

Tackling Dementia by Investing in Translational Medicine

By Angus J. Grant

The challenge posed by dementia is enormous. The World Health Organization predicts the number of people living with dementia around the world will increase from 50 million in 2018 to 150 million by 2050. In the United States, the number of people with dementia is projected to rise from 5.7 million to 14 million over the same period. These forecasts are alarming — and they should be.

The concern is not only because dementia is a cruel disease that robs people of their abilities, personality, and dignity, but also because it creates a significant burden for families and society. Dementia can last for years, and providing the necessary care for those with this condition is difficult and costly.

Contributing to this burden is the lack of effective treatments for people with dementia. Finding ways to prevent, delay, treat, and ultimately cure this condition is critical to prevent a health crisis. However, developing meaningful treatments has proved challenging for the scientific, biotech, and health care communities.

One reason dementia is hard to treat is because it is difficult to define. Dementia is a broad term for abnormal cognitive difficulties and is especially prevalent in people as they age. It does not have a single cause. It can present on its own or in combination with other conditions. It can also result from other diseases and come in multiple different forms.

Because dementia varies so much, scientists are starting to think of it like cancer. Over the past 30 years, a greater understanding of the various forms of cancer, even within a single organ or tissue type, has enabled scientists to develop highly targeted therapies.

In dementia, the well-known diseases that can underlie cognitive decline like Alzheimer's and Parkinson's may actually be segmented into different conditions that can be treated with more targeted medicines. To achieve this, the science of dementia needs to mimic the advancements made in oncology and link an understanding of the subsets and unique mechanisms of the disease to patient symptoms.

But the historic difficulty of developing treatments for dementia is not a reason to give up. Scientists at universities and in companies continue to improve their understanding of dementia and its mechanisms. In addition, governments, charities, and some companies invest in this difficult area of research.

However, turning research into treatments requires even more investment and this capital is difficult to find for dementia. Providing the funding needed to turn an idea into a viable therapy will help advancements in the field of dementia parallel the great strides made in cancer treatments and match effective, novel drugs to the patients they can benefit. This is the goal of the Dementia Discovery Fund.

Fund inception

The Dementia Discovery Fund (DDF) was established to diversify the dementia therapeutic landscape by providing the funding needed to bring innovative research from the laboratory into the clinic. It is the first ever venture capital fund to specialize in dementia. Its unique focus stems from its unusual inception following the World Dementia Council meeting in 2014.

David Cameron, prime minister of the United Kingdom in 2013, played a pivotal role in the DDF's formation. By

focusing the G8 meeting that year on the global challenges of dementia, he cemented his advocacy for more investment. Following that meeting, the newly formed World Dementia Council worked with the UK's Department of Health and Social Care to devise a framework to tackle dementia more tangibly. The result was a partnership with the charity Alzheimer's Research UK and some of the world's largest pharmaceutical companies. Together, these organizations formed the initial investment in what became the DDF.

Today, SV Health Managers LLP manages the fund — a bid championed by Kate Bingham, a managing partner at the firm. With Bingham and SV at the helm, the fund raised an astonishing £250 million, with investments from an even more diverse group. The new investors include AARP, Quest, United Health, Bill Gates, and the NFL Players Association, among others. The key theme underlying each investment: people care about dementia and are looking for a cure.

To achieve success and help change the face of dementia therapeutics, the DDF requires a unique on-the-ground team. Made up of world-class neuroscientists and drug developers, the team at SV that staffs the DDF works each day to liaise with researchers, drug companies, and patients. These interactions help the team identify novel mechanisms in dementia and find cutting-edge therapeutic technologies to address them.

The diverse investor base — which contributes scientifically to the fund through regular advisory board meetings — and the expert team are the unique combination that the DDF hopes will deliver on its mission.

Daring to be different

From the start, the DDF took an innovative approach to funding new treatments. It chose to use the lack of clarity about the mechanisms that cause dementia to invest in groundbreaking science that is closely linked to aging and cognition. Many of these hypotheses have never been tested in patients.

Aging is critical because it breaks down our biological systems. Just as knees wear out, blood vessels become clogged, and cancerous cells form, the brain and cognition also change with age.

The DDF team identified four areas of interest that may be critical to brain aging and affect cognitive health:

- (Neuro)immunology (the brain-immune system connection);
- Trafficking of molecules in and around cell membranes (how cells stay healthy);
- Mitochondrial health (the neurons' energy source); and
- Brain synapses (how neurons talk to one another).

The team is also interested in exploring new ideas about how aging can contribute to cognition and dementia and is constantly on the lookout for exciting new science.

The DDF philosophy is that providing previously unavailable investments in these new areas of interest will help link the mechanisms that support brain health to therapies that can prevent or treat dementia.

Putting it into practice

When a scientist identifies a potential new mechanism to treat dementia, the team at the DDF reviews the scientific evidence that supports the theory. The team considers the likelihood that the new idea will work to treat dementia and whether the scientist or the company

behind the new mechanism has a good plan to make a potentially safe and effective drug for patients. Asking these questions helps the DDF team determine if an idea can succeed during the process called translational development, in which scientific discoveries move from the laboratory toward manufacturing a drug for human testing.

For a dementia therapy, the path out of translational development into repeated rounds of patient testing and through regulatory approval is long and requires more money and time than developing drugs for other diseases. This lengthy process increases the financial risk of developing a dementia treatment, which is why more investment is needed at this stage for dementia.

Managing risk

Once the DDF has helped a company bring forward a new drug candidate, the group hopes that other investors will join in to help move the drugs to the market.

It takes significant resources for a candidate drug to become a therapy that will reach patients, as it has many hurdles to overcome. However, because the DDF shares the cost of translational development, more companies should continue to invest resources to develop innovative dementia therapies.

The combination of SV's proven biotech investing with the DDF team's unique expertise brings together critical venture experience and scientific rigor. This union enables the team to make the investments others will not. The DDF is committed to making a difference to the patients and families who are so desperately waiting for relief from this cruel disease. ♦



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To learn more, please visit the DDF website at <http://theddfund.com>.

DDF is managed by SV Health Managers LLP, which is authorized and regulated by the Financial Conduct Authority.