Qeios

Peer Review

Review of: "New Approach for TargetingSmall Molecule Candidates for Intrinsically Disordered Proteins"

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The authors proposed a novel computational approach, the Informational Spectrum Method for Small Molecules (ISM-SM), to infer potential ligands for intrinsically disordered proteins (IDPs), with a focus on the Alzheimer's disease-associated tau protein. ISM-SM leverages electron-ion interaction potentials (EIIP) to screen two major drug and chemical databases to identify approved drugs and natural products with potential relevance to tau pathology. The manuscript is well-written and shows promising results, especially in the identification of novel candidate compounds such as bryostatin-14.

However, I have several concerns regarding the manuscript (see below for details)

(Comment 1) How did the author identify five reported tau-binding drugs in the DrugBank database? What information in DrugBank did the author search for the five drugs? Please explain this issue in greater detail.

(Comment 2) Please provide version information about the DrugBank database and the Coconut database used for the analysis.

(Comment 3) The sliding window analysis to identify protein domains is mentioned but not detailed sufficiently. How did the authors identify the optimal window size for the analysis (used in Table 4)?

(Comment 4) Please provide the codes to perform ISM-SM on GitHub or in the supplementary materials.

(Comment 5) In section 2.2, ISM-SM method, what did (iv) mean?

(Comment 6) What did n and vi in equation (5) mean?

(Comment 7) How did the author define the values of a, b, and ti in equation (5) (e.g., {1, -5} for the values of a and b for log p)? Please explain this issue in greater detail.

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Declarations

Potential competing interests: No potential competing interests to declare.