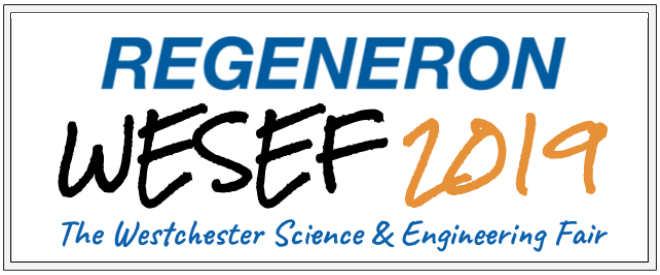

Finalist: **Madiha Qureshi Zia**

School: **Ossining High School**

Title: **Rab35: A Potential Therapeutic Target for Alzheimer's Disease**

Abstract:

The misprocessing of amyloid-β precursor protein (APP) has been genetically linked to Alzheimer's disease (AD) as a major causative factor for the disease. Cleavage of APP by β-site APP cleaving enzyme-1 (BACE) is the rate-limiting step in the formation of amyloid-beta (Aβ) peptide, a byproduct of APP whose toxicity leads to the manifestation of AD symptoms. Protein trafficking typically occurs in 'early endosomes', controlled by Rab GTPases. Peptide accumulation occurs when this process is dysregulated. We identified Rabs that decrease APP/BACE1 interaction, which may promote neuroprotection against AD by reducing amyloid beta production. We used a bimolecular fluorescence complementation assay to identify such Rabs, we co-transfected APP and BACE, each tagged with a different half of Venus fluorescent protein, into mouse neuroblastoma (N2a) cells along with a series of 16 Rab GTPases. Fluorescence here indicated the amount of APP and BACE interactions. Fluorescence microscopy and flow cytometry results revealed that Rab35 was the most successful in reducing Venus fluorescence levels in N2a cells (p=0.0001; 48% corrected total cell fluorescence; 0.35 median fluorescence intensity). Thus, these findings indicate Rab35 activity decreases the APP/BACE interaction, likely reducing amyloid-beta formation, and possibly delaying the onset of AD. These results provide novel insight into a potential therapeutic target for preventing or reducing the severity of Alzheimer's disease.