Response to Reviewer 1 Comments

Point 1: What are CTX-M genes and why you chose to develop a pipeline for such genes? It is not clear in the main text, and the reader does not have to google the acronym for understanding the objective of the study. So please, define it and better describe your aim in the introduction section.

Response 1:

At the regional level, the Manizales Antibiotic Resistance Group (GRAM) is in charge of presenting the accumulated antibiotic resistance data of the main hospitals in the city. Within the total isolation of patients in intensive citizens, general hospitalization and emergencies, the main bacteria identified are Enterobacteriaceae such as Escherichia coli, Klebsiella pneumoniae, Eneterobacter cloaca, among others; all these species with the capacity to carry genes of BLEE of the CTX-M group. In addition, according to the antibiotic susceptibility analyses carried out by the different clinics in the city, resistance to cefotaxime (cephalosporin with a broad hydrolyzable spectrum by CTX-M) ranges between 15 and 35% (Salazar, JD. et al 2018). This means that in Manizales up to one out of every three isolations of this group of bacteria is suspected of carrying a CTX-M type BLEE; the high frequency of this type of BLEE in our context highlights the importance of this type of development for antibiotic surveillance processes that take into account metagenomic data.

The validation of this pipeline allows us to point the way to the extension of the analysis for other important genes such as TEM, SHV, metalloenzines, carbapenemases type KPC or OXA-48 that are probably prevalent in our regional context considering the characteristics of populations, clinical management protocols of patients and health, asepsis in operating rooms. Since this is a common problem, the development of a pipeline that allows the identification of resistance variants becomes a fundamental step in the establishment of a modern antibiotic surveillance system. The subsequent goal will be to test this development on metagenomic data derived from the surveillance process, in collaboration with research groups for this area of knowledge.

Point 2: Please revised the format of the articles by improving the description of the methods and by describing (and not inserting) the Figures in the main text.

Response 2: The required adjustments will be made
Point 3: The English needs to be improved, in particular for section 2.1

Response 3: The required adjustments will be made

Point 4: Please provide the data you used, with a clear reference. Authors must have the possibility to repeat your experiments.

Response 4: From there, and taking into account the review of the state of the art, we started from the CTX-M database already filtered by means of phylogenetic tree.

Subsequently, the reference metagenome to be studied was selected by means of a revision in the EBI-Metagenomics database (https://www.ebi.ac.uk/metagenomics/) considering the high probability that the CTX-M gene was present by reviewing four metagenomes related below which are inputs to make the prototype, only one was selected for the study:

1.  https://www.ebi.ac.uk/metagenomics/projects/ERP001506

2.  https://www.ebi.ac.uk/metagenomics/projects/ERP020191

3.  https://www.ebi.ac.uk/metagenomics/projects/ERP016968

4.  https://www.ebi.ac.uk/metagenomics/projects/ERP009131

The metagenome selected because of the high probability of finding there CTX-M for the proposed neural network training was:

- Antibiotic resistance within the preterm infant gut.
https://www.ebi.ac.uk/ena/data/view/PRJEB15257

Point 5: Several words are written with a "-" in the middle of the words. Please correct them.

Response 5: The required adjustments will be made