**Review of NKOB Proposal “Genome architecture analysis of *Listeria monocytogenes” –* Summary**

Overall, we found the environment and resources available to the investigators to be appropriate for completion of the outlined objectives. We also found the approach outlined for data acquisition, quality control, sequence processing, mapping, analysis, and visualization to be appropriate with two exceptions. In the “SAMtools” section of the proposed methods, the authors state that “SAMtools will be utilized to generate alignments in a per-position format which will enable the calling of variants,” but SAMtools is the variant caller itself and does not generate alignments. The chosen p-value cutoff of 0.05 is also described as being “biologically relevant.” It’s worth noting here that while biologists primarily tend to use this cutoff for *statistical* significance, p values above or below 0.05 don’t necessarily say anything about *biological* significance or relevance.

The background offered for the organisms of interest was appropriate and well-cited, although the reviewers identified questions about what kind of variation the authors were looking for between these strains and what that might mean. It was assumed that SNPs or indels in genes related to virulence would be the focus, but that wasn’t outlined specifically. While the innovative aspects of the study were clearly identified, some reviewers had difficulty understanding the specific aspects of the approach described that were novel. Because the authors have already identified the innovative element, the solution is probably as simple as rewording this portion to be slightly more explicit.

The roles of the investigators were clearly defined, and a general approach for troubleshooting was offered. We suggest outlining more specific plans for potential conflicts between investigators about approaches taken. Overall, the investigators paid careful attention to detail, particularly in their proposed methods, which identify specific software, present preliminary findings, and include specifics on parameters like coverage and p values. As a result, we are generally confident in the authors’ ability to carry out their proposed analyses and produce meaningful findings.