Embargo until 2.15pm BST on Monday 17th June

Professor Veronica Kinsler and her researchers at the Francis Crick Institute and Great Ormond Street Institute of Child Health have published an article in the Investigate Dermatology Medical Journal detailing a huge breakthrough in their CMN research work.

Professor Veronica Kinsler and her CMN research team have silenced a gene called NRAS in cells in a dish and in mice. NRAS has been found to be one of several genetic mutations which can cause Congenital Melanocytic Naevus (CMN). RAS proteins are a group of proteins that regulate the normal processes of cell division and cell death (known as apoptosis). One such protein, NRAS, is manufactured by the body using the instructions found in the NRAS gene.

Normally, the NRAS protein is turned on to cause cell division and then turned off again. However, when a particular mutation occurs in the NRAS gene, the faulty NRAS protein remains turned on, causing uncontrolled cell division. It is this uncontrolled cell division which can lead to the development of benign lesions such as those seen in CMN, which can predispose those affected to developing malignant melanoma. In a person with CMN caused by the NRAS gene, all the cells in their naevi will contain the faulty NRAS gene, whereas the cells in unaffected skin will have a normal NRAS gene.

The proteins involved in cell management rely on multiple levels of a pathway or process. Inhibitors can be used to interfere with a faulty cell pathway. Melanoma, or other cancers, linked to an RAS/NRAS mutation have been difficult to target using pathway inhibitors. For example, a MEK pathway inhibitor has been used in clinical trials, proving to reduce nodules and itch in CMN, but not offering an option for melanoma. CMN occurring as a result of an NRAS mutation is currently untreatable and whenever melanoma does occur within CMN it is highly aggressive.

ARL6IP1 is a protein that plays a significant role in the stabilisation of cell processes by suppressing the death of certain cells. This protein has not previously been linked to NRAS. Professor Kinsler and her research team have found that a small interfering RNA (siRNA) molecule, targeted at CMN-affected cells, interferes with the expression of ARL6IP1 thereby allowing a cascade of cell death, which is normally suppressed, and thus a reduction in the CMN-affected cells.

Using RNA targeting of the RAS pathway, cells which are 'out of control' leading to cancers such as melanoma have been destroyed with a single dose. This is all happening at a cellular level and involves intricate cell work. The therapy was delivered through injections carrying special particles directly to the CMN cells in mice with CMN, this silenced the NRAS gene after just 48 hours. They also tested it in cells and whole skin sections from children with CMN. Importantly, silencing the gene triggered the CMN cells to self-destruct.

This approach could therefore form the basis for clinical trials to determine whether siRNA could be used to treat CMN caused by the NRAS mutation, and to reduce the risk of melanoma. This means that in the future the treatment could potentially be used to reverse the giant moles, and therefore reduce the risk of affected children and adults from developing cancer. It could also potentially reverse other commoner types of at-risk moles as an alternative to surgery.