QUESTION 3: WHAT CAUSED THIS TO HAPPEN AND CAN IT BE PREVENTED?

***IACC Strategic Plan* Objectives**	**Planning Group Summary**	**Funding 2008-2013**
3.S.A. Coordinate and implement the inclusion of approximately 20,000 subjects for genome-wide association studies, as well as a sample of 1,200 for sequencing studies to examine more than 50 candidate genes by 2011. Studies should investigate factors contributing to phenotypic variation across individuals who share an identified genetic variant and stratify subjects according to behavioral, cognitive, and clinical features. *IACC Recommended Budget: $43,700,000 over 4 years*	The recommended budget has been partially met. Progress has been made on this objective; several GWAS and sequencing projects have been funded , but more information is needed to determine whether the specific targets of 20,00 subjects for GWAS and 1,200 for sequencing studies to examine more than 50 genes has been accomplished. Invited experts may be able to comment on this.	**$38,587,633**
3.S.B. Within the highest-priority categories of exposures for ASD, identify and standardize at least three measures for identifying markers of environmental exposure in biospecimens by 2011. *IACC Recommended Budget: $3,500,000 over 3 years*	The recommended budget has not been met. There has been progress on the understanding of exposures, but more work needs to be done to apply this directly to autism research. Progress has made through projects funded by NIEHS, but those projects are not captured by the Portfolio Analysis because they are not specific to autism, but could be applied to this objective.	**$813,227**
3.S.C. Initiate efforts to expand existing large case-control and other studies to enhance capabilities for targeted gene-environment research by 2011. *IACC Recommended Budget: $27,800,000 over 5 years*	The recommended budget has been nearly met. Work still needs to continue on this objective, but is limited by the number of existing large studies that can be expanded.	**$26,903,311**
3.S.D. Enhance existing case-control studies to enroll racially and ethnically diverse populations affected by ASD by 2011. *IACC Recommended Budget: 3,300,000 over 5 years*	The recommended budget has not been met. Studies coded elsewhere (such as in 3.L.B.) may also reflect progress on this objective. It is also possible that the intended inclusion of diverse populations has happened without the use of separate supplements and thus may not be easily tracked through the portfolio analysis.	**$188,455**
3.S.E. Support at least two studies to determine if there are subpopulations that are more susceptible to environmental exposures (e.g., immune challenges related to infections, vaccinations, or underlying autoimmune problems) by 2012. *IACC Recommended Budget: $8,000,000 over 2 years*	The recommended budget has been partially met, and the intended number of studies was exceeded.	**$3,608,312**
3.S.F. Initiate studies on at least 10 environmental factors identified in the recommendations from the 2007 IOM report "Autism and the Environment: Challenges and Opportunities for Research" as potential causes of ASD by 2012. *IACC Recommended Budget: $56,000,000 over 2 years (revised in 2010)*	The recommended budget has not been met, and it appears that there has been a significant decrease in the number of studies related to this objective.Further work in this are is needed.	**$10,794,995**
3.S.G. Convene a workshop that explores the usefulness of bioinformatic approaches to identify environmental risks for ASD by 2011. *IACC Recommended Budget: $35,000 over 1 year* **This objective was completed in 2011*	The workshop identified in this objective was held in 2011, so this objective has been completed.The report from this workshop is posted at: http://www.niehs.nih.gov/health/assets/docs_a_e/autism_and_the_environment_meeting_report.pdf. .	**$46,991**
3.S.H. Support at least three studies of special populations or use existing databases to inform our understanding of environmental risk factors for ASD in pregnancy and the early postnatal period by 2012. Such studies could include: • Comparisons of populations differing in geography, gender, ethnic background, exposure history (e.g., prematurity, maternal infection, nutritional deficiencies, toxins), and migration patterns; and • Comparisons of phenotype (e.g., cytokine profiles), in children with and without a history of autistic regression, adverse events following immunization (such as fever and seizures), and mitochondrial impairment. These studies may also include comparisons of phenotype between children with regressive ASD and	The recommended budget has been partially met, and the funded projects cover the objective well; there are 32 projects that are related to this objective.. While progress is being made in this area, and it must be maintained in order to achieve this objective.	**$10,281,278**

their siblings. Emphasis on environmental factors that influence prenatal and early postnatal development is particularly of high priority. Epidemiological studies should pay special attention to include racially and ethnically diverse populations. *IACC Recommended Budget: $12,000,000 over 5 years*		
3.S.I. Support at least two studies that examine potential differences in the microbiome of individuals with ASD versus comparison groups by 2012. *IACC Recommended Budget: $1,000,000 over 2 years*	The number of projects in this area has been growing, with 6 projects in 2012. The number of funded projects is large relative to the amount of funding, indicating that the projects are each small, which suggests that these projects will not be sufficient to complete this objective. The high cost of required technology could be a barrier to the completion of this objective.	**$749,263**
3.S.J. Support at least three studies that focus on the role of epigenetics in the etiology of ASD, including studies that include assays to measure DNA methylations and histone modifications and those exploring how exposures may act on maternal or paternal genomes via epigenetic mechanisms to alter gene expression, by 2012. *IACC Recommended Budget: $20,000,000 over 5 years*	The recommended budget for this objective has been partially met, and the number of projects has been exceeded, with 22 projects supported in 2012. The current momentum in this areashould be maintained.	**$16,536,350**
3.S.K. Support two studies and a workshop that facilitate the development of vertebrate and invertebrate model systems for the exploration of environmental risks and their interaction with gender and genetic susceptibilities for ASD by 2012. *IACC Recommended Budget: $1,535,000 over 3 years*	While the recommended budget has been partially met and some projects have been funded in this area, it appears that there is a downward trend. Some projects from 2SB "Launch three studies that specifically focus on the neurodevelopment of females with ASD, spanning basic to clinical research on sex differences by 2011." may overlap with this objective. There may have been a workshop held by NIEHS that fulfilled the workshop directive of this objective, but more information is needed to determine.	**$1,287,763**
3.L.A. Conduct a multi-site study of the subsequent pregnancies of 1,000 women with a child with ASD to assess the impact of environmental factors in a period most relevant to the progression of ASD by 2014. *IACC Recommended Budget: $11,100,000 over 5 years*	The recommended budget for this objective was met, but emphasis on this objective should continue in the future. The Group is concerned about the lack of continued funding for EARLI.	**$15,194,483**
3.L.B. Identify genetic risk factors in at least 50% of people with ASD by 2014. *IACC Recommended Budget: $33,900,000 over 6 years*	While the recommended budget for this objective has been met, further work is needed to identify genetic risk factors in at least 50% of people. We can ask invited experts to give a current estimate of % of people with ASD for whom a genetic risk factor has been identified – 30%?	**$169,806,458**
3.L.C. Determine the effect of at least five environmental factors on the risk for subtypes of ASD in the prenatal and early postnatal period of development by 2015. *IACC Recommended Budget: $25,100,000 over 7 years*	The recommended budget was partially met, and several projects were funded, but it appears there is a downward trend. Epidemiological studies coded to other objectives (e.g. EARLI) may also represent progress in this area.	**$5,349,089**
3.L.D. Support ancillary studies within one or more large-scale, population-based surveillance and epidemiological studies, including U.S. populations, to collect data on environmental factors during preconception, and during prenatal and early postnatal development, as well as genetic data, that could be pooled (as needed) to analyze targets for potential gene/environment interactions by 2015. *IACC Recommended Budget: $44,400,000 over 5 years*	The recommended budget for this objective has been met, with most of the studies coded to this area relating to CADDRE.	**$63,013,714**
Not specific to any objective (Core Activities)		**$17,656,815**
Total funding for Question 3		**$380,818,136**