Qeios

Peer Review

Review of: "Candida and Long Covid: Mannan Not from Heaven"

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This commentary proposes an ambitious and integrative hypothesis linking **Candida overgrowth (CO)**, zonulin-mediated barrier dysfunction, Gq-coupled GPCR autoantibodies, altered tryptophan metabolism, and persistent spike protein signaling to the pathogenesis of Long Covid (LC) and multiple chronic diseases. The manuscript is wide-ranging, mechanistically dense, and intellectually provocative.

Despite its originality, the manuscript has significant conceptual and evidentiary limitations.

1. Hypothesis vs. Evidence Delineation

The article frequently presents speculative mechanistic connections in language that may imply causal inference. For example:

The proposed binding of hyphal mannans to lectin-like domains on Gq-coupled GPCRs remains theoretical.

The assertion that anti-GPCR autoantibodies in LC originate from Candida-induced conformational GPCR changes lacks direct experimental evidence.

The extrapolation from β-glucan elevation to pathogenic Candida overgrowth is not definitively established.

The manuscript would benefit from clearly distinguishing:

Established evidence

Correlative findings

Hypothetical extrapolations

At present, these categories are sometimes blended.

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2. Overextension Across Disease Domains

The commentary extends the Candida–LC hypothesis to dementia, cancer, obesity, aging, APS, HSD, MCAS, RA, CeD, CrD, schizophrenia, autism, and others. While mechanistic overlaps exist (e.g., NLRP3, zonulin, GPCRs), the broad generalization risks weakening the core LC hypothesis.

Declarations

Potential competing interests: No potential competing interests to declare.