Model for new generation of blood vessels challenged

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In-growth and new generation of blood vessels, which must take place if a wound is to heal or a tumor is to grow, have been thought to occur through a branching and further growth of a vessel against a chemical gradient of growth factors. Now a research team at Uppsala University and its University Hospital has shown that mechanical forces are considerably more important than was previously thought. The findings, published today in the journal *Nature Medicine*, open up a new field for developing treatments.

New generation of blood vessels takes place in normal physiological processes, such as when a wound heals, children grow, or the mucous membrane of the womb is built up to be able to receive a fertilized egg. It is also a crucial mechanism in tumor diseases, rheumatism, and certain eye disorders, for example.

How new generation and in-growth of blood vessels takes place has not been fully understood. It has been assumed that the mechanisms are the same as those that occur in embryonic development, which is probably a great over-simplification. The formation of the vascular system in the fetus takes place in a well-organized and reproducible way, which means that we all have blood vessel systems that look very much the same. On the other hand, new generation of vessels in wound healing and tumor growth, for example, occurs in a chaotic environment where it is difficult to see that there would be well-defined gradients of growth factors, and it has not been possible to find evidence of any.

"Unlike these previous models, our findings show that in wound healing, in-growth of new blood vessels takes place via mechanical forces that pull already existing blood vessels into the wound when it heals," says Pär Gerwins, who directed the study and is a physician and interventional radiologist at Uppsala University Hospital as well as a researcher with the Department of Medical Biochemistry and Microbiology at Uppsala University.

It has long been known that specialized connecting tissue cells, so-called myofibroblasts, wander in and pull the wound together. In the study being published it is shown that this wound contraction governs the in-growth of new blood vessels. Since it is a matter, at least initially, of the expansion of already existent blood vessels that have continuous blood circulation, there is a rapid in-growth of fully functional vessels, which is what we see when a wound heals.

The study not only explains a fundamental biological mechanism but also provides clues for new therapeutic goals in treating various diseases. Since myofibroblasts exist in relatively large numbers in tumors and rheumatic joints, one potential strategy to try to block the contractive capacity of these connective tissue cells. The new model can also partially explain why treatment of tumor diseases with blood-vessel inhibiting substances has not been as successful as was hoped.

Finally, the model can partially explain the mechanism behind the positive effect of "vacuum-assisted wound closure," (VAC). This is a method of treatment for hard-to-heal wounds where an air-tight bandage is applied and then the pressure is reduced in the wound with the aid of suction, which creates a continuous mechanical pull in the underlying tissue. Blood-vessel-rich wound-healing tissue is thereby generated much more rapidly, which substantially hastens healing. It is hoped that it will now be possible to understand why some wounds do not heal and also to develop new types of wound treatment.

Source: Uppsala University (news : web)