Use of Bryostatins and Bryostain Derivates to Treat Pulmonary and Systemic Vascular Diseases

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Technology description

Summary

Background Hypertension, or high blood pressure, is a cardiac condition that affects 1 in 3 adults in the United States. A specific class of hypertension called pulmonary hypertension (PH) is a disorder characterized by elevated blood pressure in the vessels carrying blood from the heart to the lung (pulmonary vasculature). This elevation in blood pressure increases the workload of the heart, and can lead to serious complications if left untreated -- these complications include heart failure, blood clots, irregular heartbeat and bleeding in the lungs. All of these complications can be fatal, and highlight the importance of immediate diagnosis and treatment of PH. The most prominent form of PH, secondary PH, is a resulting complication from lung or heart disease, and has also been linked to HIV infection and use of some diet pills (Fen-phen). Current Treatment The mainstays of current treatment for PH are: supplemental oxygen, transplant, vasodilators, endothelin receptor agonists, calcium channel blockers, anticoagulants, diuretics, and medications that stop the narrowing of blood vessels. Along with their therapeutic benefits, many of these treatments come with a range of risks and side effects: pain, diarrhea, cramps, infection, headache, possible liver damage, dizziness, vision problems, increased risk of bleeding complications. If prescribed to unstable patients, some of these side-effects can even be fatal. Additionally, a treatment may become less efficacious over time, requiring a new drug or approach to be taken. In sum, physician and patient will benefit from new therapies with fewer or less severe side effects. Also, the addition of new treatment modalities for PH will make physicians better equipped in tailoring treatments for each patient. Invention A research group led by Edward Dempsey of the University of Colorado has identified that bryostatin may be used to treat PH and other vascular diseases associated with cardiac hypertrophy. Mechanistically, bryostatins have already been shown to rapidly inactivate and degrade the signaling molecule PKC-α. This is significant, since PKC-α is involved in the narrowing of the pulmonary vasculature through signaling the growth of smooth muscle cells following low oxygen levels associated with chronic hypoxic PH (CHPH). In support of this therapeutic principle, data shows bryostatins inhibit pulmonary smooth muscle cell growth by a PKC dependent pathway . Additionally, data from a mouse model of CHPH shows bryostatins attenuate PH induced by chronic hypoxia.

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