Reviewer's report

Title: Effects of leucine supplemented diet on intestinal absorption in tumor bearing pregnant rats.

Authors:

Gislaine Ventrucci (ventrucc@unicamp.br)
Maria Alice R de Mello (mellomar@rc.unesp.br)
Maria Cristina C Gomes-Marcondes (cintgoma@unicamp.br)

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Reviewer: Dr Peter Taylor

Level of interest: A paper whose findings are important to those with closely related research interests

Advice on publication: Unable to decide on acceptance or rejection until the authors have responded to the compulsory revisions

COMPULSORY REVISIONS

1. There is some confusion throughout caused by nomenclature of experimental groups. For example, it is not immediately clear (especially in Abstract) that tumor-bearing and pair-fed rats are also pregnant. Equally, groups C, P and L are all referred to as "control" at different stages. Group names and text should be altered to fully reflect these points.

2. Was ethical approval obtained / required for these studies?

3. Some detail of perfusion system (e.g. whether perfused loop, in situ, recirculated, perfusate volume) is required.

4. Table 1. Does body weight gain represent total weight or carcass minus fetus / tumor (as appropriate)? Fetal weight in tumor-bearing rats seems to be markedly lower than in other groups, although no indication of statistical significance of these results is shown.

5. Which muscle is being studied (e.g. gastrocnemius)? It is difficult to know exactly whether tumor growth causes a real "decrease" in muscle weight rather than a reduced increase from onset of experiment.

6. I assume the absorption studies reflect disappearance of solute from recirculating perfusate, in which case "absorption" includes solute metabolised / assimilated by gut tissue as well as solute entering the blood. On this basis, the following points need to be addressed:-
   (a) Given that absorption is measured per cm of gut, it is extremely important to establish whether changes in gut mucosal mass / protein content have occurred and whether these may account for some underlying changes in absorption.
   (b) Equally, could differences in water absorption produce anomalous "apparent" rates of solute absorption?

Nevertheless, the observation that Leu, Met and glucose absorptions respond differently to treatments
excludes the above as sole reason(s) for observed changes.

7. I do not think the statements in the first paragraph of Discussion concerning "somatic parameters" are fully supported by the data and they should be modified in light of the following observations:-
(a) much of the reduction in weight gain, muscle protein balance etc in tumor-bearing rats can readily be ascribed to reduced food intake (i.e. effects of tumor-burden or pair-feeding are essentially equivalent), although there do appear to be substantial and potentially-important differences in effect on fetal weight.
(b) The major effects of Leu supplementation are to prevent experimental hypoglycaemia (Table 1) and to stimulate Amino Acid absorption / assimilation by the perfused intestine (only for Met uptake are there appreciable tumor-related differences).

DISCRETIONARY REVISIONS

1. The specific relevance to pregnancy should be made more clear in the Background section
2. BCAA are a source of metabolic fuel for skeletal muscle (particularly during prolonged exercise) but I question whether they are "the major source" (as stated in Background).
3. I think the Discussion section is too long, repetitious and contains some material of only peripheral relevance. It could easily be reduced in length by 30% without loss of coherence, particularly the long section (3 pages) on effects of Leu and cancer on muscle protein turnover.
4. The work of Diamond and colleagues (e.g. Am J Physiol 261, R793; 271, G969) on nutritional adaptations of intestinal transport processes might be further considered in the Discussion.

Competing interests:

None declared.