Viral Metagenomics – New applications for the broad-range detection of viromes in veterinary and public health settings

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Motivation and Objectives

Metagenomic methods for detection of viruses provide new diagnostic tools to the veterinary and public health laboratories, with powerful capacities to detect and to monitor the viromes in clinical samples. The Metagenomics methodology is divided into three main activities or steps: (1) wet-lab methodology ;(2) sequencing; and (3) data analysis. Integrating all three parts is of critical importance for the result as well as the interpretation of those. Our groups at the OIE Collaborating Centre for the Biotechnology-based Diagnosis of Infectious Diseases in Veterinary Medicine, Uppsala, Sweden and at the SLU Global Bioinformatics Centre, Uppsala, Sweden are working with the development and evaluation of the methodological and technological platforms for viral metagenomics. Together with the National Veterinary Institute (SVA), we develop and test methods for extraction of viromes, feasibility of sequencing platforms to deliver metagenomic data-sets and evaluate bioinformatics tools as well as combine them into software packages for analysis and exploration of metagenomes, for separation, classification, assembly and visualization of genomic data in metagenomic samples. The aim of the work is to provide insight into using the metagenomics approach for detection of emerging viruses, monitoring of wild life for known pathogens as well as providing a tool for rapid characterization of viral pathogens in outbreak situations.

Methods

Clinical samples are collected through the continued monitoring performed by the SVA, as well as through international contacts, both from wild-life and from domestic animals. Viromes are prepared for analysis by homogenization of material, DNase/RNase treatment and nucleic acid purification. The viral nucleic acids in the pre-processed samples are quantified and, depending on chosen sequencing platform, either processed directly or pre-amplified using random amplification methods. Data from sequencing is processed following a general paradigm; read QC, quality based filtering, rough assembly, homology search and visualization. The viromes are then characterized and the results are disseminated to the clinicians and to the health authorities.

Results and Discussion

The development of metagenomics as a tool for exploration of viromes has proven to be an extremely powerful technique. We have previously published several articles and are continuously developing both Wet-lab methodology, evaluating sequencing platforms and developing the bioinformatics analysis (Belák *et. al*. 2013; Granberg *et. al.* 2013).

Our current work focuses at virome isolation and amplification, development of modular bioinformatics tools for use within the diagnostic setting, and integration with the clinical sciences, as well as ongoing evaluation of sequencing technologies together with the Swedish National Infrastructure for Large-scale Sequencing and NGS equipped laboratories within Europe.

With the current development of new technological platforms, the availability of high-throughput sequencing moves from the core facilities out into the medium and small scale diagnostic labs. This provides re-emerging challenges in data analysis and interpretation as well as enormous educational needs. We aim at providing the capability to utilize these methods and

technologies in a meaningful way within the field of veterinary virology and public health.

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