

## (1)H-NMRI metabolomic profile of skeletal muscle was altered by maternal nutritional supplementation with leucine in adult offspring tumour-bearing rats.

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### Abstract

Cachexia is a cancer-associated metabolic syndrome that causes muscle spoliation, which leads to a reduced life quality of cancer patients. Maternal nutritional supplementation with the branched-chain amino acid leucine has been studied as an attempt to minimise/prevent the muscle waste, as an epigenetic effect from pregnancy and weaning periods during the environment modulatory role. Metabolomic analysis is an important technique to evaluate the preventive effects of maternal nutritional supplementation in a cachexia process. Thus, the present study analysed the possible regulatory effects of this supplementation on muscle metabolic profile of the adult offspring rats bearing a Walker-256 tumour. The skeletal muscle (gastrocnemius) was processed by <sup>1</sup>H-NMRI analysis to determine the metabolomic profiles. The tumour-bearing rats were spoiled and had an increased muscle energy expenditure. The maternal leucine supplementation improved the energy availability for muscle function and activity.

### Key words:

Cancer-cachexia; maternal nutritional supplementation; muscle metabolomic profile

### Introduction

Cancer is a set of diseases responsible for the death of 1 in 6 people around the world. Cachexia is an associated multifactorial metabolic syndrome, marked by muscle spoliation, which can reduce the life quality in cancer patients. Maternal nutritional supplementation with the branched-chain amino acid leucine has been studied as an attempt to counteract the damages caused by cachexia, ameliorating the loss of muscle mass, and also in a preventive way, since epigenetic alterations occurred by environmental modulating role during the periods of pregnancy and weaning. The nuclear magnetic resonance (<sup>1</sup>H-NMR) is an important tool to analyse the metabolic profile, identifying changes presented in cachexia state.

### Results and Discussion

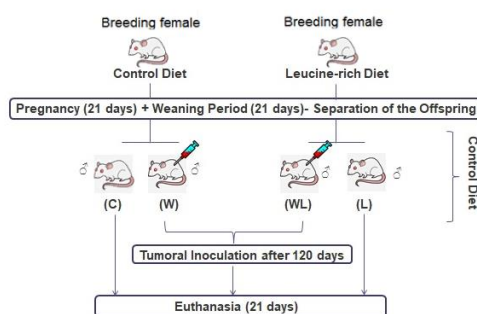


Image 1. Experimental procedure (CEUA n° 4224)

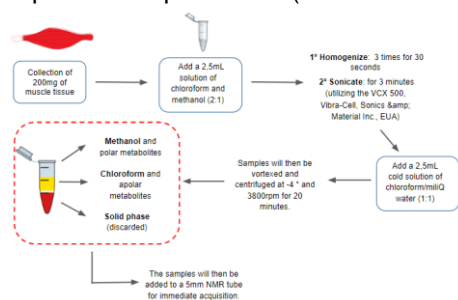


Image 2. Muscle sample preparation and <sup>1</sup>H-NMR analyze.

Our results showed 54 metabolites found. Comparisons were made among the groups WxC, LxC and WLxW. The metabolites with significant difference are shown below in Image 3:

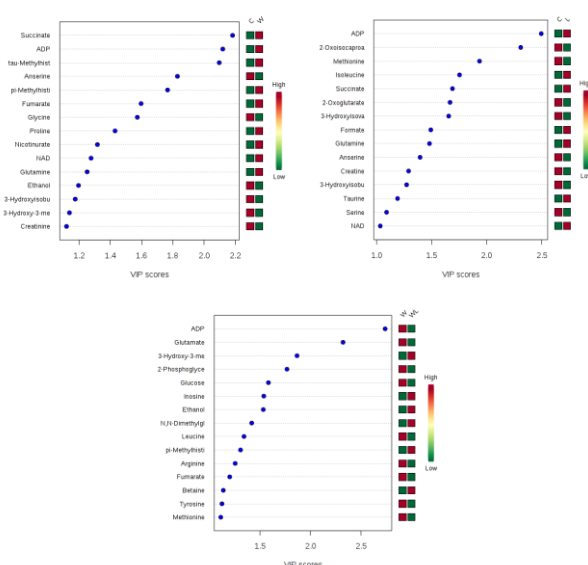


Image 3. Impacted metabolites in skeletal muscle of all three groups.

### Conclusions

The <sup>1</sup>H-NMRI analyses showed the energy expenditure impacted by tumour evolution, which led to a muscle tissue jeopardise; counteracting, the maternal nutritional supplementation with leucine attenuated the catabolic state of cachexia.

### Acknowledgement



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