Hydrogen Sulfide (H₂S) and polysulfides (H₂S_n) as signaling molecules

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Twenty years have passed since our first demonstration that hydrogen sulfide (H₂S) facilitates the induction of hippocampal long-term potentiation (LTP), a synaptic model of memory, and cystathionine β -synthase (CBS) as H₂S producing enzyme in 1996. The following year we reported that cystathionine γ -lyase (CSE) is found in vascular smooth muscles and that H₂S relaxes them in synergy with nitric oxide (NO). H₂S is recognized as a signaling molecule with various physiological roles, including the protection of tissues/organs from ischemic insults, anti-inflammatory effect, angiogenesis and oxygen sensor. We also found hydrogen polysulfides (H₂S_n), which have a higher number of sulfane sulfur atoms than H₂S in the brain, activate transient receptor potential ankyrin-1 (TRPA1) channels much more potently than does H₂S. H₂S_n also facilitate the translocation of nuclear factor-like2 (Nrf2) to the nucleus by modifying its binding partner kelch-like ECH-associated protein 1 (Keap1), regulates the activity of the tumor suppressor phosphatase and tensin homolog (PTEN), and reduce blood pressure by dilating vascular smooth muscle through the activation of protein kinase G. High performance liquid chromatography with fluorescence detection and tandem mass spectrometry analyses showed that H₂S₃, H₂S₂, cysteine- and glutathione-persulfide as well as H₂S are produced by 3-mercaptopyruvate sulfurtransferase (3MST) in the brain of the wild-type mice but not 3MST-knockout mice. We also found that H₂S₂ and H₂S₃ are produced by the chemical interaction of H₂S with NO. The production and physiological roles of H₂S and H₂S_n will be focused in this presentation.