Hydrogen sulfide, a signaling molecule across life kingdoms

Hydrogen sulfide (H$_2$S), in the past merely known as a toxic pollutant, more recently has been recognized to be an endogenous signalling molecule in higher organisms, playing key regulatory functions in the nervous and cardiovascular systems. Signalling is mostly afforded through reversible protein thiol persulfidation, currently recognized as a common post-translational modification taking place in a considerable fraction of proteins. H$_2$S is synthesized by three enzymes (cystathionine beta-synthase, cystathionine gamma-lyase and mercaptopyruvate sulfurtransferase) and degraded in the mitochondrial by an enzymatic unit coupling H$_2$S oxidation to ATP synthesis through oxidative phosphorylation. While exerting its physiological signalling action at low (nM) concentrations, at higher concentrations H$_2$S triggers cytotoxicity, and a dysregulation of H$_2$S metabolism has been documented in several neurological, cardiovascular and oncologic diseases, possibly contributing to the genesis and/or progression of those pathological states. Human enzymes implicated in H$_2$S metabolism have therefore emerged as possible drug targets. More recently, orthologs of the eukaryotic H$_2$S-synthesizing enzymes have been found to be ubiquitous in bacteria and endogenous H$_2$S biosynthesis has been recognized as implicated in bacterial resistance to antibiotics, pointing to a role of H$_2$S in bacterial physiology.

The research aims to i) elucidate how the human H$_2$S-synthesizing and -consuming enzymes are physiologically regulated; ii) identify natural or artificial compounds that, being able to modulate H$_2$S metabolism, are suitable for pharmacological applications; iii) assess the role of H$_2$S in bacterial physiology and virulence.

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References:


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