2009 IACC Scientific Workshop:

Updating the Strategic Plan for Autism Spectrum Disorder (ASD) Research

September 30 - October 1, 2009

Bethesda, Maryland

Panel 3: What caused this to happen and can this be prevented?

- Clinical Experts
  - *Robin Hansen, Susan Swedo*
- Research Experts
  - *Craig Newschaffer, Matthew State*
- Family/Personal Experts
  - *Lars Perner, Jeffrey Sell*
- Coordinated by IACC Liaisons
  - *Lee Grossman, Story Landis*

Panel 3: Noted Research Gaps in the 2009 IACC Strategic Plan

- *Gap 1 – Need to further take into account heterogeneity across autism spectrum disorders to identify risk factors*

- *Gap 2 –Need to identify factors that influence heterogeneity across autism spectrum disorders and possible bases for the identification of autism subtypes*

Panel 3: New Opportunities for Advancing Research and Knowledge about ASD

Gaps 1 and 2 – Heterogeneity of ASDs

- ***Opportunities***
  - Study phenotypic variation across ASD cases with shared genetic (or, once established, epigenetic) variation
  - Support the ability of ongoing studies of genetic and/or environmental risk factors to conduct analyses stratifying subjects according to behavioral or cognitive characteristics (e.g., social deficits, repetitive behaviors, language development) and clinical features (e.g., regression, dysmorphisms, medical co-morbidities, mitochondrial disorders, treatment response)

Panel 3: New Opportunities for Advancing Research and Knowledge about ASD

Gaps 1 and 2 – Heterogeneity of ASDs

- ***Opportunities (Continued)***
  - Support studies designed to identify clinically meaningful subgroups (i.e., based on trajectory, intervention response, etc.) as these may also represent etiologically distinct subgroups.
  - Large scale studies that aim to address gene environment interactions as well as the role of epigenetics in ASD

Panel 3: Noted Research Gaps in the 2009 IACC Strategic Plan

- *Gap 3 - Enhance information-sharing and coordination across etiologic research studies*
  - Not enough consideration has been given to the best array of common data elements, collection forms, and measures for etiologic research
  - No mechanism exists to track potential risk factors and ASD features being measured and analyzed in ongoing studies
  - Insure that, where possible, etiologic information be gleaned from intervention studies
  - Delays in data submission and accessibility impair timely meta-analyses

Panel 3: New Opportunities for Advancing Research and Knowledge about ASD

Gap 3 – Information-sharing and coordination across etiologic research studies

- ***Opportunities:***
  - Monitor portfolio of ongoing studies to identify gaps in the potential risk factors and ASD subtypes or features that are being assessed
  - Promote information exchange among investigators conducting etiologic studies

Panel 3: New Opportunities for Advancing Research and Knowledge about ASD

Gap 3 – Information-sharing and coordination across etiologic research studies

- ***Opportunities (Continued):***
  - Examine the existing array of common data elements, collection forms and measures (e.g., common history form) and consider expansions/adaptations
  - Facilitate data-sharing and rapid access to shared data for research use through resources such as NDAR and the Autism Clinical Trials Network

Panel 3: Noted Research Gaps in the 2009 IACC Strategic Plan

- *Gap 4 – Appropriate assessment of vaccination as a risk factor*
  - Need to focus on strategies to identify potentially susceptible groups
  - Need to better characterize responses (including immunological, behavioral, symptomatic, and developmental) to both vaccination and to naturally acquired illnesses that challenge the immune system

Panel 3: New Opportunities for Advancing Research and Knowledge about ASD

Gap 4 – Assessing vaccination as a potential risk factor

- ***Opportunities:***
  - Measure post-vaccine responses in children already diagnosed with an ASD, and incorporate measures of post-vaccine responses and factors that may be predictive of adverse responses into existing birth cohort studies (including baby sibs studies)
  - Examine data, as they become available, from ongoing longitudinal studies (CHARGE, SEED and EARLI) that are collecting information on immunization history. Provide additional support if required

Panel 3: New Opportunities for Advancing Research and Knowledge about ASD

Gap 4 – Assessing vaccination as a potential risk factor

- ***Opportunities (Continued):***
  - Continue to coordinate with the National Vaccine Advisory Committee (NVAC) and support efforts in public health surveillance of vaccine safety to develop the best strategy for including developmental endpoints

Panel 3: Noted Research Gaps in the 2009 IACC Strategic Plan

- *Gap 5 – Incentives and mechanisms for rapid and responsible translation of findings from etiologic research to prevention and intervention strategies designed to limit disability due to ASDs*
- ***Opportunities:***
  - Develop mechanisms to enable rapid initiation of replication etiologic studies
  - Develop effective and responsible means of applying validated findings on genetic and environmental ASD risk factors to prospective developmental, diagnostic and treatment studies

Panel 3: Areas of continued need related to existing objectives and opportunities

- Studies to identify and prioritize among potential environmental risk factors to consider in ASD research
- Efforts to promote expansion of genome-wide association studies to identify gene-environment interactions and epigenetic processes
- Biobanks and standardized procedures for collecting and analyzing tissue

Panel 3: Areas of continued need related to existing objectives and opportunities, cont.

- Rapid and reliable diagnostic tools for use in large etiologic (both genetic and epidemiologic) studies
- Assays for assessing environmental exposures
- Procedures to measure longitudinal postnatal body burden accumulation in relation to immune and physiological (metabolic, mitochondrial, neurophysiological) status to identify vulnerabilities that may develop over time from ongoing exposure

Panel 3: Summary

- Ongoing research is making progress toward identifying genetic and environmental risk factors, but could be enhanced by improvements in:
  - Understanding of heterogeneity across ASDs
  - Coordination and communication across studies
  - Diagnostic tools, measures of exposures and their physiological and immune impact, and biobanking capabilities and standards
  - Methods for investigating gene-environment interactions
- Opportunities exist to better understand whether vaccines are a risk factor in some subgroups of ASDs
- To promote translation into preventive strategies, research results related to ASD risk factors should be consistently replicated and responsibly communicated

Panel 3: Discussion points

- How can we balance the need for deep phenotyping with the need for large samples in epidemiological research?
- How should we identify new potential risk factors and set priorities for which ones to study?
- All panel members recognized and endorsed the opportunities to address gaps in our understanding of whether vaccination presents a risk factor for ASDs in specific subsets of children. Alternative strategies were proposed including a study of vaccinated versus unvaccinated children. The panel discussed the concern that ethical and selection bias may limit the utility of such a study.