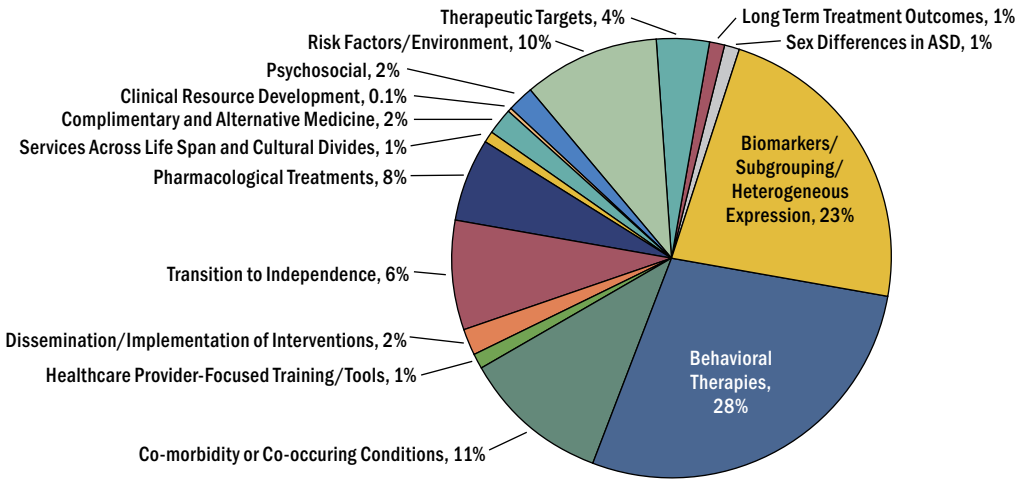
The ARP strives to obtain a balanced research portfolio focused on the gaps defined by the scientific and consumer communities. The Areas of Interest (see Figure below) are topics identified for increased emphasis and need in the scientific setting or the consumers' daily lives. The Areas of Interest are revisited every fiscal year and are changed according to the current state of need. Additionally, the Areas of Interest may be different, depending on the type of solicitation. For example, the Clinical Trial Award will have Areas of Interest that are related to dissemination and implementation of clinically validated interventions, whereas the Idea Development Award will have Areas of Interest focused on the use of preclinical models for assessments of novel therapeutics.

ARP FY07–FY22 Areas of Interest through the Years

	FY07-FY09	FY10-FY12	FY13-FY16	FY17-FY18	FY19	FY20	FY21	FY22
Clinical resource development	✓	✓						
Co-morbidity or co-occurring conditions	✓	✓	✓	✓	✓	✓	✓	✓
Identification and/or validation of therapeutic targets	✓	✓*	✓**	✓**	✓**	✓**	✓**	✓**
Biomarkers, subgrouping and mechanisms of heterogeneous expression and response to treatment	✓	✓	✓	✓	✓	✓	✓	✓
Risk factors/environment	✓	✓	✓	✓	✓	✓	✓	✓
Pharmacological treatments/interventions		✓	✓	✓	✓	✓	✓	✓
Psychosocial research and/or interventions		✓						
Complementary and alternative medicine		✓						
Behavioral and/or other non-pharmacological therapies/interventions		✓	✓	✓	✓	✓	✓	✓
Dissemination/Implementation of interventions					✓	✓	✓	✓
Key transitions to independence					✓	✓	✓	✓
Healthcare provider-focused training or tools						✓	✓	✓
Diagnosis and access to services across life span and cultural divides						✓	✓	✓
Factors influencing quality of life during geographic relocation						✓	✓	✓
Mechanisms underlying sex differences in diagnosis							✓	✓
Pragmatic Trials							✓	✓
Interventions to support Adults with ASD								✓

*Excluding gene discovery | **In preclinical models

ARP Investments in Areas of Interest FY07–FY21



Strategic Direction and Goals of the ARP

The ARP continually monitors new technological advances that may provide a better understanding of ASD, its diagnosis, and the most effective interventions for helping individuals with autism.

ADVANCE EFFECTIVE TREATMENTS:

Behavior Therapy for Irritability and Aggression in Adolescents with Autism

Dr. Denis Sukhodolsky, Yale University (AR190136)

Irritability and aggression are common in children and adolescents with ASD that tend to persist into adulthood and contribute to disability over and above the core ASD symptoms. There is also a major gap in treatments for adolescents on the autism spectrum. This study will investigate the clinical efficacy of a novel behavioral intervention for irritability and aggression in adolescents with ASD complicated by high levels of disruptive behavior. The intervention, Behavior Therapy for Irritability and Aggression, consists of 15 ninety-minute weekly sessions delivered by an experienced therapist using a detailed manual that targets both common and ASD-specific mechanisms of irritability. It includes structured, illustrated activities for teaching emotion regulation and problem-solving skills to the adolescent; a functional assessment to identify unique triggers of aggressive behavior; a parent component that teaches antecedent management and reward strategies; and a school component for disruptive behavior at school. If proven effective, this intervention may provide a useful treatment option for adolescents with ASD complicated by behavioral problems.

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UNDERSTANDING CAUSES, MECHANISMS, AND SIGNS:

Molecular Studies to Identify Mechanisms that Underlie Symptom Improvement in Microbiota Transfer Therapy Patients

Dr. Stephen Walker, Wake Forest University Health Sciences (AR190127)

One novel treatment strategy that has recently shown significant promise for the treatment of children with ASD and chronic GI symptoms is microbiota transfer therapy (MTT). In a small open-label study that enrolled 18 ASD-diagnosed children, it was found that children given MTT displayed significant improvements in both GI and behavioral symptoms that persisted for at least 8 weeks post-transplant. In addition, a follow-on phase 2 clinical trial is ongoing to evaluate the safety and efficacy of MTT, determine whether a longer treatment course is beneficial, and determine long-term safety and efficacy. In this current study, Dr. Walker will utilize peripheral blood collected from the study participant to investigate differences in gene expression and metabolite profiles at three specific time points. The goal of these studies is to provide mechanistic detail to explain the positive outcomes being observed and to provide new therapeutic targets. The impact of having the additional (mechanistic) information would be significant because it would enable the development of more targeted microbial-based therapeutic approaches.

Based on the current state of ASD research, the funding landscape provided by other federal and private organizations, and the needs of the ASD community, the ARP developed its overall strategic direction, into five key elements:

- Fund high-impact research to address major knowledge gaps
- Invest in projects with potential for immediate implementation
- Invest in projects with potential for broad dissemination
- Focus on novel ideas that fulfill the needs of the ASD community and maintain high scientific rigor
- Support the development of an early stage diverse investigator cohort for autism research

The ARP identified four near- to medium term goals to achieve its strategic direction. Here, we highlighted a few studies within each strategic goal poised to impact the ASD community as they continue to make progress.

ADDRESS NEEDS OF PERSONS:

Community Participation, Service Needs, and Health Outcomes Among Adults with Autism

Dr. Lindsay Shea, Drexel University (AR190018)

Programs and services supporting community participation among adults with ASD are a critical part of comprehensive health services, but research about best practices to construct and deliver them is lacking. The objective of this study is to capture a longitudinal trajectory of participation experiences and preferences of adults with ASD and examine the overall service utilization and contextual factors that are associated with participation over time, by building upon large, existing data sets. The team will examine how participation frequency, volume, type, preferences, and satisfaction change over time and identify key barriers to and facilitators of participation among adults with ASD, including sociodemographic and clinical characteristics. Additionally, they will identify overall service utilization and health outcomes and see how they are associated with participation over time. Findings will be relevant for individuals and families who are choosing participation services, policymakers developing participation-related policies, and the design and delivery of Medicaid services at the federal and state levels.

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SUPPORT THOSE CARING FOR THE AUTISM COMMUNITY:

A Novel Provider-Focused Training Program to Serve Transition-Age Youth and Adults with Autism Spectrum Disorder

Dr. Beth Malow, Vanderbilt University Medical Center and Dr. Micha Mazurek, University of Virginia (AR180072/P1)

There is a shortage of healthcare providers with knowledge and expertise in ASD. This study will develop and pilot test a novel primary care provider (PCP) training program with the goal of increasing high-quality, community-based healthcare for adults with ASD. Specifically, this team has developed the Project Extension for Community Healthcare Outcomes (Project ECHO). Utilizing this framework, they will develop a specific training curriculum and protocol for autism transition/adult healthcare training. They will implement and test this curriculum with PCPs caring for transition-age youth and adults with ASD. Building capacity to meet the healthcare needs of individuals with ASD as they transition to and enter adulthood is critical and timely, given estimates of a half-million youth with ASD entering adulthood over the next decade. The proposed research is relevant to ASD now because the team is developing an innovative educational program that will build capacity in PCPs to serve this population, including those caring for military personnel and their families.

Investing in the Next Generation of ASD Researchers

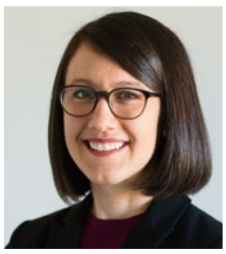
To ensure the continuation of highly innovative and impactful research for the ASD community, the ARP is committed to investing in the next generation of autism researchers through one of the core elements to support the development of an early-state, diverse investigator cohort for autism research. Over the past several years, the ARP provided funding for those early career investigators interested in pursuing a career as a clinical trials researcher by partnering these researchers with an experienced mentor. Recently, the ARP began offering the Career Development Award mechanism which is designed to support early career, independent investigators as well as established investigators from other research fields.

Clinical Trial Award - Early Career Investigator Recipients:

Examining the Efficacy of the TEACCH School Transition to Employment and Post-Secondary Education Program

Dr. Laura Klinger and Dr. Briane Tomaszewski, University of North Carolina, Chapel Hill (AR180178/P1)

The overall goal of this proposal is to conduct one of the first clinical trials examining the effectiveness of an intervention designed by Drs. Klinger and Tomaszewski, the TEACCH School Transition to Employment and Postsecondary Education (T-STEP) program. This community college-based program aims to support adolescents and young adults with ASD transitioning into adulthood and specifically supports common challenges experienced by autistic individuals as they transition from high school into adult life. This trial will allow the team to assess whether the T-STEP works as designed to improve problems with planning and organization, professional social skills, and coping skills that are often barriers to success in employment and post-secondary education for autistic adolescents and adults. The long-term impact of this intervention is to promote a more positive quality of life for autistic adolescents and young adults. The T-STEP intervention may help autistic young adults be more successful in post-secondary education and employment, thereby increasing their quality of life.



Randomized Trial of Telehealth Parent-Implemented Intervention to Improve Social-Communication Outcomes in Young Children with ASD

Dr. Rebecca Landa and Dr. Rachel Reetzke, Hugo W. Moser Research Institute at Kennedy Kreiger (AR200061/P1)

With the recent COVID pandemic, many intervention services for young children with ASD shifted from in-person to telehealth with no evidence of their efficacy. This study will be the first to examine whether telehealth parent coaching yields effects that are not less effective than in-person coaching on child social-communication outcomes and parent fidelity in implementing evidence-based intervention strategies. The researchers will assess the efficacy of coaching parents of toddlers with ASD to implement Naturalistic Developmental Behavioral Intervention (NDBI) strategies via telehealth compared to in-person modalities. The goal of this parent-implemented intervention is to help parents use NDBI strategies to improve their children's social-communication skills throughout daily home routines. Parents are the primary sources of interaction and learning for toddlers with ASD. Therefore, validating that coaching parents' NDBI implementation via telehealth is not less effective than providing in-person coaching will provide the evidence needed to enable families to access services in the modality most suited to their needs and preferences. This could translate into better continuity of care for military or other families that may need to relocate during their child's intervention and increase accessibility and intensity of intervention for young children with ASD anywhere internet capabilities exist. This study will also provide information to help clinicians and families in their decision-making regarding the selection of telehealth versus in-person services for NDBI parent coaching. Finally, empowering parents to effectively use NDBI strategies with their child with ASD may enable families to tailor services to their child's needs and the family's preferences, likely improving parent implementation fidelity and child social-communication outcomes.

Career Development Award Recipients:

Dismantling the "Visual Ease Assumption": Cross-Modal Examinations of Narrative Comprehension in Individuals with Autism: Dr. Emily Coderre, University of Vermont

Area of Interest: Address Needs of Persons with Autism into Adulthood

Dr. Coderre is studying the use of visual narratives in autism. This study will provide a comprehensive examination of narrative comprehension in ASD by determining which underlying skills might be leading to comprehension impairments in ASD and whether there are differences in those skills across visual and linguistic modalities. The results will significantly alter how we conceptualize reading and narrative comprehension difficulties in individuals with ASD and support the development of more evidence-based practices in literacy interventions.

Is There a Point of Convergence Between Congenital Heart Disease and Autism?: Dr. Jason Tchieu, Children's Hospital, Cincinnati

Area of Interest: Understand Causes, Mechanisms, and Signs of ASD

Dr. Tchieu is studying congenital heart defects (CHD) in patients with autism. This study will investigate major developmental pathways and a subclass of genes mutated in CHD and ASD using a human pluripotent stem cell developmental platform. This work will utilize different cell types to pinpoint key pathways shared between the brain and heart, and assess cellular composition of ASD-related heart and brain organoids. Dr. Tchieu's study holds promise to uncover shared pathways and mutations and lay a foundation for further insight and treatment pathways for these highly complex disorders.

Atypical Thalamocortical Connectivity and Its Relationship to Sleep Problems and Sound Processing in Young Children with Autism Spectrum Disorders:

Dr. Annika Linke, San Diego State University

Area of Interest: Understand Causes, Mechanisms, and Signs of ASD

Dr. Linke is studying sleep disturbances in the autism population. The team will look at the relationship between disrupted sleep and atypical sensory processing using multimodal MRI, comprehensive diagnostic and behavioral measures, and objective measures of sleep in children. This study will broaden the understanding of the neurobiology of autism and provide additional background on evidence-based guidelines for treatment of sleep problems in autism.

Brainwide Social Network in Mice Underlying Autism Spectrum Disorder:

Dr. Ariel Gilad, Hebrew University of Jerusalem

Area of Interest: Understand Causes, Mechanisms, and Signs of ASD

Dr. Gilad is studying brain-wide network deficits in a mouse model of autism during social interactions. This study will assess brain networks in individual mice, specifically their personality and social interactions, and will assess dysfunction in socially related networks of the amygdala, prefrontal cortex, and nucleus accumbens. Finally, the team will activate specific areas of the brain using light to determine whether they can rescue aspects of normal social behavior. This work is crucial to understanding the complexity of social impairment in autistic persons and may pave a way towards targeted personalized treatment in autism using non-invasive brain stimulation.

Epigenetics in Autism: An In Vivo PET Imaging Study: Dr. Nicole Zurcher-Wimmer, Massachusetts General Hospital

Area of Interest: Understand Causes, Mechanisms, and Signs of ASD

Dr. Zurcher-Wimmer is studying environmental influences associated with autism risk, specifically related to the epigenetic enzymes, histone deacetylases (HDACs). To study this, the team will utilize a PET scan to quantify overall HDAC expression in adults with autism and compare to controls, and then quantify sex-specific HDAC differences in autistic adults compared to controls. Finally, they will quantify the relationship between HDAC expression and symptom presentation in autistic persons. This study may reveal atypical in vivo expression of HDAC in autistic persons, specifically whether these differ in a sex-specific manner. Furthermore, regional HDAC expression levels may be associated with behavioral phenotypes and provide key understandings of how epigenetic enzymes contribute to autism pathobiology.

For more information, visit:
http://cdmrp.health.mil
or contact us at:
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