

## **Conference Call for Interagency Autism Coordinating Committee (IACC) Scientific Workshop Panel Two**

Strategic Plan Questions II: *"How can I understand what is happening?"*

Thursday, September 17, 2009

**Call Participants:** Alison Singer (Co-Chair), Cathy Rice (for Edwin Trevathan, Co-Chair); Panelists: Ashura Buckley, Denise Resnick, Pauline Filipek, Emanuel DiCicco-Bloom, and Sarah Spence; Susan Daniels (Office of Autism Research Coordination (OARC) Staff)

### **Summary:**

The panelists introduced themselves and Ms. Alison Singer, co-chair, began by reviewing the outline for the phone call. The agenda covered three topics areas; 1) to discuss the data provided by OARC, including the research opportunities in the IACC Strategic Plan for Autism Spectrum Disorder (ASD) Research, its short and long term objectives, and any gaps that might exist, 2) to prioritize these ideas, and 3) to formulate short questions from which the panel will draft slides for its presentation at the scientific workshop.

The panelists began by discussing the first business item. Ms. Singer reported that the 2008 ASD Research Funding Portfolio Analysis indicated that more than 50% of the research funding for Question II falls outside of the Strategic Plan objectives. The panel noted that some of these studies listed in the analysis under Question II—Other should have been classified as being under specific objectives. These studies included, but were not limited to brain imaging studies, which should have been included as part of the Short-Term Objective #2, or the Long-Term Objective #1. The panel recommended that the portfolio analysis be updated to reflect these comments.

Ms. Singer mentioned that two of the objectives in Question II (Short-Term #3, the neurodevelopment of females, and Short-Term #4, awareness of tissue and brain donation) did not have any funded projects in 2008. The panel discussed how to assure that in the coming year projects would be funded to address these objectives, and that the objective language may need to be adjusted in order to capture their true priority. Dr. DiCicco-Bloom asked the panel if Short-Term Objective #3 is truly a high priority; that a better focus might be to compare individuals with High-Functioning ASD (HFA) to individuals with Low-Functioning ASD (LFA). The panel then discussed if the study of HFA/LFA might fit under the subtyping project found under the Research Opportunities, and indicated that encouraging research into LFA is very important.

The panel talked about the merits of studying females in relation to ASD, specifically, that the reason why this topic was given such a priority is because the ratio of ASD occurrence is one female to every four males. The panel concluded that instead of the objective focusing on females, to the exclusion of males, that Short-Term Objective #3 should include the term "sex-differences", as a way to indicate that there is not enough basic biology known about why the male brain is more susceptible to ASD. It was also suggested that the language of "sex differences" should also be added to both Short-Term

Objectives #1 and 2, or even to expand the research to look more broadly into why the male developing brain appears to be more susceptible to mental retardation, autism and a variety of other mental disorders. Ms. Singer noted that the use of the term “sex differences” and broadening the scope beyond autism may water-down the focus of the objective, which was intended by the IACC to address a very specific and noted research gap.

As the group continued to discuss possible changes to research opportunities and objectives in the strategic plan, Ms. Singer pointed out that if a new research opportunity was identified by the panel, then the same idea should also be included in a short or long term objective, because it is those specific objectives that are tracked and reported on, not the items listed under research opportunities. Ensuring that each idea that is represented in the research opportunities section is articulated as a research objective will make it easier to track progress on the implementation of the plan.

Reviewing biobanking and biomarkers (Short Term Objective #1 and Long-Term Objective #2), the panelists agreed that information on American Reinvestment and Recovery Act (ARRA) funding is needed before conclusions can be drawn, but they identified potential data pools from which biomaterials would be easy to collect, including The High Risk Baby Siblings Research Consortium and the Children’s Health Study. They discussed the merits of biological biomarkers for diagnosis, as well as the use of the 2008 Summary of Advances to indicate new areas of biomarker research, including the use of the amyloid precursor protein. The panelist concluded that though biomarkers may not be currently used as a diagnostic tool, their collection and analysis can yield new therapeutic and research targets, as well as new risk factors. The collection of biospecimens could be accomplished by supplementing existing grants (such as the Children’s Health Study).

In discussing research topics unique to Question II, the panelists mentioned tissue donation awareness research (Short-Term Objective #4) and co-occurring conditions (Research Opportunities). Dr. DiCicco - Bloom recommended that tissue donation awareness is very important and should be a priority. Dr. DiCicco -Bloom also noted that current biobanks should be modified to include ASD tissues, phenotype information and have tighter regulations. The panelists commented that research into the underlying biology of co-occurring conditions needs to be highlighted in the objectives, and that known syndromes with high incidence of ASD will help in understanding the basic pathways of ASD.

Specific areas of potential biomarkers that are not mentioned in the Strategic Plan are proteomics, maternally-derived antibodies and mitochondrial markers. Mitochondrial markers might fit under the metabolic section of Short-Term Objective #2, but expansion of the objective might be necessary. Expansion of the objective will also allow other studies on co-occurring conditions to be performed as well, such as understanding the relationship between sleep disorders and ASD. Dr. Filipek suggested that mitochondrial disorders might deserve to be highlighted specially in the plan, while Dr. DiCicco Bloom suggested that focusing attention on mitochondrial disorders might discourage research on equally important areas of cellular function that may also play a role in development of ASD. Ms. Singer suggested capturing all relevant ideas in a parenthetical note in the objective.

In reviewing the Deferred Topics to be Considered for the 2010 IACC Strategic Plan Update document, the panel concurred that understanding the biological mechanisms behind social, linguistic, and cognitive deficits in people with ASD would be useful as one or more specific objectives. This could be done via various approaches, including brain structure-function studies and imaging studies. The panelists also mentioned that there are studies already included in the 2008 ASD Research Portfolio Analysis under the Other-Other category that address some of these topics.

The panel deferred discussing the topic of launching human and animal studies that examine immune, infectious and environmental factors in the occurrence of ASD until after the panelists review Question III.

Other areas of research that were discussed were the use of skin fibroblast, reversing them into pluripotent stem cells and re-differentiating them into neurons (induced pluripotent stem cells or iPSCs). This is an emerging research area that is not reflected in the 2008 research projects list or the 2009 strategic plan. The use of stem cells from post-mortem brains of people with ASD was also mentioned, and that this work will enable the creation and testing of functional "Autistic" neurons. Another area that the panelists noted as important were studies that combined genotyping and functional analysis. These studies can yield important information about the contribution of specific genes to the development of ASD. The panel also discussed that the Aspirational Goal of Question II included a translational component, and that the integration of both clinical and basic biological research is a crucial component to be included in the discussion of these objectives.

The meeting closed with an encouragement for the panel to continue to think about these issues and to share any new ideas via e-mail. The next meeting is scheduled for Wednesday, September 23, 2009 at 3:00 p.m. ET.

#### ACTION ITEMS:

- Review Question III in order to discuss the deferred topic of launching human and animal studies that examine immune, infectious and environmental factors in the occurrence of ASD (All panelists)
- Translate short statements to go on draft slides from the meeting summary (Alison Singer)