S1 Text. Additional details comparing the JHMM approach to previous methods used for analyzing var DBLa population structure (S18 and S19 Figs). A binary presence/absence matrix was built by clustering the global dataset at 96% pairwise sequence identity using the pipeline described in [1]. The resulting matrix indicated which DBLα type (clustered at 96%) was present in each isolate. A principal component analysis (PCA) was then performed (S18 Fig). The first principal component indicated a separation between the South American isolates and the rest of the world. This was consistent with the proportions identified using the JHMM approach, which indicated that the South American isolates were the most distinct. The third and fourth principal components indicated a separation among the African isolates (S19 Fig). By applying t-Distributed Stochastic Neighbor Embedding (t-SNE) [2], we were able to better resolve the global structure from the binary presence/absence matrix (Fig 2B). t-SNE is able to distinguish structure at multiple scales in high dimensional settings whilst preserving local structure. To compare with the approach of Tessema et al. (2015) [3], we built a phylogenetic tree using RAxML [4], based on treating each isolate's binary presence/absence vector as a binary sequence (Fig S8). Finally, to compare with the approach of Rougeron et al. (2017) [5] we used the same binary matrix as input to Admixture in order to estimate underlying historical populations [6] (S9 Fig). Using cross-validation as a measure of clustering error, we found that two latent clusters were most strongly supported (S10 Fig). Whilst approaches based on clustering at a global sequence identity threshold of 96% identified broadly similar structure in the global var population, the JHMM approach is better able to disentangle more subtle or distant relationships such as the affinity between species and the relationship between countries within Africa.

To compare with an approach not reliant on clustering at 96% pairwise sequence identity we used the alignment-free Feature Frequency Profile approach of Sims et al. (2009) [7]. Alignment-free algorithms have proved useful in analyzing large complex datasets where recombination, genetic shuffling and other genetic events make generating accurate alignments difficult [8,9]. Using Jensen-Shannon divergence as a distance measure between the resulting k-mer frequency profiles for each isolate, we built a neighbor-joining tree using FastME v2.1.4 [10]. The resulting phylogeny is shown in S11 Fig.

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