Multiplex targeted mass spectrometry assay for one-shot flavivirus diagnosis

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Significance

With pandemic emergence and increasing magnitude of flavivirus outbreaks in recent years, there is an urgent need for robust and easily extendable technologies for flavivirus diagnosis and typing to facilitate better disease management, surveillance, and control. Here, we report a single-shot mass spectrometry assay for distinguishing Dengue virus serotypes, <u>Zika</u>, Yellow fever, and <u>Kunjin</u> viruses, including coinfections in a multiplex assay with high specificity and sensitivity. This assay is easily extendable to a wider panel of flaviviruses and addresses the shortcomings of current diagnostics, holding high promise as a future flavivirus diagnostic tool.

Abstract

Targeted proteomic mass spectrometry is emerging as a salient clinical diagnostic tool to track protein biomarkers. However, its strong analytical properties have not been exploited in the diagnosis and typing of flaviviruses. Here, we report the development of a sensitive and specific single-shot robust assay for flavivirus typing and diagnosis using targeted mass spectrometry technology. Our flavivirus parallel reaction monitoring assay (*fv*PRM) has the ability to track secreted flaviviral nonstructural protein 1 (NS1) over a broad diagnostic and typing window with high sensitivity, specificity, extendibility, and multiplexing capability. These features, pivotal and pertinent to efficient response toward flavivirus outbreaks, including newly emerging flavivirus strains, circumvent the limitations of current diagnostic assays. *fv*PRM thus carries high potential in positioning itself as a forerunner in delivering early and accurate diagnosis for disease management.

Figure



Figure: The image portrays targeted mass spectrometry technology as a powerful analytical tool for precise diagnosis and typing of flaviviruses (fv) – the group of pathogens causing vector, mainly mosquito, - borne diseases such as dengue, zika, West Nile and yellow fever. The article describes this extendable multiplexed fvPRM assay with high potential in clinical and epidemiological utility for disease management. *Mosquito photo courtesy of Deng Lu* (*Environmental Health Institute, National Environment Agency, Singapore*) and flavivirus structure in the blood drop adapted from PDB.