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Dear Editorial Board,

We are pleased to resubmit our manuscript, **“*mspms*: A Comprehensive R Package and Graphic Interface for Multiplex Substrate Profiling by Mass Spectrometry Analysis,”** for consideration in *GigaScience*.

Since our initial submission, the *mspms* software has successfully completed peer review at Bioconductor and is now an accepted part of its ecosystem. This process led to significant enhancements, including a more intuitive user interface and seamless integration with Bioconductor’s extensive analytical tools.

In response to the editorial feedback, we have substantially revised the manuscript. These revisions include a more clearly articulated rationale for the work, an improved logical flow, and a restructured methods section to ensure clarity and accessibility. We believe these updates have strengthened the manuscript significantly.

We have also revitalized the *mspms* graphical interface. Key improvements include enhanced error-handling, loading indicators, refined graphics, and new features such as user-defined thresholds, publication-quality plot downloads, and interactive feature selection.

The core message of our manuscript remains unchanged: we present *mspms*, a novel, open-source R package now available through Bioconductor, designed to streamline and democratize the analysis of multiplex substrate profiling by mass spectrometry (MSP-MS) data. Benchmarking against established ground-truth data for cathepsins A-D demonstrates that *mspms* reliably infers substrate specificities across diverse proteases. With its robust functionality and user-friendly design, *mspms* is poised to become a standard tool in protease research, significantly advancing the study of proteolytic enzymes and their roles in health and disease.

We chose to resubmit this manuscript to *GigaScience* because we believe it is the ideal venue for our work, given the journal’s emphasis on high-quality research that prioritizes reproducibility, usability, and practical utility. Additionally, the open-access model and global reach of *GigaScience* align with our mission to make the *mspms* package broadly accessible to the research community.

We have no conflicts of interest to declare. All authors have approved the manuscript for submission, and the content has not been published or submitted for publication elsewhere.

Thank you for considering our manuscript for publication. We look forward to the opportunity to share our research with the scientific community through *GigaScience*.

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