Green tea chemical combined with another may hold promise for treatment of brain disorders

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Scientists at Boston Biomedical Research Institute (BBRI) and the University of Pennsylvania have found that combining two chemicals, one of which is the green tea component EGCG, can prevent and destroy a variety of protein structures known as amyloids. Amyloids are the primary culprits in fatal brain disorders such as Alzheimer's, Huntington's, and Parkinson's diseases. Their study, published in the current issue of *Nature Chemical Biology* (December 2009), may ultimately contribute to future therapies for these diseases.

"These findings are significant because it is the first time a combination of specific chemicals has successfully destroyed diverse forms of amyloids at the same time," says Dr. Martin Duennwald of BBRI, who co-led the study with Dr. James Shorter of University of Pennsylvania School of Medicine.

For decades a major goal of neurological research has been finding a way to prevent the formation of and to break up and destroy amyloid plaques in the brains and nervous systems of people with Alzheimer's and other degenerative diseases before they wreak havoc.

Amyloid plaques are tightly packed sheets of proteins that infiltrate the brain. These plaques, which are stable and seemingly impenetrable, fill nerve cells or wrap around brain tissues and eventually (as in the case of Alzheimer's) suffocate vital neurons or brain cells, causing loss of

memory, language, motor function and eventually premature death.

To date, researchers have had no success in destroying plaques in the human brain and only minimal success in the laboratory. One reason for these difficulties in finding compounds that can dissolve amyloids is their immense stability and their complex composition.

Yet, Duennwald experienced success in previous studies when he exposed amyloids in living yeast cells to EGCG. Furthermore, he and his collaborators also found before that DAPH-12, too, inhibits amyloid production in yeast.

In their new study, the team decided to look in more detail at the impact of these two chemicals on the production of different amyloids produced by the yeast amyloid protein known as PSI+. They chose this yeast amyloid protein because it has been studied extensively in the past, and because it produces varieties of amyloid structures that are prototypes of those found in the damaged human brain. Thus, PSI+ amyloids are excellent experimental paradigms to study basic properties of all amyloid proteins.

The team's first step was to expose two different amyloid structures produced by yeast (e.g., a weak version and a strong version) to EGCG. They found that the EGCG effectively dissolved the amyloids in the weaker version. To their surprise, they found that the stronger amyloids were not dissolved and that some transformed to even stronger versions after exposure to EGCG.

The team then exposed the yeast amyloid structures to a combination of the EGCG and the DAPH-12 and found that all of the amyloid structures broke apart and dissolved.

The next steps for the research team will be to explore the mechanism

and potency of such a combinatorial therapy for the treatment of diverse neurodegenerative diseases.

"Our findings are certainly preliminary and we need further work to fully comprehend the effects of EGCG in combination with other chemicals on amyloids. Yet, we see our study as a very exciting initial step towards combinatorial therapies for the treatment of amyloid-based diseases," says Duennwald.

Source: Boston Biomedical Research Institute