ORAL SUPPLEMENTATIONS WITH L-GLUTAMINE OR L-ALANYL-L-GLUTAMINE DO NOT CHANGE METABOLIC ALTERATIONS INDUCED BY LONG TERM HIGH-FAT DIET IN THE B6.129F2/J MOUSE MODEL OF INSULIN RESISTANCE

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Introduction Obesity and diabetes are major worldwide causes of cardiovascular disease which is associated with a general state of low-grade inflammation. Conversely, some nutrients, such as L-glutamine (GLN) and L-alanyl-L-glutamine dipeptide (DIP) have been shown to potentiate the expression of the 70 kDa family of heat shock proteins (HSP70), which are strongly anti-inflammatory. **Materials and Methods** In this work we aimed to investigate the effects of long-term supplementations with GLN or DIP, in the high-fat diet (HFD)-fed B6.129SF2/J mouse model, over insulin sensitivity and signaling, oxidative stress markers, metabolism and HSP70 expression. Mice were fed in a standard low-fat diet (STA) or a HFD for 20 weeks. In the 21th week, mice from the HFD group were allocated in five groups and supplemented for additional 8 weeks with GLN, DIP or its constituint amino acids: 1) HFD controls, 2) HFD+DIP group, 3) HFD+L-alanine group, 4) HFD+GLN group or 5) HFD L-alanine+L-glutamine group. Procedures were approved by the Federal University of Rio Grande do Sul Ethics Committee on Animal Experimentation (CEUA #21293/2011). **Results** HFD induced higher body weight, fat pad, fasted glucose and total cholesterol in comparison with STA group. Amino acid supplementations did not induce any modifications in these parameters. Although insulin tolerance tests indicated insulin resistance in all HFD groups, any amino acid supplementation could improve insulin sensitivity in the model. There were also no significant differences in the immunocontents of insulin receptor. Notably, HSP70 contents in the liver were markedly increased in HFD controls as compared to STA group, which suggest that insulin resistance is only in the beginning. **Conclusion** Apparently, B6.129SF2/J mice are more resistant to the harmful effects of HFD through a mechanism that may include gut

adaptation, reducing the absorption of nutrients, including amino acids, which may explain the lack of improvements in our intervention.

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