28th ECSS Anniversary Congress, Paris/France, 4-7 July 2023

ATHLOME: Genetic predispositions to outstanding athletic performance

Diedhiou, N., Heyer, V., Alouane, T., Simon, A., Ohana, M., Laporte, J.

IGBMC

INTRODUCTION:

There is a link between genetic predispositions, diseases and exceptional physiological and athletic abilities. As an example, a mutation of the HFE gene, encoding a protein involved in iron homeostasis, leads to hemochromatosis when present in two copies in the genome, while the presence of a single copy was found enriched in top-level athletes engaged in sports which require either a large capacity for oxygen transfer or high muscular performance. With the present ATHLOME project, we aim to discover new genes and genetic variants modifying neuromuscular and respiratory performances, that would be potential therapeutic targets for diseases affecting these physiological functions.

METHODS:

A first international cohort of thirty-one freedivers with a national or international level was recruited based on their high abilities in comparison to the common population (more than 6 min static apnea for women and 7 min for men, lung vital capacity >110%). Physiological (lung vital capacity, glossopharyngeal respiration...) and biological (blood cell counts and protein levels) data were gathered. Saliva samples were collected allowing DNA extraction and genome sequencing after anonymization. Also, lung MRI was performed to decipher mechanisms of the glossopharyngeal breathing.

RESULTS:

For the analysis of the DNA sequencing raw data, benchmarking of several in-house and commercial pipelines was performed before optimization of the most efficient pipeline. As a first approach, a list of candidate genes implicated in the physiology of breathing, oxygen transport and muscle function was screened and both novel genetic variants as well as known variants were found enriched in the freedivers cohort compared to the control population. A second approach aimed to screen for very rare variants with a high predicted impact on the encoded protein leading to a modification of its expression or function. Two hits with a statistically relevant frequency were found and require further functional investigations. Lung area and height evolution were measured during glossopharyngeal breathing from MRI data from one athlete, documenting a consequent lowering of the diaphragm during this process. CONCLUSION:

The study design and pipeline of analysis were validated by those first results as variants already reported linked to athletic performance were identified in our cohort. However, validation of implicated genes or genetic variants at the statistical and molecular levels may require a larger cohort. In addition, other athletes whose field necessitates resistance to hypoxia and high muscular performance may be recruited and investigated. Also, enrollment of families of athletes would be an asset allowing genetic segregation.

Topic: Health and Fitness

Presentation

Poster

European Database of Sport Science (EDSS)

Supported by SporTools GmbH

