

IX. Autism Research Program

“I was honored to be chosen to be a Consumer Reviewer for the first year of CDMRP Autism Research Program grants. The experience was intense, even grueling at times, and yet the extraordinarily high quality of the CDMRP grant review process provided a welcome example of the grant review process done right. In fact, this was by far the best-organized and most ethical grant review I have ever participated in. After 10 years of participating in grant reviews, I appreciated the excellent overall organization, the meticulous attention to detail, and the expediency of the process that the CDMRP had put into place. Clearly a lot of thinking and experience had gone into the process.”

Portia Iversen
Cure Autism Now Foundation and
Autism Genetic Resource Exchange
FY07 Peer Review Panel Member





A scenic view of a river with a bridge and buildings in the background, framed by green leaves in the foreground. The text "Harnessing Hope" is overlaid on the right side of the image.

Harnessing Hope



Vision

Improve the lives of individuals with autism spectrum disorders now.

Mission

Promote innovative research that advances the understanding of autism spectrum disorders and leads to improved treatment outcomes.



The Disease

Autism is a complex developmental disorder that recent evidence indicates may affect as many as 1 in 166 children. With this prevalence rate, it is estimated that in the United States there are approximately 500,000 individuals between the ages of 0 and 21 years with autism.¹ The manifestations of autism vary widely from mild to severe, leading to their general classification as autism spectrum disorder (ASD). ASD is described by serious impairments in social, emotional, and communication skills as well as the presence of unusual behaviors and physical manifestations, such as sleep disorders and depressed immune function. Only about 10 percent of individuals with ASD develop autism secondary to a known genetic disorder. The cause of ASD in the remaining individuals is not certain. However, progress is being made on several fronts. Like autism itself, the answer to this question will likely be multifaceted.

Red Flags of Autism

ASD usually develops before 3 years of age. In clinical terms, there are a few “absolute indicators,” often referred to as “red flags,” that suggest that a child should be evaluated.² These red flags, representing certain symptoms or behaviors, should indicate to parents that a child should be screened to ensure that he or she is progressing developmentally. However, no two individuals with ASD exhibit the same symptoms, and, conversely, some individuals without ASD may present some of these behaviors.

- ❖ No big smiles or other warm, joyful expressions by 6 months or thereafter
- ❖ No back-and-forth sharing of sounds, smiles, or other facial expressions by 9 months or thereafter
- ❖ No babbling by 12 months
- ❖ No back-and-forth gestures, such as pointing, showing, reaching, or waving, by 12 months
- ❖ No words by 16 months
- ❖ No two-word meaningful phrases (without imitating or repeating) by 24 months
- ❖ Any loss of speech or babbling or social skills at any age

¹ Centers for Disease Control and Prevention, Autism Information Center, <http://www.cdc.gov/ncbddd/autism/>

² This information has been provided by First Signs, Inc. © 2001–2005. Reprinted with permission. For more information about recognizing the early signs of developmental and behavioral disorders, please visit <http://www.firstsigns.org> or the Centers for Disease Control and Prevention at www.cdc.gov/actearly.



Program Background

The CDMRP began managing the Department of Defense Autism Research Program (ARP)³ in response to fiscal year 2007 (FY07) Appropriations Conference Committee Report No. 109-676, which provided \$7.5 million (M) for research on ASD. In the first year of the program, 18 awards were made to promote innovative research that advances the understanding of ASD and leads to improved treatment outcomes. In FY08, the ARP was continued with a congressional appropriation of \$6.4M (see Figure IX-1, ARP Funding History). The FY08 program sought to fill unique needs and gaps of the scientific and advocacy communities into specific emphasis areas and award mechanisms, as detailed under The Program Today.

³ Formerly known as the Autism Spectrum Disorder Research Program.

“The Department of Defense’s Congressionally Directed Medical Research Programs has significantly contributed to the overall needs of autism research. The funding process involves parents of affected children from the formulation of the mission statement to the final program consideration for funding. This process adds a valuable perspective to funding decisions not based solely on scientific merits.”

Alice Kau, Ph.D.
National Institute of Child Health and
Human Development
FY07–FY08 Integration Panel Member

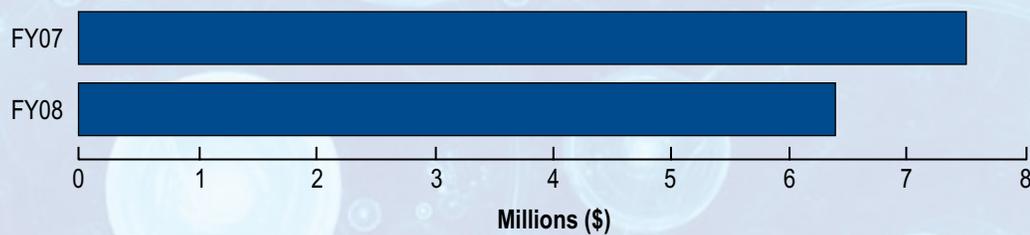


Figure IX-1. ARP Funding History

Extraordinary People

The ARP partners with highly qualified people—consumer advocates, peer review panel members, Integration Panel (IP) members, and the scientific community—to improve the lives of individuals with ASD.

Consumer Advocates

Consumer advocates for the ARP represent the voice and vision of hundreds of thousands of individuals in the United States affected by ASD. Consumer advocates for the program are family members of individuals living with autism, or they are individuals living with autism who are active participants in an autism-related support, outreach, or advocacy organization. Consumer advocates are active participants in practically all aspects of program execution. They work collaboratively with leading scientists and clinicians in setting program priorities and funding proposals to which they contribute their unique perspectives and a sense of urgency. Consumer advocates also serve as liaisons between their constituencies and the scientific community and are able to increase awareness about the ARP in the consumer community. Additional details about consumer advocate participation can be found in Section I, Overview.

Peer Review Panel Members

The primary responsibility of scientific peer review is to determine the scientific and technical merit of proposals submitted to the program. Scientific reviewers for peer review are selected for their subject matter expertise in ASD and experience with scientific peer review. Consumer reviewers are nominated by an advocacy or support organization and are selected on the basis of their commitment to advocacy, interest in science, and ability to represent the collective views of the autism consumer community. Additional information about peer review can be found in Section I, Overview.

“The CDMRP’s process of having both scientific reviewers as well as consumer reviewers ensures that the highest quality and most relevant proposals are selected for funding. The CDMRP is to be lauded for creating such an effective review process.”

Dean E. Calcagni, M.D.
Autism Speaks

FY07 Consumer Peer Review Panel Member



Integration Panel Members

The ARP IP is composed of visionary scientists, clinicians, and consumer advocates who are committed to serving the interests of the ASD community. Individual panel members recommend program priorities, innovative investment strategies, and a broad portfolio of research projects for funding. Further details about the functions of the IP can be found in Section I, Overview.

Scientific Community

The scientific community is a driving force in the ARP’s vision to improve the lives of individuals with ASD. In the first year of the program, 22 renowned researchers across the United States were funded by the program. Selected ARP-funded investigators and their accomplishments are highlighted throughout the remainder of this chapter.

“Innovative brain imaging research can be used to link abnormalities of anatomy, function, and chemistry to symptom expression and developmental course that will help unravel the mysteries of autism and allow us to develop targeted interventions. The ARP, through its focused funding and dedication to innovation, has the potential to bring novel imaging and other promising techniques to bear on diagnosis and treatment of the autism spectrum disorders.”

Stephen Dager, M.D.
University of Washington
FY07–FY08 Integration Panel Member



FY08 ARP IP Members

Gary Goldstein, M.D. (Chair)
Kennedy Krieger Institute

Peter Bell (Alternate Chair)
Autism Speaks

Linda Brzustowicz, M.D.
Rutgers University

Stephen Dager, M.D.
University of Washington

Lee Grossman
Autism Society of America

Susan Hyman, M.D.
University of Rochester

Alice Kau, Ph.D.
National Institute of Child Health and Human Development

Lyn Redwood, R.N., M.S.N.
*National Autism Association/
 SafeMinds*

Shelley Reynolds
Unlocking Autism

Christopher Stodgell, Ph.D.
University of Rochester

Harnessing Hope



A Prospective Multi-System Evaluation of At-Risk Infants with Autism

Martha Herbert, M.D., Ph.D.

Margaret Bauman, M.D.

Massachusetts General Hospital

Children who receive an earlier autism diagnosis and receive intensive early interventions typically do better than those who are diagnosed at a later time. Additionally, many children with autism suffer from a host of associated medical complications. The connection between autism and the associated biomedical complications has not been fully explored. Drs. Martha Herbert and Margaret Bauman received an FY07 Clinical Partnership Award to developmentally track several autism-associated medical indicators in at-risk siblings. This study will lay the foundation for a systematic medical evaluation of every infant at risk for or showing signs of autism, potentially leading to an earlier diagnosis. Additionally, it may provide insight into the proper treatment of biomedical complications; such insight could improve the quality of life for those with autism or help ameliorate the symptoms of autism itself since they may contribute to each other.

3D Facial Pattern Analysis for Autism

Ye Duan, Ph.D.

University of Missouri-Columbia

While clinical observations indicate that autism is a heterogeneous disorder, there are no readily available means to differentiate subtypes within the patient population. Distinguishing the subtypes would aid in the development and utility of more individualized therapies and a better understanding of different etiologies. FY07 Concept Award recipient, Dr. Ye Duan, proposes to determine if there is a consistent facial pattern in the core group of idiopathic autism patients, which is often referred to as essential autism. If such a pattern is confirmed, in addition to defining a subgroup of autism patients, Dr. Duan believes it will indicate that essential autism is a neurodevelopmental syndrome and may provide a prescreening tool to assist in early diagnosis.

Y-Chromosome Regulation of Autism Susceptibility Genes

Yun-Fai Chris Lau, Ph.D.

Northern California Institute for Research and Education

Boys are disproportionately represented in the number of autism cases, suggesting a potential sex-based link to autism development. Recently, a study indicated that genes on the Y (male) chromosome may influence the function of suspected autism susceptibility genes in gonadal cells of the developing fetus. In his FY07 Concept Award, Dr. Yun-Fai Chris Lau proposes to study the effect of the Y- chromosome-associated transcription factor called SRY on the expression of autism susceptibility genes in neurons, which may elucidate the mechanisms involved in the sexual dimorphism of brain development and physiology and potentially explain the gender difference in the clinical manifestation of autistic disorders.

Autism and Associated Neurobehavioral Functioning Among Patients in a Psychiatric Hospital

David Mandell, Sc.D.

University of Pennsylvania

Addressing an often neglected consumer community and area of research, Dr. David Mandell, recipient of an FY07 Concept Award, proposes to examine adults in a psychiatric hospital to determine the prevalence of autism among patients who may have been misdiagnosed with other disorders. Dr. Mandell hypothesizes that many of the patients diagnosed with other disorders, such as schizophrenia, may actually be autistic but have been misdiagnosed due to poor screening criteria or a lack of awareness of ASD. While participants in the study potentially may receive immediate benefits through more appropriate treatment, the results may also benefit the entire community by aiding in the development of better methods to differentiate autism from other psychiatric disorders, particularly in adults.



The Program Today

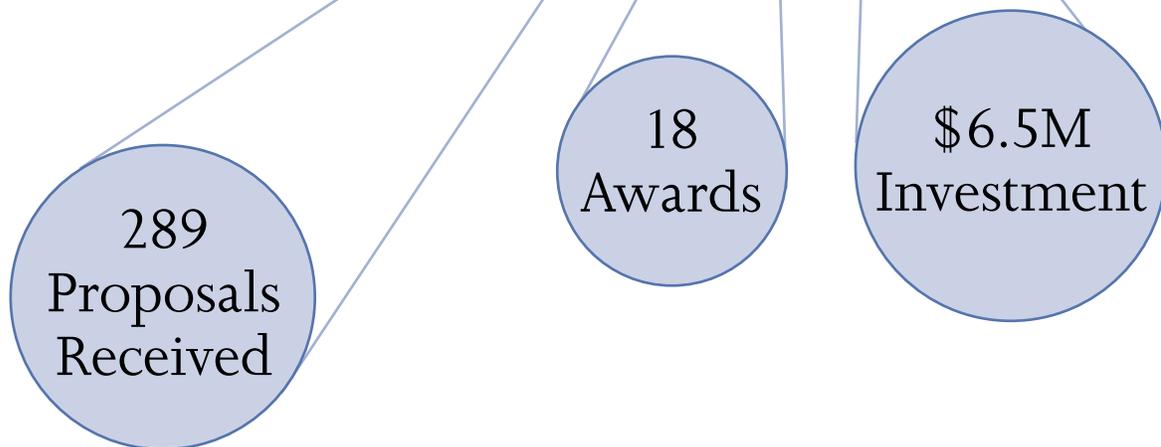
FY07 Summary

A congressional appropriation of \$7.5M in FY07 marked the first year of the ARP. To invigorate the field of ASD research, the program offered 3 award mechanisms, Clinical Partnership, Concept, and Idea Development Awards. Both the Concept and Idea Development Awards supported innovative research to advance the understanding of ASD while the Clinical Partnership Awards supported the development of translational research collaborations to address a central problem or question in ASD. Enthusiasm from the scientific community was observed, as 289 proposals were submitted across the 3 award mechanisms. A total of 18 awards were made, as shown in Table IX-1.

Table IX-1. Funding Summary for the FY07 ARP

Categories and Award Mechanisms	Proposals Received	Awards	Investment
Clinical Research			
Clinical Partnership	26	1	\$0.5M
Innovative Research			
Concept	154	7	\$0.8M
Idea Development	109	10	\$5.2M
TOTAL	289	18	\$6.5M

Note: An additional 4 awards (\$2.8 million) were funded using FY08 ARP appropriations.



The Vision for FY08

Congress appropriated \$6.4M in FY08 to continue the newly established ARP. A total of \$2.8M of the FY08 appropriation was used to fund promising research reviewed in the FY07 program. The balance of the FY08 program funds is allocated for program announcements that seek to promote research that will (1) improve clinical outcomes of ASD, (2) lead to a better understanding of ASD across the lifespan, including adulthood, of an affected individual, and (3) integrate basic science and clinical observations. Two award mechanisms were offered to encourage innovative avenues of research in the field of ASD. Concept Awards were retained to facilitate the development of novel ideas and observations in ASD research into larger, hypothesis-driven research, as well as serve as a vehicle for researchers to enter ASD research. Synergistic Idea Awards were launched to support collaborative efforts that would foster novel insights into ASD. The following areas of research were particularly encouraged:

- ❖ Comorbidity (e.g., manifestations such as gastrointestinal disorders, sleep disorders, seizures, tics, and immune disorders)
- ❖ Targets for Treating (e.g., clinical, molecular, and cellular)
- ❖ Biomarkers and Pathology (e.g., brain and other tissues)
- ❖ Environment (e.g., clinical and basic toxicology and gene/environment interaction)

A total of 102 proposals were received across the 2 award mechanisms and approximately 7 awards are anticipated, as shown in Table IX-2. Appendix B, Table B-8, summarizes the congressional appropriations and the investment strategy executed by the ARP for FY07 through FY08.

Table IX-2. Award Mechanisms Offered and Proposals Received for the FY08 ARP

Categories and Award Mechanisms	Proposals Received
<i>Innovative Research</i>	
Concept	66
Synergistic Idea	36
TOTAL	102

The ARP Team

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