Are Circulating Type 2 Vaccine-Derived Polioviruses (VDPVs) Genetically Distinguishable from Immunodeficiency-associated VDPVs?

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Abstract—Vaccine-Derived Polioviruses (VDPVs) may emerge during person-to-person transmission (circulating VDPV [cVDPV]) or during prolonged replication in individuals with primary immunodeficiency (iVDPV). To prevent the emergence of type 2 vaccine-derived polioviruses (VDPV2s) which represents >90% of the VDPV during the past two years, WHO implemented a worldwide synchronized switch from trivalent oral poliovirus vaccine (tOPV; types 1, 2, and 3) to bivalent OPV (bOPV; types 1 and 3) in April 2016. When planning the scope of a post-switch outbreak response, it is important to know if the recently identified VDPV is likely to be cVDPV or iVDPV, as the public health responses dramatically differ in the two events: outbreak requires a community immunization response while chronic infection requires careful patient monitoring and potential individual treatment. Here we demonstrate that genetic distinctions between cVDPV and iVDPV sequences can be calculated (to some extent) to inform global poliovirus outbreak response, particularly for VDPV2. We performed a survey of cVDPV and iVDPV nucleotide sequences of the VPI capsid region (~900 nucleotides) from GenBank. A non-redundant dataset contains 33 cVDPV2 isolates and 33 iVDPV2 isolates was built. We compared each sequence to its Sabin 2 parental strain to determine the number of genetic nucleotide (NT) and amino acid (AA) substitutions. cVDPV2 and iVDPV2 sequences show similar profiles for NT and AA frequencies, codon usage, and AA conservation. Simple counts of NT, AA, and codon substitutions in comparative analyses between cVDPV2 and iVDPV2 were insufficient for a clear distinction between the two VDPV2 categories. However, the combined measures of NT and AA substitutions (from VP1 and neutralizing antigenic site sequences) were more informative, with more non-synonymous (AA changes) in iVDPV2 than cVDPV2. This work highlights that the genetic variations between iVDPVs and cVDPVs may be reflect the differences of the viral micro-environments, interactions between virus and host, and the selective pressures during person-to-person transmission compared with chronic infections in immune-deficient patients. The dataset was small but the issue is certainly deserving of attention and suggesting the needs for further data collections from poliovirus surveillance. This is the first attempt using computational techniques to quantify the genetic difference between cVDPVs and iVDPVs.

Keywords—Vaccine-Derived Polioviruses; Immunodeficiency; Circulation; Outbreak