Tissue Factor Pathway Inhibition as a Treatment Strategy for Severe Pulmonary Arterial Hypertension

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Technology description

Description

The invention proposes a novel therapeutic strategy for the treatment of severe pulmonary arterial hypertension (PAH) by targeting Tissue Factor (TF) pathway. Preliminary human and animal data have demonstrated that TF is associated with PAH. By blocking TF pathway, the progression of PAH would be stopped and early pathological vascular changes could be potentially reversed. Blockade of TF pathway can be currently implemented by administration of TF pathway inhibitor (TFPI) (invented by Chiron) to PAH patients. Future effort should be directed toward developing an orally active drug for inhibiting TF pathway. Strategies (including gene therapy) that selectively blocked TF activation in the pulmonary circulation would be the most useful. PAH is currently treated with two different FDA approved strategies (3 drugs total). Despite the two available FDA-approved strategies as well as the off-label use of sildenafil (Viagra), some patients still progress to death or lung transplantation. TF pathway blockade offers a number of theoretical benefits in PAH. It would prevent in situ thrombosis, known to occur in PAH, as well as reduce the production of thrombin and Xa, which likely contribute to PAH. TF blockade can reduce platelet activation/ aggregation and release of platelet mediator, probably attenuating the pathologies of PAH.

Advantages

The main advantage of this novel strategies is that it is distinctive and would likely be additive (or even synergistic) to the 2 FDA-approved strategies.

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