Repurposed cancer treatments could be potential Alzheimer's drugs

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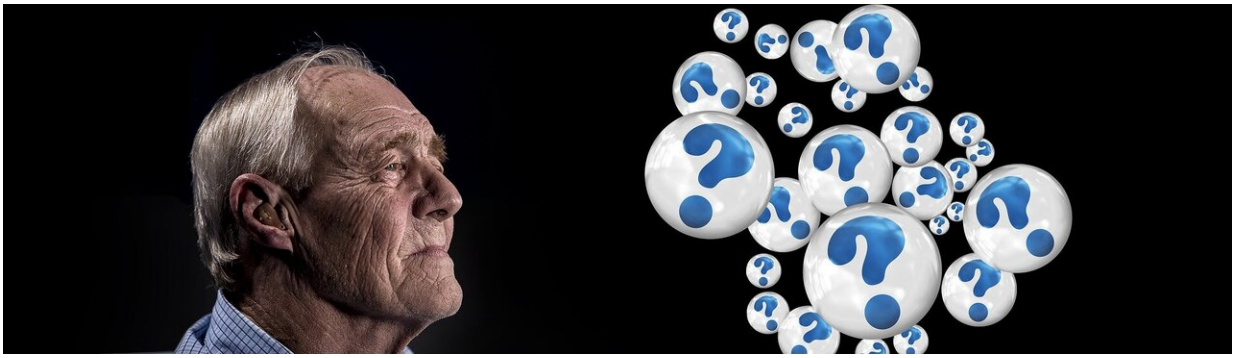

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Existing and emerging cancer drugs could be repurposed as therapies to be tested in clinical trials for people at genetic risk of Alzheimer's disease, according to a new study published in *Science Advances*. Research combining analysis of brain protein alterations in these individuals as well as laboratory experiments in animal models and cell cultures could help scientists identify existing drugs to test for their potential as Alzheimer's interventions more quickly.

The findings represent efforts from researchers at the National Institute on Aging (NIA), part of the National Institutes of Health; and NIA-supported teams at the University of California, San Francisco; Rush University, Chicago; and the Icahn School of Medicine at Mount Sinai,

New York City.

The scientists identified brain protein changes related to the APOE4 genetic risk variant in young postmortem study participants (average age at death was 39 years) and compared these changes with those in the autopsied brains of people with Alzheimer's and those without (average age at death was 89 years).

The analyses included brain samples from the Baltimore Longitudinal Study of Aging, the Religious Orders Study, and other NIA-funded studies. The researchers then tested whether existing Food and Drug Administration-approved or experimental drugs for other diseases act upon some of these proteins.

Their findings show an experimental drug for liver cancer and Dasatinib, approved for chronic myeloid leukemia, act upon some of these Alzheimer's disease-related proteins, suggesting they could be potential Alzheimer's therapies. The drugs also reduced neuroinflammation, amyloid secretion, and tau phosphorylation in cell culture experiments, underscoring their potential as candidates to be tested in Alzheimer's clinical trials.

These findings add to evidence from another recent study showing the value of this kind of data-driven approach to drug repurposing research. Next steps could include testing these drugs in clinical trials. For those already FDA-approved or that have already been tested for safety in other trials, the timeline for testing could be decreased.

NIA leads NIH's systematic planning, development, and implementation of research milestones to achieve the goal of effectively treating and preventing Alzheimer's and related dementias. This research is related to Milestone 7.B, "Initiate research programs for translational bioinformatics and network pharmacology to support rational drug

repositioning and combination therapy from discovery through clinical development" and Milestone 7.C, "Continue to develop resources, capabilities and partnerships to advance data-driven drug repositioning and combination therapy."

More information: Jackson A. Roberts et al, A brain proteomic signature of incipient Alzheimer's disease in young APOE ε4 carriers identifies novel drug targets, *Science Advances* (2021). DOI: 10.1126/sciadv.abi8178

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