AGM2017: Current HSP Research - Prof Andrew Crosby

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Professor Andrew Crosby gave a presentation on current HSP research.

He began by giving an overview of some of the HSP characteristics. HSP is described as being "heterogeneous" - but what does this mean? Simply, it means "variable", genetically in this context. There are 73 different HSP genes identified, of which about 40 have been confirmed in follow up studies covering several families. Prof Crosby speculates that there will be hundreds of HSP genes in the end. There is also variability within one variation - he mentioned Silver Syndrome (also known as SPG17, which inherits dominantly) which he described as HSP plus hand muscle wasting. First symptoms are usually observed in teenagers. One example mentioned had a parent who was normal at 48, but it is not known why.

Background information: Our genes are responsible for producing proteins which have jobs to do in our body. The proteins are made from the DNA in our genes, although they have to go through several steps to do this. Should a gene be faulty there may be a problem with the proteins that are produced. Neurological conditions are often referred to as "upper" where the brain and/or spinal cord are affected, or "lower" when the nerves between the spine and the muscles are affected. Some motor neuron diseases may affect the upper, lower or both sections. HSP is a motor neuron disease.

By considering all motor neuron diseases together provides a bigger family of conditions and knowledge of one genetic alteration may help all motor neuron diseases, and the more confident researchers can be of finding a genetic route for changes.

Prof Crosby described the Amish community, who live in the Pennsylvania and Ohio/Indiana areas of the USA. They originated from the Swiss/German borders and two waves of migration happened, in 1737 and 1815. The Amish population keep good genealogical records and tend to marry within the existing communities. There are 4 types of HSP in the Amish which are not found elsewhere. Given the records they can trace the current population back to the original migrants, and one person out of a couple carried a recessive form of HSP. SPG20 is one of the types found in the Amish. In this type one C in the DNA becomes an A, the result of which is that no protein is made.

There are 13 HSP genes which are known to feature in at least one other condition. Drugs for other conditions with similar nerve problems could be looked at for treatment trials.

The work that Prof Crosby is doing at Exeter is to try to develop a blood test for HSP. Such a test may be able to prevent other clinical tests being done. If a test can identify a gene which is different then this can give information on: what has gone wrong, opportunities to improve the molecule, and help to develop a treatment.

Although HSP is a neurological condition there is a biochemical process. In order to develop a blood test it is a question of identifying the pathways that are affected. Such a blood test would look for biochemical signals and, if successful, may be able to test whether people might develop HSP.

The issue with genetic testing is that some parts of DNA are more susceptible to change than other parts. Genetic tests on two people with the same genetic mutation would not, for example, prove that they are related to each other (they may be related some generations back). Tests will show a number of changes, but it is not always clear which change gives rise to HSP. With analysis of family trees this can help, and if a genetic change is identified to cause HSP with certainty, then this can be added to an HSP panel test.

The Caucasian population has been studied more than other populations and so there is more certainty on which genes cause which conditions. Genetic tests from people from other backgrounds are more difficult to interpret as there is less data available.