

How studying Alzheimer's in China could unlock its secrets

October 27 2017, by Nancy Ip

Alzheimer's disease (AD) is the most common form of dementia, affecting some 46 million people globally, and a leading cause of mortality in the elderly.

There are two major hurdles to overcome in developing effective treatments. First, our understanding of the disease pathology is still incomplete. Second, by the time an individual is diagnosed, the disease is already at an advanced stage where it is more difficult to treat. Meanwhile, recent studies indicate that genetic factors also contribute to disease risk with a heritability estimate of 60–80%, though these are not well defined.

To address these hurdles, my laboratory at the Hong Kong University of Science and Technology has taken a two-front offensive, aiming to:

1. Decipher the mechanisms underlying disease pathophysiology,
2. Determine the unique genetic contribution to AD in the Chinese population.

Research into novel mechanisms

One of our studies discovered that a cell surface protein EphA4, which regulates communication between nerve cells, is hyperactivated in the AD brain. By blocking this excess activity, we reversed the neuronal communication impairment in AD mice. What is more, we identified a

compound derived from a traditional Chinese medicine herb, with EphA4 inhibitory activity, as a potential drug candidate.

Another significant study revealed how modulating the immune response is beneficial in treating AD. The immune protein interleukin (IL)-33, found in the human body, functions as an alarm signal upon cellular damage. However, its action is compromised in individuals with mild cognitive impairment (those at increased risk of developing AD). When administered to AD mice, IL-33 significantly improved memory and reduced disease pathology, thus highlighting its significance as a potential treatment for AD.

My team is now working with strategic partners to translate both these findings into viable clinical treatments for humans.

Research into the genetics of AD

It is well established that early-onset AD, which accounts for less than 10% of all cases, is hereditary and caused by rare genetic mutations. Meanwhile, recent studies show that late-onset AD, the more frequent type of AD that predominantly affects the elderly, also has a genetic association. Late-onset AD, however, is not caused by specific gene mutations. Instead, certain genetic risk factors affect an individual's risk of developing the disease.

To date, several genes that contribute to AD have been identified. For example, mutations in amyloid precursor protein, presenilin 1 and presenilin 2 are associated with early-onset AD, while the $\epsilon 4$ allele of apolipoprotein E is a strong [genetic risk factor](#) for both early-onset and late-onset AD. Existing genetic studies, however, have been predominantly conducted in Caucasian populations. But genetic diversities exist among different ethnic groups. Good examples are the differences in hair, skin and eye colours, which are caused by specific

genetic variants.

To understand the genetic basis of AD in the Chinese population, my team recently conducted a large study in collaboration with clinicians in mainland China. With one of the fastest growing elderly populations, China is projected to have 22.5 million cases of Alzheimer's by 2050.

Our findings have confirmed known [genetic risk](#) factors (e.g. apolipoprotein E) for late-onset AD as well as unveiled new ones. Further characterization has revealed that the identified AD risk factors are associated with the immune system, thus shedding new light on [disease pathology](#).

The study marks one of the first comprehensive genetic analyses undertaken on the Chinese population and provides new insights into the disease. The ultimate goal of this work is to contribute to the global quest of understanding AD. Furthermore, given the looming epidemic, it is my hope that such studies will enable both early diagnosis as well as early intervention with novel therapies to prevent or slow the progression of the disease.

Provided by The Hong Kong University of Science and Technology

Citation: How studying Alzheimer's in China could unlock its secrets (2017, October 27)
retrieved 2 May 2024 from

<https://medicalxpress.com/news/2017-10-alzheimer-china-secrets.html>

<p>This document is subject to copyright. Apart from any fair dealing for the purpose of private study or research, no part may be reproduced without the written permission. The content is provided for information purposes only.</p>
--