New method for identifying most aggressive childhood cancers

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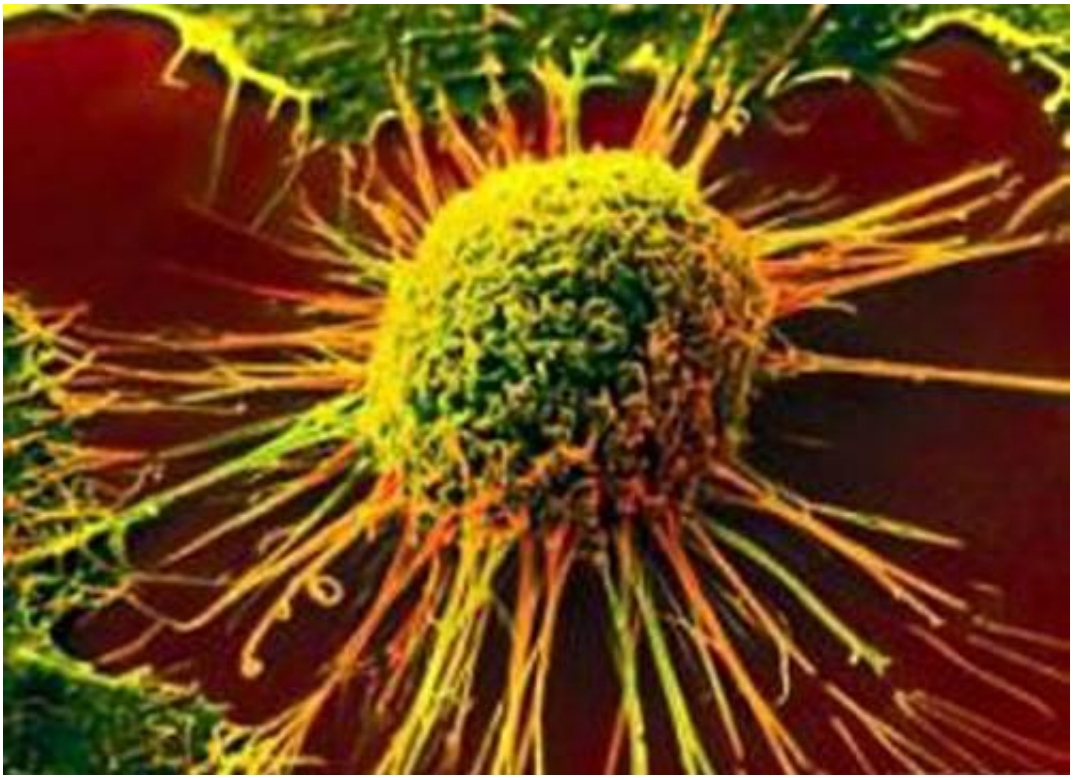

A research group at Lund University in Sweden has found a new way to identify the most malignant tumours in children. The method involves studying genetic 'micro-variation', rather than the presence of individual mutations.

In adult cancers, the tumour cells are more genetically variable than healthy cells. When a cancerous cell divides, the chromosomes often end up in the wrong place, or break and combine in incorrect ways. However, it has been unclear whether this is also the case in childhood cancers, and whether variability in the tumour DNA is linked to the severity of the cancer.

"We have now been able to confirm that both of these are the case. Tumours in children are also genetically unstable, and the greater the variation between the cells, the more malignant the cancer", said David Gisselsson Nord, a researcher in clinical genetics at Lund University.

Dr Gisselsson Nord and his colleagues Linda Holmqvist Mengelbier and Jenny Karlsson have studied 44 cases of Wilms' tumour, the most common type of kidney cancer in children. All 44 patients had been treated with chemotherapy and most recovered, but a few developed metastases and died. The latter patients were those whose cancers demonstrated the greatest variation between cells.

The Lund researchers' study explains why for many forms of childhood cancer it has been difficult to predict which patients have the highest risk of the cancer reoccurrence. Despite much searching, very few markers have been found in childhood kidney cancer that can differentiate between aggressive and less dangerous cancers.

"The reason for this is that researchers have been looking for certain characteristics, such as mutations, in a single sample from each patient. However, when there is so much variation between the cells, one sample is not enough to determine the properties of the tumour", said Dr Gisselsson Nord.

Thankfully for patients, taking many samples from each tumour is not the only solution. The present study shows that it is sufficient to study

'micro-variation' (the degree of genetic variation between the cells) within a millimetre-sized sample. This type of genetic variation appears to form a foundation for the larger changes that in the long run cause the cancer to return and spread.

"The micro-variation is a much better predictor of the risk of metastasis and death than the presence of individual mutations. This is an entirely new way of assessing how dangerous a tumour is", explained David Gisselsson Nord.

The research findings have been published in the renowned journal *Nature Communications*. The researchers now hope to move on to a larger study of all new cases of kidney cancer in children in Europe over the next five years. If the results bear out, the degree of genetic variation in tumour cells could become the marker used to determine the strength of treatment required to save the child's life.

More information: "Intratumoral genome diversity parallels progression and predicts outcome in pediatric cancer." *Nature Communications*, www.nature.com/ncomms/2015/150 … full/ncomms7125.html

Provided by Lund University