MedicalXpress

Alternatively spliced tissue factor identified as promising new biomarker for aggressive cancers

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A recently discovered form of the protein that triggers blood clotting may play a key role in the molecular mechanisms leading to the growth of certain metastatic cancers, according to new research reported by an international team of scientists.

The protein, called "Tissue Factor," is present in various tissues, but is most prominent in vascular structures such as blood vessels. Previous studies have shown that alternatively spliced Tissue Factor (asTF) contributes to cancer growth, but the molecular events leading to this were previously unknown.

In a preclinical study, an international team of collaborators including Vladimir Bogdanov, PhD, of the University of Cincinnati (UC), and Henri Versteeg, PhD, of the Einthoven Laboratory of Experimental Vascular Medicine at Leiden University Medical Center in the Netherlands, has described in detail how asTF works to contribute to cancerous cell growth.

They report their findings in an early edition of *Proceedings of National Academy of Sciences* (PNAS). This is the first study to report the specific mechanisms of action that lead to increased angiogenesis when alternatively spliced Tissue Factor is present.

"This is an important breakthrough in cancer research because we are

able to draw a more complete molecular picture of how Tissue Factor contributes to cancer growth," says Bogdanov, who discovered asTF while a postdoctoral fellow and is currently the director of the newly established hemostasis research program at the UC College of Medicine. "This will help translate basic research into real-life for therapies targeted to stop angiogenesis."

Angiogenesis is the process by which tumors grow vessels to fuel their growth and ability to reach out and metastasize to other tissues.

Originally, researchers believed that this shorter Tissue Factor acts similarly to the well known "full length" Tissue Factor. What they discovered actually occurred, however, was asTF binding to the surface molecules called integrins on endothelial cells to induce signaling cascades triggering angiogenesis.

This resulted in increased cell adhesion, cell migration and development of new vessels in both cellular and animal models. High levels of asTF were also found in specimens of human cervical cancer.

"When we started this research, we expected that asTF would influence cancerous growth in a manner similar to full length Tissue Factor, namely the activation of blood clotting," says Versteeg. "The clotting of blood activates the so-called protease activated receptors on cell surfaces and these receptors have been thought to be the bad guys in tumor growth. That asTF does not influence tumor growth through blood clotting was a completely unexpected finding. How exactly asTF activates integrins, and in which types of cancer, remains to be uncovered and should keep us busy for some time."

"Our findings introduce a whole new way of studying how the Tissue Factor gene influences tissue formation process, including angiogenesis," explains Bogdanov. "This is another level of understanding the molecular

actions behind Tissue Factor."

Expression of the Tissue Factor gene is increased in many forms of cancer. Researchers hope their findings will help guide development of new ways of targeting specific forms of Tissue Factor to stop cancerous cell growth while producing minimal impact on the body's capability to stop bleeding.

Source: University of Cincinnati (news : web)