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List of Abbreviations

AD= Alzheimer Disease

Ab= Amyloid beta

p-TAU= phosphorylated TAU

HSV-1= Herpes simplex virus-1

IgM= Immunoglobulin M

HSE= Herpes simplex encephalitis

VZV= Varicella zoster virus

HIV= Human immunodeficiency virus

PNS= Peripheral nervous system

PPI= Protein-protein interaction network

Kbp= Kilo base pair

ORF= Open reading frame

U_L= Long unique

U_S= Short unique

DNA= Deoxyribonucleic acid

gC= Glycoprotein C

gD=Glycoprotein D

gH=Glycoprotein H

gL= Glycoprotein L

HVEM= Herpes virus entry mediator

MHC= Major histocompatibility complex

ICP-4=Infected cell protein 4

CD8+= Cluster of differentiation type 8

CTL= Cytotoxic T-lymphocyte

VHS= Virus host shutoff

LAT= Latency associated transcript

RNA= Ribo nucleic acid

NRSF= Neuronal restrictive silencing factor

REST= Repressor element silencing transcription

ICP0= Infected cell protein 0

Abstract

Protein–protein interactions form the basis for a vast majority of cellular events, including signal transduction and transcriptional regulation. Herpes Simplex Virus-I infection is very common among human population. It is most common pathogenic cause of acute encephalitis in humans and has been suggested as an environmental risk factor for Alzheimer disease. Major problem with HSV-1 is that it resides within neurons and gets reactivated whenever there is immunosuppression or stress. In this study we are bridging the common HSV-1 infection with that of Alzheimer.Huge amount of data is available for viruses and host interaction and this data can be used by computational network construction methods to construct virus-host interaction. Taking this into consideration; data for Alzheimer and HSV-1 was collected from different sources. By this data, protein-protein interaction network of Alzheimer [AA network] and Host-HSV-I[HV network] was prepared. After that, all first interacting neighbors of HV network were collected by using APID2NET[HA network]. Then common proteins present in AA and HA networks were found. By this intersection we found 6 proteins that are direct target of viruses and are also directly linked to Alzheimer. They are APOE (Apolipoprotein E), APOA1 (Apolipoprotein A-I), A4 (Amyloid beta A4 protein/ APP), LMNA (Prelamin-A/C), PARP1 (Poly [ADP-ribose] polymerase 1) and TAU (Microtubule-associated protein TAU); out of these APOE and A4 are already known risk factors for Alzheimer. Clustering reveals RGS6 (regulator of G-protein signaling), EPC2 (Enhancer of polycomb homolog 2), CR1 (Clusterin-1) and CD2AP (CD2 associated protein), they are indirectly associated with AD. Here we represent APOA1, LMNA, PARP1, SG6, EPC2, CR1 and CD2AP as new candidate risk factors. These were then classified based on Pathways, GO and Subcellular localization. This classification suggests new possible protein targets which can be utilized for development of better therapeutic techniques for Alzheimer's disease.

Aim and Objective

1. To construct Alzheimer protein-protein interaction network.
2. To construct HSV-1 protein-protein interaction network.
3. To find common proteins in the two network.
4. To identify new risk factors that may initiate Alzheimer pathology.
5. To cluster common proteins based on pathways and GO.
6. To identify location where majority of AD proteins and HSV-1 targets are clustered.