SHMF MND Research Update

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Profilin' the genes behind MND

An international research team have uncovered a new MND gene called *Profilin 1* that plays a role in some people with family history of MND. *Profilin 1* is involved in building scaffolds and structural networks inside nerve cells that give them their characteristic shape and enable them to haul cargoes along distances up to 1 metre in people.

An old and new player in MND?

Using next generation DNA sequencing technology, the researchers identified mistakes in the *Profilin 1* gene in Caucasian and Jewish families affected by MND. The mistakes occur in a region of the gene involved in binding actin protein - the equivalent of bricks in nerve cells - and necessary to build scaffolds. *Profilin 1* acts to cement actin together forming long chains and networks. Mistakes in *Profilin 1* prevent nerve cells from branching out, effectively stunting the growth of motor neurones.

This is not the first time that *Profilin 1* is linked to disease, however. Profilin 1 forms a partnership with *survival motor neuron* protein in nerve cells. *Survival motor neuron* is linked to the childhood disease spinal muscular atrophy, providing important links between *Profilin 1* and motor neurone defects.

Although *Profilin 1* is a very rare cause of MND (estimated at 0.1-0.2% of cases), it adds to a growing list of genes involved in building and maintaining scaffolds inside nerve cells and presents an important target for genetic diagnosis.

Further reading: Wu *et al.* (2012) *Nature* vol 488, pages 499-503.

Correcting TDP-43 misbehaviour

TDP-43 is the major culprit protein in MND where it forms deposits resembling junk piles in sick motor neurones. The reason why *TDP-43* goes rogue in MND is a mystery and may offer important clues to new treatment angles.

Researchers from the USA used a genetic screen in bakers yeast, a simple laboratory organism, to find molecules that block *TDP-43* accumulation. Yeast are ideal for such screens, because they have fewer genes (6,000) than humans (23,000) and can be rapidly screened in days. Among 2,000 hits, they identified a gene called *DBR1* that strongly blocked *TDP-43* accumulation. Excitingly, *DBR1* also blocked accumulation of a second rogue protein implicated in MND called *FUS*. Importantly, they confirmed the protective effect of *DBR1* in nerve cells. *DBR1* belongs to a family of molecules involves in gene splicing and may help soak up rogue *TDP-43* in motor neurones as its normal function. Blocking *DBR1* and similar genes may offer a new strategy for targeting abnormal *TDP-43* in MND and results from animal models are keenly awaited.

Further reading: Armakola *et al.* (2012) *Nature Genetics*, *in press.*

Help now and donate

Profilin 1 and *DBR1* are new exciting players in the MND field, but there is much work ahead in translating these findings into strategies that will enhance diagnosis, management or treatment of MND. Funds raised by the *Susie Harris Memorial Fund* will contribute directly to this global MND research effort. Please donate now.