Biomarker associated with poor outcome in aggressive childhood cancer

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Results from a new study identify a biomarker that may be useful for predicting the outcome of treatment for neuroblastoma, the most common cancer in young children. The research, published by Cell Press in the April 7th issue of the journal *Cancer Cell*, also provides new information about the molecular signals that are involved in the progression of this often devastating pediatric cancer.

Retinoic acid (RA) is a metabolite of Vitamin A that has important influences over the processes of growth and differentiation. RA mediates gene expression by interacting with retinoic acid receptors (RARs) that, in the presence of RA, switch from repressing target genes to activating them. Because many targets of RA induce differentiation or cell death, RA is used as a therapeutic agent in many cancers, including neuroblastoma.

"Many neuroblastoma patients exhibit aggressive tumors with poor clinical outcome," explains senior study author Dr. Rene Bernards from The Netherlands Cancer Institute. "While some of these aggressive tumors exhibit increased expression of the MYCN oncogene, little is known about the other genetic factors that control neuroblastoma progression." Dr. Bernards and colleagues performed a genome-wide RNA interference screen to search for additional components of the RA signaling pathway that might be linked to neuroblastoma.

The researchers identified ZNF423 as a critical cofactor of RA-induced differentiation. Reduced expression of ZNF423 was led to a growth

advantage and resistance to RA differentiation in neuroblastoma cells while increased expression of ZNF423 led to growth inhibition and enhanced differentiation. The researchers went on to show that ZNF423 interacts with the RAR?/RXR? nuclear receptor that is necessary for activation in response to retinoids.

Importantly, low expression levels of ZNF423 were associated with poor disease outcome in neuroblastoma patients, suggesting that the gene might be useful as a prognostic biomarker. "Expression levels of ZNF423 could significantly affect responses to both endogenous and pharmacological concentrations of RA in cancer patients, which may in turn influence the outcome of neuroblastoma," offers Dr. Bernards. "Therefore, ZNF423 may be a useful biomarker for predicting responses to RA-based therapies, which are increasingly being used to treat neuroblastoma."

Source: Cell Press (news : web)