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Research links huntingtin to neurogenesis

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New research finds that a protein that is often mutated in Huntington's disease (HD) plays an unexpected role in the process of neurogenesis. The research, published by Cell Press in the August 12 issue of the journal *Neuron*, provides new insight into HD pathology and has even broader implications for human health and disease.

HD is an inherited neurodegenerative disease that causes uncontrolled movements, emotional disturbances, and severe mental deterioration. Previous research has demonstrated that abnormal huntingtin protein (htt) is associated with HD pathology. "Given the predominant neurological signs and striking neuronal death in HD, most studies on htt function have focused on adult neurons," explains senior study author, Dr. Sandrine Humbert from the Institut Curie in Orsay, France. "However, although htt is not restricted to differentiated neurons and is found at high levels in dividing cells, no studies have investigated a possible role for htt during cell division."

Cell division, known as mitosis, is the process where a single cell divides into two new but identical daughter cells. It is a complex and highly regulated sequence of events that occurs in a series of well-defined stages. One key step of mitosis involves the assembly and orientation of a structure called the "mitotic spindle." During mitosis, the proteins dynein and dynactin must interact with the spindle. Because htt is known to facilitate dynein/dynactin activity, Dr. Humbert's group investigated whether htt played a functional role during mitosis.

The researchers discovered that htt was specifically localized to the

mitotic spindle during mitosis in mouse neurons and that htt was required for recruitment of dynein/dynactin to the spindle. Importantly, interference with htt led to misorientation of the spindle in both mice and flies. The researchers went on to show that htt was critical for both mitosis and cell fate determination. "Our findings demonstrate a previously unknown function for htt protein and open new lines of investigation for elucidating the pathogenic mechanisms in HD," concludes Dr. Humbert. "Our work also identifies htt as a crucial part of spindle orientation and neurogenesis."

Provided by Cell Press