SPEECH INFORMATION (For Conference Program Book)	
Topic	**Multi-Omic Insights into the Gut–Brain Axis in Autism Spectrum Disorder: Microbiome, Metabolomics, and Therapeutic Intervention**
Abstract	Advances in microbiome science and metabolomics have increasingly highlighted the gut–brain axis as a central pathway shaping neurodevelopment, cognition, and clinical outcomes in autism spectrum disorder (ASD). Integrating microbiome ecology, blood metabolomics, structural neuroimaging, and early-phase microbial intervention, this body of work elucidates multi-level mechanisms through which gut-derived signals influence the developing brain and contribute to autistic phenotypes, while also exploring their therapeutic potential. The first line of investigation conceptualizes the gut microbiota as an interconnected ecological system and develops a quantitative Autism Dysbiosis Index (ADI) to capture ASD-specific microbial disturbances. In a cohort of 143 ASD and 99 typically developing controls, full-length 16S rRNA sequencing and ecological network modeling revealed distinct alterations involving taxa such as *Cutibacterium acnes*, *Gemmiger formicilis*, and *Marseillibacter massiliensis*. Dysbiosis patterns mapped onto reduced orbitofrontal gray matter volume and poorer performance on executive function tasks, supporting a microbiota–frontal–cognitive axis. The ADI not only differentiated ASD from controls but also correlated with symptom severity, providing a scalable biomarker for gut–brain involvement. Complementing these ecological findings, a second study integrates untargeted metabolomics with brain MRI to investigate biochemical precursors of altered neurodevelopment. Among 140 individuals with ASD and 52 controls, tryptophan metabolism emerged as the most affected pathway. Elevated circulating L-tryptophan in ASD was associated with reduced gray matter volume in serotonin-relevant regions—including the medial prefrontal cortex, amygdala, hippocampus, and parahippocampal gyrus—and these structural differences mediated relationships between tryptophan levels and core autistic symptoms. These results highlight metabolomic perturbations, particularly in the tryptophan–serotonin pathway, as mechanistic drivers influencing brain structure and behavioral phenotypes. Building upon these mechanistic insights, an open-label pilot trial examined GKB7 as a microbial-based intervention. In 20 children with ASD, 12 weeks of supplementation were well tolerated and associated with improvements in reciprocal social interaction, stereotyped behaviors, emotional regulation, and global functioning, along with reductions in externalizing behaviors and peer-related difficulties. Together, these studies provide convergent evidence for a multi-level microbiome–brain–behavior framework in ASD. By linking ecological dysbiosis, metabolic alterations, neural substrates, and preliminary clinical benefits of microbial supplementation, they point toward the promise of microbiome-informed precision medicine and novel gut-targeted therapies for ASD.