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Backlinks

- Medical papers
- Regulation of Oxygen Homeostasis at the Intestinal Epithelial Barrier Site

Abstract

The unique biology of the intestinal epithelial barrier is linked to a low baseline oxygen pressure (pO2), characterised by a high rate of metabolites circulating through the intestinal blood and the presence of a steep oxygen gradient across the epithelial surface. These characteristics require tight regulation of oxygen homeostasis, achieved in part by hypoxia-inducible factor (HIF)-dependent signalling. Furthermore, intestinal epithelial cells (IEC) possess metabolic identities that are reflected in changes in mitochondrial function. In recent years, it has become widely accepted that oxygen metabolism is key to homeostasis at the mucosae. In addition, the gut has a vast and diverse microbial population, the microbiota. Microbiome-gut communication represents a dynamic exchange of mediators produced by bacterial and intestinal metabolism. The microbiome contributes to the maintenance of the hypoxic environment, which is critical for nutrient absorption, intestinal barrier function, and innate and/or adaptive immune responses in the gastrointestinal tract. In this review, we focus on oxygen homeostasis at the epithelial barrier site, how it is regulated by hypoxia and the microbiome, and how oxygen homeostasis at the epithelium is regulated in health and disease.

Introduction:

a. Overview of oxygen homeostasis regulation

b. Focus on intestinal epithelial barrier site

c. Importance of maintaining oxygen balance in the body

d. Role of intestinal epithelium in maintaining systemic oxygen homeostasis

e. Review of existing knowledge and research gaps

Oxygen Homeostasis:

a. Definition and significance

b. Factors affecting oxygen homeostasis

c. Mechanisms for regulating oxygen levels

d. Role of the intestinal epithelial barrier in maintaining systemic oxygen balance

e. Comparison with other barriers (e.g., blood-brain, alveolar)

Oxygen Sensing at the Intestinal Epithelial Barrier:

a. Overview of oxygen sensing mechanisms

b. Key players in oxygen sensing (e.g., HIF-1, PHDs, IREs)

c. Oxygen sensing pathways in intestinal epithelium

d. Regulation of oxygen transport across the barrier

e. Impact of dietary factors on oxygen sensing and homeostasis

Intestinal Epithelial Barrier Function:

a. Structure and function of the intestinal epithelium

b. Role in maintaining systemic oxygen balance

c. Regulation of paracellular and transcellular oxygen transport

d. Factors affecting barrier integrity (e.g., inflammation, infection)

e. Potential therapeutic targets for modulating oxygen homeostasis

Conclusion:

a. Summary of the current understanding of oxygen homeostasis at the intestinal epithelial barrier site

b. Gaps in knowledge and future research directions

c. Importance of further investigation into this area

d. Potential implications for human health and disease

Key Takeaways:

1. Oxygen homeostasis is crucial for maintaining overall body function.
2. The intestinal epithelial barrier plays a significant role in regulating systemic oxygen balance.
3. Oxygen sensing mechanisms, including HIF-1, PHDs, and IREs, are involved in this process.
4. Dietary factors can influence oxygen sensing and homeostasis.
5. Further research is needed to understand the intestinal epithelial barrier's role in oxygen regulation and its implications for human health.