

Research Spotlight: Fungus may lead to treatment for Alzheimer's Disease

Research Spotlight provided by **Dr. Robin Couch**, Department of Chemistry and Biochemistry

Nerve growth factor (NGF), a protein that is secreted by specialized cells within the brain, induces the differentiation and survival of nerve cells. NGF secretion is triggered by various physiological perturbations to the nervous system, including nerve lesions and the presence of damaging toxic agents. Under these conditions, a local increase in NGF is elicited, which promotes nerve cell survival by binding to receptors located on the surface of the effected cells and initiating a survival response. NGF therapy has been suggested as a method of preventing or reducing nerve cell loss and atrophy that occurs during a stroke or in neurodegenerative disorders such as amyotrophic lateral sclerosis (ALS), Alzheimer's disease (AD), and Huntington's disease. In fact, clinical trials in which NGF-secreting cells are surgically implanted in the brains of AD patients have shown a positive impact on cognitive function. However, NGF is a protein with non-drug-like properties, seriously limiting its direct therapeutic use.

To overcome these limitations, Dr. Robin Couch, Assistant Professor of Chemistry and Biochemistry at George Mason University, is focused on the development of small drug-like molecules that are metabolically stable and can upregulate the natural production of NGF in the brain. One promising class of molecules are known as the cyathanes, and include the fungal natural products erinacine C, scabronine A, and cyathin A3. Elucidating the mechanism by which these molecules confer their activity will significantly aid in the future development of these compounds into drugs. In collaboration with [Dr. Dennis Wright](#) (a synthetic chemist) and [Dr. Akiko Nishiyama](#) (a neurobiologist) at the University of Connecticut, the Couch lab will utilize a derivative of cyathin A3 and a technique known as affinity column chromatography to identify the specific protein target responsible for initiating the cyathane-induced NGF release. Dr. Emanuel Petricoin, Dr. Lance Liotta, and Dr. Mark Ross in the [Center for Applied Proteomics and Molecular Medicine](#) at George Mason University will also contribute to this project by providing expertise with their state-of-the-art protein analysis equipment. Once the protein target of the cyathanes has been identified, the team of scientists will work to rationally develop derivatives in order to obtain compounds with suitable properties to become a clinically useful drug.



*Dr. Robin Couch, Assistant Professor of Chemistry and Biochemistry at Mason.
 Picture - Evan Cantwell*

For more information about this research:

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