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Deep sequencing of the yellow fever vaccine strain 17D reveals low diversity compared to wild-type parent Asibi virus and population stability for primary and secondary seed lots of 17D vaccine

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Yellow fever virus (YFV) is controlled by the use of live-attenuated vaccine strain 17D that was empirically derived by passage of wild-type Asibi strain in chicken tissue. For RNA viruses such as YFV, the quasi species model is now the paradigm for understanding diverse population structures that arise during the viral lifecycle and provides a powerful and novel context to study the genomic determinants of live vaccine attenuation, stability, and safety. We hypothesized that low diversity is an indicator of vaccine stability and attenuation, and performed a massively parallel genomic analysis (also known as Deep Sequencing) to compare the commercial vaccine substrain 17D-204 produced in the United States (YF-Vax®) with the wild-type parental strain Asibi from which the vaccine was derived. YF-Vax® was found to be of significantly lower diversity than Asibi virus suggesting that attenuation of 17D was due to lack of diversity in the vaccine strain to revert to a virulent phenotype. Analyses were extended to investigate a panel of YFV vaccine primary and secondary seeds representing distinct subculture histories and different producers. Results indicate a low presence of sequence variant substructure across seed lineages for the modern YFV vaccine substrains 17D-204, 17D-213 and 17DD. We hypothesize that low diversity of the RNA population for 17D vaccines contributes to a mechanism of attenuation and provides a paradigm for investigating other live attenuated vaccines. Furthermore, the low diversity among multiple vaccine seeds and lots suggests deep sequencing can contribute to the quality control of live attenuated RNA virus vaccines.

Biography

Alan D T Barrett obtained his BS, MS and PhD in the area of arbovirology from the University of Warwick followed by a Post-doctoral fellowship at the London School of Hygiene and Tropical Medicine. He is currently Director of the Sealy Center for Vaccine Development and World Health Organization Collaborating Center for Vaccine Research, Evaluation and Training for Emerging Infectious Diseases. He was an editor of the Journal of General Virology and an Associate Editor for Vaccine. He has authored/co-authored more than 270 research papers, reviews and book chapters.

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