Innovations
UNIVERSITY OF COLORADO
ANSCHUTZ MEDICAL CAMPUS

Neprilysin for the Treatment of Pulmonary Hypertension

Category

Technology: Therapeutic- New Use or Method of Treatment

Problem

Chronic Pulmonary Hypertension

Technology Overview

Method of using Neprilysin agonists for the treatment or prevention of PH

IP Status

- Patents issued
- Available for Exclusive or Non-Exclusive Licensing

Value Proposition

- Neprilysin is protective in the lung and plays a different role in the lung than it does in the systemic circulation
- Lung -targeted strategies to increase Neprilysin levels could have major therapeutic benefits

Market Attractions

- No current direct treatments for pulmonary hypertension
- PH effects millions of Americans

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Problem: Chronic pulmonary hypertension is a major clinical problem, complicating most lung and heart disorders including chronic obstructive pulmonary disease (COPD). Pulmonary Hypertension (PH) occurs when the pressure in the arteries of the lung is elevated, increasing resistance for the right side of the heart. This added burden causes shortness of breath, fluid retention and, ultimately, right heart failure. Several forms of PH afflict millions of Americans. The only established therapy for secondary PH (like that seen with COPD) is treatment of underlying conditions, prevention of further injury, and supplemental oxygen. Selected patients with severe PH are treated with expensive drugs that have side effects and are rarely curative. There is need for new approaches.

Solution: Dr. Edward Dempsey, a Pulmonologist at the University of Colorado, discovered that Neprilysin activity and expression are substantially decreased in human lungs with advanced COPD. Neprilysin (NEP) is a cell surface enzyme that degrades bioactive peptides that maintain normal lung vascular function and is widely expressed in pulmonary vasculature. He has developed a method of using NEP agonists for the treatment or prevention of PH. Neprilysin may be protective against chronic hypoxic (and likely other forms of) pulmonary hypertension in the lung, at least in part by attenuating the growth of smooth muscle cells. Lung -targeted strategies to increase Neprilysin levels could have therapeutic benefits in the treatment of this disorder.

Investigators used a genetic approach to show that Neprilysin is protective in the lung and plays a different role in the lung than it does in the systemic circulation. Of note, newer Neprilysin inhibitors have been shown to decrease systemic hypertension and decrease cardiac remodeling. Their data is still consistent with these effects and demonstrate that targeted deletion of NEP in the C57BL/6 mouse predisposes to exaggerated pulmonary hypertension and vascular remodeling in response to chronic hypoxia. Thus, NEP may protect the lung against hypoxia-induced vascular remodeling, in large part by limiting the magnitude of neuropeptide-induced proliferative, migratory and/or contractile responses.

Increased pulmonary vascular remodeling and cell proliferation is observed in figure 10, PA SMCs from normoxic $NEP^{+/+}$ and $NEP^{-/-}$ mice were isolated from the proximal medial PA. Representative staining of the PA SMC for α-SMA is shown in Figure 10 C and D. PA SMCs from $NEP^{-/-}$ mice have increased levels of proliferation markers compared to $NEP^{+/+}$

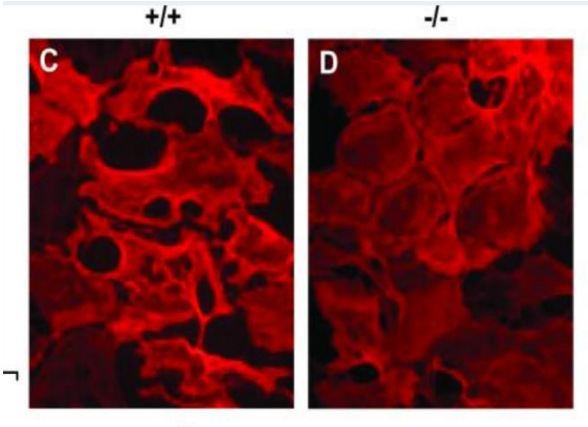

Figure 10

Additional Documents and Sources:

Patent #s 8,883,144 and 9,950,044 issued. Filed September 1, 2011 and October 9, 2014; Available under NDA
Dempsey EC, Wick MJ, Karoor V, et al. Neprilysin null mice develop exaggerated pulmonary vascular remodeling in response to chronic hypoxia. *Am J Pathol*. 2009;174(3):782–796. doi:10.2353/ajpath.2009.080345

About CU Innovations

CU Innovations is the technology transfer office for the University of Colorado Anschutz Medical Campus. CU Innovations seeks to bring together industry partners, entrepreneurs and investors to translate discovery into impact. http://innovations.ucdenver.edu

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