Is there a significant overlap between "Autism" and In-Born Errors of Immunity?

Yes, **inborn errors of immunity** frequently present with **autistic behavioral symptoms**, though the overlap is partial and mechanistic rather than diagnostic.

Is there a significant overlap between autism and inborn errors of immunity? N = 8

Yes 75% · Possibly 25% · Mixed 0% · No 0%

FIGURE 1 Research consensus on overlap between autism and inborn errors of immunity

Inborn errors of immunity (IEIs) are monogenic immune disorders whose expanding scope has revealed pathogenic gene variants that manifest overlapping clinical features with ASD, including dysregulated immune activation, chronic inflammation, and altered CNS morphogenesis (Jyonouchi, 2023). A substantial subset of IEI patients present with neurodevelopmental disorders such as autism spectrum disorder, intellectual disability, or ADHD, arising through shared genetic pathways governing both immunity and brain development (Xiao et al., 2025).

Evidence for ASD–IEI Overlap

Evidence Strength	Claim
Moderate	IEIs such as **DiGeorge syndrome** are developmental immunodeficiencies often initially diagnosed as autism, and ataxia-telangiectasia causes immunodeficiency with cerebellar degeneration (Xiao et al., 2025).
Moderate	Some ASD patients show **neuroinflammation markers** resembling those in IEI patients, suggesting shared inflammatory pathways may be targetable with IEI-directed treatments (Jyonouchi, 2023).
Moderate	Genetic overlaps between immunity and brain development — including defects in **DNA repair, chromatin remodeling, and cytokine signaling** — produce combined immunological and neurological phenotypes (Xiao et al., 2025).

FIGURE 2 Evidence strength for claims linking ASD and inborn errors of immunity

Shared Immune Dysregulation Mechanisms

The immune and nervous systems share common signaling mechanisms and affect each other as part of the neuroimmune network, providing a biological basis for the overlap (Jyonouchi, 2023). Multiple ASD risk genes encode immune system components, and immune-related genetic variants in ASD also control neurodevelopmental processes such as neuronal and synaptic plasticity (Estes & McAllister, 2015; Arenella et al., 2023). Genome-wide analyses confirm a genetic relationship between ASD and immune phenotypes, with ASD positively correlated with allergic diseases and locally correlated with rheumatoid arthritis, C-reactive protein, and lymphocyte counts (Arenella et al., 2023).

Chronic neuroinflammation driven by dysregulated immune activation is a convergent feature: IEIs cause chronic inflammation affecting multiple organs including the CNS, while ASD brains show elevated pro-inflammatory cytokines, microglial activation, and altered blood-brain barrier function (Jyonouchi, 2023; Briceno Noriega & Savelkoul, 2013; Hsiao et al., 2012). Maternal immune activation during gestation — a well-established ASD risk factor — produces offspring with permanent immune dysregulation and ASD-like behaviors in animal models, further bridging the two conditions (Hsiao et al., 2012; Hughes et al., 2022).

Clinical and Translational Implications

- IEI patients often present with a **puzzling array of clinical features**, and some are diagnosed with ASD or other neuropsychiatric conditions before an underlying immune defect is identified (Jyonouchi, 2023).
- Progress in understanding IEI disease mechanisms at the molecular level has enabled **gene-specific treatments** in some disorders, which may be applicable to ASD patients with overlapping inflammatory profiles (Jyonouchi, 2023).
- Recognizing neurological involvement in IEIs can improve **early diagnosis and multidisciplinary care**, while deeper understanding of immune-neural crosstalk opens avenues for targeted anti-inflammatory or gene therapies (Xiao et al., 2025).

The overlap is significant but not universal: ASD is a behaviorally defined syndrome with multiple etiologies, and only a subset of cases involve immune mechanisms traceable to inborn errors (Jyonouchi, 2023; Gładysz et al., 2018). Whether immune dysregulation is a primary cause or secondary consequence of ASD remains unresolved, and the heterogeneity of both conditions complicates efforts to define the full extent of their intersection (Hughes et al., 2018; Ormstad et al., 2018).

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