TECHNICAL BULLETIN

Developmental Zinc Status: A Potential Link Between Gut, Immune and Neurological Function

Introduction

Autism spectrum disorder (ASD) is a complex neurodevelopmental condition influenced by both genetic and environmental factors. While hundreds of ASD-associated genes and numerous prenatal risk factors have been identified, many appear to converge on common biological pathways involved in brain development, immune regulation, gastrointestinal function and cellular signaling. Zinc (Zn), an essential trace mineral required for growth and development, plays critical roles in each of these processes. Emerging evidence suggests that developmental Zn deficiency may represent a common mechanism through which diverse ASD risk factors influence neurodevelopment. This technical bulletin reviews current Sauer et al. (2026) evidence linking Zn biology to ASD and examines the potential role of developmental Zn status in pathways frequently altered in affected individuals.

Developmental Zinc Deficiency as a Common Biological Framework

Prenatal Zn deficiency has emerged as one of the most consistently reported nutritional risk factors associated with ASD. Human observational studies, meta-analyses and animal models have repeatedly identified associations between reduced Zn status and ASD-related outcomes. Prenatal Zn-deficient animal models exhibit alterations in social behavior, communication, anxiety-related behaviors, immune regulation, gastrointestinal function and neurodevelopmental processes that overlap with many clinical features observed in ASD.

The review proposes that developmental Zn deficiency may serve as a biological framework for understanding how genetically and environmentally distinct ASD risk factors converge on common cellular pathways. Rather than acting through independent mechanisms, many ASD-associated risk factors appear to influence shared processes that are highly dependent on normal Zn signaling.

Zinc-Dependent Biology is Overrepresented Among ASD Risk Genes

One of the strongest quantitative findings reviewed in the paper is the significant enrichment of Zn-binding proteins among ASD-associated genes. Analysis of the SFARI ASD gene database revealed that Zn-binding proteins are significantly overrepresented among ASD candidate genes, particularly among high-confidence and syndromic ASD categories.

These findings suggest that many genes implicated in ASD participate in biological processes influenced by Zn signaling, including synaptic organization, neuronal communication, mitochondrial regulation, oxidative stress responses and inflammatory pathways. Consequently, disruptions in Zn-dependent biology may influence multiple ASD-associated processes simultaneously.

Developmental Zinc Deficiency Produces ASD-Relevant Features in Animal Models

Prenatal Zn-deficient animal models reproduce a broad range of biological and behavioral changes frequently associated with ASD. These models demonstrate evidence of neuroinflammation, altered gut microbiota composition, increased intestinal permeability, impaired synaptic development, social behavior deficits, communication abnormalities, anxiety-related behaviors and altered neurodevelopment.

Animal and mechanistic studies have also demonstrated that Zn deficiency affects mitochondrial function, oxidative stress pathways, immune signaling, gastrointestinal barrier integrity and neuronal connectivity. Importantly, many of these biological disturbances overlap with pathways implicated in ASD by genetic and clinical research.

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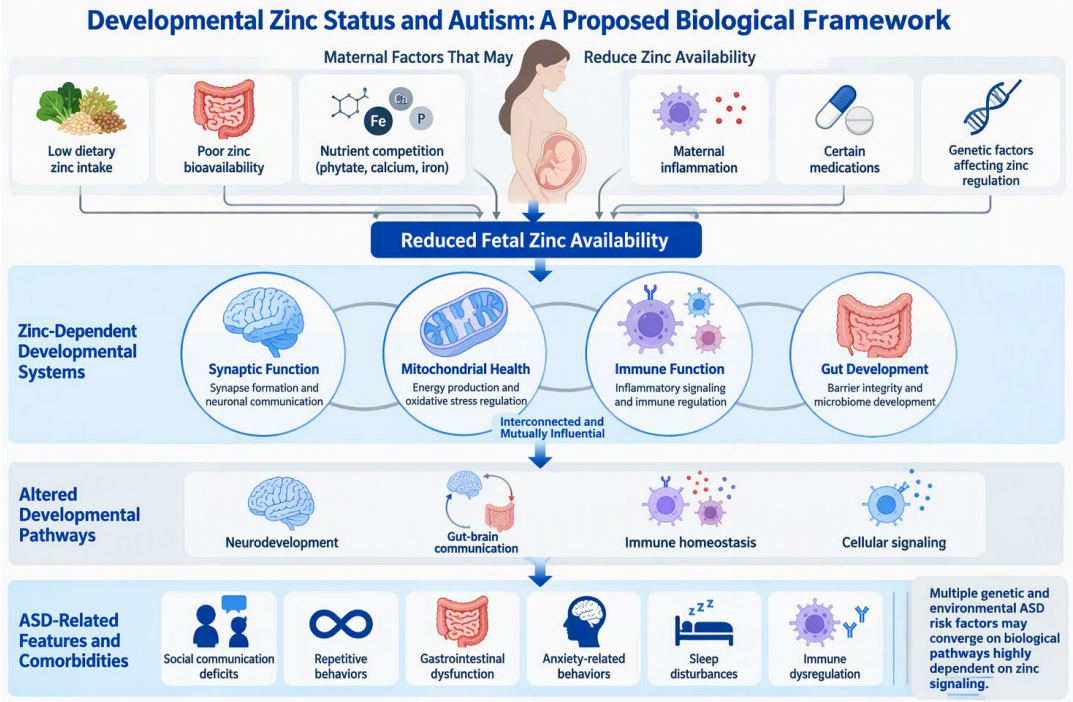


Figure 1. Proposed Biological Framework Linking Developmental Zn Status with Systems Frequently Altered in Autism Spectrum Disorder
Emerging evidence suggests that multiple ASD risk factors may converge on Zn-dependent biological processes involved in neurodevelopment, immune function, mitochondrial health and gastrointestinal integrity.

Examples reported in prenatal Zn-deficient animal models include:

- Increased neuroinflammatory signaling and astrocyte activation
- Altered gut barrier function and microbiota composition
- Reduced synaptic proteins such as SHANK family proteins
- Impaired social interaction and communication
- Increased anxiety-like behaviors
- Altered cognitive and motor function

Together, these findings support the concept that developmental zinc deficiency can affect multiple systems involved in neurodevelopment.

Proposed Model Linking Developmental Zinc Deficiency and ASD

The review proposes that maternal factors capable of reducing fetal Zn availability may influence Zn-dependent developmental pathways. These factors include inadequate dietary Zn intake, nutrient competition, maternal immune activation, toxic exposures, genetic variants affecting Zn regulation and certain medications. Reduced fetal Zn availability may subsequently affect synaptic development, immune regulation, gastrointestinal function, mitochondrial health and endocrine signaling.

The resulting multisystem dysfunction may contribute to both the core features of ASD and many of its associated comorbidities. Importantly, the authors emphasize that this model remains a hypothesis requiring further validation through well-controlled human clinical studies.

Implications for Nutritional Strategies

Current evidence supports an important role for Zn in neurodevelopment, immune regulation, gastrointestinal function and cellular signaling. Developmental Zn deficiency has been associated with biological pathways frequently altered in ASD and animal studies have demonstrated that prenatal Zn deficiency can produce ASD-relevant phenotypes. However, definitive human clinical trials evaluating prenatal Zn supplementation and ASD risk are still lacking.

Maintaining adequate Zn status before and during pregnancy may support healthy fetal development and normal function of Zn-dependent biological systems. Additional clinical research is needed to determine whether targeted nutritional strategies that support Zn homeostasis can influence developmental outcomes and ASD risk in humans.

Source: Sauer et al., 2026. Clinical Nutrition Volume 58. Article ID 106592 doi: 10.1016/j.clnu.2026.106592

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