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## Molecular Evolution of the RNA-Dependent RNA Polymerase and Capsid Genes of Human Norovirus Genotype GII.2 in Japan during 2004-2015.

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### Abstract

The RNA-dependent RNA polymerase (*RdRp*) and capsid (*VP1*) genes of 51 GII.2 human norovirus (HuNoV) strains collected during the period of 2004-2015 in Japan were analyzed. Full-length analyses of the genes were performed using next-generation sequencing. Based on the gene sequences, we constructed the time-scale evolutionary trees by Bayesian Markov chain Monte Carlo methods. Time-scale phylogenies showed that the *RdRp* and *VP1* genes evolved uniquely and independently. Four genotypes of GII.2 (major types: GII.P2-GII.2 and GII.P16-GII.2) were detected. A common ancestor of the GII.2 *VP1* gene existed until about 1956. The evolutionary rates of the genes were high (over  $10^{-3}$  substitutions/site/year). Moreover, the *VP1* gene evolution may depend on the *RdRp* gene. Based on these results, we hypothesized that transfer of the *RdRp* gene accelerated the *VP1* gene evolution of HuNoV genotype GII.2. Consequently, recombination between ORF1 (polymerase) and ORF2 (capsid) might promote changes of GII.2 antigenicity.

**KEYWORDS:** RNA-dependent RNA polymerase; capsid; molecular epidemiology; molecular evolution; norovirus; phylogeny

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