World Alzheimer's Day, 21 September 2017
A focus on early diagnosis

Over the past six years, World Alzheimer's Day has sought to raise awareness of Alzheimer's disease, in addition to challenging the stigma that patients and their families and caregivers face as a result of the lack of understanding of dementia. This year, the focus of the World Alzheimer's Day campaign is the importance of early detection and diagnosis of dementia. Even though there is currently no cure for Alzheimer's disease, early diagnosis provides patients with the opportunity to access symptomatic treatments and prepare for the future impact of this progressive neurodegenerative condition, before neurodegeneration has progressed extensively.

As treatment strategies vary to some extent between patients with different types of dementia, diagnoses need to be early as well as accurate. A factor that may complicate the routine differential diagnosis of Alzheimer's disease and other dementias is the overlap of symptoms and pathologies between neurodegenerative diseases. For example, at least 50% of people with vascular dementia have some concurrent Alzheimer's disease pathology, and some patients with Alzheimer's disease have α-synuclein deposits, which are the pathological substrate of Parkinson's disease and dementia with Lewy bodies.

Currently, working diagnoses are made in the clinic using psychological assessments, supported by imaging scans when required. Biomarker measurement in cerebrospinal fluid (CSF) can provide diagnostic information, although CSF biomarkers are not always routinely used in practice because the procedure for CSF collection is invasive and variability in results can be high. Currently, a conclusive diagnosis of Alzheimer's disease can only be made by carrying out a post-mortem brain examination. There is a clear, unmet need for simple, inexpensive, non-invasive biomarker tests that identify patients at early stages of different types of dementia, so patients can be provided with optimal care strategies.

Biomarker information can also be used to elucidate disease mechanisms, which supports the development of new treatments. Many trials in Alzheimer's disease have failed to produce an effective drug that has been approved, and clinical, social and economic factors drive the continuing search for treatments and diagnostic tests. Alongside the impact on the patient and their family, providing treatments and care for people over the course of a progressive disorder such as Alzheimer's disease involves extensive use of clinical, caregiver and economic resources.

By 2015, global dementia care costs had soared to US$818 billion – a staggeringly high cost. This value is so high that it is frequently quoted alongside the market values of Apple (>US$800 billion) and Google (>US$600 billion), and compared with the economies of G20 countries, just to provide an appropriate context. It is currently estimated that over 46 million people across the globe are affected by dementia, and this figure is predicted to have almost trebled by 2050 because people are living longer and healthcare improvements are likely to continue to prolong the lives of patients. As the number of people with dementia increases, we can expect the associated costs and requirements for care resources to rise considerably too. Biomarkers have a key role to play in identifying patients with dementia (to allow effective planning and management of healthcare budgets and resources), and also in the development of new therapeutic targets.

So far in 2017, research has been published on potential dementia biomarkers ranging from antimicrobial proteins in saliva and inflammatory markers in blood, to observations from imaging studies of the eye and α-synuclein in skin nerve fibres. One study, published in the *Proceedings of the National Academy of Sciences*, has drawn media attention because it reported that it was possible to identify patients with Alzheimer's disease using a blood sample. Biomarker analysis of blood samples was carried out through vibrational spectroscopy, which provides a 'spectral fingerprint' of the molecules within the sample. The test was at least as specific and sensitive as currently used clinical and molecular methods, and was even able to distinguish between Alzheimer's disease and dementia with Lewy bodies. This method is not only rapid, cost-effective and relatively non-invasive, but also provides an overview of a wide range of molecular patterns in the samples. While providing data to support a diagnosis, if samples are also analysed in healthy people and in patients at different stages of dementia, this could provide data to elucidate the key mechanisms that take place at different stages of the neurodegenerative process. A better understanding of these mechanisms is a key initial step in drug development.

As the numbers of people with dementia and their healthcare costs continue to soar, strategies that can support both diagnostic and therapeutic advances will be of great importance in preparing for the years to come.

Molecular biomarkers

Psychological tests

Imaging

Diagnosis and symptomatic treatment

Drug development