American Journal of Physiology-Cell Physiology theme: hypoxia

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THIS ISSUE of the American Journal of Physiology-Cell Physiology begins the publication of a series of theme reviews focused on adaptive responses to cellular hypoxia. The original conception of this series came from AJP-Cell Physiol Associate Editor Michael Goligorsky, who kindly invited me to serve as guest editor and has assisted me in bringing his concept to publication.

The maintenance of oxygen homeostasis is an important principle for understanding development, physiology, and disease pathogenesis. All cells sense and respond to hypoxia. Some of the adaptive responses to hypoxia are cell autonomous, such as the switch from oxidative to glycolytic metabolism, whereas others are non-cell autonomous, such as the changes in cardiovascular and respiratory function that are initiated by depolarization of carotid body glomus cells or the increased red blood cell production that is triggered by increased erythropoietin secretion from the kidney.

In the first article of this series, Toshio Miyata of Tohoku University tackles the interrelated topics of hypoxia and oxidative stress. He focuses on two transcription factors: hypoxia-inducible factor 1 (HIF-1) and nuclear factor-erythroid 2-related factor 2 (NRF-2) that mediate responses to hypoxia and oxidative stress, respectively. Interestingly, they are both negatively regulated under nonstress conditions by ubiquitination and proteasomal degradation. Through this mechanism, cells are poised to respond rapidly to decreased levels of O2 or increased levels of reactive oxygen species. Miyata discusses the role of these systems in disease processes and how targeting them pharmacologically may have therapeutic benefits.

In the following months, reviews will focus on the effect of hypoxia on cell metabolism (Navdeep Chandel, Northwestern University, Chicago, IL), neurotransmitter synthesis (Ganesh Kumar, University of Chicago, Chicago, IL), ion channel function (Larissa Shimoda, Johns Hopkins University, Baltimore, MD), and genetic changes that alter hypoxic responses in humans (Josef Prchal, University of Utah, Salt Lake City). I will conclude the series by discussing the role of hypoxic adaptation in regulating cell proliferation and survival.

Reduced oxygen availability represents a fundamental physiological stimulus. The depth and breadth of the impact of oxygen homeostasis on physiology and medicine are remarkable and continues to increase as more and more investigators establish connections to their areas of interest. The reviews in this series will provide a roadmap for continued exploration.

DISCLOSURES

No conflicts of interest, financial or otherwise, are declared by the author(s).