

## Publication

# The Metabolic Signature of Cardiorespiratory Fitness: A Systematic Review.

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Cardiorespiratory fitness (CRF) is a potent health marker, the improvement of which is associated with a reduced incidence of non-communicable diseases and all-cause mortality. Identifying metabolic signatures associated with CRF could reveal how CRF fosters human health and lead to the development of novel health-monitoring strategies.; This article systematically reviewed reported associations between CRF and metabolites measured in human tissues and body fluids.; PubMed, EMBASE, and Web of Science were searched from database inception to 3 June, 2021. Metabolomics studies reporting metabolites associated with CRF, measured by means of cardiopulmonary exercise test, were deemed eligible. Backward and forward citation tracking on eligible records were used to complement the results of database searching. Risk of bias at the study level was assessed using QUADOMICS.; Twenty-two studies were included and 667 metabolites, measured in plasma (n = 619), serum (n = 18), skeletal muscle (n = 16), urine (n = 11), or sweat (n = 3), were identified. Lipids were the metabolites most commonly positively (n = 174) and negatively (n = 274) associated with CRF. Specific circulating glycerophospholipids (n = 85) and cholesterol esters (n = 17) were positively associated with CRF, while circulating glycerolipids (n = 152), glycerophospholipids (n = 42), acylcarnitines (n = 14), and ceramides (n = 12) were negatively associated with CRF. Interestingly, muscle acylcarnitines were positively correlated with CRF (n = 15).; Cardiorespiratory fitness was associated with circulating and muscle lipidome composition. Causality of the revealed associations at the molecular species level remains to be investigated further. Finally, included studies were heterogeneous in terms of participants' characteristics and analytical and statistical approaches.; CRD42020214375.

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