Reviewer’s report

Title: Milk is not just food but most likely a genetic transfection system activating mTORC1 signaling for postnatal growth

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Reviewer: Ernesto Bernal-Mizrachi

Reviewer’s report:

In this review the authors provide intriguing support for the hypothesis that milk is a potent stimulus for postnatal growth via the mTOR pathway. This article is similar to the 2012 J Obesity article with the addition of primary data from 10 healthy subjects and the discussion of the exosome.

Major compulsory revisions:

1. Do the exosomes survive the pasteurization process? The data presented about miRNA are from raw cow’s milk and human milk. If the exosome is not a factor in pasteurized dairy products then the direct effects of branched chain AA remain as the major driver of cell growth.

2. The data provided from the healthy adult subjects needs to be put into the context of other typical meals or perhaps one that would also be high in branched chain amino acids to highlight the additional effects of milk.

3. Teleologically speaking there are undoubtedly beneficial effects of human milk on the growing neonate. For instance, the attenuation of BAT thermogenesis may be a developmentally appropriate postnatal event. At what point would the authors suggest that this mTORC1 signaling becomes pathogenic or in excess.

4. The authors should include a discussion of the effects of BCAA on the liver as another major metabolic organ.

Minor essential revisions:

1. For the section “Leucine-insulin-mTORC1 pathway” please provide evidence that mTORC1 regulates insulin secretion. In addition, there is evidence from animal models that mTORC1 enhances beta-cell mass in genetic models. Please provide references for this.

2. For the section “AA-IGF1-insulin-mTORC1 pathway promoting peripheral cell growth” could the authors be more specific about the meaning of “peripheral”.

Quality of written English: Needs some language corrections before being published

Statistical review: No, the manuscript does not need to be seen by a
statistician.

Declaration of competing interests:

"I declare that I have no competing interests"