

Licensing Opportunity



A novel target and therapeutic agent for endothelial barrier dysfunction and edema

- Short term treatment with imatinib protects against vascular leakage and edema formation
- Imatinib prevents endothelial barrier dysfunction via inhibition of the tyrosine kinase Abl-related gene (Arg)
- Abl-related gene (Arg) forms a novel target in the treatment of vascular leakage
- No side effects have been reported for short term treatment with imatinib

Imatinib | endothelial barrier dysfunction | Abl-related gene | tyrosine kinase | edema

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Background

Endothelial barrier dysfunction is a significant pathogenic phenomenon, underlying a wide variety of diseases. Because endothelial barrier dysfunction importantly contributes to edema formation, it is associated with high morbidity and mortality. Though life-threatening, no pharmacological therapy is available to counteract endothelial barrier dysfunction and edema formation. Our recent studies indicate that the anti-cancer drug imatinib potentially reduces endothelial barrier dysfunction, providing novel treatment options for edema.

The Technology

Imatinib was proven to protect against endothelial barrier dysfunction in vitro and in vivo. In various endothelial cell types of both macro- and microvascular origin, imatinib attenuated the barrier disruptive effect of inflammatory mediators such as thrombin and histamine. Imatinib exerts its protective effects via inhibition of the tyrosine kinase Abl-related gene (Arg). Arg was shown to mediate cytoskeletal rearrangements required for endothelial barrier disruption. Furthermore, imatinib improves binding of endothelial cells to the extracellular matrix. Animal studies confirmed protective effects of imatinib. In mice, pretreatment with imatinib reduced vascular leakage in the skin and development of edema in the lung [1]. In a recent case report, short term imatinib treatment was associated with fast and significant resolution of pulmonary edema, indicating the clinical relevance of imatinib in edema treatment [2].

Intellectual Property

Protection against endothelial barrier dysfunction through inhibition of the tyrosine kinase abl-related gene (ARG), PCT filed 2 May 2011, applicant was legal party of VU University and medical center.

Inventors

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Key publications

1. J. Aman et al. Unpublished data
2. M. Overbeek et al. Eur Respir J, 2008