

Research finds new Rx target for childhood cancer

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Research led by Michael Lan, Ph.D., Professor of Pediatrics and Genetics at LSU Health New Orleans School of Medicine, found that a compound named 5'-iodotubercidin (5'-IT) suppresses the growth of neuroblastoma cells and identified a potential new therapeutic approach for the disease. The paper, currently available online [here](#), will be

published in the April 12, 2019, issue of the *Journal of Biological Chemistry*.

Neuroblastoma is the most common non-brain solid tumor in children. It is a cancer of neuroendocrine cells—cells that have characteristics of both nerve cells and hormone-producing cells. Neuroblastomas start in immature nerve cells, called neuroblasts, of the sympathetic nervous system. They form when there are abnormal changes in the genes controlling the development of these young cells into specialized cells. While some neuroblastomas resolve on their own, others can be fatal. The objective of the research was to find a new drug for the treatment of aggressive neuroblastoma tumors.

Dr. Lan's laboratory studies a DNA-binding protein, INSM1, made from the gene that regulates the development of immature or undifferentiated neuroendocrine [cells](#). INSM1 is activated by another protein called N-Myc, and both are overproduced in neuroblastoma.

"Too much N-Myc occurs in roughly 30% of neuroblastoma tumors and strongly correlates with advanced-stage disease and poor outcome," Lan notes. "INSM1 has emerged as a critical factor in neuroblastoma cell growth."

The researchers were looking for a compound that would suppress excessive INSM1 and discovered that 5'-IT inhibits INSM1 protein expression and also affects cellular signaling molecules leading to neuroblastoma cell death.

"Taken together, we developed a unique INSM1 promoter-driven reporter assay to identify drugs that specifically inhibit INSM1 promoter activity," concludes Lan. "The identification of new signaling pathways that control the proliferation of aggressive neuroblastoma suggests new options for combination therapy of neuroblastoma patients."

According to the American Cancer Society, neuroblastoma accounts for about 6% of all cancers in children. There are about 800 new cases of neuroblastoma each year in the United States. The average age of children when they are diagnosed is about 1 to 2 years. In rare cases, [neuroblastoma](#) is detected by ultrasound even before birth. Nearly 90% of cases are diagnosed by age 5. In about two of three cases, the disease has already spread to the lymph nodes or to other parts of the body when it is diagnosed.

More information: Chiachen Chen et al, 5'-Iodotubercidin represses insulinoma-associated-1 expression, decreases cAMP levels, and suppresses human neuroblastoma cell growth, *Journal of Biological Chemistry* (2019). [DOI: 10.1074/jbc.RA118.006761](https://doi.org/10.1074/jbc.RA118.006761)

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