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TO: U.S. Senate Committee on Environment and Public Works

FROM: Dr. Isaac N. Pessah, Director  
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Re: State of Research on Potential Environmental Health Factors With Autism and Related  
Neurodevelopment Disorders

Autism Spectrum Disorders (ASD) are highly heterogeneous conditions that are diagnosed using only behavioral criteria due to a lack of concrete biological markers. The American Psychiatric Association's *Diagnostic and Statistical Manual of Mental Disorders* (DSM-IV) defines ASD as a disorder characterized by deficits in verbal and nonverbal communication, stereotyped behaviors and interests, and impaired social interactions. ASD encompasses a wide range of phenotypic severities and co-morbidities. ASD likely encompasses several disorders with distinct etiologies and pathologies that converge on a common set of behavioral diagnostic criteria. Although autism risk has strong heritability, no single locus alone appears to be sufficient to account for the full clinical phenotype. Results from many genome-wide autism screens indicate that potential susceptibility genes are spread across the entire genome. Recently several very rare genetic mutations, single nucleotide polymorphisms (SNPs), *de novo* copy number variations, and epigenetic factors that influence DNA methylation were shown to contribute complexity in the transmission of autism risk. Yet genetics alone cannot account for the majority of autism cases currently being diagnosed. There is lack of full concordance between monozygotic twins, with some estimate ranging as low as 60%, and the prevalence of ASD among siblings has been reported as high as 14%. Interactions among multiple genes are likely to contribute to various types of autism, and heritable epigenetic factors and/or non-heritable environmental exposures are likely to significantly contribute to susceptibility and variable expression of autism and autism-related traits. It is therefore likely that constellations of epigenetic and environmental factors are contributing to the increasing prevalence of ASD, a rise that cannot be fully accounted for by changes in diagnostic criteria.

There is a critical need to identify environmental factors, including exposure to xenobiotic chemicals and changes in diet that contribute to autism risk and severity. The vast majority of public and private resources has, and continues, to support work on identifying genetic impairments associated with autism risk. From these studies we have learned that genetics alone cannot predict the majority of autism cases, the patterns of impairments, severity, nor can they predict success for current treatment modalities. Moreover, we have learned that many of the molecular and cellular systems that are associated with autism are the very same ones that are the target of environmental chemicals currently of concern to human health because of their widespread use. Further research is needed on modifiable factors that contribute to causing or protecting against autism. It is accepted that autism is 'multi-factorial,' meaning that there are multiple factors that combine to impair brain development. Increased efforts to identify environmental factors that contribute risk to developing autism spectrum are therefore essential to improve our understanding of the constellations of genes that confer differential sensitivity to distinct environmental exposures during gestational and neonatal development. Such approaches will likely prove useful in defining subgroups of children that differ in susceptibility to specific types of environmental exposures that promote autism risk, severity, and responsiveness to clinical and behavioral interventions.

We know that autism prevalence continues to increase dramatically clearly implicating environmental factors in autism risk. We must identify which environmental exposures and combination of exposures are contributing to increased overall risk in the population and identify the most susceptible groups. Only by bringing together the concerted effort of multidisciplinary teams of scientists can we identify which of the >80,000 commercially important chemicals currently in production promote developmental neurotoxicity consistent with the immunological and neurological impairments identified in individuals with idiopathic autism. It is clear that there is a critical need to identify which chemicals in the environment that influence the same biological pathways known to be affected in autism. Limiting exposure to these chemicals is the only way to mitigate or prevent autism in susceptible individuals.

Respectfully Submitted,

  
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