IACC Strategic Plan Question 3 Outline

January 2017

Chapter Title: What Causes ASD, and Can Disabling Aspects of ASD Be Prevented or Preempted?

I.   **Introduction**
- **Aspirational Goal: Causes of ASD will be discovered that inform diagnosis, prognosis, and treatments and lead to prevention or preemption of the challenges and disabilities of ASD.**
- Describe the chapter's emphasis on addressing the challenges, disabilities, and comorbidities associated with ASD
- Acknowledge the recognition that there are positive aspects of ASD, sometimes including enhanced abilities
- Acknowledge that individuals on the autism spectrum can vary in the level of ability and disability across many domains. Therefore, some may require several interventions or intensive interventions, and others may need or desire few or no interventions
- Provide a general description of this question (can refer to previous version of the SP for guidance – Q3)

II.   **For each of the following three sections, describe 1) what is known, 2) what are the gaps, barriers, and opportunities, 3) are there policy/services implications? If so, what are they?**

- **Topic 1: Genetic Risk Factors**
  - Autism heritability
  - Identification of risk genes in diverse human populations
  - Genomic studies, including sequencing and array studies
  - Genomic architecture, including how factors combine to result in phenotype
  - Sex differences
  - Shared risks and the specificity of autism risk with other disorders (related phenotypes)
  - Data access and data sharing
  - Workforce needs
  - Genetic testing
  - Risk communication
  - Policy implications

- **Topic 2: Environmental Risk Factors, Individually and in Combinations Over Time**
  - Environmental exposures – chemical, nutritional, social stressors, etc. – in diverse populations
  - Prenatal and postnatal influences
  - Epidemiological studies of risk factors, including addressing the current major challenges in these studies, such as:
    - Sufficient samples size to study subgroups
    - Ability to differentiate risk factors (e.g. antidepressant use vs. depression)
  - Application of exposomics technologies to identify environmental risk factors

- o Advances in exposome science
- o Identification and utilization of biomarkers of exposure as a surrogate for detecting primary environmental risk factors
- o Data access and data sharing
- o Workforce needs
- o Public health implications and communication regarding exposure
- o Risk score, the prospect of future exposure testing, and the ability to predict risk

III.   Topic 3: Linkages between Genes and Environment
- o Capitalize on existing studies to forge real linkages between gene and environmental studies, and encourage the creation of new studies leveraging these linkages
    - ▪ Studies examining how genetic and environmental risk factors interact in the broader physiological environment to contribute to phenotype
- o Understanding multivariate risk across complex systems, such as:
    - ▪ Microbiome
    - ▪ Immune system
    - ▪ Endocrine system
- o Model systems (animal models, cellular models, iPSCs)
- o Understanding biological mechanisms of genetic and environmental pathways, including through the use of:
    - ▪ Epigenetics
    - ▪ Metabolomics
    - ▪ Transcriptomics
    - ▪ Proteomics
    - ▪ Functional genomics
- o Need for multidisciplinary workforce and approaches
- o Data access and data sharing
- o Emphasis on diverse populations in genetic and exposure studies

IV.   Summary/Progress towards Aspirational Goal
V.   Objectives

- **Objective 1:** Strengthen understanding of genetic risk factors for ASD across a large population representing the full diversity and heterogeneity of those with ASD, enabling development of strategies for reducing disability and comorbidities in ASD.

- **Objective 2:** Understand the effects on ASD risk of individual and multiple exposures in early development, enabling development of strategies for reducing disability and comorbidities in ASD.

- **Objective 3:** Expand knowledge about how multiple environmental and genetic risk factors act interact through specific biological mechanisms to manifest in ASD phenotypes.