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A Mechanism for Blood Flow-Induced Capillary Maintenance

What is this research about?

Blood flow, or shear stress, plays an important role in keeping blood vessels healthy. In the small vessels of our muscles which are called capillaries, abnormally low amounts of shear stress cause capillaries to regress and die. This reduction in blood vessels causes a common symptom of type II diabetes. This symptom causes severe leg pain, tissue death and, in worst case scenarios, foot amputation. This is called peripheral ischemia. High shear stress keeps the capillaries healthy by getting the cells of the capillary, or endothelial cells, to form strong connections with each other. High shear stress also inhibits the production of proteins that would break these tight connections and damage the capillary. These proteins are called proteases. Proteases are normally inhibited by protease inhibitor proteins, but it is not known how shear stress inhibits proteases. If shear stress does cause production of protease inhibitors, it is important to find out how this production is occurring. One protein that is known to cause production of protease inhibitors in endothelial cells is called Ets-1.

What you need to know:

High blood flow is important for the proper functioning of blood vessels. One of the ways this occurs is by production of protease inhibitors, which maintain vessel wall integrity.

What did the researcher do?

The researcher treated rats with a vasodilator to increase blood flow to the leg muscles, and then measured the amount of Ets-1 present in the blood vessels. They also exposed isolated endothelial cells to shear stress and measured the amount of Ets-1, as well as its activity. Finally, the researchers measured the amount of protease inhibitors produced in endothelial cells by shear stress, both under normal conditions and when the amount of Ets-1 in the cells was reduced.

What did the researcher find?

Elevated blood flow increased the amount and activity of Ets-1, both in rat leg muscles and in endothelial cells alone. Shear stress also increased the amount of 3 different protease inhibitors in endothelial cells. Reducing the amount of Ets-1 in the endothelial cells prevented the production of all 3 protease inhibitors in response to increased flow.

How can you use this research?

This research expands our understanding of how blood flow regulates endothelial cell function, leading to properly functioning blood vessels. A complete understanding of this process could be used in the future to treat cardiovascular diseases in which blood flow is impaired, such as diabetes-induced peripheral ischemia.

About the Researchers

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Citation

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Keywords

Blood flow, Capillaries, Gene expression, Protease inhibitors, Diabetes

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