

New model to further understand causes of Alzheimer's disease

March 9 2020



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Scientists from Cardiff University have brought together all known risk factors for Alzheimer's disease for the first time to produce a new model



of the disease which it is hoped will help speed up the discovery of new treatments.

The Multiplex Model is a new way of looking at Alzheimer's <u>disease</u> developed by Professor Julie Williams, Dr. Rebecca Sims and Dr. Matt Hill of the University's UK Dementia Research Institute (UKDRI) and unveiled in the journal *Nature Neuroscience*.

The <u>model</u> was produced by looking at all known <u>genetic risk factors</u> to further understanding of what triggers Alzheimer's and how it develops.

More than 50 risk genes have already been identified and this new theory uses these—and the impact of thousands of other genes—to create the most detailed look at the basis of the disease yet.

There are 850,000 people with dementia in the UK and Alzheimer's is the most common form. There is no cure for the disease, which causes problems with memory and thinking.

Professor Williams, director of the UKDRI at Cardiff, said: "The genetic breakthroughs we and other scientists have made over the past 20 years have shown us that Alzheimer's is a multi-component disease.

"The Multiplex Model assumes that changes to one or all of these components work together to form a disease cascade. In other words, we now know that Alzheimer's can be triggered by a number of different defects in the genetic make-up.

"By using this multi-faceted approach, we can pinpoint our research and work even faster towards developing new therapies."

Researchers are already able to predict those likely to get Alzheimer's with about 80% accuracy through looking at the combined effect of all



contributing genes. For those with highest genetic risk they can currently predict the likelihood in most cases.

The model of Alzheimer's used for the past 20 years—known as the amyloid hypothesis—has been limited to looking at one component of the disease, namely that plaques of amyloid protein form in the brain triggering dementia, but this approach has yet to yield new treatments that work.

This new model looks at the combined effects of many genes, along with a breakdown in <u>cellular processes</u> linked to Alzheimer's, such as abnormalities in the brain's immune response or differences in the way the brain processes cholesterol. It also considers environmental factors, such as ageing and vascular issues.

"Alzheimer's disease begins some 20 years before symptoms emerge," said Professor Williams, "and at the moment we just don't know what triggers it.

"This new approach allows us to look at all of the different factors and components involved—once we know more about exactly what is happening in the earliest stages of disease at a cellular and genetic level we can identify new targets for treatment and preventative therapies.

Bart De Strooper, director of the UKDRI, said: "We are proud of this great overview of the genetic basis of Alzheimer's disease from one of our world-leading teams in the UK Dementia Research Institute. The huge progress in understanding the complex genetics underlying this condition will greatly help us in deciphering the early disease phases, when treatment intervention is most likely to be effective.

"This further emphasises the need for a multi-angle, holistic approach to studying neurodegenerative disease. In order to make breakthroughs, we



will have to harness wide-ranging expertise from across the research field, ensuring new knowledge gained is brought together to provide a complete picture of the causes and drivers of dementia."

More information: Rebecca Sims et al. The multiplex model of the genetics of Alzheimer's disease, *Nature Neuroscience* (2020). <u>DOI:</u> <u>10.1038/s41593-020-0599-5</u>

Provided by Cardiff University

Citation: New model to further understand causes of Alzheimer's disease (2020, March 9) retrieved 11 May 2024 from <u>https://medicalxpress.com/news/2020-03-alzheimer-disease.html</u>

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