Abstract

Lethal Encephalitis of Unknown Origin—Elucidation by Metagenomics †

Martin Beer

Institute of Diagnostic Virology, Friedrich-Loeffler-Institut, Suedufer 10,
17493 Greifswald-Insel Riems, Germany; Martin.Beer@fli.de
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Abstract: Novel and (re)emerging viruses cause frequent threats to both human and animal health. Diagnostic metagenomics using unbiased next-generation sequencing (NGS) is the key method for the identification of new pathogens. With today's available state-of-the-art platforms, NGS can be broadly used to also identify novel and unknown pathogens in different sample materials (even in point-of-care diagnostics) or to characterize the complete genomes of all types of pathogens. Nevertheless, the extreme numbers of sequence fragments resulting from NGS analyses requires not only novel diagnostic pipelines including powerful software tools for big data analysis but also a new dimension of knowledge and resources. We therefore developed and validated a universal workflow for metagenome diagnostics for the analysis of disease syndromes in both animals and humans. The metagenomics pipeline will be presented, and several examples with the detection and characterization of novel viruses will be shown. The power of diagnostic metagenomics will be presented with different examples focusing on lethal encephalitis cases in both animals and humans where we were able to identify a series of novel or unexpected viral pathogens. Furthermore, the detection of zoonotic pathogens was only possible by a "one-health" approach and the close relationship between veterinary and human medicine. The major aim of the presentation is to give an idea about the capabilities of modern NGS-based metagenomics and to learn more about the newly detected viral pathogens. Since a large proportion of severe encephalitis cases still remain unexplained, a main conclusion is the recommendation that those cases should be analyzed by using a modern and powerful metagenomics workflow.

Keywords: next-generation sequencing (NGS); metagenomics; virus discovery; encephalitis; virus infection; "one-health"; zoonosis