

# New way to combat cancer

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In many forms of cancer the tumor encounters a lack of oxygen, a condition that the tumor tries to prevent in various ways. A research group with its base at Lund University in Sweden is now presenting findings that may make it possible to attack the tumor precisely via these defense mechanisms in the future. The discovery is being honored with a cover illustration in the international journal *Cancer Cell*.

The natural thing for tissue to do when there is a lack of oxygen is to try to stimulate the formation of new blood vessels in the area. Tumors adapt in this way, too. Two substances that are key to this process are called HIF-1 and HIF-2 (hypoxia inducible factors). Both help the tumor create new blood vessels.

HIF-1 has been an object of interest to scientists for several years and is already seen as a treatment target in the drug industry. Under the direction of Professor Sven Pålman, researchers at Lund University together with colleagues at the Karolinska Institute and in Valencia have now managed to show that HIF-2 also plays a crucial role in the reaction of the tumor. Their studies of the pediatric tumor neuroblastoma show that HIF-1 plays the most important role initially, whereas HIF-2 is of greater importance if the lack of oxygen is prolonged.

“In other words, merely attacking HIF-1 might not be enough. You need a treatment that knocks out both factors,” says Sven Pålman.

The supply of oxygen to tumors is a complex and partly controversial chapter in cancer care. Many drugs now on their way to market aim to

stop the flow of oxygen to the tumor in order to get them to die. But the principle is not always easy to put into practice. The flow of oxygen to the tumor must be eliminated completely-a tumor that ‘merely’ experiences a shortage of oxygen risks becoming even more aggressive.

“One reason for this is that the tumor gets help from HIF-1 and HIF-2, for instance, to stimulate the growth of new blood vessels. Through these vessels they can release cells that lead to metastases, daughter growths in other parts of the body. Another reason is that oxygen-deprived tumors become more resistant to both chemotherapy and radiation,” explains Sven Pahlman.

His research team has now been able to demonstrate that high levels of HIF-2 in the pediatric tumor neuroblastoma are associated with a poor prognosis. It should therefore be possible to use the level of HIF-2 as a marker for the diagnosis and prognosis of neuroblastoma. It should also be feasible to develop the blocking of HIF-2 into a future treatment of the disease. The researchers have carried out experiments on laboratory animals to this effect and have attained favorable results.

Source: The Swedish Research Council

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