February 26, 2021

**DEPARTMENT OF MICROBIOLOGY AND IMMUNOLOGY**

1520A MEDICAL SCIENCE RESEARCH BUILDING I

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Dear Dr. Imperiale,

I am happy to submit my manuscript, **Amplicon sequence variants artificially split bacterial genomes into separate clusters,** for your consideration at *mSphere*. This work quantifies the risk of splitting bacterial genomes into multiple clusters when researchers use amplicon sequence variants or too finely defined operational taxonomic units to analyze 16S rRNA gene sequence variants. The main conclusion is that the use of these practices artificially splits genomes into separate units of inference and creates a situation where researchers could unknowingly claim that different copies of the *rrn* operon from the same genome have different ecologies.

The manuscript has also been submitted to bioRxiv as a preprint.

Sincerely,

A picture containing text, weapon, gun, black

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Patrick D. Schloss, PhD

Professor