



November 14, 2019

Ms. Claire Palmer
Directory Alumni Council
P.O. Box 828
Byfield, MA 01922

Dear Claire:

As a loyal supporter of the *Foundation for Neurologic Diseases* (FND), you have had a direct impact on our innovative research on Alzheimer's disease (AD) and other chronic brain disorders. You and our other public-spirited donors have enabled our scientists to engage in the most promising directions in applied neurobiological research, leading to ground-breaking discoveries that are informing the current search for therapeutic treatments for this devastating disorder. Virtually no other research group has been able to achieve this level of ability to pursue novel scientific ideas and discoveries that attract philanthropic donors as well as funding through grants or industry, all of which are needed to bring complex biomedical research to fruition. Time and again, seed funding from the FND has provided the basis for ideas and discoveries that we would otherwise be unable to achieve due to lack of funding.

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This year, we are proud to share our excitement around a two-day Scientific Symposium and dinner that was held in June as a celebration of the long-term (~40-year) collaboration of the FND's founders and co-leaders, Drs. Dennis Selkoe and Howard Weiner. More than 300 people from around the world attended the Symposium, followed by a celebratory dinner held at the Museum of Fine Arts in their honor. All of the scientific presentations were given by former or current trainees of Drs. Selkoe and Weiner over these many years. This event serves to underscore the unique scientific environment created in large part by ongoing support from the Foundation over three decades.

Karen Hodge, CPA

As we approach the year's end, we are pleased to provide this update on highlights of our scientific progress and our perspective on where the field of AD research stands today. It is our hope that this news will inspire you to include the Foundation in your charitable giving this year.

A signal advance of our work in the laboratory in 2018-19 has been the production of unique antibodies to the amyloid b-protein (A β) unlike any others that have been created to treat AD. We developed a method to identify novel antibodies that potently neutralize the bad effects of so-called "oligomers" (small clumps) of the A β protein that we isolate from the brains of patients dying with AD. We discovered and characterized these new antibodies by testing a great many candidate antibodies that we made on cultured human neurons specially derived from human stem cells. Our unique monoclonal antibodies potently neutralized the human A β oligomers we placed on the human neurons, and they worked better than the most advanced antibodies tried in AD patient trials heretofore. Now, we are using your support to the FND to decipher why these antibodies have such unique properties. Importantly, we have conducted this work with a biopharmaceutical company that can choose to advance one or more of these special antibodies into human trials in AD patients. This work exemplifies the advances we can make as a result of the existence of the FND, founded in 1988.

Another area of progress in our lab and only a handful of others is the creation of inexpensive, sensitive blood tests to detect AD *before symptoms develop*. FND-supported scientists published in late 2018 that we can detect elevated levels in the blood of a fragment (called NT-1) of the tau protein that comprises the “tangles” of AD. Our data suggest that we can distinguish normal people from those with clinical AD with a high degree of accuracy using this NT-1 immunoassay. Even more significantly, we obtained in 2019 the first evidence that elevated blood levels of NT-1 tau can predict the rate of cognitive decline over the next several years in still-normal people. In short, we have developed a biomarker in blood whose level predicts the progressive advancement of the AD process, beginning even before the first clinical forgetfulness. Our next step is to take advantage of the Harvard Aging Brain Study (HABS) led by our close colleague, Dr. Reisa Sperling, whose work is also supported by the FND. Dr. Sperling’s HABS cohort allows us to assay NT-1 tau longitudinally over 6-8 years, as she collects blood each year from her >500 subjects, all of whom were cognitively normal at entry into her study. We look forward to letting you know next year how effective the NT-1 assay and other blood tests we have also developed are in predicting the advent of AD, so we can enroll subjects into early pre-clinical trials.

In closing, let us share that the initially disappointing news suggesting failure of an anti-A β antibody trial in 2019 has been reversed! Biogen’s antibody called “aducanumab” has been found to slow memory decline as well as decline of everyday functions in the home (cooking, finances) when analysis of twice as many (all) of the subjects in the trial was completed. The antibody also markedly removed amyloid plaques, definitely proving the amyloid hypothesis we’ve been working on at the FND for 30 years. If approved by the FDA, aducanumab would become the first therapy to reduce the clinical decline of Alzheimer’s disease and would also demonstrate that removing amyloid beta results in better clinical outcomes.

It is also important to note, a seemingly re-effective anti-A β antibody (called BAN2401) from the Japanese pharma company Eisai is now in Phase 3 (final) trial, and we are enrolling early AD patients in that global trial. Moreover, our colleague Dr. Reisa Sperling will use BAN2401 in her new AD prevention study, the best way, we think, to address AD *before* memory decline is noticeable.

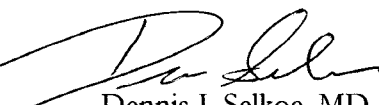
More than five million people currently suffer from Alzheimer’s disease in the US alone (and perhaps 40 million worldwide). The US number is projected to grow to seven million by 2025. We are hopeful that we and many other AD scientists are closing in on a time when this tragic disease loses its grip as a major cause of disability and death in older people. As we re-double our efforts at the FND to find a way to treat and prevent AD, can we count on your support? Your year-end contribution to the Foundation will have an immediate impact in keeping the positive trajectory of our research moving forward into the New Year. As always, 100% of each dollar you donate goes directly into our research, without diverting any portion of your gift to overhead or indirect costs. Very few non-profit organizations you will hear from this holiday season can make this statement. We are inspired to proceed, and we are grateful for your continuing friendship and support of our mission for science... and for health.

We wish you all the best for a joyous holiday season and a Happy New Year!

With sincere gratitude,



Karen Hodge
Executive Director
Foundation for Neurologic Diseases



Dennis J. Selkoe, MD
Founder and President
Foundation for Neurologic Diseases