Reviewer’s report

Title: Antimicrobial characteristics of Berberine against Prosthetic Joint Infection-related Staphylococcus aureus of Different Multi-locus Sequence Types.

Version: 2 Date: 09 Mar 2019

Reviewer: Cornelia Braicu

Reviewer's report:
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In order to be published to BMC complementary and Alternative medicine, this paper need to be accompanied by major revisions and entirely restructured, being focused on mechanistic insights.

Additional analysis on the NGS data for MLSTcheck needs to be performed.

A flow chat with work flow for the transcriptome assembly and annotation for Staphylococcus aureus will be very useful.

The main issue is related to the figure 3, additional information related to the altered transcriptomic pattern should be presented, the data need to have a biological significance using specific bioinformatics tools (KEEG, Reactome, Ingenuity…). Therefore the 'hub gene' investigation and 'Protein-Protein Interaction (PPI)' analysis resulted in insignificant housekeeping genes is mandatory to increase the value of the paper. Volcano plot gives only information related to the number of altered transcript, no information related to the biological significance. Therefore gene ontology classification and some networks are mandatory.

The conclusion section needs to be sustained by a proposed mechanism of action for exerting antibacterial activity for S aureus. These should be sustained by in vitro data, to sustain the hypothesis related to PJI.

The data from figure 1, can be represented as % of control, in this case can be much easy demonstrated the antimicrobial activity of berberine.

Additional information related to the berberine solution, please define GC for figure 2 and 3.

Are the methods appropriate and well described?
If not, please specify what is required in your comments to the authors.

No
**Does the work include the necessary controls?**
If not, please specify which controls are required in your comments to the authors.

No

**Are the conclusions drawn adequately supported by the data shown?**
If not, please explain in your comments to the authors.

No

**Are you able to assess any statistics in the manuscript or would you recommend an additional statistical review?**
If an additional statistical review is recommended, please specify what aspects require further assessment in your comments to the editors.

I am able to assess the statistics

**Quality of written English**
Please indicate the quality of language in the manuscript:

Needs some language corrections before being published

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