QUESTION 2: HOW CAN I UNDERSTAND WHAT IS HAPPENING?

***IACC Strategic Plan* Objectives**	**Planning Group Summary**	**Funding 2008-2013**
2.S.A. Support at least four research projects to identify mechanisms of fever, metabolic and/or immune system interactions with the central nervous system that may influence ASD during prenatal-postnatal life by 2010 (Fever studies to be started by 2012). *IACC Recommended Budget: $9,800,000 over 4 years*	The recommended budget for this objective was met and many projects were funded in this area, but the field is still developing and emphasis on this objective should continue in the future. Scientific advances have been made in linking maternal innate immune function and immune-system challenge to aspects of ASD. Methodological advances in the field include the development of animal models for study of the role of the immune system in ASD and PET ligands for imaging microglial activation. There is a need for a well-designed, multi-site clinical study of fever and to develop standard measures for fever. Questions about fever could be added into funded epidemiological studies. There is also interest in further work on metabolic and mitochondrial issues, but oxidative stress appears not to be specific to autism. More guidance is needed on the key questions for this field to answer – a workshop may be helpful.	**$16,997,853**
2.S.B. Launch three studies that specifically focus on the neurodevelopment of females with ASD, spanning basic to clinical research on sex differences by 2011. *IACC Recommended Budget: $8,900,000 over 5 years*	The recommended budget for this objective was partially met, and more than 3 studies were launched, but further work is needed in this area. Studies of protective and compensatory effects in females and differential response to treatment based on gender are promising areas that could help with future prevention and effective, personalized treatment efforts.	**$5,856,783**
2.S.C. Identify ways to increase awareness among the autism spectrum community of the potential value of brain and tissue donation to further basic research by 2011. *IACC Recommended Budget: $1,400,000 over 2 years*	The recommended budget for this objective has been partially met as of 2012. In 2013, Loss of autism brain samples in 2012 due to a freezer malfunction has caused a loss of progress and there is a need for new samples to replace and build the amount of available brain tissue for ASD research. The Autism BrainNet initiative is a multi-site privately funded effort that will target autism specifically and will include and autism-specific brain donation outreach campaign that addresses this objective. NIH launched the NIH Neurobiobank ($5M), which includes samples for research on autism as well as other brain disorders. The NIH Neurobiobank has a web publication "Why Brain Donation? A Legacy of Hope." to increase awareness about brain donation.	**$856,031**
2.S.D. Launch three studies that target improved understanding of the underlying biological pathways of genetic conditions related to autism (e.g., Fragile X, Rett syndrome, tuberous sclerosis complex) and how these conditions inform risk assessment and individualized intervention by 2012. *IACC Recommended Budget: 9,000,000 over 5 years*	The recommended budget for this objective has been met and a large number of projects funded that address this objective. Investment in this area has doubled since 2009, and there is an ACE center focused on tuberous sclerosis. This objective is on track. The next step will be to translate findings in this area into clinically useful therapies.	**$53,147,645**
2.S.E. Launch three studies that target the underlying biological mechanisms of co-occurring conditions with autism, including seizures/epilepsy, sleep disorders, wandering/elopement behavior, and familial autoimmune disorders, by 2012. *IACC Recommended Budget: $9,000,000 over 5 years*	The recommended budget for this objective was met, and more than twenty projects were funded, but further efforts are needed, especially on wandering, metabolic and immune conditions related to ASD, as well as a systems-biology approach to understand how these co-occurring conditions are related to ASD. In order to more accurately assess progress, wandering/elopement could be considered separately from seizures/epilepsy/sleep, and familial autoimmune disorders could be moved to 2.S.A to be grouped with other immune-related issues. Scientific advances in this area include mechanistic and mutation linkages of epilepsy and ASD-like behaviors, as well as circadian rhythm disruptions downstream of ASD-associated mutations. While studies on co-occurring conditions have been initiated, a greater depth of understanding is needed.	**$16,531,078**
2.S.F. Launch two studies that focus on prospective characterization of children with reported regression to investigate potential risk factors by 2012. *IACC Recommended Budget: $4,500,000 over 5 years*	The recommended budget for this objective has been partially met. The number of recommended projects has been met and progress is being made, but further work is needed to understand how autism develops. Some recent data suggest that regression may be more of a continuum than regression vs. non-regression as distinct types of autism, and several studies have provided new descriptions of ADS developmental trajectories, but further work is needed to better understand subtypes and potential biomarkers. High-risk siblings may present an opportunity for studying regression prospectively.	**$993,134**
2.S.G. Support five studies that associate specific genotypes with functional or structural phenotypes, including behavioral and medical phenotypes (e.g., nonverbal individuals with ASD and those with cognitive impairments) by 2015.	The recommended budget for this objective has been met, over 40 projects have been funded in this area, and the projects cover the areas described, so the objective appears to be on track. With so many studies initiated, the next step is to encourage multi-site collaboration in order to achieve the large number of subjects required for	**$41,777,028**

	meaningful data interpretation.	
IACC Recommended Budget: $22,600,000 over 5 years		
2.L.A. Complete a large-scale, multidisciplinary, collaborative project that longitudinally and comprehensively examines how the biological, clinical, and developmental profiles of individuals, with a special emphasis on females, youths, and adults with ASD, change over time as compared to typically developing people by 2020.	The recommended budget for this objective was partially met and several projects have been funded in this area. More clinical studies are needed over a longer trajectory to identify issues faced as people with ASD age, especially with regard to risk factors for other medical conditions. Another remaining need is that of standardization of data collection and analysis methods.	**$20,690,241**
IACC Recommended Budget: $126,200,000 over 12 years		
2.L.B. Launch at least three studies that evaluate the applicability of ASD phenotype and/or biological signature findings for performing diagnosis, risk assessment, or clinical intervention by 2015.	The recommended budget for this objective was partially met, and more than 3 studies were launched, but more funding and work in this area is needed. This objective also requires standardization of data collection and analysis methods, as well as collaboration among investigators to pool data.	**$3,599,806**
IACC Recommended Budget: 7,200,000 over 5 years		
Not specific to any objective		**$201,661,561**
Total funding for Question 2		**$362,111,160**