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Tumor suppressor gene in flies may provide insights for human brain tumors

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In the fruit fly's developing brain, stem cells called neuroblasts normally divide to create one self-renewing neuroblast and one cell that has a different fate. But neuroblast growth can sometimes spin out of control and become a brain tumor.

Researchers at Duke-NUS Graduate Medical School in Singapore have found a tumor-suppressing protein in the fly's brain, with a counterpart in mammals, that can apparently prevent brain tumors from forming.

"Our data explicitly show that the fruitfly protein PP2A (protein phosphatase 2A) suppresses brain tumor formation and controls the balance of self-renewal and differentiation of neural stem cells," said Hongyan Wang, Ph.D, assistant professor of neuroscience and behavioral disorders, and senior author of a paper published online in the journal *Development*.

"Given that mechanisms for stem cell division in flies and mammals are likely to be similar, our study on fly PP2A may provide useful insights for certain types of human brain tumors and possibly in a wide variety of cancers," Wang said.

By studying flies that had a PP2A mutation, the researchers learned that flies with missing or abnormally expressed PP2A had ten times the amount of stem cell growth in their larval brains. The flies' neural stem cells did not become neurons (nerve cells) in the brain, the types of cells needed for normal function. Instead, they effectively grew into a tumor

mass.

Dr. Wang's previous work had identified a protein kinase called Polo as a tumor suppressor. Because phosphatases like PP2A usually have the opposite biochemical function to kinase, the scientists predicted that PP2A would stop the tumor suppressor Polo and allow for unchecked cell growth. "We were very surprised when we found that PP2A also suppressed tumors," Wang said.

Follow-up experiments showed that PP2A is important for regulating Polo kinase function, and showed that these two critical brain tumor suppressors work together to control neural stem cell divisions.

"Our discovery suggests that PP2A and Polo, both of which are crucial brain tumor-suppressors and cell cycle regulators, can function in the same pathway to regulate stem cell self-renewal and tumor development," Wang said. The research team plans to uncover novel proteins in this pathway by learning which protein functions between PP2A and Polo during the neural stem cell division process.

Source: Duke University Medical Center (news : web)