Biology for Physiological Hydrogen Sulfide
Introduction

Hydrogen sulfide (H\textsubscript{2}S), which is known as a toxic gas, has emerged as the third gaseous signaling molecule along with nitric oxide (NO) and carbon monoxide (CO). H\textsubscript{2}S has been reported to regulate physiological functions such as vascular relaxation, cellular protection, insulin secretion and neurotransmission \textsuperscript{1-4} (Fig. 1).

Physiological hydrogen sulfide is mainly produced from L-cysteine as a substrate by cystathionine-β-synthase (CBS), cystathionine γ-lyase (CSE) and 3-mercaptoppyruvate sulfurtransferase (3-MST). Hydrogen sulfide functions as a physiological mediator and it is stored in proteins as bound sulfane sulfur. It binds mostly to sulfhydryl groups of cysteine. Although hydrogen sulfide is a gaseous molecule, about 80% of hydrogen sulfide exists as hydrogen sulfide anion (H\textsubscript{2}S\textsuperscript{-}) at physiological conditions because of its pK\textsubscript{a} (approximately 7). Hydrogen sulfide also easily binds to proteins and produces, under oxidative conditions, sulfur species of different structures. Therefore, functional mechanisms of hydrogen sulfide need to be further studied.

This review gives you a brief overview of the latest hydrogen sulfide research.

![Fig.1 Physiological Functions of H\textsubscript{2}S](image-url)
1. **Biosynthesis of hydrogen sulfide**

Biological hydrogen sulfide is enzymatically produced by CBS, CSE or 3-MST from L-cysteine and L-homocysteine as substrates. These enzymes are expressed in various tissues and cells. Their catalytic activities are regulated by many kinds of physiologically active substances. This chapter focuses on the activities and functions of these enzymes.

![Fig. 1-1 Biosynthesis of H₂S](image)

1-1. **Cystathionine-β-synthase (CBS)**

CBS is a homodimeric enzyme which is composed of two 63 kDa subunits. Each subunit is organized into a N-terminal heme-binding domain, a central PLP (pyridoxal phosphate)-binding catalytic domain, and a C-terminal SAM (S-adenosyl methionine)-binding domain. The activity of CBS is highly regulated by various factors such as PLP, SAM and CO, which inhibits the activity by binding to the N-terminal heme-binding domain \(^5\). CBS is known as an enzyme that synthesizes L-cystathionine from L-serine and L-homocysteine. However, the productions of L-cystathionine and hydrogen sulfide are promoted if the substrate is L-cysteine or L-homocysteine. Furthermore, CBS generates L-serine or L-lanthionine, along with hydrogen sulfide when only L-cysteine is used as a substrate \(^6\)–\(^8\).

The expressions of CBS are mainly observed in the liver, kidney \(^9\) and brain \(^10\).