Journal of
Aesthetic Surgery and Medicine
ISSN: 3068-5311
ScitechJournals
Open Access

Building Muscles: The Molecular Regulation of Muscle Regeneration by Hydrogen Sulfide (H_2S)

Abstract

Hydrogen sulfide (H_2S) was originally considered toxic at elevated levels; however, over the past decade it has emerged as an important gasotransmitter alongside Nitric oxide and Carbon monoxide. H_2S is generated endogenously from L-cysteine by several enzymes and regulates diverse cellular and pathophysiological processes. Many of its biological effects are mediated through S-sulfhydration of cysteine residues on target proteins, altering enzymatic activity, protein stability, localization, and molecular interactions. Rapid growth in H_2S research reflects its expanding importance in biology and medicine. Given its critical role in health and disease, understanding H_2S metabolism and molecular signaling mechanisms may facilitate the development of novel therapeutic strategies. Recent findings indicate that H_2S plays an essential role in myogenesis and skeletal muscle regeneration following injury, suggesting potential applications in preventing age-related sarcopenia and treating muscle damage.

Review Article

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Received: 24 Feb, 2026; **Accepted:** 09 Mar, 2026; **Published:** 24 Mar, 2026.

Introduction

Skeletal muscle is a highly plastic tissue capable of regeneration in response to injury, exercise, and disease. This regenerative capacity depends on tightly coordinated molecular signaling pathways that regulate satellite cell activation, proliferation, differentiation, and fusion [1,2]. Dysregulation of these processes contributes to muscle-wasting conditions such as sarcopenia, cachexia, and muscular dystrophy [3].

Gasotransmitters—small gaseous signaling molecules—have emerged as key modulators of muscle physiology. Among these, H_2S has gained attention as the third major endogenous gasotransmitter after nitric oxide (NO) and carbon monoxide (CO) [4,5]. Once considered merely a toxic environmental gas, H_2S is now recognized as a critical regulator of redox balance, mitochondrial function, inflammation, and cellular metabolism [6].

This mini-review summarizes current knowledge on H_2S biosynthesis, molecular mechanisms of action, and its emerging role in skeletal muscle regeneration and repair.

Biosynthesis and Metabolism of H_2S

Endogenous H_2S is synthesized primarily from L-cysteine through the enzymatic actions of cystathionine β-synthase (CBS), cystathionine γ-lyase (CSE), and 3-mercaptopyruvate sulfurtransferase (3-MST) [7,8]. These enzymes exhibit tissue-specific expression patterns and contribute to finely tuned regulation of H_2S levels.

H_2S metabolism is tightly controlled by mitochondrial oxidation pathways, ensuring physiological concentrations are maintained [9]. Dysregulation of H_2S production or clearance has been implicated in cardiovascular, neurological, and metabolic diseases [10].

In skeletal muscle, CSE and 3-MST are particularly relevant, suggesting localized control of H_2S production during muscle repair [11].

Molecular Mechanisms of H_2S Signaling

S-Sulfhydration

A primary mechanism of H_2S signaling involves S-sulfhydration (also termed persulfidation), a post-translational modification in which a sulfur atom is added to cysteine residues on target proteins [12]. This modification alters protein conformation, enzymatic activity,

and interaction networks.

S-sulfhydration has been shown to regulate key signaling molecules involved in oxidative stress responses and cytoskeletal organization [13].

Redox Regulation and Mitochondrial Function

H_2S plays a dual role in redox biology. At physiological concentrations, it acts as an antioxidant by enhancing glutathione levels and activating nuclear factor erythroid 2–related factor 2 (Nrf2) pathways [14]. It also modulates mitochondrial respiration by interacting with electron transport chain components [15].

Given that mitochondrial health is critical for muscle regeneration, these effects position H_2S as an important metabolic regulator during myogenesis.

Interaction with Other Gasotransmitters

H_2S signaling interacts with nitric oxide pathways, influencing vascular tone and perfusion in skeletal muscle [16]. Cross-talk between H_2S and NO may enhance angiogenesis and nutrient delivery during muscle repair [17].

Role of H_2S in Myogenesis and Muscle Regeneration

Satellite Cell Activation and Differentiation

Satellite cells are skeletal muscle stem cells responsible for regeneration [2]. Emerging evidence suggests that H_2S promotes satellite cell proliferation and differentiation by modulating key transcription factors such as MyoD and myogenin [18].

Experimental models indicate that inhibition of H_2S-producing enzymes impairs muscle regeneration, whereas H_2S donors enhance myogenic differentiation [19].

Anti-inflammatory Effects

Muscle injury triggers inflammatory responses that are essential for regeneration but detrimental when excessive. H_2S exhibits anti-inflammatory properties by suppressing pro-inflammatory cytokines and modulating NF-κB signaling [20]. These effects contribute to a favorable microenvironment for muscle repair.

Protection Against Muscle Atrophy and Sarcopenia

Age-related sarcopenia is characterized by reduced muscle mass and function. Declining H_2S production has been associated with aging tissues [21]. Preclinical studies suggest that H_2S supplementation may counteract oxidative stress and mitochondrial dysfunction in aging muscle, positioning it as a candidate therapeutic strategy.

Therapeutic Potential and Clinical Implications

The therapeutic application of H_2S relies on controlled delivery systems, as excessive levels can be cytotoxic. Slow-releasing H_2S donors and hybrid compounds are being developed to achieve physiological effects without toxicity [6].

In muscle injury models, H_2S donors have demonstrated improved regeneration and reduced fibrosis [19]. These findings suggest potential clinical applications in:

- Sports-related muscle injuries
- Age-related sarcopenia
- Muscular dystrophies
- Cachexia associated with chronic diseases

However, further translational and clinical studies are necessary to determine optimal dosing, timing, and safety.

Conclusion

Hydrogen sulfide has evolved from being considered a toxic gas to a recognized endogenous signaling molecule with profound biological effects. Through mechanisms such as S-sulfhydration, redox regulation, mitochondrial modulation, and anti-inflammatory signaling, H_2S plays a critical role in skeletal muscle regeneration. Emerging evidence supports its involvement in satellite cell activation and protection against muscle degeneration.

A deeper understanding of H_2S metabolism and molecular targets may facilitate the development of novel therapeutic strategies aimed at enhancing muscle regeneration and preventing age-related sarcopenia. Continued research will be essential to translate these promising findings into clinical practice.

References

1. Xiao ZL, Chen SB, HE HQ, Xu YD, Liu XQ, et al. (2003) Infectious atypical pneumonia: the first case report. Xin Yi Xue 34(6):10-12.
2. Feng CG. (2003) Development and Academic Progress of SARS (January 2003 to April 19, 2003). Ke Ji Dao Bao. (6).
3. Chan-Yeung, Moira, and W. C. Yu. “Outbreak of severe acute respiratory syndrome in Hong Kong Special Administrative Region: case report.” Bmj 326, no. 7394 (2003): 850.
4. Twu, Shiing-Jer, Tzay-Jinn Chen, Chien-Jen Chen, Sonja J. Olsen, Long-Teng Lee, Tamara Fisk, Kwo-Hsiung Hsu et al. “Control measures for severe acute respiratory syndrome (SARS) in Taiwan.” Emerging infectious diseases 9, no. 6 (2003): 718.
5. Huang JH, Zhang WW, Chen LQ, Wang XH, Tan CJ, et al. (2003) Analysis on Infections Status of SARS Contact in Dongcheng Distric. Ji Bing Jian Ce 18(10):371-373.

6. Song ZF, Liu G, Wu HY, Wang DZ, Wu XP, et al. (2003) The effective measures to intercept the infection chain of severe acute respiratory syndrome (SARS) in Sichuan province. Zhongguo Xun Zheng Yi Xue Za Zhi 3(2):144-149.
7. Neuzil, Kathleen M., Cynthia Hohlbein, and Yuwei Zhu. "Illness among schoolchildren during influenza season: effect on school absenteeism, parental absenteeism from work, and secondary illness in families." Archives of pediatrics & adolescent medicine 156, no. 10 (2002): 986-991.
8. World Health Organization. Consensus document on the epidemiology of severe acute respiratory syndrome (SARS). No. WHO/CDS/CSR/GAR/2003.11. World Health Organization, 2003.
9. Lin, Zeming. Predictive and generative models of protein sequence and structure. New York University, 2024.
10. 叶殿秀, 杨贤为, and 张强. "An analysis of the relationship between SARS and meteorological conditions in Beijing area." 气象英文版 29, no. 10 (2003): 42-45.
11. Wang, Chen, Peter W. Horby, Frederick G. Hayden, and George F. Gao. "A novel coronavirus outbreak of global health concern." The lancet 395, no. 10223 (2020): 470-473.
12. WHO, Geneva. "Statement on the second meeting of the International Health Regulations (2005) Emergency Committee regarding the outbreak of novel coronavirus (2019-nCoV)." World Health Organization 30 (2020).
13. WHO, Geneva. "Statement on the second meeting of the International Health Regulations (2005) Emergency Committee regarding the outbreak of novel coronavirus (2019-nCoV)." World Health Organization 30 (2020).
14. Holshue, Michelle L., Chas DeBolt, Scott Lindquist, Kathy H. Lofy, John Wiesman, Hollianne Bruce, Christopher Spitters et al. "First case of 2019 novel coronavirus in the United States." New England journal of medicine 382, no. 10 (2020): 929-936.
15. Riley, Steven, Christophe Fraser, Christl A. Donnelly, Azra C. Ghani, Laith J. Abu-Raddad, Anthony J. Hedley, Gabriel M. Leung et al. "Transmission dynamics of the etiological agent of SARS in Hong Kong: impact of public health interventions." Science 300, no. 5627 (2003): 1961-1966.
16. Donnelly, Christl A., Azra C. Ghani, Gabriel M. Leung, Anthony J. Hedley, Christophe Fraser, Steven Riley, Laith J. Abu-Raddad et al. "Epidemiological determinants of spread of causal agent of severe acute respiratory syndrome in Hong Kong." The lancet 361, no. 9371 (2003): 1761-1766.
17. Dye, Chris, and Nigel Gay. "Modeling the SARS epidemic." Science 300, no. 5627 (2003): 1884-1885.
18. Liang WN, Mi J. (2003) Epidemiological Analysis of SARS in Beijing. Zhonghua Liu Xing Bing Xue Za Zhi 24(12):1096-1099.
19. Wang, Ming, Lin Du, D. H. Zhou, Biao Di, Y. F. Liu, P. Z. Qin, X. W. Wu, X. S. Chen, J. C. Qiu, and Z. R. Li. "Study on the epidemiology and measures for control on severe acute respiratory syndrome in Guangzhou city." Zhonghua liu Xing Bing xue za zhi= Zhonghua Liuxingbingxue Zazhi 24, no. 5 (2003): 353-357.
20. Gully, Paul R. "National Response to (SARS): Canada." In WHO global meeting. Geneva, Switzerland: World Health Organization, p. 2003. 2003.
21. Li, X. Q., W. F. Cai, L. F. Huang, Chun Chen, Y. F. Liu, Z. B. Zhang, Jun Yuan, T. G. Li, and Ming Wang. "Comparison of epidemic characteristics between SARS in 2003 and COVID-19 in 2020 in Guangzhou." Zhonghua liu xing bing xue za zhi= Zhonghua liuxingbingxue zazhi 41, no. 5 (2020): 634-637.
22. Li Z, Wang XJ, Wang M, Lin Y, Ding SJ, et al. (2003) Analysis of serum antibody of SARS and type IV collagen in different populations. Shan Dong Yi Yao. 43(22):5.

Citation: Guangdong Yang. "Building Muscles: The Molecular Regulation of Muscle Regeneration by Hydrogen Sulfide (H_2S)." J Aesthetic Surg Med (2026): 111. DOI: 10.59462/3068-5311.3.1.111.