Hepatic hydrogen sulfide levels are reduced in mouse model of progeria

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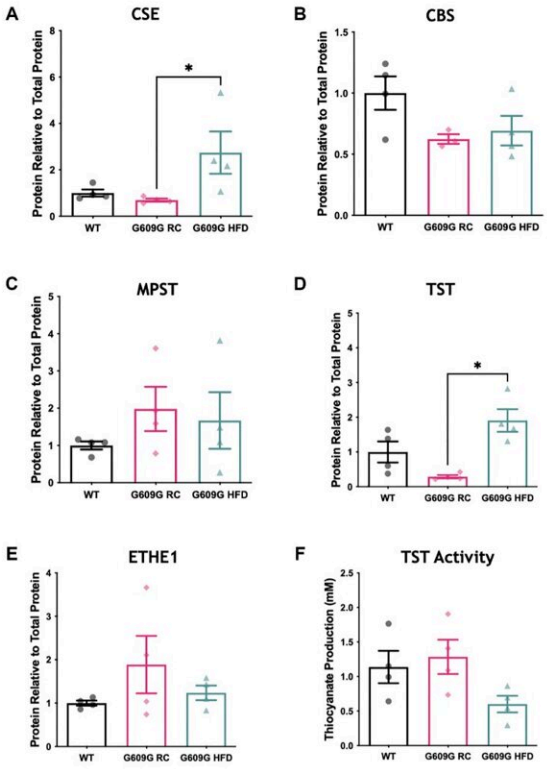

Hepatic protein levels of H2S producing enzymes. Credit: 2023 Wilkie et al.

Hutchinson-Gilford progeria syndrome (HGPS) is a rare human disease characterized by accelerated biological aging. Current treatments are limited, and most patients die before 15 years of age. Hydrogen sulfide (H_2S) is an important gaseous signaling molecule that is central to

multiple cellular homeostasis mechanisms. Dysregulation of tissue H_2S levels is thought to contribute to an aging phenotype in many tissues across animal models. Whether H_2S is altered in HGPS is unknown.

In a new study published in the journal *Aging*, researchers Stephen E. Wilkie, Diana E. Marcu, Roderick N. Carter, Nicholas M. Morton, Susana Gonzalo, and Colin Selman from the University of Glasgow, University of Edinburgh, Saint Louis University, and Karolinska Institute investigated hepatic H_2S production capacity and transcript, protein and enzymatic activity of proteins that regulate hepatic H_2S production and disposal in a mouse model of HGPS (G609G mice, mutated Lmna gene equivalent to a causative mutation in HGPS patients).

"This study was designed and undertaken due to the lack of understanding in the mechanistic targets of known treatments against HGPS and considering the positive association between H_2S and longevity in model organisms," say the researchers.

Here, the researchers employed the HGPS mouse model G609G to test the hypothesis that, in contrast to anti-aging increases in H_2S production, the accelerated aging typical of progeroid mice is associated with reduced hepatic H_2S production. G609G mice were maintained on either regular chow (RC) or high fat diet (HFD). HFD has been previously shown to significantly extend lifespan of G609G mice, and compared to wild type (WT) mice maintained on RC.

RC-fed G609G mice had significantly reduced hepatic H_2S production capacity relative to WT mice, with a compensatory elevation in mRNA transcripts associated with several H_2S production enzymes, including cystathionine-γ-lyase (CSE). H_2S levels and CSE protein were partially rescued in HFD fed G609G mice. The data acquired here confirmed some aspects of the relevance of H_2S in HGPS but raises more questions

about the specific mechanisms at play.

"Regardless, the work presented here addresses an area of research that remains critically understudied and provides new evidence that the accelerated aging phenotype observed in HGPS may be partially explained by a reduction in hepatic H_2S levels," state the researchers.

More information: Stephen E. Wilkie et al, Hepatic hydrogen sulfide levels are reduced in mouse model of Hutchinson-Gilford progeria syndrome, *Aging* (2023). DOI: 10.18632/aging.204835

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