Hydrogen sulfide and inflammatory-based vascular diseases

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Hydrogen sulfide (H2S) is an endogenous signaling molecule that, together with CO and NO, constitutes the gaseous mediators class defined 'gasotransmitters'. In mammalian cells, H2S is produced from L-cysteine through the action of cystathionine beta-synthase (CBS) and cystathionine gamma-lyase (CSE), both pyridoxal-phosphate (PLP) dependent enzymes. There is also a third pathway that involves 3-mercaptopyruvate sulfurtransferase (3-MST) and it is PLP independent. These enzymes are expressed in many tissues and organs: CBS is mainly located within the central nervous system (Kimura 2010), CSE primarily accounts for H2S production in the vasculature while (3MST) pathway is emerging in controlling intestinal mucosa physiology (Flannigan et al., 2013). Recent literature clearly shows that H2S has a protective action in many pathological conditions, however the mechanism of tissue protection in inflammation is a point of debate. In cardiovascular district, it has been recently demonstrated that H2S, either increasing its biosynthesis or administrating it exogenously, attenuates myocardial injury, protects blood vessels, limits vascular inflammation and regulates blood pressure. These pleiotropic actions indicate H2S as a critical cardiovascular signaling molecule similar to nitric oxide (NO) and carbon monoxide (CO) with a pivotal role in systemic circulation. In this context, we have investigated on the role of H2S in vascular function in both physiological and physio-pathological conditions. In particular, we found reduced levels of tissue and circulating H2S in different models of inflammatory-based vascular diseases such as diabetes and SHR-model of hypertension. Starting from these evidences, our studies aimed to evaluate the impact of l-cysteine/CSE /H2S pathway in vascular inflammation development and the use of H2S-donors as therapeutic agents to ameliorate inflammatory-based vascular dysfunction.