

The best model of human disease is the human

Neurodegenerative diseases are debilitating incurable conditions that cause decline in movement, thinking and behaviour. Amyotrophic Lateral Sclerosis (ALS) accounts for up to 10,000 deaths in Europe and costs over €600 million each year in care. It occurs in midlife, mainly causing degeneration in motor pathways but also affecting thinking and behaviour. In the Academic Unit of Neurology, we have worked on ALS for the past 25 years, identifying different subtypes with various degrees of cognitive and behavioural change, and showing a link between ALS and schizophrenia. Finding that genetic factors account for about half of the risk of developing ALS, we helped discover many new genes for ALS. Two, SOD1 and C9orf72, are the target of a precision medicine-based approach toward therapy. Our early-phase gene therapy studies of C9orf72 look promising.

However, for the forms of ALS with no established genomic basis, clinical trials of

over 70 compounds have failed to demonstrate benefit despite successes in animal models.

“Our goal is to find the right drug for the right patient in the right dose, at the right time.”

Professor Orla Hardiman

Professor of Neurology, Consultant Neurologist and Leader, ALS/MND Clinical and Research Group

We adopted a new perspective. We shifted our focus from laboratory-based work to applied clinical research in patients (<https://rmn.ie/>). We study patients as individuals – their genetic makeup, key biomarkers, prior treatment, family history, environmental factors and behaviour – as these all affect how diseases progress. This in turn influences design and testing of new treatments. Within the European consortium TRICALS (www.tricals.com)

we combine insights from epidemiology, clinical assessment, family history studies, imaging, neuro-electric-signalling, genomic and biomarker datasets to investigate the causes and progression of ALS, and develop better treatments.

We focus on human disease in humans with the same scientific rigour that was applied to laboratory work and animal modelling. With colleagues at the ADAPT Centre and internationally, we process clinical data at scale, aiming to build a unique multimodal assessment of the disease for each individual and so create more effective treatments.

