Press release

HKU-led Team Wins 2021 and 2022 US National Academy of Medicine Healthy Longevity Catalyst Award

An Expert-led AI and Big Data-driven Approach for Breakthrough Drug Discovery of Alzheimer's Disease

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The HKU led team comprises: Professor Victor O.K. Li (HKU Department of Electrical & Electronic Engineering (EEE), Associate Professor Jacqueline C.K. Lam (HKU EEE), Dr. Jocelyn Downey (HKU EEE), Professor Illana Gozes (Tel Aviv University), Mr. Han Yang (HKU EEE), and Mr. Tushar Kaistha (HKU EEE).

Around 50 million people worldwide currently suffer from Alzheimer's Disease (AD) and related forms of dementia, including 10 million people in China. AD is an irreversible, progressive and ultimately fatal brain disorder that slowly destroys memory, thought capability, and eventually the ability to carry out the simplest tasks. Despite the urgent need for treatments and intensive research, there is a lack of effective restorative treatments or preventative therapeutics for AD. Even though the US Food and Drug Administration approved Aduhelm as a treatment for AD in 2021, the first newly approved drug for treating AD since 2003, controversy remains as regards to whether Aduhelm, which has been proven to reduce Amyloid (a protein) plaques in AD patient's brains, can actually delay cognitive decline. It is thereby urgent to search for more effective treatments which target at the root cause of AD. The international research team, led by Professor Victor On-Kwok Li and Dr. Jacqueline Chi-Kei Lam from HKU Engineering, with collaborators Prof. Illana Gozes from the Tel Aviv University and Dr. Jocelyn Downey from HKU Engineering, aim to apply new causal AI techniques and domain-specific pathological knowledge to accelerate the search for more effective drugs for AD. Our AI and big data driven interdisciplinary AD studies have been richly rewarded with two consecutive winnings of the US National Academy of Medicine Healthy Longevity Catalyst Award in 2021 and 2022, making us the only team in HK to win the prestigious grant twice in two consecutive years.

To identify breakthrough AD treatments, the research group developed a novel AI and big data-driven methodology. First, a heterogeneous biomedical graph is constructed, consisting of complex and interconnected genes, proteins, and drug information to capture the network characteristics of the AD pathology, taking into account the known expert knowledge about the associations between different AD pathways. Second, the curated graph is taken as an input to an artificial intelligence (AI)-driven graph neural network (GNN), with embeddings of drug and gene nodes as the outputs. Third, a drug scoring and selection analysis is conducted to generate the drug-gene scores and identify possible drug candidates. The HKU-led interdisciplinary team, combining AI with neuroscience and immunology, contributes a methodological breakthrough, by incorporating expert knowledge in GNN-based biomedical graph construction, which covers genetic mutations and pathological knowledge. Our

novel approach, both AI- and expert-led, capturing the best of both worlds, is expected to greatly improve the speed and accuracy of drug discovery for AD.

AD is the fifth leading cause of death worldwide, comprising 60-80% of dementia cases. In the US, AD and other dementias are ranked number 4 in years of life lost due to premature mortality. Furthermore, AD imposes a huge cost both on the quality of life for sufferers themselves, their families, and friends. Globally, the World Health Organization (WHO) estimates the societal costs of dementia to be approximately USD1.3 trillion; if dementia was a country, it would be in the top 15 economies globally and roughly the size of the Australian or Spanish economy. Additionally, the prevalence of AD and dementia increases with age; the number of sufferers is expected to increase as people live longer. As estimated by WHO, nearly 80 million people will suffer from dementia and the associated costs will plumet to US$ 2.8 trillion by 2030. The discovery of new drugs that treat the root causes of AD will avert the course of irreversible AD neurodegeneration. Our AI- and expert-led methodology will not only transform the drug discovery methodology for AD and other neuro-degenerative diseases, but all diseases. Our ground-breaking work brings hope to the AD sufferers, and sets a promising pathway for early neurodegenerative disease detection and treatment in the future.

The Healthy Longevity Catalyst Award, organized by the U.S. National Academy of Medicine (NAM), as part of its Healthy Longevity Global Competition, is given to bold, innovative and potentially transformative ideas to extend human healthspan. Globally, more than 1,000 applications are received each year with a success rate of approximately 10%. This award was first made in Hong Kong in 2021, with 51 applications and 5 awards made. The HKU team led by Prof. Li and Dr. Lam was the only awardee from Engineering. In 2022, the Research Grants Council of Hong Kong collaborates with the NAM, and ten awards were made in Hong Kong. Our HKU-led Engineering team won again in 2022, making us the only team in HK to win this prestigious award twice.

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