

Peer Review

Review of: "Candida, the Gut Microbiome, and the Epidemic Levels of Cancer and Autoimmune Disease in Young Women, Dementia, and Obesity"

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The manuscript presents a wide-ranging hypothesis that Candida overgrowth (CO) is a central, underappreciated driver of gut dysbiosis, altered tryptophan metabolism, increased intestinal permeability, estrobolome dysregulation, and subsequent risks of autoimmune disease, dementia, obesity, and hormone-driven cancers. It integrates multiple pathophysiologic pathways and epidemiologic observations into a provocative model linking dietary patterns, fungal overgrowth, and modern epidemics of chronic disease.

The article is interesting, well-referenced, and thought-provoking, but as a commentary or hypothesis paper, it relies heavily on circumstantial associations and extrapolation. While the review of mechanistic pathways is detailed, some arguments lack critical balance and could be misinterpreted as stronger than the evidence currently supports.

This article connects microbiome science, immunology, endocrinology, and epidemiology in a comprehensive framework.

Raises important questions that may stimulate further research.

Major Concerns

The manuscript frequently frames associations (e.g., Candida, zonulin, estrogen reabsorption) as though causation were likely. Stronger caveats are needed to emphasize the speculative nature, particularly in linking Candida directly to rising cancer rates in young women.

The breadth of conditions included (cancer, dementia, obesity, cardiovascular disease, autoimmune disease, COVID-19, long COVID, connective tissue disorders) is impressive but may overwhelm the reader. A tighter focus or clearer hierarchy of evidence would improve clarity.

Many pathways are supported by animal models, in vitro findings, or indirect biomarkers. The manuscript would benefit from distinguishing robust evidence (e.g., Candida biofilms in periodontitis) from emerging hypotheses (e.g., Candida as a central driver of the young women's cancer epidemic).

Some mechanistic descriptions (e.g., opposing roles of Candida vs. mammalian IDO, estrogen's dual immunomodulatory roles) need clarification.

Figures are hypothetical but could be misread as empirically demonstrated; they should be labeled more explicitly as models.

Being a commentary, there is no systematic search strategy reported. Still, a short statement on how references were selected (databases, timeframe) would improve transparency.

Minor Issues

Occasional repetition across sections (NF- κ B, Th17, β -glucuronidase) could be synthesized more tightly.

Some grammatical and stylistic polishing would improve readability.

A concluding section with specific testable hypotheses or research priorities (e.g., longitudinal studies of CO and estrogen-positive cancers, clinical trials of antifungal or probiotic interventions) would strengthen impact.

For Editor

Recommendation

Major Revision

The manuscript is provocative and potentially impactful, but before acceptance it should:

- Sharpen distinctions between speculation and evidence.
- Streamline scope to avoid dilution of key messages.
- Add a more critical appraisal of limitations and alternative explanations.
- Clearly label figures as hypothetical.
- Provide future research directions and clarify clinical translation relevance.

Declarations

Potential competing interests: No potential competing interests to declare.