CALIFORNIA STATE SCIENCE FAIR
2010 PROJECT SUMMARY

Name(s)

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Project Number

S0415

Project Title

Prion and Lipid Membrane Interactions: The Role of Dilauroylphosphatidylethanolamine in Fatal Prion Disease Propagation

Abstract

Objectives/Goals

Fatal prion diseases have no cure, with malicious prions eventually spreading throughout the brain. How prion proteins (PrP) propagate themselves is largely unknown. Lipids have been linked with misfolding of the malicious PrP. This project provides specific evidence that energy changes occurring in the PrP-lipid interactions are involved in infectious prion misfolding.

Methods/Materials

Specifically, the biomolecular dynamic simulation analysis done shows significant changes in inter-atomic energies in PrP in a lipid environment. PrP interactions with lipid versus water were simulated using NAMD, VMD, Charmm. Using molecular modeling and dynamic simulations, the specific energies in the region of the misfolding were investigated with Chimera.

Results

Results found that electrostatic energies of PrP immersed in a Dilauroylphosphatidylethanolamine (lipid) box differed widely from PrP in a water box. Visual changes were observed in the Octarepeat Domain (OD). There was also extra twisting directly adjacent to the E200K region which codes for the hereditary susceptibility of prion diseases and is the region where misfolding occurs.

Conclusions/Discussion

The energy differences only occur in nonbonded energies. A lipid membrane environment leaves openings for misfolding and the PrP moves differently in the lipid solution rather than a water one. It is likely that the polar nature of water reduces PrP#s internal electrostatic energy. It is conclusively shown that PrP interaction with a lipid membrane induces stresses within the protein and affects the region of misfolding. With this knowledge of PrP-lipid interactions, additional information can be extracted to better identify the nature of the linkage.

Summary Statement

Kinking found in the examined region of a prion during a simulation of prions in a lipid membrane demonstrates that the conditions induce misfolding.

Help Received

Dr. Glenn Millhauser helped answer conceptual questions, parents helped with putting together the board and editing the report.