Elucidation of Common Molecular Mechanisms of Parkinson’s, Alzheimer Diseases, and Diabetes Research Intern

Aggregation of specific proteins is associated with a number of diseases including Parkinson’s (PD), Alzheimer’s (AD), and other neurodegenerative diseases. Type II diabetes (T2D) is also linked to aggregation of Islet amyloid polypeptides (IAPP). IAPP is found to be significantly accumulated as extracellular amyloid deposits in the pancreas of T2D patients; it is shown that early oligomers are significantly cytotoxic species that lead to beta-cell apoptosis. The mechanisms through which IAPP leads to T2D are unclear. Various lines of evidence appeared to support the contention that IAPP oligomers built in the early stages of aggregation form annular protofibrils and consequently pores in the membranes the same way as amyloid-beta and alpha-synuclein correspondingly create pores in the cell membrane in AD and PD. Increase of calcium influx to the cells can lead to apoptosis in case of all these diseases.

The specific tasks of the project are using computer modeling and simulations to accomplish the following goals: (1) To characterize the interactions between IAPP, amyloid beta, and alpha-synuclein molecules in oligomers, and interactions between molecules and the membranes. (2) To validate a concept of self-assembly of these molecules, using a set of mutants known to enhance or inhibit IAPP aggregation process with identifiable structural properties.

The task will include extensive analysis of research articles in the field, related to modeling and simulations abovementioned proteins and their interactions with the membrane. Computational molecular modeling and molecular dynamics simulations.

2. Number of Students to be supported: 1

3. Name of Lead person: Dr. Igor Tsigelny, Dept. of Neurosciences, SDSC

4. Plan to Integrate Student into Group Activity

The student will be a part of the research team working on the larger scale project that includes the project described here. He or she will attend the group meetings and communicate with the team members using other methods of communication. The student will work closely with the lead person and the other personnel involved.

5. Student Prerequisite

We are looking for a student who is interested in both biology and computation.

6. Number of hours per week: 15-20 hours

7. Relevant link:

San Diego Supercomputer Center: http://www.sdsc.edu