Tumor mechanism identified

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Researchers from the Peninsula Medical School in Plymouth (UK), the Memorial Sloan-Kettering Cancer Center in New York, Cornell University in New York, Weil Medical College in New York and the Center for Neural Tumour Research in Los Angeles, have for the first time identified a key mechanism that makes certain cells become tumorous in the brain. The resulting tumours occur most often spontaneously but can also occur in numbers as part of the inherited disease Neurofibromatosis type 2.

The research is published in the highly respected journal, *Cell*.

The tumours are caused by mutations affecting a protein called Merlin, which in turn causes cancers in a range of cell types including Schwann cells. Schwann cells produce the sheaths that surround and insulate neurons.

The new research investigates for the first time the role of Merlin in the cell nucleus. It explains how Merlin regulates cell proliferation, and how it regulates gene expression. Normally Merlin inhibits the development of tumours at a cell nucleus level - mutations affecting Merlin affect its ability to inhibit. By understanding this mechanism for the first time, the way is open for the development of effective therapies for a condition in which no treatment other than surgery exists.

In neurofibromatosis 2 the sheer number of the tumours can overwhelm a patient, often leading to severe disability and eventually death. Patients can suffer from 20 to 30 tumours at any one time, and the condition

typically affects older children and young adults.

No therapy, other than invasive (radio)surgery aiming at a single tumour and which may not eradicate the full extent of the tumours, exists.

The condition of multiple tumours , neurofibromatosis type two (NF2), affects one in every 2,500 people worldwide. It can affect any family, regardless of past history, through gene mutation and currently there is no cure.

Professor Oliver Hanemann, who led the research from the Peninsula Medical School, commented: "This has been an exciting collaboration with colleagues in the United States resulting in a landmark publication. Until now, there has been no meaningful work on the role of Merlin in the nucleus. The results of our research show a greater understanding of the fundamental part played by Merlin in the repression of tumorous cells, and how this part is undermined when the protein is mutated. Identification of the difference in mechanisms will allow us to develop therapies for the future."

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