Review of: "AI-Generated Hallmarks of Aging and Cancer: A Computational Approach Using Causal Emergence and Dependency Networks"

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Potential competing interests: No potential competing interests to declare.

I think the authors did a good job, overall. There are some aspects that need further investigation, but overall they have made an interesting proposal. The issue of conducting genomic inference based on aggregating information is an old one, and of course, pathway analysis and networks have determined significant progress. It is correct to consider ML and AI right now and exploit their potential value in generating hypotheses. The authors did this, supported by some ideas related to causal emergence, pathways, and network dependency, and demonstrating the feasibility of their methodological framework and also a certain relevance of outcomes.

A few remarks:

a) Causal emergence has a quick presentation while it would deserve a major assessment in view of the importance of the word causality.

b) Networks are very popular and extremely useful, but in this approach, the topological potential seems utilized in quite limited terms.

c) Pathways have a few inherent limitations that call for further evaluation. Redundancy of terms, for instance, needs to be controlled. Pathways rarely respond to isolated dynamics or perturbations; they rather show collective influences that should be considered.

d) Validation is a key aspect, and the paper lacks some specific treatment.

e) Conceptually, the approach describes the importance of having distinct phases and/or features to perform well, but in reality, any clear separation is quite artificial and often limited in terms of hypotheses. Thus, it remains an ideal concept. This is an aspect of complexity that the authors should elaborate on and refine in view of the contribution that ML and AI can offer.