Foundations can be a critical source of funding for biomedical research as NIH budgets flatten and further cuts are made. An exciting example of this comes from research on Alzheimer’s Disease which currently affects 5.4 million Americans and is expected to reach 16 million by 2050.

While NIH dollars concentrate on conservatively funding research focused on the biological basis of Alzheimer’s disease, there is little support for studies on the preclinical development of drugs to treat the disease, or for innovative “high risk/high reward” studies. These “funding gaps” can often be addressed by foundations which can quickly identify and fund promising research. This particular “funding gap” in Alzheimer’s research was identified by The Medical Foundation, which advised the Edward N. and Della L. Thome Memorial Foundation to support the best researchers conducting Preclinical Drug Discovery studies. In this case, foundation funding led to a breakthrough with enormous therapeutic potential.

This bright spot in Alzheimer’s research was recently reported in the journal Science last February, by a team of researchers led by Dr. Gary Landreth at the Case Western Reserve University School of Medicine in Cleveland Ohio. While it has been known for over twenty years that Alzheimer’s is characterized by an abnormal accumulation of a protein called amyloid-beta in the brain, attempts to therapeutically remove it or block its formation, continue to be unsuccessful despite decades of effort.

Dr. Landreth proposed an unconventional approach to remove amyloid-beta through the function of another protein called Apolipoprotein E (ApoE), a cholesterol carrier in the brain that facilitates the normal removal of amyloid-beta. Landreth and his research team tested an FDA approved drug called bexarotene, which is currently used to treat skin cancer. Dr. Landreth hypothesized that bexarotene could activate retinoid X receptors (RXRs) that increases levels of ApoE and lead to the enhanced removal of amyloid-beta.

To test his theory, bexarotene was given to mice strains that were genetically engineered to recapitulate many of the trademarks of Alzheimer’s disease. These animals have excessive amounts of beta-amyloid in their brains, and exhibit behavioral problems reflecting deficits in memory, such as the ability to remember painful stimuli, or how to build nests in their cages. A remarkable aspect of their results was the rapidity of bexarotene action, and within hours the elevated levels of ApoE dramatically dropped by 25% and at 3 days had been stably reduced by 50%. The leading treatments to date take months to reduce beta-amyloid levels and are not nearly as effective.

Even more amazing was the restoration of the behavioral deficits in these animals. They were able to learn in performance tests, and began to make nests in their cages, just like normal mice. The exciting ability for bexarotene treatment to affect a wide spectrum of behaviors in the brain holds tremendous hope for the utility of this type of treatment in future Alzheimer’s therapies.

It is critical to note that while this drug is already approved for use in humans to treat cancer, Dr. Landreth sternly warns against its being used by Alzheimer’s patients prior to the careful clinical trials needed to test its safety for use in Alzheimer’s treatment. The drug was given in megadoses to the mice, and while no ill effects were observed, it is important to note that drugs that work in mouse models do not always work in humans, and can have serious side effects. Nevertheless, this study is clearly an exciting breakthrough that provides much hope for a field that has failed to identify a successful treatment over the last twenty years.

Importantly, when Dr. Landreth proposed to do these studies, he was unable to garner immediate support from NIH. Luckily, his research did fall within the funding focus of the Edward N. and Della L. Thome Memorial Foundation and work leading up to these studies was generously supported by the Blanchette Hooker Rockefeller Foundation. Dr. Landreth adds, “I had spent almost all of the (research) money when I applied to the Thome Foundation and we were running on fumes. The Foundation awarded the grant and I had funds almost immediately...We simply could not have completed the work in the Science paper without their support.”

After the publication of his findings Dr. Landreth has obtained significant funding to continue these studies and move bexarotene into clinical trials on humans. But his encouraging story highlights the critical role of foundations, not only in their ability to rapidly provide research support, but in their ability to identify ‘funding gaps’ that can maximize funding impact. Such judicious use of philanthropic funding can contribute effectively and significantly to fill gaps in the research path towards improving treatments for those suffering from devastating diseases such as Alzheimer’s.

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