

17 Visualizing the Evolution of RNA Viruses: A Web-Based platform for Tracking Genetic and Antigenic Changes



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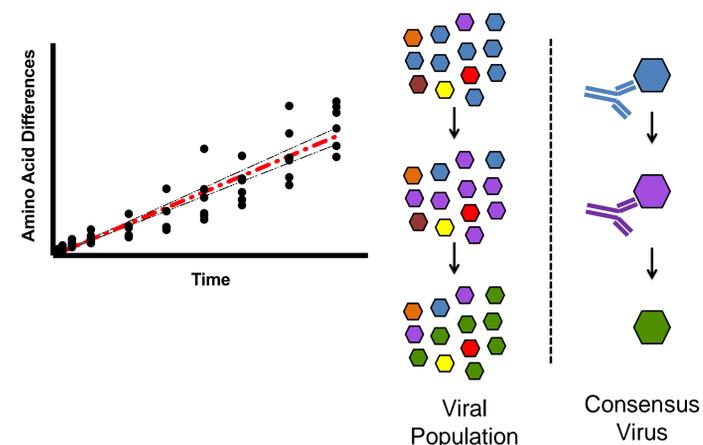
Abstract

RNA viruses, such as noroviruses and influenza viruses, are notorious for their ability to rapidly mutate. This facilitates adaptation to new environments and evasion of immune responses, posing a significant challenge to vaccine development. While online tools exist to track the evolution of influenza viruses, there is a lack of similar resources for human noroviruses. To address this gap, we have developed a web-based application that provides a global, spatiotemporal view of norovirus genotype distribution over the past three decades, as well as a tool to track the temporal diversification of residues involved in the antibody-mediated neutralization of GII.4 noroviruses, the most common norovirus genotype. This innovative tool allows users to visualize the changes occurring in viruses circulating each year, including the combination of multiple residues. By combining this tool with antibody binding information, we have demonstrated that current GII.4 norovirus strains have reconstituted conformational epitopes from ancestral variants. The web application, built using the Shiny R platform, is highly flexible and can be easily expanded to track the evolution of other medically relevant viruses, such as influenza H5 and H7 viruses. We anticipate that this tool will facilitate the surveillance and antigenic characterization of emerging noroviruses and influenza viruses with pandemic potential,

Introduction

RNA Viruses Present an Extreme Diversity that Challenge Vaccine Design

RNA Viruses can Accumulate Mutations Overtime Resulting in a Virus-Host Arms Race (Antigenic Drift)

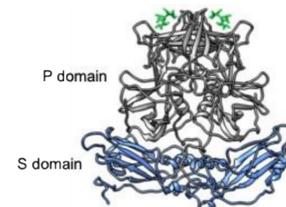


Motivation: Can we develop a simple web-based tool that can be used to plot and track genetic and antigenic diversity of medically-relevant RNA viruses?

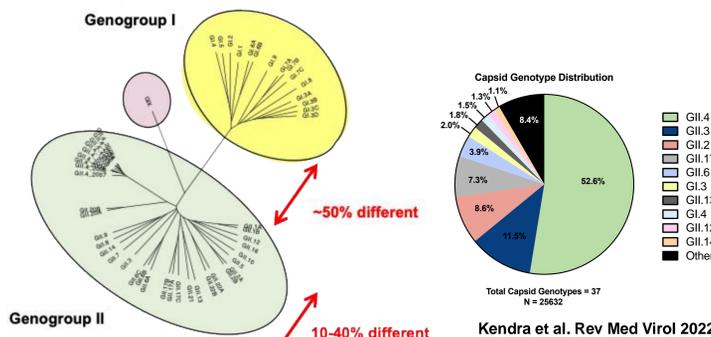
Model to Build the Tool

Human Norovirus

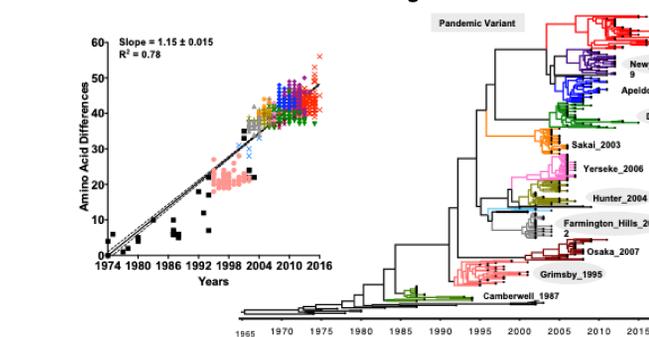
Norovirus Capsid Protein Determine the Genotypes and Antigenicity



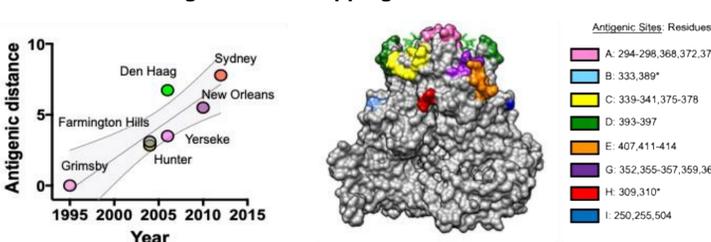
Human Noroviruses Present Multiple Genotypes, with Genotype GII.4 being Predominant



Chronological Emergence of GII.4 Variants Results in Accumulation of Amino Acid and Antigenic Differences



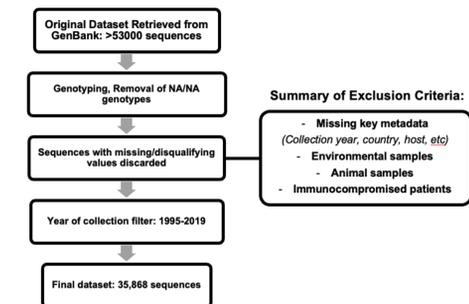
Antigenic Differences of GII.4 Variants Are Associated with Mutations on Antigenic Sites Mapping on the P domain



Parra et al. Virus Evol 2019
Tohma et al. Cell Rep 2022

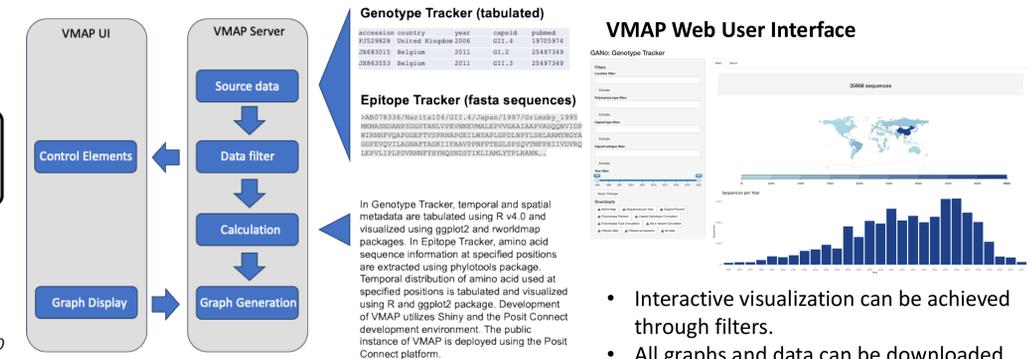
Materials and Methods

Norovirus Database



Genotyping was done using **Norovirus Typing Tool Version 2.0** (<https://www.rivm.nl/mpf/typingtool/norovirus/>)

Viral Mutational and Antigenic Profiler Tool (VMAP)

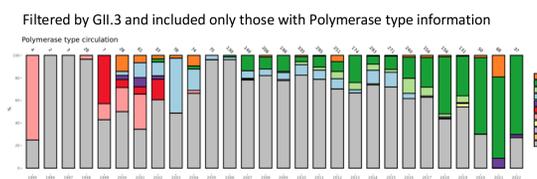
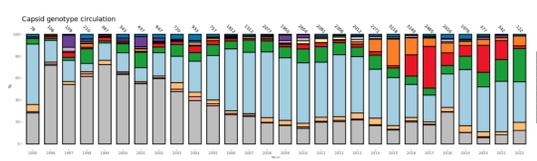
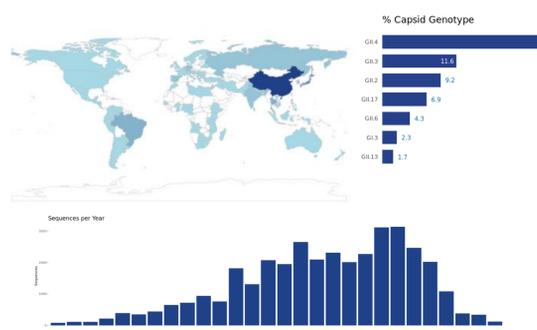


- Interactive visualization can be achieved through filters.
- All graphs and data can be downloaded.
- Graph are publication ready.

Results and Discussion

Genotype Tracker Tool

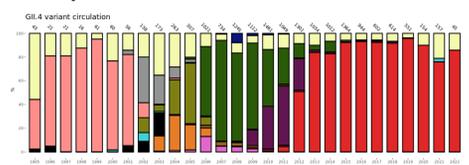
Spatiotemporal distribution of sequences and genotypes



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Epitope Tracker Tool

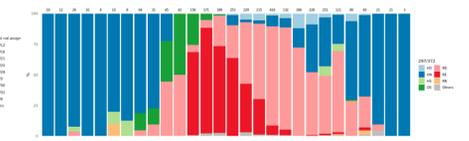
Temporal distribution of GII.4 variants



Temporal distribution of positive selected residues of the GII.4 norovirus capsid. Note the similarity with the temporal distribution of GII.4 variants in the human population (above).

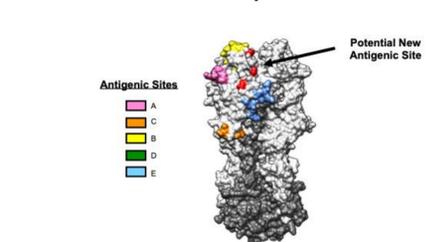


Temporal distribution of coevolving residues 297 and 372



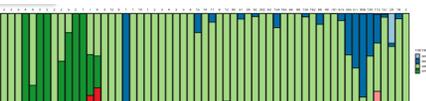
Future Updates

H7 Influenza virus HA protein



H7 dataset was downloaded from GSAID and curated (n = 5175).

Temporal distribution of residues from a potential new antigenic site. (unpublished data)



- This tool will be implemented to study the genetic diversity of H5 and other influenza viruses as well.
- Please do not hesitate to contact us (gabriel.parra@fda.hhs.gov) if you are interested in developing this tool for your virus of interest

VMAP is available at: <http://dnahive.fda.gov/vmap> or

