### Question 1 (Screening and Diagnosis)

**Walter Koroshetz**


*Early ASD diagnosis can facilitate early intervention, but the diagnostic stability of ASD in children younger than 18 months is not known. This prospective study followed 1269 toddlers diagnosed with ASD after initial referral through a universal screening program and found that ASD diagnosis becomes stable starting at 14 months of age. In this study, 23.8% of children were diagnosed with ASD after receiving a non-ASD diagnosis at their initial evaluation, and only 1.8% of children initially diagnosed with ASD transitioned to a final diagnosis of typical development.*

### Question 2 (Underlying Biology)

**Louis Reichardt**


*This paper shows the surprising importance of Ube3A in the nucleus in reproducing rodents the phenotypes of Angelman Syndrome. Ube3A has before been assumed to exert its actions at the synapse.*

**Walter Koroshetz**


*Mutations affecting the synaptic scaffolding protein SHANK3 are linked to language and communication impairments in Phelan-McDermid syndrome and other forms of ASD. In this study of mice lacking the Shank3B gene, the authors find disrupted functional connectivity and abnormal gray matter anatomy in the prefrontal cortex, and they show that these abnormalities correlate with socio-communicative deficits. The observations add to other research in people and animal models suggesting that disrupted functional connectivity in higher-level cortical areas may be a shared mechanism across different forms of ASD.*

**Walter Koroshetz**


Prior studies have suggested that the gut microbiome may differ between typically developing individuals and those with ASD. Here, the authors transplanted gut microbiota from human donors with or without ASD into germ-free mice and showed that gut colonization with ASD-donor microbiota induced ASD-like behaviors and alternative splicing of ASD-relevant genes in the brain. Treating an ASD mouse model with certain microbial metabolites improved behavioral abnormalities and modulated neuronal excitability in the brain. Although further study should determine whether these findings apply to ASD in people, the results add to research suggesting a role for gut-brain connections in ASD.

**Joshua Gordon**


Despite the clinical and genetic heterogeneity of autism, this disorder has been shown to converge and affect specific cellular pathways in the patients’ brains. In the current study the research team took advantage of recent methodological advances to further try and understand the distinct roles of the array of cortical brain cells in autism pathology. They performed single-nucleus RNA sequencing of cortical tissue from patients with autism to identify autism-associated transcriptomic changes in specific cell types. Results identified that synaptic signaling of upper-layer excitatory neurons and the molecular state of microglia are preferentially affected in autism. Moreover, findings point to a correlation between dysregulation of specific groups of genes in cortico-cortical projection neurons and the clinical severity of autism. These findings suggest that molecular changes in upper-layer cortical circuits are linked to behavioral manifestations of autism and provide preliminary findings on regional cell specific dysfunction in this disorder.

### Question 3 (Risk Factors)

**Diana Bianchi**


This study focuses on the relative importance of inherited vs non-inherited causes of autism using population data from the 5 MINERvA countries, i.e., Denmark, Finland, Sweden, Israel, and Western Australia, the largest family-based database for autism research. The analysis applied to full
Birth cohorts of children born between January 1, 1998, and December 31, 2011 (N=2,001,631). The heritability of ASD was estimated to be about 80%.

**Geraldine Dawson**


With a marked sample-size increase from a unique Danish population resource, the authors report a genome-wide association meta-analysis of 18,381 individuals with ASD and 27,969 controls that identified five genome-wide-significant loci. They identified seven additional loci shared with other traits at equally strict significance levels, and also found both quantitative and qualitative polygenic heterogeneity across ASD subtypes. These results highlight biological insights, particularly relating to neuronal function and corticogenesis, and establish that GWAS performed at scale will be much more productive in the near term in ASD.

**Question 4 (Treatments and Interventions)**

**Alison Singer**


This study used a meta-analysis approach to examine how clinic-based interventions were working in real world, community-based settings. Unfortunately, the effect sizes for improvement across multiple outcomes across the same intervention were significantly smaller in community-based settings than in research settings. There may be many reasons for this, but the message is clear: we need to do a better job implementing research findings in the community.

**Larry Wexler**

The AFIRM modules were created to educate practitioners on the identified evidence-based practices for students with autism. This study sought to identify who uses the AFIRM modules, what knowledge gains did they make, and their perception of the modules. Results indicate AFIRM is used across the country and the nation with users from various practitioner roles (i.e., SLPs, general education, special education, administrators, and interventionists). Gains were seen in modules completed with practitioners indicating they felt the modules were useful and relevant to their work. These modules align with IAAC’s goal of supporting school-based interventions by disseminating learning modules teaching how to implement evidence-based practices in the school.

### Question 5 (Services)

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Families and individuals with ASD often experience financial difficulties in meeting their service needs related to an autism diagnosis, especially among ethnically diverse and low-income households. And many states have used the availability of Medicaid Home and Community-based Services (HCBS) waivers to bridge the gap in unmet needs and services. HCBS waivers can be used to expand Medicaid coverage to include more services for individuals with ASD, and expand eligibility to include individuals who would not typically qualify for Medicaid. Using data from the National Survey of Children’s Health (2003, 2007, & 2011) and the National Survey of Children with Special Health Care Needs (2005 & 2010), the findings showed that states with more generous HCBS waivers showed a significantly reduced odds of having unmet need for black children with ASD compared with white children with ASD; and unmet needs among black children with ASD were roughly cut in half or approximately 13%.

### Question 6 (Lifespan Issues)

**David Mandell**


In this research, the authors studied changes in the number of services received before and after high school exit in a large sample of individuals with ASD. With each passing year during high school, individuals with ASD received fewer services. At the time of high school exit, there was a sharp drop in the number of services received, particularly for those with co-occurring intellectual disability. This study found not only that there is a post-high school service cliff, but also that the loss of services begins long before high school exit.

### Question 7 (Infrastructure and Surveillance)

**Alison Singer**


Although current global estimates suggest the proportion of the population with autism who have intellectual disability (ID) is approximately 50%, this study found a selection bias due to under-inclusion of populations with ID across all fields of autism research. The review covers all original research published in 2016 in autism-specific journals with an impact factor greater than 3. The results were stark: meta-analysis estimated 94% of all participants identified as being on the autism spectrum in the studies reviewed did not have ID (95% CI 0.91–0.97). Eight out of ten studies demonstrated selection bias against participants with ID. The reporting of participant characteristics was generally poor: information about participants’ intellectual ability was absent in 38% of studies (n = 114). Where there was selection bias on ID, only 31% of studies mentioned lack of generalisability as a limitation.
Autism research must be more transparent about the underlying severity and characteristics of the individuals being studied, and we must find strategies for inclusion for children and adults with severe forms of autism.