Reviewer's report

Title: Kinetics of mycolactone in human skin during antibiotic therapy for Mycobacterium ulcerans disease.

Version: 1 Date: 8 February 2014

Reviewer: Tim Stinear

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Sarfo et al tackle an important question here, looking at the relationship between mycolactone levels, bacterial burden and disease state in different presentations of M. ulcerans infection.

I have a few issues that the authors should consider.

Major:

I would have liked to have seen substantially more detail on the establishment of mycolactone detection sensitivity for the cytotox assay and MS assays. These data should be included in the main body of the manuscript, rather than an additional file. In this vein, rather than just showing fitted curves for these experiments (Supp figure 1) it would be more informative to see the original data plotted too, including biological replicates or means of replicates with error spread indicators for these spiking experiments. Spiking different tissue samples would be particularly important to understand method variability. There was simply not enough information in the methods or results to assess how the spiking experiments were performed. At the moment it reads that only a single dose of mycolactone was spiked, but Supp Fig 1 shows dose response curves. Much more detail is needed in this section to give the reader an understanding of the variation in the extraction method used and the inherent variability of the assays used. Establishing the limit-of-detection for these methods developed together with an understanding of the variability of the assay is critical to enable sensible interpretation of the data from real clinical specimens. Once a more sophisticated assessment of the methods has been performed then the data from the real clinical specimens may need to be reinterpreted.

Minor:

1. Abstract: "We sought to measure the concentration of mycolactone concentration within lesion"...too many "concentrations"

2. Why use both Pearson and Spearman correlation analysis? Spearman rho correlation coefficients were not cited in the ms. Were the data normally distributed? Perhaps use Spearman instead of Pearson as the former is a non-parametric test, based on rank and does not assume normality.

3. Background: " Variations in the side chains can give rise to small differences among the family of mycolactones." Meaning not clear here.
4. Monitoring The Clinical Response To Antibiotic Treatment: "The maximum diameter and the diameter at right angles were measured and the average diameter was used". What is being referred to here? I assume its the lesion but need to make clear.

5. Eighty patients with clinically confirmed Mu were all PCR positive. One hundred percent clinically confirmed correct cases is unusually high. Would it be more accurate to say 80 patients with laboratory-confirmed (IS2404 PCR) were selected for the study?

Level of interest: An article of importance in its field

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

Statistical review: Yes, and I have assessed the statistics in my report.

Declaration of competing interests:

I declare that I have no competing interests