DoD Autism Research Program (ARP)

Each year, the Department of Defense's office of the Congressionally Directed Medical Research Programs (CDMRP) assesses scientific opportunities to advance research in specific areas. The investigators supported by individual programs are making significant progress against targeted diseases, conditions, and injuries. This list is not intended to be a full representation of accomplishments, but rather a sampling of the broad portfolio of research and advances resulting from congressional appropriations.

Year	ARP Research Contributions	Additional Information and Hyperlinks
2007	Drs. Alberto Ascherio, Susan Santangelo, and Marc Weisskopf from Harvard University, using the Nurses' Health Study II, identified maternal environmental risk factors before and during pregnancy that may increase the incidence of autism in these children. Dietary intake of polyunsaturated fat was associated with lower risk of autism, whereas pollutants, and exposure to abuse of the mother was associated with an increased risk.	• Roberts AL, Lyall K, et al. 2013. Perinatal air pollutant exposures and autism spectrum disorder in the children of nurses' health study II participants. Environ Health Perspect 121:978-84. • ARP Research Highlight
2007	Dr. Yun-Fai Lau of the Veterans Affairs Medical Center, UCSF, discovered a potential cause of sexual bias in autism by showing that the Y chromosome-encoded transcription factor sex-determining region Y (SRY) regulates the X chromosome-encoded monoamine oxidase A, an important enzyme in deamination of neurotransmitters, therefore demonstrating a novel mechanism of sexual dimorphism for neural function and potential disorders.	• Wu JB, Chen K, et al. 2009. Regulation of monoamine oxidase A by the SRY gene on the Y chromosome. FASEB J 23:4029-38.
2008	Dr. John Shoffner of Georgia State University found that children with defects in the genes of the mitochondrial oxidative phosphorylation pathway are at risk for neurological regression during periods of high fever, and therefore screening for mitochondrial diseases may aid in therapies that could minimize neurological regression associated with fever.	• Shoffner J, Hyams L, et al. 2010. Fever plus mitochondrial disease could be risk factors for autistic regression. J Child Neurol 25:429-34. • ARP Research Highlight
2008	Drs. Andrew Feinberg and Walter Kaufmann of Johns Hopkins Medical Center and Children's Hospital, Boston, respectively, isolated differentially methylated regions within the genome of patients with autism as compared to their monozygotic twin. These epigenetic changes may help to determine if environmental factors influence the development of neurological disorders such as autism.	• Ladd-Acosta C, Hansen KD, et al. 2014. Common DNA methylation alterations in multiple brain regions in autism. Mol Psychiatry 19(8):862-71. • ARP Research Highlight
2009	Dr. Brooke Ingersoll from Michigan State University developed an internet-based training program, ImPACT Online, a highly innovative, web-based, distance learning program that teaches parents to support their child's social communication development using a novel blend of evidence-based intervention techniques. ImPACT Online uses effective adult learning tools to help parents acquire these intervention techniques and integrate them into their daily interactions with their children.	• Ingersoll B and Wainer A. 2013. Initial efficacy of project ImPACT: A parent-mediated social communication intervention for young children with ASD. J Autism Dev Disord 43(12):2943-52. • ARP Research Highlight

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2009	Dr. Armin Alaedini from Columbia University used samples from a cohort of well-characterized patients diagnosed with autism, their unaffected siblings, and unrelated controls to find that patients with autism had Immunoglobulin G antibodies to gluten linked to gastrointestinal symptoms which were different than that of celiac disease. Dr. Alaedini received a Fiscal Year 2013 Idea Development Award for "Proteomic Mapping of the Immune Response to Gluten in Children with Autism."	• Lau NM, Green PH, et al. 2013. Markers of celiac disease and gluten sensitivity in children with autism. PLoS One 8(6):e66155. • ARP Research Highlight
2010	Dr. Daniel Cox of the University of Virginia developed a virtual reality driver simulator (VRDS) to train and evaluate driving skill in teens with ASD. The success of the VRDS with eye tracking led to the award of a new Idea Development grant, a partnering project between Dr. Cox and Dr. Timothy Brown from the University of Iowa. In the follow-on Fiscal Year 2011 award, Drs. Cox and Brown are studying key predictors of driving performance and safety.	• Cox NB, Reeve RE, et al. 2012. Brief report: Driving and young adults with ASD: Parents' experiences. J Autism Dev Disord 42(10):2257-62.
2010	Dr. Eric Klann from New York University showed that increased EIF4E gene expression in mice results in aberrant behaviors reminiscent of autism. The results from this study led to a collaboration with Egenix Pharmaceuticals to conduct pre-clinical testing of compounds that will target EIF4E for the treatment of ASD.	• Santini E, Huynh TN, et al. 2013. Exaggerated translation causes synaptic and behavioural aberrations associated with autism. Nature 493(7432):411-15.
2010	Dr. Tali Kimchi developed a novel video-RFID tracking system that automatically tracks the locations of multiple animals, such as mice, allowing for the evaluation of the effects of group characteristics on individual behavioral traits. The Kimchi laboratory demonstrated that their automated tracking and behavioral characterization system can be used to accurately classify the strain, sex, and social hierarchy. This system may allow rapid standardization, systematic screening, and quantification of sets of socio-behavioral phenotypes in autistic-related wild-type and genetically modified models for neuropsychiatric disorders. The Video-RFID tracking and behavioral phenotyping technology is registered with the U.S. patent office.	• Weissbrod A, Shapiro A, et al. 2013. Automated long-term tracking and social behavioural phenotyping of animal colonies within a semi-natural environment. Nat Commun 4(2018).
2010	Sarkis Mazmanian found that within a mouse model of ASD these animals also display GI abnormalities similar to those found in ASD patients. Treating young mice harboring disrupted gut bacteria with Bacteroides fragilis improved gut function and alleviated ASD-like behaviors in these mice. These findings suggest that probiotic therapy may be a useful treatment for individuals with ASD.	• Hsiao EY, McBride SW, et al. 2012. Modeling an autism risk factor in mice leads to permanent immune dysregulation. Proc Natl Acad Sci U S A 109(31):12776–81.
2011	Drs. Elisa Hill, Joel Bornstein, and Heather Young from the University of Melbourne investigated the expression patterns of the neuroligin 3 (NL3) protein that are localized in myenteric neurons in the colon and the jejunum in wild-type mice and the NL3 mouse model of ASD, finding that the number of cell bodies staining for NL3 is reduced in the affected mice.	• Hill-Yardin EL and Hannan AJ. 2013. Translating preclinical environmental enrichment studies for the treatment of autism and other brain disorders. Behav Neurosci 127(4):606-9. • Argyropoulos A, Gilby KL, and Hill-Yardin EL. 2013. Studying autism in rodent models: Reconciling endophenotypes with comorbidities. Front Hum Neurosci 7:417.

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2011	Dr. Janine LaSalle investigated whether epigenetic alterations in human placenta may serve as autism biomarkers. Dr. LaSalle and her colleagues performed MethylC-seq in full-term human placenta and demonstrated, for the first time, normal tissue showing clear evidence of partially methylated domains. The results provided a comprehensive reference map of the human methylome in the human full-term placenta. The researchers demonstrated differential methylation between autism and typically developing individuals, and 10 potential gene targets were identified.	• LaSalle JM, Powell WT, and Yasui DH. 2013. Epigenetic layers and players underlying neurodevelopment. Trends Neurosci 36(8):460-470. • Schroeder DI, Blair JD, et al. 2013. The human placenta methylome. Proc Natl Acad Sci U S A. 110(15):6037-6042.
2011	Dr. Cade Nylund examined Department of Defense Military Health System medical records to understand comorbid conditions and risk factors for autism. Several co-morbid conditions such as obesity and nutritional deficiencies in children with ASD were identified. Additionally, the team identified potential prenatal and early infancy ASD risk factors.	• ARP Research Highlight
2011	Dr. Dwight German used screening of a combinatorial peptoid library to search ASD patient blood for biomarkers that could indicate ASD. He found that when combining the levels of the peptoid, ASD1, with thyroid stimulating hormone (TSH) the predictive accuracy for ASD in boys was 73%.	• Zaman S, Yazdani U, et al. 2016. A search for blood biomarkers for autism: peptoids. Sci Rep 6:19164.