LETTER

H_2S and O_2 sensing

Oxygen-sensing cells in the carotid body, blood vessels, airways, and adrenal gland initiate vital homeostatic responses to hypoxia and hypoxemia. Inappropriate activity of these cells is associated with a variety of pathophysiologies, but despite intense research and obvious clinical applicability, there is no consensus regarding the oxygen sensor that directly couples oxygen availability to the eventual physiological response.

In the recent article "H_2S mediates O_2 sensing by the carotid body," Peng et al. (1) showed that the hypoxic responses of carotid bodies were significantly decreased in mice lacking cystathionine γ lyase (CSE), one of the enzymes involved in H_2S biosynthesis. They also provided evidence for H_2S-mediated hypoxic responses in both chemoreceptor and adrenal chromaffin cells. The authors state in their introduction that "given that carotid bodies are peripheral organs and that H_2S is redox active, we hypothesized that CSE-derived H_2S plays a role in hypoxic sensing by the carotid body"; in their discussion, they state that the "present study established a physiological role for H_2S generated by CSE in mediating hypoxic sensing" (1). This leads the reader to believe that the authors have identified a novel oxygen-sensing mechanism. Actually, this is not a novel hypothesis (1).

Peng et al. (1) failed to cite that the concept of H_2S-mediated O_2 sensing was first proposed by us (2) in 2006. In our model, tissue H_2S concentration is established by the simple balance between constitutive production and oxygen-dependent inactivation. In subsequent work (reviewed in ref. 3), we showed that H_2S and hypoxic responses were identical and that the latter could be blocked by inhibitors of H_2S biosynthesis. We measured H_2S production in many living tissues in real time and showed that H_2S concentration was inversely related to tissue Po_2 at Po_2s encountered during hypoxia. We also showed that H_2S was readily consumed by mitochondria, also at physiologically relevant Po_2s. Clearly, there was substantial evidence for H_2S-mediated O_2 sensing before the study by Peng et al. (1).

Furthermore, Peng et al. (1) failed to acknowledge that we had previously shown H_2S-mediated O_2 sensing in fish chromaffin cells (4) and that these cells are homologous to the mammalian cells. In fact, the only reference to any of our papers was this brief sentence: "It is interesting to note that H_2S has been demonstrated to mediate O_2 sensing by the trout gill chemoreceptors, indicating that it is an ancient well-conserved system across phyla" (1). Actually, this is more than a phylogenetic curiosity. Not only did we present evidence for a H_2S-mediated O_2 sensing mechanism, we clearly pointed out that these chemoreceptors are homologous to, and the antecedent of, mammalian chemoreceptors (5). In our opinion, our work established the precedent for H_2S-mediated O_2-sensing mechanisms in both chemoreceptors and chromaffin cells.

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The authors declare no conflict of interest.

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