

## Metabolic profiling of elite athletes with different cardiovascular demand

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### Abstract

**Background:** Intensive exercise of elite athletes results in physiological changes in response to increased cardiovascular demand. This study aims to profile metabolic changes in elite athletes from different sport disciplines. **Methods:** Metabolic profiling of serum samples from 500 elite athletes from different sports disciplines who participated in national or international sports events and tested negative for doping abuse at anti-doping laboratories, was performed using non-targeted metabolomics-based spectroscopy combined with ultrahigh-performance liquid chromatography. Multivariate analysis was conducted using orthogonal partial method of least squares discriminant analysis. Differences in metabolic levels between athletes with varying cardiovascular demands were assessed by univariate linear models. **Results:** Out of 743 analyzed metabolites, 112 novel metabolites that changed significantly with increased cardiovascular demand were detected. These included markers of carboxylic acid beta oxidation, oxidative stress and energy-related metabolites. GGM sub-networks identified 6 subnetworks that captured the main metabolic pathways perturbed in reference to cardiovascular demand including fatty acids beta oxidation. **Conclusion:** Data provide evidence that athletes with high cardiovascular demand exhibit a definite metabolic profile which will reflect a singular life style characterized by a strict exercise and a special diet. Metabolic signatures related to elite athletes could potentially be used as biomarkers for his or her overall health and response to their strict environment.

Intensive exercise of elite athletes can cause physiological alterations within the circulatory system in response to increased stroke volume and vital sign, known collectively as cardiovascular demand (CD). This study aimed to match metabolic differences in elite athletes with high vs low/moderate CD and to reveal their underlying metabolic pathways as potential biomarker signatures for assessing health, performance, and recovery of elite athletes. Metabolic profiling of serum samples from 495 elite athletes from different sport disciplines (118 high CD and 377 low/moderate CD athletes) was conducted using non-targeted metabolomics-based spectroscopy combined with ultra-high-performance liquid chromatography.

Results show that DAGs containing arachidonic were enriched in high CD along side branched-chain amino acids, plasminogens, phosphatidylcholines, and

phosphatidylethanolamines, potentially indicating increased risk of disorder within the high CD group. Gamma-glutamyl amino acids and glutathione metabolism were increased in low/moderate CD group, suggesting more efficient oxidative stress scavenging mechanisms than the high CD group. This first most comprehensive metabolic profiling of elite athletes provides an evidence that athletes with different CD show a singular metabolic signature that reflects energy generation and oxidative stress and potentially places the high CD group at a better risk of disorder. Further studies are warranted for confirmation and validation of findings in other sport groups in light of potential confounders related to limited available information about participants.

Excessive training of professional athletes causes alterations in their blood metabolic profile that depends largely on the sort and duration of their training regimen [1, 2]. Various behavioral, biochemical, hormonal, and immunological markers are routinely used to assess athletes' physical status during a training program [3, 4]. Previous studies, however, have demonstrated that conventional tests could not detect the physiological differences between endurance athletes and control subjects, or differences before and after training sensitively [5, 6]. Therefore, a more comprehensive metabolic profiling has been considered in order to identify global physiological changes in response to training. Metabolomics offers a quantitative measurement of the metabolic profiles related to exercise in professional athletes so as to spot biomarkers related to their performance, response to fatigue, and potentially their respective sports-related disorders [5, 7]. Non-targeted metabolomics allows the detection of changes in response to various physiological states such as pre-/post-exercise and offers identification of metabolic signatures with potential translational impact for both professional athletes and general public [8]. These changes include metabolites related to glucose, lipid, aminoalkanoic acid, and energy metabolism [1, 5], like those involved in ATP (ATP) synthesis, beta-oxidation of free fatty acids, and ketone bodies [8]. Previous studies in healthy volunteers have

## *Extended Abstract*

demonstrated significantly reduced excretion of amino acids with increased fitness levels and increased fat oxidation rate during exercise [9]. Furthermore, metabolomics profiling of athletes undergoing intensive exercise revealed increase in plasma lactate [10, 11] and adenine breakdown products [12], indicating anaerobic metabolism and ATP cycling, respectively. Further studies of the effect of exercise showed elevated tricarboxylic acid (TCA) cycle intermediates, markers of aerobic energy production, in skeletal muscle biopsies [13, 14]. Intensive exercise was also shown to trigger changes within the levels of amino acids, including a moderate uptake of glutamate in striated muscle resulting in release of alanine to promote ammonia metabolism [11, 15, 16], with corresponding changes in plasma concentrations of these metabolites [17, 18]. Elevation in serum levels of sex steroid hormones was also reported in endurance athletes only in response to high exercise intensities [19].

## **Biography :**

Mohamed A Elrayess has completed his PhD at University College London (UCL) in Cardiovascular Genetics in 2002, then studied the therapeutic utilization of hematopoietic stem cells in disorder at the Department of Medicine at UCL for one year. He then spent over seven years working as a somatic cell Scientist in Eisai Ltd., a serious international drug company , leading projects that specialize in somatic cell therapy in various neurodegenerative diseases. He is currently a Senior Scientist at Anti-Doping Lab Qatar, where he leads projects that specialize in the role of stem cells in diabetes and genetics and metabolomics of elite athletes and holds an Honorary Senior Lectureship at UCL.

This work is partly presented at International Conference on Metabolomics and Diabetology

May 23-24, 2018 | New York, USA