Molecular Biology of Alzheimer's Disease

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Figure 1: Anu Ramachandran's project on how a faith healer affected HIV education in Tanzania earned her the interdisciplinary award in the humanities category during the 14th annual USC Undergraduate Symposium for Scholarly and Creative Work.

Background

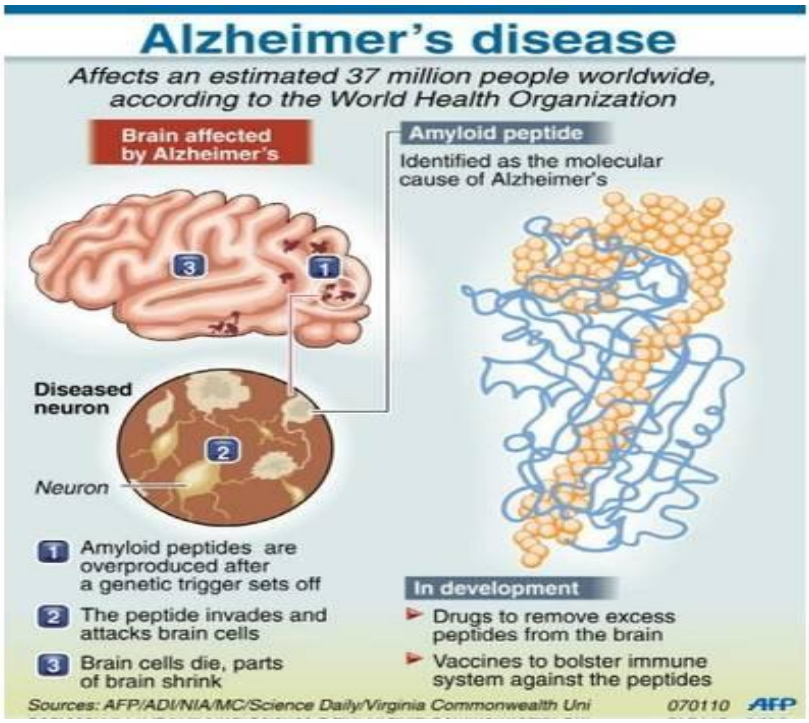
Anu Ramachandran is currently a senior majoring in Neuroscience B.A., and Philosophy B.A.. She is a true Renaissance scholar, who has exposed herself to many facets of student life at USC, and has gained a wealth of experience both from her academics and her extracurricular involvements. She is currently president of the USC Support for International Change program, a member of the Alpha Epsilon Delta Pre-Medical Honor Society, an Organic Chemistry Supplemental Instruction (SI) Leader, and a research assistant in Dr. Carol-Anne Miller's lab at the USC Alzheimer's Disease Research Center. Anu has worked in Dr. Miller's lab since her freshman year and has deepened her understanding of the scientific method with her involvement in numerous research projects over the past three years.

After participating in a USC Problems without Passports trip exploring the influence of spiritual healing in rural Brazil, Anu was inspired to learn more about teaching and spreading public health. The following summer, she participated in a public health service trip combating the spread of HIV/AIDS in rural Tanzania. Drawing upon her research experience in the field in Brazil and in the lab at USC, Anu took the initiative to research a local spiritual healer and publish a paper in the *Journal of Global Health* on the effects of spiritual healing on public health education in rural Tanzania. While traversing a wide variety of commitments at USC, Anu has remained passionate, purposeful, and most of all, open to new sources of knowledge. Her experiences abroad have fueled her commitment to research at Dr. Miller's lab, where her lab work has produced invaluable results that may soon merit publication.

Research

At Dr. Carol Miller's lab, Anu has researched the GluR2 AMPA receptor and its involvement in the pathophysiology of Alzheimer's disease. Most recently, her research has focused on revealing the clustering of GluR2 mRNA around neuronal nuclei in the FAD mouse model of Alzheimer's disease. Anu uses in situ hybridization to label the GluR2 mRNA in mounted mouse brain tissue using an anti-sense DNA marker, which binds to the GluR2 mRNA. A series of antibodies and probes are then applied to the tissue so that the locations of the GluR2 mRNA will visibly fluoresce under a microscope. When observed under a microscope, Anu's experimental brain slices revealed a difference in GluR2 mRNA localization between normal mice and FAD mice, which have a set of mutations that lead to increased Amyloid-Beta peptide accumulation and subsequent Alzheimer's disease. Anu found that in Alzheimer's-affected mice with the FAD mutation, GluR2 mRNA clusters around neuronal nuclei and does not migrate through the neuron to the synapse as it does in unaffected mice.

This finding of GluR2 mRNA clustering is found in all Alzheimer's affected mice, but is much more noticeable in mice that have had Alzheimer's disease for longer periods of time.



Significance

The GluR2 mRNA does not migrate to the synapse in Alzheimer's-affected mice; it is not being expressed in adequate concentrations. In other words, the cell's DNA is producing an appropriate amount of GluR2 mRNA, but then that mRNA is getting 'stuck' and not being translated into GluR2 protein subunits of the AMPA receptors. This means that the Alzheimer's-affected brain has neurons, which do not have a sufficient concentration of AMPA receptors, the most common type of receptor in the mouse and human nervous system. A decrease in the function of this receptor can cause a variety of symptoms amounting to an overall decline in cognitive function, similar to that seen in Alzheimer's disease.

The AMPA receptor, and especially the GluR2 subunit, has been the focus of much research in the field of Alzheimer's research. However, most of the focus has been on changes in the AMPA receptor's activity at the synapse. At Dr. Carol Miller's lab, Anu is researching what happens to the AMPA receptor before it arrives at the synapse, and she is finding that the receptor subunits face issues in mRNA translation. If the process of mRNA translation is understood more deeply, this could yield a broad avenue of Alzheimer's treatments. As of yet, no cure has been found for Alzheimer's disease, but Anu's research and that of the Miller laboratory could prove a major step towards understanding and effectively treating Alzheimer's disease.