

Blood clotting finding may lead to new treatments

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A key protein that causes the blood to clot is produced by blood vessels in the lungs and not just the liver, according to new research published today in the journal *PLoS One*, led by scientists at Imperial College London.

The findings may ultimately help scientists to develop better treatments for conditions where the blood's ability to clot is impaired, including deep vein <u>thrombosis</u>, where dangerous <u>blood clots</u> form inside the body, and haemophilia A, where the blood cannot clot sufficiently well.

It has long been known that an agent called factor VIII plays a key role in enabling the blood to clot. Too much factor VIII puts people at risk of excessive clots. Low levels of factor VIII cause bleeding in people with haemophilia A and factor VIII replacement is used to treat this.

Prior to recent research it had been believed that most factor VIII was produced by the liver. Therapeutic options for patients with haemophilia have included replacing <u>liver cells</u>, for example through transplantation.

Dr Claire Shovlin, the lead author of the study from the National Heart and Lung Institute at Imperial College London, said: "Our study suggests that the blood vessels in the lung are playing a crucial role in altering how blood clots form in the body. There are a huge number of these blood vessels - they cover an area equivalent in size to a squash court, effectively 20 times the surface area of all other blood vessels combined.



"This means it's really important for us to understand exactly how the behaviour of the lung blood vessels might be affecting diseases where blood clotting is a factor. Further research on how the lungs modify the clotting potential of the blood flowing through them could open up new avenues for treatments," added Dr Shovlin.

In 2006, researchers from the University of Leuven in Belgium published a study in the journal Blood looking at donated lung tissue. The researchers passed fluid through the tissue and found that in three of the four lung samples studied, the levels of factor VIII increased in the fluid after passing through the lungs. They also provided evidence that some lung blood vessels could produce factor VIII in cell culture.

The researchers behind today's study have confirmed that the <u>blood</u> <u>vessels</u> in the lungs should be an important site for regulating the formation of clots, both in the lungs themselves and also, potentially, in the rest of the body. They used different microscopic and biochemical techniques to look at samples of lung tissue and blood samples in minute detail.

Tissue and blood samples for the work leading up to this study were donated by patients from Imperial College Healthcare NHS Trust, with tissue processed through the Hammersmith Hospital Tissue Bank.

The team found that factor VIII could be seen in the lung tissue and was present on the surface of blood vessel cells in the lungs. They also found that factor VIII localises in the lungs with a protein called von Willebrand factor, which protects factor VIII from degradation. The work also showed that how the factor VIII gene may be decoded is much more complicated than previously thought. This could potentially alter how scientists approach the treatment of the many conditions where blood clotting is a factor.



The researchers hope that ultimately new drugs can be developed that target production of <u>factor VIII</u> in the lungs, to improve the body's ability to ensure that the blood clots properly. By targeting the lungs, the researchers think it may be possible to make more effective drugs that produce fewer side effects than current treatments.

Provided by Imperial College London

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