Conference Call #2 for IACC Scientific Workshop Panel Two
Strategic Plan Questions II: *"How Can I Understand What is Happening?"*
Wednesday, September 23, 2009

Call Participants: Ms. Alison Singer (Co-Chair), Dr. Ed Trevathan (Co-Chair); *Panelists:* Dr. Pauline Filipek, Dr. Sarah Spence, Dr. David Amaral, Dr. Emanuel DiCicco-Bloom, Dr. Ashura Buckley, Ms. Denise Resnick; Dr. Susan Daniels (Office of Autism Research Coordination (OARC) Staff)

Dr. Daniels welcomed the panelists, liaisons, and members of the public listening to the conference call, and conducted roll call. The panel identified the goals of the call: to review additional gaps and new opportunities developed since the last call, review the slides on objective prioritization, discuss the comments received through the Request for Information (RFI), and assign presenters for the Scientific Workshop. The panelists also wanted to address the issue of overlap with Question III: What caused this to happen and can it be prevented?

The panelists began by reviewing the draft slide set developed by Ms. Singer, based on the panel's first conference call. Dr. Spence asked Ms. Singer how research gaps differed from new opportunities and Ms. Singer said that she considered anything missing from the existing plan to be a "gap," while any new scientific advances or initiatives would be considered "new opportunities." Dr. DiCicco-Bloom noted that the distinction was not critical, as the slides were simply meant to generate discussion during the Workshop.

The panelists discussed the slide on noted research gaps and Dr. DiCicco-Bloom noted that many RFI respondents suggested specifically studying underlying neuroconnectivity, neurotransmitters, and the auditory system. The panelists decided to omit the specific mention of cellular function as an example of the type of underlying biology to be studied, to keep the area broader. The panelists also felt that the parenthetical list of co-occurring disorders should be expanded to include autoimmune disorders, in addition to seizures and sleep disorders. The group recommended expanding the recommendation to study the biology of other known syndromes to specify studying syndromes that frequently co-occur with ASD, such as Fragile X, Rett syndrome, and tuberlosclerosis complex (TSC). Dr. Spence explained that studying the known pathway aberrations in these frequently co-occurring disorders may help to understand the pathways contributing to ASD.

The panelists discussed the use of the word biomarker, saying that the term in the medical field specifically means a ubiquitous diagnostic marker. As used by the panel, "biomarkers" was intended to mean biologic indicators (e.g., antibodies, cytokines) that could be used to discover different or abnormal pathways. These biological indicators would not be immediately useful for diagnosis and therefore are not "biomarkers" in the traditional sense of the term. The panelists recommended moving away from the term "biomarker" and adopting "biological signature" instead.

The panelists noted that proteomics is an approach to look for biological signatures, not a type of biomarker, and raised concerns about the strength of the evidence indicating maternally-derived antibodies. Dr. DiCicco-Bloom said that the emerging research on mitochondrial markers is very

suggestive and is an area of interest for the public. Dr. Spence concurred, saying that studies about metabolic abnormalities, oxidative stress, and markers of redox and balance warranted more research. She also stated the need to collect the types of biological samples that could be used by researchers conducting biological signature studies. She said metabolism experts should be consulted to determine what types of samples would be most useful.

The group discussed the biobanking initiative in the Strategic Plan and noted that there was currently no funding to improve public awareness of the need for brain and other tissue samples from people with ASD. The group discussed how this was an implementation issue rather than a research issue, and recommended addressing it in the future (possibly in coordination with the National Institute of Child Health and Human Development (NICHD)).

The group recommended rewording the recommendation to conduct studies that "combine genotyping and functional analysis" to clarify that this meant studies that associate specific genotypes with functional or structural phenotypes. The panelists discussed the recent opportunities related to creating induced pluripotent stem cells from skin fibroblasts and corrected the wording of the opportunity to specify "in vitro" analysis.

Dr. DiCicco-Bloom recommended removing the reference to amyloid precursor protein from "Research Opportunities" because he said that the finding came from a small, unreplicated study. The panelists reviewed deferred topics and Dr. Amaral said that he felt that much research was currently being conducted on the biological mechanisms behind social, linguistic, and cognitive deficits, but not specifically in relation to ASD. Dr. Spence said that the objective to study biological mechanisms in processing environmental exposures had much overlap with Question III and might be best to address during that presentation.

The group discussed studies focused on nonverbal or minimally verbal people with ASD, and agreed that it was an understudied group because most research focuses on individuals with greater functional language ability. Dr. Spence said that approximately 50 percent of people with ASD are low-communicating and many assume that these individuals are also cognitively impaired, but in some cases, when provided with assistive communication technologies, these individuals demonstrate higher level cognitive abilities/verbal IQ than was expected. Dr. Spence explained that there can be many reasons why autistic people may be nonverbal, including intellectual impairment, motor apraxia and other causes, which need to be distinguished and treated differently. The panel emphasized the importance of understanding the biology of people across the spectrum, examining nonverbal people with cognitive impairments, as well as those who are nonverbal but cognitively intact. Ms. Singer explained that a goal of the previous IACC (prior to the Combating Autism Act) was or 80% of nonverbal autistic children to develop functional language ability. The group discussed the use of alternative and augmentative communication devices, as it relates to Questions V and VI (Services and Supports/Outcomes). All agreed to recommend making nonverbal research a higher priority.

The panelists discussed whether to make specific mention of including females in ASD research and Ms. Singer noted that there was a related objective in the Strategic Plan, but that no funding was currently being put toward it. However, she noted that they had not yet received information about the grants supported through ARRA.

The panel reviewed the Summary and Discussion slide and recommended emphasizing that biological research would be used to build the evidence base for risk factor research, interventions, services and supports. The panel noted the importance of translating risk factor research to the community in understandable language and to explain how studies are designed, to allay frustration. (For example, communicating that a researcher must first develop a hypothesis about a potential risk factor before embarking on a large study, that environmental studies can be very costly, and multiple risk factors cannot be studied simultaneously.) Dr. Amaral recommended developing a task force to develop strategies for improving communication with the public about the challenges associated with environmental studies and about the research findings of such studies.

The panel noted that much overlap occurred with Question III when studying the biological pathways that could potentially be triggered by environmental factors. Ms. Singer said that panelists would have a chance to engage in discussion with other panels during the Workshop.

The group discussed the RFI, noting that there were many comments related to studying subgroups of ASD, including regressive autism, “recovered” autism, and ethnic minorities on the spectrum. The group discussed whether sensory-motor processing was worthy of study, because it is an area not specific to ASD. Dr. DiCicco-Bloom described the difficulties of measuring sensory-motor processing (it is based primarily on self-report, poor assessment measures, etc.). He recommended specific mention of co-occurring autoimmune disorders in their presentation, citing recent evidence that mothers with celiac disease and rheumatoid arthritis are more likely to have children with ASD. Dr. Spence asked whether the panel should mention prioritizing items already in the plan, such as the phenotyping studies, and Ms. Singer said that the requested prioritization was primarily to be used to determine the importance of including new items/objectives in the plan.

Ms. Singer and Dr. Trevathan said that they would nominate presenters after the call and Ms. Singer volunteered to update the slide presentation and send to the group for final input. She recommended that the panelists prepare a list of items that they would like to discuss during other panel presentations.

Action Items:

- Finalize slide set for Scientific Workshop
- Appoint presenters
- Prepare list of items to discuss during other panel presentations