Scientists gain insight into the cause and possible treatment of motor neurone disease

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BBSRC-funded researchers at UCL along with collaborators at King's College London have identified a molecule that could be the key to understanding the cause of neurodegenerative diseases such as motor neurone disease (MND). This insight opens up the possibilities for developing new treatments to treat these devastating progressive conditions. The research is published today (17 November 2008) in the *Proceedings of the National Academy of Sciences* (*PNAS*) and is funded by BBSRC (Biotechnology and Biological Sciences Research Council) with the Medical Research Council and the Wellcome Trust.

Lead researcher Professor Patricia Salinas said: "For decades we have been studying how nerves communicate with their target muscles and we know that in diseases like MND the sites of contact between nerves and muscles become weak. However, many mysteries remain as to how these contacts form under normal circumstances and therefore it has been very difficult to see what has gone wrong in MND. The work we are publishing today puts another important piece of the puzzle in place and offers up a new possibility for developing drugs to treat MND and other neurodegenerative diseases."

Professor Salinas, with her husband Dr Simon Hughes – a researcher at King's College London – has found that a signalling molecule called Wnt3 plays a crucial role in creating the connections, or synapses, between nerves and the muscles they control. It does this by assisting another molecule called Agrin, which coordinates construction of the synapse and organises the elements that make up the connection.

Professor Salinas continued: "Without properly formed synapses the muscle cannot receive the nerve signal that tells it to contract and hence we see the muscle weakness that is classic in MND. If we can build up a thorough picture to show how synapses are normally formed between nerves and muscles we can start to look for any elements that aren't working properly in people with MND. This might also lead to strategies for nerve repair after an injury."

The team of researchers have looked at the function of Wnt signals in chickens, mice and in cells and in all three cases it was shown to enhance the effectiveness of Agrin.

Professor Salinas added: "Chickens that don't have the Wnt signal in their developing wings have all of the muscle tissue that we would expect to see, but they don't make strong connections between nerves and muscles. So we know that Wnt is definitely affecting synapse formation rather than anything else to do with muscles. Now that we understand the role Wnt plays we can begin to explore any role it plays in MND and whether it could be a good target for treating this type of neurodegenerative disease."

Professor Janet Allen, BBSRC Director of Research said: "We are delighted to see that work funded by BBSRC is making an impact on the understanding of serious conditions like MND. When scientists ask questions about normal biological processes they are often doing work that underpins better health and well being for people in the future."

Dr Belinda Cupid, Research Manager, MND Association, said: "We know from recent research that signs of motor neurone damage, on a cellular level, in models of MND occur very much earlier than the symptoms appear, so any new knowledge of how healthy motor neurones and muscles interact will give us new clues about what might be going wrong in those people affected by this cruel disease."

Source: Biotechnology and Biological Sciences Research Council