[BIOINFO 2024]

Development of a drug candidate discovery pipeline for Alzheimer's disease based on drug-transcriptomes

Min-Kyeong Kwon[1], Hyunjung Kim[1], and Sun Shim Choi[1*]

[1]Division of Biomedical Convergence, College of Biomedical Science, Institute of Bioscience & Biotechnology, Kangwon National University, Chuncheon, Korea

**Corresponding author: schoi@kangwon.ac.kr*

Alzheimer's disease (AD) is a progressive neurologic disorder that causes the brain to shrink and brain cells to die. Despite the big worldwide efforts to develop treatments for preventing, delaying the onset, slowing the progression, improving cognition, or reducing behavioral disturbances of AD, most drugs have been unsuccessful. In the present work, we built AD-specific reference datasets consisting of 8 brain-associated cell lines and extracted AD-associated drug transcriptome data from the datasets named "positive control drug data." The AD-associated drugs are FDA-approved AD drugs or drugs that are effective in AD studies. In addition, we collected AD transcriptome data from 3 brain regions (temporal lobe, frontal lobe, and parietal lobe) from several studies. We also collected drug target gene information from LINCs, DrugBank, and SEA and grouped drugs into each target gene set targeting the same gene. First, we selected drugs with a similar trend with positive control drug data and an opposite trend against AD transcriptome data. Second, clustering selected drugs, we assumed that if a cluster is significantly overlapped with a target gene set, drugs in the cluster are supposed to target the target gene. Finally, AD drug candidates were identified using the supposed target gene-edited transcriptome data from LINCS and CMap.