Innovations
UNIVERSITY OF COLORADO
ANSCHUTZ MEDICAL CAMPUS

Cystathionine Treatment Regenerates Vascular Tissue

Category

Amino Acid Therapeutic Developed in 2011

Problem

Atherosclerosis, vascular disease, and diabetes

Technology Overview

Cystathionine protects against ER stress, and regenerates vasculature.

IP Status

- Patent Pending
- Available for Exclusive Licensing

Value Proposition

- Effective in multiple animal models of ER stress
- Excellent safety profile expected.
- Ease of Manufacturing.

Market Attractions

- Significant Markets
- Unmet needs
- Low cost

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Problem: Vascular calcification (VC) is common in aging, and is a major contributing pathogenic factor in atherosclerosis, peripheral vascular disease, diabetes, and a number of genetic and metabolic disorders (Alexopoulos et al. (2009) Nat. Rev. Cardiol. 6:681-688). Calcific deposits in arteries complicate the prognosis and increase the morbidity in atherosclerosis, diabetes and chronic kidney disease (CKD) (Yahagi et al. (2017) Arterioscler. Thromb. Vasc. Biol. 37:191-204). VC is now recognized as a strong predictor of cardiovascular events in diabetic and CKD patients and the general population (McCullough et al. (2008) Am. Soc. Nephrol. 3:1585-1598). VC almost invariably occurs in patients as a consequence of renal dialysis during end stage renal disease; this patient population has expanded as a consequence of increased type 2 diabetes cases (Foley et al. (1998) J. Am. Soc. Nephrol. 9(12 Suppl):S16-23). Despite the fact that millions of individuals incur the life-threatening pathological consequences of VC, there is currently no drug or therapeutic treatment able to even partially reverse this condition.

Technical Solution and Key Value Propositions:

Efficacy: Using animal models, the Maclean lab has shown that the non-protein amino acid, cystathionine, protects against a wide range of pathologies induced by endoplasmic reticulum (ER) stress, including vascular calcification. Cystathionine was found to completely block hepatic injury and acute tubular necrosis induced by the ER stress-inducing agent tunicamycin in mice. Cystathionine also prevents aortic vascular calcification induced by supra-physiological levels of vitamin D and nicotine.

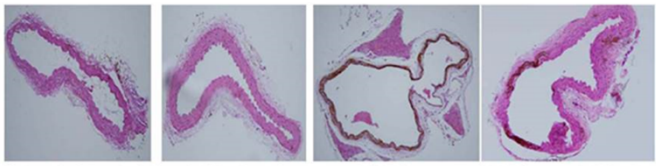

Figure 1. Cystathionine treatment exerts highly significant protective effects in a mouse model of vascular calcification Von Kosssa staining of aortas from mice treated with VitD3 to induce massive calcification (bronze stain) in the presence and absence of cystathionine treatment. Figures shown are representative sections taken from an n of 5 per group.

Safety: In mammals, cystathionine is formed as an intermediate in a metabolic pathway that converts methionine into cysteine. People born with a genetic defect in an enzyme in that pathway (cystathionine gamma lyase) accumulate high levels of cystathionine but experience no adverse clinical effects (Kraus et al. (2009) Mol. Genet. Metab. 97:250-9).

Manufacturing: Cystathionine is commercially available at >98% purity.

Data Update:

The Maclean lab now has evidence that cystathionine can reverse pre-existing VC and other forms of ER stress-induced injury (paper pending).

Key Documents and Sources:

"*Uses of and Methods of Treatment with Cystathionine*." US Patent application pending; priority date June 3, 2011.

Maclean, et al., *Cystathionine protects against endoplasmic reticulum stress-induced lipid accumulation, tissue injury, and apoptotic cell death.* J. Biol. Chem. 2012 Sep 14; 287(38):31994-2005.