

Leucine-rich diet alters the (1) H-NMRI serum metabolomic profile of tumour-bearing adult rats from offspring of mothers supplemented with this branched-chain amino acid.

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Abstract

Cancer-cachexia is a multifactorial chronic disease associated with high inflammation and loss of muscular and adipose tissues and affects 30% of cancer patients. A maternal diet with leucine could alter the inflammatory state and regulate protein synthesis positively, modulating the effects of cachexia. Metabolomic analyses are an important technique to value the effects of cachexia because of the identification of altered metabolites in serum samples and consequently evaluate the impacted metabolic pathways in these patients. Thus, we analysed the regulatory effects of maternal nutritional supplementation with leucine over the serum metabolic profile (using the $^1\text{H-NMR}$ analysis) of the adult offspring rats bearing the Walker 256 tumour. The cachexia leads to a characteristic metabolic profile related to an increase in the glycolytic pathway, which is likely modulated by maternal leucine-rich diet that altered the $^1\text{H-NMRI}$ serum metabolomic profile, improving the oxidative pathway.

Key words:

Cancer-cachexia; maternal nutritional supplementation; serum metabolomic profiling

Introduction

Cancer is a worldwide health problem, and cachexia is a syndrome associated with this disease, which is responsible for 30% of cancer patients death. Studies are investigating the potential of nutritional supplementation with the branched-chain amino acid leucine in modulating the cachexia state. The intrauterine and weaning periods are susceptible to epigenetic changes due to the influence of environmental factors, such as the mother's nutrition. So, we studied the preventive potential of the maternal nutritional supplementation with leucine in cancer-cachexia state. Nuclear magnetic resonance ($^1\text{H-NMR}$) was used to characterise the metabolic profiles of serum, allowing the identification of the impacted metabolic pathways in cancer-cachexia state.

Results and Discussion

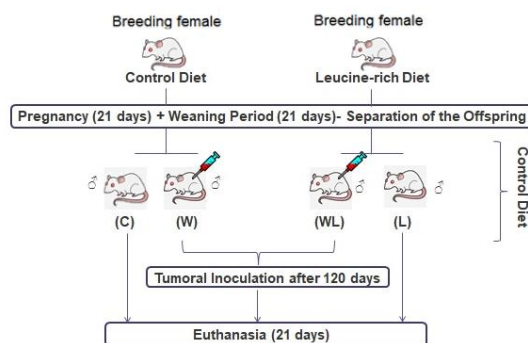


Image 1. Experimental procedure (CEUA nº 4224)

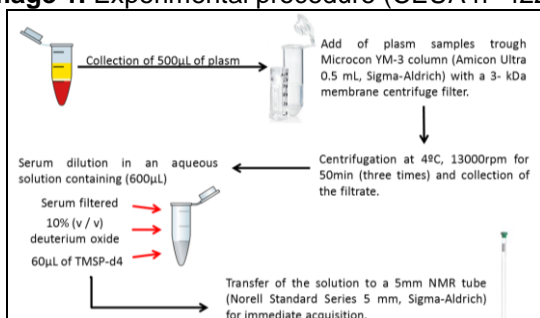


Image 2. Serum sample preparation and $^1\text{H-NMR}$ analysis.



In our results, 66 metabolites were found. Comparisons were made between the groups WxC, LxC and WLxW. The metabolites with significant difference are shown in Image 3 and Table 1:

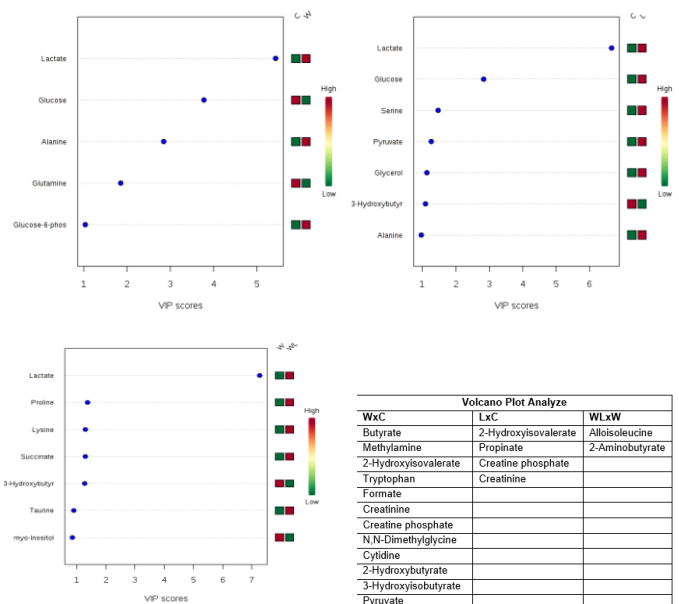


Image 3 and Table 1. VIP and Volcano Plot analyses of impacted metabolites found in WxC, LxC and WLxW groups.

Conclusions

Cachexia state leads to a characteristic metabolic profile mainly associated with an increase in the glycolytic pathway. Maternal leucine-rich diet alters the $^1\text{H-NMRI}$ serum metabolomic profile, improving the oxidative pathway.

Acknowledgement



World Health Organization. Cancer. (2018), on line version; Metabolic profiling, metabolomic and metabonomic procedures for NMR spectroscopy of urine, plasma, serum and tissue extracts. *Nat. Protoc.* 2, 2692–2703 (2007);