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Identification of changes in serum analytes and possible metabolic pathways associated with canine obesity-related metabolic dysfunction

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ABSTRACT

The main objective of this study was to identify analytes that could change and that could help to clarify the metabolic and physiopathological changes related to canine obesity-related metabolic dysfunction (ORMD). For this, serum from 35 overweight/obese dogs, with and without ORMD, was submitted to a comprehensive panel of biochemistry analysis, a gel-free tandem mass tag isobaric label-based proteomic analysis, and, finally, selected proteins were used as a starting point for creating a protein interaction network.

Dogs with ORMD showed significantly higher serum concentrations of alanine aminotransferase (ALT), alkaline phosphatase (ALP), Ca, total proteins, albumin, total cholesterol, triglycerides, glucose, and butyrylcholinesterase (BChE) activity in comparison with dogs without ORMD. Proteomic analysis revealed that 23 proteins related to lipid metabolism, the complement factor system, cellular adhesion and functionality, inflammation, and coagulation were altered in dogs with ORMD. Finally, the obtained protein interaction network highlighted that the central term of this network was the negative regulation of the immune response. These data suggest that canine ORMD is associated with changes in analytes that reflect altered lipid metabolism, and liver and immune function impairment and suggests the potential for a prothrombotic state and lung function alterations.

Introduction

Metabolic syndrome (MetS) in humans is associated with increased risks of cardiovascular disease, liver dysfunction, and/or type 2 diabetes and decreased lifespan (Grundy et al., 2004). In veterinary medicine, MetS in horses is a risk factor for laminitis among other pathologies (Frank et al., 2010; Frank, 2011). Around 20% of overweight/obese dogs were shown to have metabolic derangements and exhibit MetS criteria (Tvarijonaviciute et al., 2012b; Lahm Cardoso et al., 2016). However, since dogs do not experience some of the consequences of MetS identified in humans, mainly atherosclerosis or type 2 diabetes mellitus, the clinical value of the canine MetS has been questioned (Verkest, 2014). Nevertheless, dogs with MetS (or obesity-related metabolic dysfunction, ORMD) present with modest insulin resistance, hyperlipidemia and hypoadiponectinemia (Tvarijonaviciute et al., 2012b; Piantedosi et al., 2016). Furthermore, proteins associated with lipid metabolism, the complement system, coagulation, immune response, the hyaluronan metabolic process, and antioxidants were identified as being altered through the use of fluorescence two-dimensional differential gel electrophoresis (2D DIGE) and mass spectrometry in the plasma of obese dogs with ORMD relative to dogs without ORMD, indicating the need of further studies (Tvarijonaviciute et al., 2016).

A traditional way to study the possible changes in the metabolism is the performance of a panel of biochemistry analytes in serum. In addition, the use of proteomics has the potential for the identification of many other proteins involved in metabolism and homeostasis. Quantitative gel-free proteomics using isobaric labeling reagents has a high sensitivity, precision, and signal-to noise ratio, and a broad dynamic range (Thompson et al., 2003).

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