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The importance of hypoxia sensors in detecting HIF-1 biomarker at high altitude

Abstract

The episode of prolonged exposure to high altitude can cause hypoxia and potential significant health consequences. In people with high altitude disorder, the body reaction to high altitudes starts with the formation of a protein called hypoxia-inducible factor (HIF), which triggers a series of other physiological changes and plays a central role in the hypoxia response; its activity is regulated by the oxygen-dependent degradation of the HIF-1α protein. This deserving condition provides an opportunity to study the effect of low oxygen tension of flying at high altitude that could lead to hypoxia using hypoxia sensor.

Keywords: hypoxia sensors, biomarker, high altitude

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Introduction

Physiological and complication of hypoxia at high altitude

The definition of hypobaric hypoxia (HH) is the partial pressure of PO_2 decrease in the body as ascent to altitudes of >2500m.[1] This condition will cause hypoxemic which is decreased amount of O_2 in the blood due to low maximal oxygen uptake (VO_2 max) in tissue that causes by low atmospheric pressure of high altitudes.[2] In meanwhile, the barometric pressure and ambient partial pressure of oxygen (PO_2) also will drop as ascent to the high altitude with reduce in the PO_2 at every point along the oxygen transport cascade from inspired air to the arterial blood, alveolar space, tissue and venous blood.[3] The reduction of PO_2 in human body becomes greater as ascent to higher altitude and stays at the longer duration space of flight. These will lead to physiological changes and responses in the cardiovascular system over a period of minutes to weeks after exposure to altitude hypoxic that enable the body to adapt to or compensate for the hypoxic environment changes. Besides that, exposure to short-term altitude would directly or indirectly affect the vascular tone of systemic resistance vessel and enhance the respiratory system by increase the respiratory rate and sympathetic activity by activate the peripheral chemoreceptor.

Ascent to high altitude is associated with physiological responses that counter the stress of hypobaric hypoxia by increasing oxygen delivery and by altering tissue oxygen utilization via metabolic modulation.[4] At the cellular level, the transcriptional response to hypoxia is mediated by the hypoxia-inducible factor (HIF) pathway and results in promotion of glycolytic capacity and suppression of oxidative metabolism. Hypoxia inducible factor-1 (HIF-1) plays a key role in oxygen homeostasis by facilitating oxygen supply to the tissues under hypoxic conditions, as during acclimatization to hypobaric hypoxia or in the hypoxemia/inflammation molecular response.

Hypoxia inducible factor-1 is found in almost all body tissues. Under normoxic conditions it is degraded through hydroxylation, but does not undergo degradation in the presence of hypoxia. Therefore, HIF-1 is a key transcription factor in the adaptive responses to low oxygen. HIF-1 is involved in the cellular adaptation to injury, inflammation, infection and cancer.[5]

Biomarker correlated with hypoxia in high altitude

Formenti's (2010), studied the effects of altitude training in patients with a rare genetic disorder, called Chuvash polycythemia or CP, and a group of equally fit people without CP (as control). In people without the disorder, the body's reaction to high altitudes starts with a protein called hypoxia-inducible factor (HIF), which triggers a series of physiological changes.[6] But in those with the disorder, a person's level of HIF protein remains elevated even when they are at sea level. This condition offered the researchers and opportunity to study the metabolic effects of most prolonged in the "high-altitude" state. The results showed those with CP had to quit the test early and achieved a work rate that was 70 percent that of those without CP. The metabolism of CP patients is different and leads to poorer physical performance and endurance. The differences seen in those with Chuvash polycythemia were large, and five patients with positive finding. Because the people with CP did more poorly than those without it, the researchers concluded that there are limits to the benefits of training at high altitudes, could be due to increased levels of HIF in the body.

Thus, this study will be determining whether genetic and inflammatory biomarker would potentially be used as a diagnostic tool in detecting physiological change's effects at high altitude for a long space flight. The exploitation of biomarker detection would promise a novel potential role in detect and prevent the risk of developing hypoxia that can cause poor prognosis in the future.

The importance of sensor in detecting new biomarker of hypoxia

In numerous applications, such as environmental monitoring, clinical diagnostics, DNA sequencing, biological warfare agent detection, and even health condition, the detection and quantification of biological and chemical substances are becoming increasingly important.[7] A desirable sensor should not only be highly sensitive and selective, but also capable of directly viewing results on the device, making it portable.

Fluorescence-based instruments have made significant contributions to chemical and biological sensing over the past few decades. On the basis of the fluorescence parameters being measured,

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various types of fluorescence-based instruments can be distinguished. The most fundamental function of a fluorometer is to measure the fluorescence intensity at fixed wavelength values of excitation and emission, also known as steady-state measurements.

As an alternative to fluorescent techniques, an immunoassay technique is one of the well-known approaches for examining bimolecular interactions would be advantageous. Immunoassay techniques are less labor-intensive (they do not require labels), will provide more accurate binding information (less non-specific binding), and, with the proper instrument, will allow for direct measurement of on/off rates.[8]

Over the past few decades, lateral flow immunoassays (LFIA) have emerged as crucial diagnostic tools for a vast array of applications. Reasons for its use include sensitivity, suitability for detecting a wide range of compounds, and a relatively quick time to obtain a response.[9] Therefore, these devices can be utilized in settings with limited resources, close to the patient, and non-laboratory situations.

In humans, animals, food, and the environment, lateral flow tests are used to detect pathogens, medications, hormones, and metabolites. Due to their ability to detect a variety of drugs, these tests are utilized not just by individuals with certain diseases or food allergies, but also in hospitals and police stations when a yes/no response is required.[10] However, a better LFIA system that can detect new biomarkers and offer faster, more accurate, and quantitative data is desired.

The physiological response to hypoxic stress highly depends on inflammation

Tissues undergo hypoxia when injury, infection, hypoperfusion, ischemia, or hypoxemia as a result of sleep apnea, lung illness, anemia, or other reasons including high altitude exposure.[11] Hypoxia within a cell can induce the expression of inflammatory mediators that signal tissue injury and activate survival responses. Despite the fact that hypoxia-induced inflammation may serve a protective function by initiating an immune response and supporting tissue recovery, it can also contribute to a number of diseases, especially in the context of persistent hypoxia.[12] Therefore, maladaptive hypoxia-induced inflammation may have repercussions on the body's physiology. These hypoxic markers could be used to determine the acute effects of hypoxia and inflammatory responses on jet fighter pilots in high-altitude. The emerging function of HIF in systemic physiology, as outlined here in terms of the response to high altitude, is applicable to any clinical scenario involving hypoxia. In addition, hypoxia has been discovered to stabilize HIF-1a.[13]

Conclusion

These sensor and biomarker may be used as an indicator to detect the hypoxia in the air forces of prolonged exposure to high altitude. The exploitation of biomarker detection is a promised method as novel potential way to detect and prevent the risk of developing hypoxia that can cause poor prognosis in the future.

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Conflicts of interest

The authors declare that there is no conflict of interest.

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