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Refinement Efforts on CBER’s Reference Virus Database (RVDB) to Enhance Accuracy and Specificity of Virus Detection

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The potential of next generation sequencing (NGS) for broad adventitious virus detection in biological products was demonstrated by the unexpected detection of porcine circovirus type 1 (PCV1) in a licensed rotavirus vaccine (Victoria et al., J. Virol. 2010) and the discovery of a novel rhabdovirus in Sf9 insect cells, a commonly used cell substrate for baculovirus-expressed products (Ma et al., 2014). NGS is now being recognized by regulatory agencies and health authorities as an alternative method for adventitious virus detection to supplement or replace the currently recommended in vivo and in vitro assays. However, the qualification and validation of NGS methods relies on the public availability of reference materials.

Reference materials are needed to evaluate the entire NGS workflow, including the upstream wet-bench steps for sample and library preparation to the downstream bioinformatics analysis pipeline. CBER’s non-redundant, reference viral database (RVDB; https://rvdb.dbi.udel.edu/) was developed to enhance bioinformatics analysis for detection of known and novel viruses. This included all viral, virus-related, and virus-like nucleotide sequences (excluding bacteriophage) with a reduced cellular sequence content to enhance broad virus detection with less computational burden (Goodacre et al., 2018). This talk will describe the improvements and ongoing work on RVDB for identifying and removing or annotating some of the non-viral sequences that are present in RVDB due to direct input of sequences from GenBank.