A First-in-Class Anti-Hypertensive Therapy

Despite the number of available treatments, nearly one third of the over 73 million patients with hypertension respond poorly to current treatment options. This presents a significant commercial opportunity for new therapies with novel mechanisms of action. The cGMP dependent protein kinase (PKG) has long been identified as a master regulator of vasodilation and target for drug development, but previous attempts have failed to develop a cGMP independent activator. The Dostmann lab is developing a library of synthetic peptides (S-tides) that are first in class agonists of PKG1α with the potential to treat resistant hypertension and acute hypertensive crisis. S-tides are rationally designed peptides, which bind to and activate PKG1α with nanomolar efficacy, leading to 20-50% blood pressure reductions when administered to rats. S-tides may have immediate clinical utility as an IV-administered drug for acute hypertensive crisis or may serve as a platform for the development of orally available therapeutics for the treatment of resistant hypertension and other diseases that involve PKG biology.

Applications:
- Chronic hypertension and acute hypertension crisis.
- Treatment of other diseases that involve PKG, such as CHF, PAH, kidney disease, GI dysfunction and genitourinary disorders.

Advantages:
- First-in-class peptide therapeutic for hypertension.
- cGMP independent activation of a master regulator of vasodilation.
- Activates PKG with nanomolar efficacy.
- S-tides provide a framework for ligand and structure based virtual screening of small molecules.

Intellectual Property and Development Status:
US Patent No. 9,260,486
Establishing the safety profile of the S-tides and completing in vivo efficacy studies. Looking for start-up funding and collaborators for small molecule development, as well as licensing opportunities.

References:
Synthetic Peptides as cGMP-Independent Activators of cGMP-Dependent Protein Kinase Iα
Chem Biol. 2015 Dec 17;22(12):1653-61

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