

Endogenous Simian Retrovirus Variations in Vero Cells: Implications for Quality Control of a Human Vaccine Cell Substrate

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The Vero cell lineage, a permanent cell line established from the kidney tissue of an African green monkey (AGM), is susceptible to various types of viruses. Vero cells have pseudo-diploid karyotypes, and are non-tumorigenic unless they are extensively passaged. Due to these characteristics, Vero cells have been utilized as not only a biological material in research laboratories but also a cell substrate for human vaccines in pharmaceutical industries. The Vero cell genome harbors a variety of simian endogenous type D retrovirus (SERV) sequences. In this study, a transcriptome analysis suggested that DNA hypomethylation released the epigenetic repression of SERVs in Vero cells. Moreover, comparative genomics among three Vero cell sublines and an AGM reference revealed that the genomes of the sublines have ~80 SERV integrations, and that the same integration events are shared with the three cell sublines. In addition, apparently intact retroviral integrations were found to commonly exist in the genome of Vero cells. These results strongly suggest that SERVs integrated in the genome of Vero cells did not retrotranspose after the establishment of the cell lineage as far as cells were maintained under standard culture and passage conditions, providing a scientific basis for controlling the quality of pharmaceutical cell substrates and their derived biologics.

(CS and TS equally contributed to this study, and are the co-first authors. NO and KH are co-correspondence)