

# Vascular protection in endotoxemic shock: inhibition of vascular permeability and mortality using ANGPTL4



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## **Short summary**

Microvascular leak plays a critical role in the outcome of sepsis. Counteracting vascular permeability has recently raised a huge interest in the field but therapeutic targets and translation studies are crucially lacking. We previously showed that ANGPTL4 is induced by hypoxia and protects vascular integrity at reperfusion of acute myocardial infarction (*Galaup, Circulation 2012*) and stroke (*Bouleti, Eur. Heart J. 2013*). We here hypothesized that ANGPTL4 might also modulate vascular permeability in endotoxemic shock. In the present study, we show that giving human recombinant ANGPTL4 to mice prevents vascular injury and mortality induced by LPS. We further demonstrate that ANGPTL4 suppresses vascular permeability by stabilizing endothelial cells. The power of this finding is that it may hit a central control node; i.e; control of vascular endothelial homeostasis and barrier. In conclusion, we demonstrate that suppressing vascular permeability by ANGPTL4 could be a novel therapeutic strategy against sepsis. Either

alone or in combination with existing drugs, ANGPTL4 could contribute to the reduction of mortality in patients with severe infectious diseases.

### **List of the most relevant publications:**

Galaup A, Gomez E, Souktani R, Durand M, Cazes A, Monnot C, Teillon J, Le Jan S, Bouleti C, Briois G, Philippe J, Pons S, Martin V, Assaly R, Bonnin P, Ratajczak P, Janin A, Thurston G, Valenzuela DM, Murphy AJ, Yancopoulos GD, Tissier R, Berdeaux A, Ghaleh B, **Germain S.** [Protection against myocardial infarction and no-reflow through preservation of vascular integrity by angiopoietin-like 4.](#) *Circulation*. 2012 Jan 3;125(1):140-9.

Bouleti C, Mathivet T, Coqueran B, Serfaty JM, Lesage M, Berland E, Ardidie-Robouant C, Kauffenstein G, Henrion D, Lapergue B, Mazighi M, Duyckaerts C, Thurston G, Valenzuela DM, Murphy AJ, Yancopoulos GD, Monnot C, Margail I, **Germain S.** [Protective effects of angiopoietin-like 4 on cerebrovascular and functional damages in ischaemic stroke.](#) *Eur Heart J*. 2013 Dec;34(47):3657-68.