International Progressive MS Alliance identifies targets for future research

INTERNATIONAL
PROGRESSIVE MS ALLIANCE
CONNECT TO END PROGRESSIVE MS

The International Progressive MS Alliance is a growing global initiative to end progressive MS. MS Research Australia, along with MS organisations from around the world, have joined the Alliance, and play an active role in its management. The Alliance encourages collaborative international research to accelerate breakthroughs for the treatment of progressive MS. The Alliance has, to date, run two major grant schemes designed to fast-track the transformation of knowledge into solutions for people with MS.

In March 2015, the Alliance bought international MS researchers, industry representatives and scientists from other disease fields together in Boston. The aim was to discuss the current state of knowledge in progressive MS and determine how the translation of this knowledge into treatments for progressive MS can be accelerated despite there still remaining gaps in our understanding. As a result, several of the world's leading MS researchers have condensed the main findings of the meeting into a summary paper, published recently in the *Multiple Sclerosis Journal*.

This paper provides insight into the innovative work that is happening all over the world to further our understanding of the causes of progressive MS, current drugs being trialled and their mechanisms of action. Importantly it also summarises how we might learn from the drug development techniques being used in other diseases to explore new treatment options for progressive MS.

The biology of progressive MS and the cells involved
A great deal of knowledge has accumulated on a range of biological mechanisms and cells that may play a significant role in progressive MS. B cells of the immune system, as well as astrocytes and microglia (which both have inflammatory and support roles in the brain) are all key players in progressive MS. Energy production by mitochondria in the cells of the brain, as well as the barriers and enhancers for myelin repair are also under intensive investigation. While these areas of research have been separately developed and investigated, the focus for the Alliance and MS researchers now will be to prioritise these for the most relevance and 'druggability' to speed the translation of this knowledge into treatments.

Drug screening offers promise for identifying new potential treatments
High-throughput drug screening involves using specialised software that can screen large numbers (100,000+) of molecules at a time, to identify potential new drug compounds. This method has already been used to identify several compounds such as benztropine, which has since been found to enhance remyelination in animal models of MS.

The future use of cells to enhance accuracy of drug screening
Researchers are investigating whether normal adult cells taken from people with MS can be re-programmed into the earliest type of stem cell, and grown in the laboratory into different types of nerve and brain cells. With further research, there is potential that these cells could then be used to rapidly screen the effectiveness of large panels of potential drugs for inducing myelin growth and repair.

Accurate animal models of progressive MS are urgently needed
The most widely used mouse model of relapsing MS, known as EAE, does not accurately reflect the features of progressive MS. New models need to be developed that better reflect the progressive disease state. One model being used involves the use of a compound called cuprizone to cause demyelination and mimics the effects of progressive MS. It has already helped to support the idea that long-term inflammation can trigger neurodegenerative processes that then progress beyond the period in which inflammation is active.

Innovative methods for maximising available data
Network Biology is a new concept developed in other disease models which involves using large databases or 'maps' containing information on the functions and interactions between genes, molecules, and cells. This allows virtual experiments to replicate the real-life state, in order to test very early and novel hypotheses in the lab before they are applied to animals or humans. Importantly, information from the mass drug screening approaches mentioned above will also be able to be overlayed into these computational models to accelerate the identification of suitable drug candidates.

Collaborating for progress
This meeting pulled together the many complex facets of progressive MS and highlighted that a solution is unlikely to be discovered without a concerted, worldwide effort. Catalysing this collaborative and integrated approach is the goal of the Progressive MS Alliance. The result of these efforts will be the accelerated identification of the critical pathways that will lead to new therapies for the estimated one million people who live with a progressive form of MS.