Dr Luke McAlary; Post-Doctoral Fellow, University of Wollongong, New South Wales

Dr McAlary and his lab focus on molecular causes of disease, understanding how they happen in a cell and how they can be treated. In this presentation Dr McAlary discussed why his team focus their research specifically on superoxide dismutase 1 (SOD1) MND and outlined their studies in drug screening at a cellular level. Below is a synopsis of the presentation. You can listen to the recording here.

A combination treatment for SOD1-associated MND

Features of SOD1 include:

- First known genetic cause of ALS/MND
- When mutated it results in pure ALS phenotype
- Contains copper and zinc
- Over 160 possible types of mutation that are associated with MND and can destabilise this protein

Dr McAlary explained how MND is associated with protein aggregation and why preventing protein aggregation or prompting proper folding may slow disease progression. Luke discussed how folding occurs in the formation of SOD1 protein and how small molecule drugs may help improve the folding of SOD1.

Dr McAlary's discussed the CuATSM drug trial happening in Australia. CuATSM surrounds copper and deliveries copper to Central Nervous System which can help promote copper input into SOD1. Dr McAlary has worked on a project using a compond Ebselen which can promote formation of disulphate bond in the protein. Both these compounds have been found to help stabilise the effects of SOD1 protein.

Dr McAlary has completed drug screening at a cellular level for SOD1 examining the combination of CuATSM and Ebselen. The combination of these compounds appears to be

beneficial in a cell model of MND, enhancing performance and increasing stabilisation of protein for some of the main SOD1 mutations.

CuATSM works on mutations that can bind copper however it is less effective if a SOD1 mutation is not able to bind the copper. Similar Ebselen is not as effective on some SOD1 mutations. It is therefore important to understand the underlying cause of the disease e.g., through genetic testing.

Once out of lockdown the team want to complete further research in CuATSM and Ebselen moving it from cellular testing to animals and examine other compounds including Zinc in their formulation. Further testing is required, to determine if this model could also be applied to TDP and FUS proteins.