



International Journal of
Cancer Research

ISSN 1811-9727



Academic
Journals Inc.

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Potential New Anti-Cancer Mechanism

Scientists attached to VIB and K.U.Leuven have succeeded in decoding a potential new anti-cancer mechanism. The researchers discovered that normalizing abnormal tumor blood vessels through HRG (Histidine-Rich Glycoprotein) prevents metastasis of tumor cells and enhances chemotherapy efficiency. In tumors, vessels formation is disturbed, leading to inefficient delivery of chemotherapeutic drugs and allowing cancer cells to escape to other parts of the body (metastasis).

The normalization of tumor blood vessel formation through HRG works by repressing the production of the Placental Growth Factor PIGF. Anti-PIGF therapy is now being tested as a new agent against cancer by ThromboGenics in collaboration with Roche. The recently discovered mechanism offers alternative possibilities for cancer treatment.

Cancer and the formation of blood vessels (angiogenesis) Every growing tissue is supplied with oxygen and nutrients through our blood vessels. However, tumors grow much faster than normal tissue and have a higher need for nutrients. Consequently, tumor cells start generating growth factors to stimulate the growth of new blood vessels. However, the resulting blood vessels are of abnormal shape, causing poor blood flow and little oxygen supply to the cancer cells. The oxygen shortage encourages cancer metastasis and eventually leads to a malignant cancer. Furthermore, the abnormal shape of the blood vessels hampers the supply and efficiency of anti-cancer drugs.

Conventional anti-angiogenic therapy Conventional anti-angiogenic cancer therapy in which a growth factor is eliminated may aggravate tumor metastasis, because. Because of this, there has in recent years been a greater focus on anti-angiogenic therapies which normalize the blood vessels supplying the tumor. This would reduce the oxygen shortage, with the result that the cancer cells will tend to travel less to other parts of the body and anti-

cancer drugs can be delivered more efficiently.

Histidine-rich glycoprotein (HRG) Charlotte Rolny, Max Mazzone and their colleagues from the VIB Vesalius Research Center, K.U.Leuven, have under the direction of Peter Carmeliet and in collaboration with VIB researchers from the Vrije Universiteit Brussel and colleagues from Sweden studied the mechanism behind the known anti-cancer activity of the protein HRG. The results of their experiments show that HRG, a protein distributed in the tumor stroma, displays anti-cancer activity by combating tumor progression and spread and stimulating normalization of tumor blood vessels. The underlying basis of this action is the capacity of HRG to suppress the angiogenic factor PIGF.

Towards an alternative cancer therapy Revealing the mechanism behind the anti-cancer activity of HRG opens up new horizons for cancer treatment. The larger a tumor becomes, the higher its oxygen requirement. However, the tumor vessels that are formed are abnormal in shape, leading to poor blood and oxygen flow. This oxygen shortage stimulates cancer cell metastasis. Stimulating HRG in the tumor stroma counters tumor progression and spread while at the same time being conducive to normalization of tumor blood vessels which enhances the efficacy of chemotherapy. Moreover, these data also support eliminating PIGF for the treatment of cancer.

Source: Cancer Cell, 2011; DOI: 10.1016/j.ccr.2010.11.009