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Dear Editorial Board,

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

Our work introduces **mspms**, a novel, open-source R package designed to streamline and democratize the analysis of multiplex substrate profiling by mass spectrometry (MSP-MS) data. Following rigorous benchmarking with ground-truth data for cathepsins A-D, we demonstrate that **mspms** reliably infers substrate specificities across a broad spectrum of proteases. With its robust functionality and user-friendly design, **mspms** fills a critical need in proteomics, offering researchers a powerful tool to accelerate the study of proteolytic enzymes and their roles in health and disease.

The **mspms** package has been officially accepted into the Bioconductor ecosystem following an independent peer-review process. This ensures seamless compatibility with established analytical pipelines. The package also features an intuitive graphical user interface, making it accessible to researchers regardless of their programming expertise. These capabilities are tailored to support several popular modern proteomics workflows, broadening its appeal and usability across a wide range of researchers.

We believe *Molecular & Cellular Proteomics* is an ideal venue for this work, given the journal’s focus on advancing proteomics tools, technologies, and applications. By combining the power of open-source software with reproducible workflows, **mspms** directly aligns with MCP’s mission to promote innovative and accessible solutions for the global proteomics community.

All authors have approved the manuscript for submission. We confirm that this work has not been published or submitted elsewhere, and we have no conflicts of interest to disclose.

Thank you for considering our manuscript. We look forward to the opportunity to share **mspms** with the proteomics community through *Molecular & Cellular Proteomics*.

Sincerely,

Charlie Bayne

On behalf of all authors