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## Estimated Timing of the Last Common Ancestor of the SARS Coronavirus

TO THE EDITOR: Using the viral sequences derived from clinical specimens collected in Hong Kong between February and April 2003 from 139 patients with the severe acute respiratory syndrome (SARS), we attempted to estimate the timing of the last common ancestor of the coronavirus associated with the recent outbreaks of SARS. We previously reported the results of phylogenetic analysis, using the same set of spike-gene sequences as that in the SARS-associated coronavirus (SARS-CoV) isolated during the early phase of the outbreak (February to April) in Hong Kong and southern China, together with those available in the public data base. 1

Assuming that the mutation rate was uniform, we carried out a linear regression analysis that was similar to the approach used for the timing of the origin of human immunodeficiency virus type 1.2 The divergence (i.e., branch length), based on the genetic distance between the isolates and the root of the phylogram, was plotted as a function of the sampling time (Fig. 1).2,4 The root was defined as the first diverging point<sup>2</sup> of the hypothetical common ancestor of SARS-CoV. The best-fit line was generated by the linear regression analysis extrapolated back to the past. The divergence of the sequences from the common ancestor was found to have a linear relation with time (P<0.001), in a progressive manner. The last appearance of the common ancestor of SARS-CoV was estimated to be on December 12, 2002 (95 percent confidence interval, September 26, 2002, to January 13, 2003), when the value of the divergence was zero. This finding suggests that the first deviation of the ancestral virus may have occurred in late 2002, close to the time of the first reports of SARS in southern China.<sup>5</sup> Although additional sampling of sequences, involving a longer time frame, is needed, the current findings shed some light on the origin of SARS-CoV and thus may help elucidate its evolution.

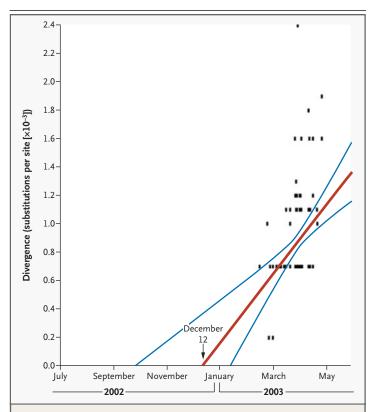


Figure 1. Timing of the Most Recent Common Ancestor of the Hong Kong SARS-CoV.

The divergence of the sequence from the ancestral sequence was plotted against sampling time (GraphPad Prism, version 4.00).<sup>3</sup> The red line represents the best-fit line obtained by linear regression analysis, and the blue lines indicate the 95 percent confidence intervals.

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