

Combination therapy shows promise in fighting neuroblastoma

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A study by a multidisciplinary team of researchers from The Saban Research Institute of Children's Hospital Los Angeles sheds further light on the role of the cytokine TGF β 1 in the growth of neuroblastoma, and suggests the possibility for a small molecule drug/antibody combinatorial therapy to treat this cancer. Their data has been published online by the journal *Clinical Cancer Research*.

Neuroblastoma (NB) is a type of solid cancer that arises from nerve tissues. It is the most common type of childhood cancer with nearly half of its incidence in children under two years of age and accounts for 15 percent of all [childhood cancer](#) deaths. Currently available therapy involves the use of an antibody called dinutuximab which targets a type of modified carbohydrate sugar (GD2) found to be expressed at high levels in NB tumors. However, this antibody-based treatment is often not sufficient to prevent cancer relapse.

In addition to directly targeting molecules involved in disease, in many cases antibody-based therapy is thought to also involve the activation of natural killer (NK) cells. NK cells are a subset of immune cells that have a proven capacity to kill tumor cells upon activation by antibodies. Proteins such as TGF β 1 (transforming growth factor beta 1) have recently been shown to suppress the anti-cancer functions of NK cells in the tumor microenvironment.

TGF β 1, part of the superfamily of cytokines, is a secreted protein that performs many cellular functions including control of cell growth,

proliferation, and cell death. The CHLA researchers demonstrate a unique mechanism for tackling NB by employing a combinatorial therapy involving dinutuximab and a small molecule drug, galunisertib, which inhibits TGF β 1. Grafting NB cell lines or tissue from a patient with neuroblastoma into immunodeficient mice, the authors demonstrate that galunisertib-mediated inhibition of TGF β 1 allows dinutuximab and NK cells to effectively kill the NB tumors.

"The addition of galunisertib to adoptive cell therapy using [natural killer cells](#) in addition to the drug dinutuximab reduced tumor growth and increased the survival of mice injected with either neuroblastoma cell lines or patient-derived tumor tissue," said principal investigator Robert Seeger, MD, of CHLA's Center for Childhood Cancer and Blood Disease. Seeger is also a professor of pediatrics with the Keck School of Medicine of the University of Southern California (USC). He added that galunisertib reverses the TGF β -1-induced suppression of cytotoxicity and may improve antibody-based immunotherapy for neuroblastoma.

More information: R. C. Seeger et al, TGF R1 Blockade with Galunisertib (LY2157299) Enhances Anti-Neuroblastoma Activity of Anti-GD2 Antibody Dinutuximab (ch14.18) with Natural Killer Cells, *Clinical Cancer Research* (2016). [DOI: 10.1158/1078-0432.CCR-16-1743](#)

Provided by Children's Hospital Los Angeles

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