Reviewer's report

Title: Metabolic phenotype of methylmalonic acidemia in mice and humans: the role of skeletal muscle

Version: 4 Date: 11 September 2007

Reviewer: Carlos Mello

Reviewer's report:

General
In this interesting study Chandler et al. elegantly show that a large portion of circulating MMA has an extra-heptorenal origin and likely derives from the skeletal muscle in a murine model with a null allele at the methylmalonyl-CoA mutase locus, which is correctable by lentiviral transduction. The authors discuss, based on the evidence provided by the analysis of a series of patients, that transplantation does not correct the biochemical phenotype of the affected patients probably because of organ specific contributions to MMA production, and suggest that modulating skeletal muscle metabolism may represent a strategy to increase metabolic capacity in methylmalonic acidemia.

Major Compulsory Revisions (that the author must respond to before a decision on publication can be reached)

Minor Essential Revisions (such as missing labels on figures, or the wrong use of a term, which the author can be trusted to correct)

Please use the greek letter "mu" instead of "u" throughout the manuscript, but particularly in the inset and y axis title of figure 5 (in which units should be between parentheses).

Discretionary Revisions (which the author can choose to ignore)

What next?: Accept after minor essential revisions

Level of interest: An article of importance in its field

Quality of written English: Acceptable

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.