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POSTER PRESENTATION – P4

ACUTE HYPOBARIC HYPOXIA INDUCES COORDINATED DNA METHYLATION ALTERATIONS AND IMMUNE CELL REDISTRIBUTION IN LOWLANDERS

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Background: Acute hypobaric hypoxia rapidly affects oxygen transport, endocrine regulation, and immune function. However, how short-term hypoxic stress links immune cell redistribution with changes in blood DNA methylation remains unclear.

Objectives: We aimed to characterize coordinated immune and DNA methylation responses to acute hypobaric hypoxia in lowlanders and to distinguish methylation changes caused by altered blood cell composition from potentially cell-intrinsic responses.

Subjects and methods: 18 healthy lowlanders were exposed to simulated altitude (3,500 m) for 75 minutes. Blood samples collected before and after exposure underwent genome-wide DNA methylation analysis using Illumina EPIC arrays. Differential methylation, functional enrichment, and immune cell deconvolution analyses were performed, and EPIC v1 and v2 datasets were integrated to identify methylation changes independent of blood cell composition.

Results: Acute hypobaric hypoxia induced widespread blood DNA methylation changes, particularly in immune-related pathways. Most signals reflected shifts in immune cell composition, with increased neutrophils and decreased lymphocytes. After adjustment, only a few hypoxia-associated loci remained, including an enhancer region of ECE1, a gene involved in vascular responses to hypoxia.

Conclusions: Even brief hypobaric hypoxia induces coordinated immune redistribution and detectable changes in blood DNA methylation. These findings highlight the importance of accounting for blood cell composition and support DNA methylation as a sensitive molecular indicator of acute hypoxic stress.

Keywords: Acute hypobaric hypoxia; Epigenetics; Cell composition deconvolution; DNA methylome; Remodelling; Innate-adaptive immune axis.

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