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Study suggests way to attack deadly, untreatable nerve tumors

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Scientists Shrink MPNSTs After Cracking Their Genetic Code.

Singapore- Genomic profiling of mostly untreatable and deadly nerve sheath tumors led scientists to test a possible therapeutic strategy that inhibited tumor growth in lab tests on human tumor cells and mouse models, according to research in the journal Cancer Cell.

When the international team of researchers analyzed complete screens of genes and genetic material in malignant peripheral nerve sheath tumors (MPNSTs), it revealed previously unknown genetic information about the disease.

"This uncovered potential therapeutic targets we did not expect for these untreatable tumors, but our findings also need further study before knowing whether they will be relevant to patient treatment in the clinic," said Q. Richard Lu, PhD, lead author and scientific director of the Brain Tumor Center at the Cincinnati Children's Cancer and Blood Diseases Institute.

Researchers show a gene called *Lats1/2* suppresses cancer, and losing the gene's expression reprograms cells so they rapidly expand and become cancerous. Loss of *Lats1/2* also causes other genes in the HIPPO signaling pathway (which controls tissue growth) to become hyperactive. These hyperactive genes and their associated proteins (TAZ and YAP) then work with the protein TEAD1 to activate molecular cancer programs that form MPNSTs.

In their future work, Lu and his colleagues want to identify small-molecule agents that will inhibit TAZ-YAP and the downstream cancer programs they activate, he said. The researchers also need to identify druggable locations on the surface of MPNST cells or HIPPO signaling cascade inside cells. This would allow small molecular inhibitors to attach to and attack the tumor cells.

The study's first author is Lai Man Natalie Wu, PhD, a research fellow in Lu's laboratory. The research also is a collaboration between multiple scientists at Cincinnati Children's and University Hospital in Dusseldorf, Germany, the German Cancer Consortium and German Cancer Research Center in Heidelberg, the Washington University School of Medicine in St. Louis, the MD Anderson Cancer Center in Houston, the University of Texas Southwestern Medical Center in Dallas, the Harvard Medical Schoolin Boston.

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