disparate pipeline processes self-contained and reproducible. Furthermore, we moved all pipeline settings into a separate JSON file. After every analysis, the pipeline settings and virtual-environment recipes will be archived (immutably) under a persistent unique identifier. This allows long-term precise reproducibility. Likewise, after every run the raw data and final products will be automatically archived, complying with data retention laws/guidelines. All the disparate processes in the pipeline are parallelized and automated via Snakemake1 (i.e. end-users need no coding skills). In addition, interactive web-reports such as MultiQC [http://multiqc.info] and Krona2 are generated automatically. By combining Snakemake, Conda, and containers, our pipeline is highly portable and easily scaled up for outbreak situations, or scaled down to reduce costs. Since patient privacy is a concern, our pipeline automatically removes human genetic data. Moreover, all source code will be stored on an internal Gitlab server, and, combined with the archived data, ensures a clear audit trail. Nevertheless, challenges remain: (1) reproducible reference databases, e.g. being able to revert to an older version to reproduce old analyses. (2) A user-friendly GUI. (3) Connecting the pipeline and NGS data to in-house LIMS. (4) Efficient long-term storage, e.g. lossless compression algorithms. Nevertheless, this work represents a step forward in making user-friendly clinical diagnostic workflows.

A44 Genome analysis of bovine enterovirus variants isolated from cattle in Thailand

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Bovine enteroviruses (BEV) are non-enveloped RNA viruses of the genus Enterovirus, family Picornaviridae, which are commonly found in cattle. They have been classified into two species, enterovirus E (EV-E) and enterovirus F (EV-F). The viruses were previously considered non-pathogenic, but recent evidences suggest their association with pathogenesis in cattle. BEV-like enteroviruses have also been increasingly isolated from a wide range of animals, such as sheep, goats, horses, geese, possum, and deer, from many countries. The isolation and characterization of novel enteroviruses expands the range of the genus. Our data show that both EV-E and EV-F are circulating in cattle in Thailand. The viruses have been detected in 35–67 per cent of dairy and meat cattle feces in Kanchanaburi Province. Recently, we retrieved EV-E isolates from cattle feces by virus isolation in Madin-Darby Bovine Kidney cells. Four virus isolates were subjected to whole-genome sequencing using Illumina next-generation sequencing. A phylogenetic analysis of VP1 capsid protein, which is used for virus genotyping, suggested that there are at least two EV-E genotypes circulating in cattle in the area of study. Two virus strains, closely related to EV-E1 with amino acid sequence identities >88 per cent were identified as EV-E1. The other two strains, closely related to EV-E2 with amino acid sequence identities < 85 per cent, were likely to constitute a new EV-E genotype separate from the existing EV-E2.

A45 Genetic diversity of anelloviruses in the blood virome

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The microbiome has an important impact on human health. The microbiome is a complex ecosystem that contains of a wide variety of microorganisms shaped by the immune system, host genetic factors, and the environment. Studies of the human virome have identified a diverse group of viruses in different compartments of the body, including viruses of the Anelloviridae family. These viruses are widespread among the general population. In various clinical conditions an association has been found between the Anelloviridae abundance and the patient's immune status. However, no pathological consequences have been identified for this viral family. In this study, we analyzed the Anelloviridae diversity in plasma samples of liver transplant recipients. The virome contents of plasma samples from liver transplant recipients were sequenced by next-generation sequencing techniques on an Illumina platform (NextSeq). Complete Anelloviridae ORF1 contigs were extracted from metagenomic data and aligned with 66 RefSeq anellovirus sequences for phylogenetic analysis. The study included 144 plasma samples of 24 liver transplant recipients who had been infected by the hepatitis B virus and developed end-stage liver disease. The identified Anelloviridae viruses belong to the Alphatorquevirus, Betatorquevirus, and Gammatorquevirus genera. In total, we were able to retrieve 142 unique anellovirus contigs that were less than 95 per cent identical on the nucleotide level. A phylogenetic tree was constructed from these contigs with 65 RefSeq sequences retrieved from GenBank. The majority of the identified Anelloviridae sequences were assigned to the Alphatorquevirus genus, which represents the largest group of anelloviruses. We were able to identify a high diversity of Anelloviridae viruses in serum samples of liver transplant recipients. Phylogenetic analysis showed that the majority of anelloviruses belonged to the Alphatorque genus. Future research should focus at elucidating the role of these commensal viruses in both immunocompromised and healthy individuals.

A46 Hand, foot, and mouth disease in Vietnam

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Hand, Foot, and Mouth Disease (HFMD) is a major public health issue in the Asia-Pacific region. Our research program aims to address unanswered questions about clinical, epidemiology, pathogen evolution, cost of illness, and host-genetic makers associated with severe HFMD in Vietnam. A multi-hospital-based observational study has been conducted at three referral hospitals in Ho Chi Minh City, Vietnam since 2013. Demographic, clinical data, and cost of illness were collected alongside clinical specimens. Multiplex PCR and next-generation sequencing were employed to identify enterovirus serotypes and to study pathogen evolution, respectively. A genome-wide association-based approach was used to explore genetic markers of disease severity. From 2013 to 2017, 2,191 HFMD patients were enrolled. More than twenty enterovirus serotypes were detected in 84.3 per cent of patients. EV-A71 was the major cause, accounting for 22 per cent of total number of cases, followed by CV-A6 (21%), CV-A16 (13%), and CV-A10 (8%). Interestingly, these four common enteroviruses replaced each other during the study period. EV-A71 and CV-A6 were the two most predominant viruses detected in 2013 and 2014. However, CV-A6 was replaced by CV-A16 and CV-A10 in 2015 and 2016, respectively. A total of 396 whole-genome sequences (EV-A71 ($n = 200$), CV-A6 ($n = 98$), CV-A10 ($n = 66$), and CV-A16 ($n = 32$)) were obtained. Phylogenetic analysis showed that EV-A71 subgenogroup B5 has replaced C4 in 2012, and, since then, B5 has continued to circulate predominantly, while C4 has been sporadically detected. All Vietnamese CV-A6 isolates belonged to genogroup A, which has caused large outbreaks of HFMD worldwide. Costs of illness varied between disease severities, ranging from $USD 244 [95% confidence interval (95% CI): 230–258] per patient for grade 2A (mild) to $USD 1984 (95% CI: 1,752–2,227) for grade 3 (severe). The genome-wide association study identified two genetic markers potentially associated with severe HFMD. The results highlight that active surveillance and understanding pathogen evolution are essential to inform public health in prioritizing the development of intervention strategies. Efforts to unravel the evolutionary process of Vietnamese CV-A10 and CV-A16 in relation to global strains are ongoing. An independent cohort is needed to replicate the preliminary findings of the genome-wide association study.