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AI-based mining of biomedical literature: Applications for the drug repurposing for the treatment of HIV-Associated Neurocognitive Disorder.

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Repurposing the approved drugs or small molecules in the advanced stages of clinical development drastically reduces drug development time. Biomedical data and literature are exponentially growing, making it harder for individual investigators to keep up with, much less analyze and discover hidden connections in these datasets. The datasets, such as PubMed, PMC, ClinicalTrials, and others, have vast information that can be mined to generate new disease development and progression hypotheses. Moreover, this data could be mined to discover the potential application of existing small molecules for disease treatment. We have developed and employed AGATHA, an AI-based literature mining system that discovers novel interactions that potentially lead to a new therapeutics discovery. This system prioritizes plausible term pairs among entity sets through learned ranking criteria, allowing us to recommend new research directions. The AGATHA has been applied to discover new HIV-associated neurocognitive disorder (HAND) and Substance Use Disorder (SUD) treatments. With the AGATHA, we generated a list of HAND-associated genes corresponding to small molecules, including FDA - approved drugs. We tested the activity of small molecules targeted against the proteins of five prioritized genes to protect against the combined neurotoxicity of HIV-Tat and cocaine in primary neuronal cultures and determined FDA-approved drugs and compounds in the late stage of clinical and preclinical development. The analysis of transcriptomics modulations by the compounds determined the mechanistic inside and opened an avenue for developing combinational therapy harnessing HIV and SUD-induced neuroinflammation. These findings show that literature mining accelerates drug repurposing for HAND treatments.