Background
Cystathionine is an intermediate in the synthesis of cysteine, in a reaction catalyzed by cystathionine β-synthase (CBS). Pathogenic mutations in CBS result in CBS-deficient homocystinuria (HCU) which, if untreated, results in mental retardation, thromboembolic complications and connective tissue disorders. Currently there is no other recognized function for cystathionine.

Kidney and Liver Injury
A CU research group has discovered that cystathionine reduces the development of toxin-induced liver and/or kidney disease. For instance, using both mouse and cell-culture models, the group found that cystathionine blocked development of fatty liver disease and acute tubular necrosis, as well as other forms of toxin-induced apoptotic cell death. Not only does this indicate a key role for cystathionine synthesis in the pathology of HCU, it also suggests that cystathionine may be a new treatment option in many disease states where cell death is triggered by stress to the endoplasmic reticulum (ER), including several kidney and liver disease states as well as some kinds of cardiovascular disease (see Data Update below).

Chemotherapy Potentiation
The group also found that cystathionine is capable of blocking tunicamycin-mediated tissue injury and apoptosis; preliminary work indicates that this protective effect may be far enough 'upstream' to protect against multiple intracellular disturbances in addition to ER stress. In particular, neuroblastoma (the commonest and most deadly solid tumor in children under five years) is marked by massive accumulation of cystathionine. The research group’s work suggests that this accumulated cystathionine has the potential to allow the neuroblastoma cells to resist cytotoxic treatments such as chemotherapy, and that the use of a CBS-inactivating drug could increase chemosensitization and improve clinical outcome in neuroblastoma patients.

Partnering Needs
⇒ Medicinal chemistry work on cystathionine to improve bioavailability, or collaboration to develop optimal cystathionine delivery approach or formulation to best reduce kidney, liver and cardiovascular injury.
⇒ Collaboration to validate neuroblastoma chemosensitization via inhibition of cystathionine accumulation in vivo.

Data Update
The research group has recently generated in vivo data that validates the protective role for cystathionine in liver disease, and has further discovered that cystathionine confers a protective effect against general vascular calcification.

Key Documents

Uses Of and Methods of Treatment with Cystathionine. PCT filed June 1, 2012.