Reviewer’s report

Title: Oral intake of Phenylbutyrate and vitamin D3 upregulates the Cathelicidin LL-37 in human macrophages: A dose finding study for treatment of tuberculosis

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Reviewer: eduardo sada

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The author presents a study that demonstrated the induction of cathelicidin LL37 after receiving Phenylbutyrate (PB) and vitamin D3 by oral route in humans. They presented data from 24 healthy subjects who received PB either with vitamin D3 or without, interesting only 500 mgs associated to vitamin D have the expected results of induction of LL37, production of peptide and bactericidal activity against MTB by MDM. The results are clear and valuable, the methods appear to be adequate as well as the analysis of the results. The conclusions are correct and the results suggested a treatment scheme useful for PB trials in patients with TB. I only have some questions about the study.

Major Compulsory Revisions

The results of bactericidal activity in the model of MTB infection are clear however the authors did not include a control group of healthy subjects without any intervention (No PB no vitamin D) I think if the authors have this results it should be included in the manuscript and make the analysis against this group. Other recommendation is that probably the results could be more reliable if in the bactericidal assay the authors use lower rate of infection 5:1 instance to multiplicity of infection (MOI) of 25:1.

Minor Essential Revisions

Only 500 mgs of PB with vitamin D were effective and 500 mgs twice a day did not demonstrate this effect. It could be interesting to discuss for the authors why this administration did not work as well as just 500 mgs.

It is interesting that they detected LL37 in lymphocytes besides to MDM. There very few information in the literature about thea and deserve some comments in the manuscript.

Level of interest: An article of outstanding merit and interest in its field

Quality of written English: Acceptable

Statistical review: Yes, but I do not feel adequately qualified to assess the statistics.