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Norovirus: The Pervasive Pathogen behind Gastrointestinal Upheaval

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Abstract

Norovirus, also known as Norwalk virus and sometimes referred to as the winter vomiting disease, is a highly contagious virus that is the leading cause of gastroenteritis worldwide.

Keywords: Norovirus; Norwalk virus; vomiting disease; Norovirus infections

Introduction

Norovirus, also known as Norwalk virus and sometimes referred to as the winter vomiting disease, is a highly contagious virus that is the leading cause of gastroenteritis worldwide. Gastroenteritis is an inflammation of the stomach and intestines, typically resulting in symptoms such as diarrhea, vomiting, and abdominal pain. Norovirus infections are characterized by sudden onset and can affect people of all ages, though they are particularly common among children and older adults. The virus is notorious for causing outbreaks in various settings, including schools, cruise ships, hospitals, and nursing homes, due to its ability to spread rapidly from person to person and through contaminated food, water, or surfaces. Despite its widespread prevalence, there is no specific treatment or vaccine for norovirus, and management primarily involves supportive care to relieve symptoms and prevent dehydration. Proper hand hygiene and sanitation practices are essential for preventing the spread of norovirus, particularly in high-risk environments [1].

The left side shows NSW-2012 VLPs have a T=4 icosahedral symmetry (symmetry axis labeled 2, 3, and 5). These VLPs were composed of 240 copies of VP1. The VP1 adapted four quasiequivalent conformations (A, B, C, and D) that gave rise to two distinct dimers (A/B and C/D). At the icosahedral twofold axis, the B, C, and D subunits were alternating, while the A subunit is positioned at the fivefold axis. The right side shows a cutaway section of these VLPs and indicates that the inner and outer diameters are 32 nm and 50 nm, respectively. The P domains are elevated ~21 Å off the S domain (Figure 1) [2].

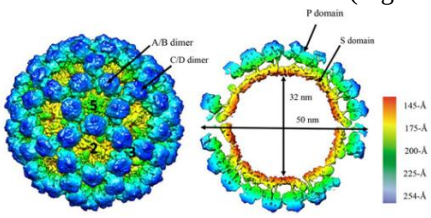

Figure 1: *Cryo-EM reconstruction structure of NSW-2012 VLPs.*

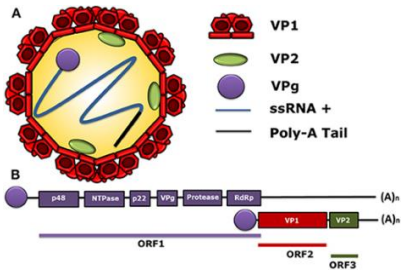

Figure 2*: Molecular structure of human norovirus (HuNoV).*

(A) A schematic representation of the human norovirus virion showing its 90-dimer protein surface of the VP1 structural protein of the capsid. The structural protein VP2 (1–8 proteins per virion) is shown within the viral capsid. The non-structural VPg protein, covalently bound to the 5′ end of the RNA genome (ssRNA+) in a positive sense and a poly-adenine tail at the 3′ ends are also displayed. (B) General scheme of the HuNoV genome organization. ORF1 encodes the non-structural proteins: p48,

NTPase, p22, VPg, Protease, and RdRp. The ORF2 encodes for the major structural protein VP1 and the ORF3 encodes for the minor structural protein VP2. The sub genomic RNA bound to VPg encoding VP1 and VP2 is indicated below the ORFs. VPg is represented as a circle linked to genomic and sub genomic RNAs (Figure 2)[3].

Classification

Norovirus belongs to the family Caliciviridae and the genus Norovirus. It is classified into several Geno groups and genotypes based on genetic sequencing of the viral genome. As of my last update, there are at least seven Geno groups (GI to GVII), with Geno groups GI, GII, and GIV being the most commonly associated with human illness. Within each Geno group, there are multiple genotypes. For example, within Geno group GII, there are more than 20 genotypes. These genotypes can undergo genetic mutations over time, contributing to the diversity and evolution of the virus. Understanding the genetic diversity of norovirus is important for tracking outbreaks and developing strategies for prevention and control.

Genome Structure

Norovirus has a single-stranded, positive-sense RNA genome. This means that the RNA strand can be directly translated by host cell machinery into viral proteins. The genome of norovirus is approximately 7.5 to 7.7 kilobases in length and is organized into three open reading frames (ORFs).ORF1 encodes a large polyprotein that is cleaved into multiple non-structural proteins involved in viral replication and other essential functions. ORF2 encodes the major capsid protein (VP1), which forms the outer shell of the virus particle and is responsible for binding to host cells.ORF3 encodes a minor structural protein (VP2) which is found within the viral particle. The genome also contains untranslated regions (UTRs) at both ends, which play important roles in viral replication and translation. Norovirus exhibits considerable genetic diversity, with multiple genotypes and variants circulating in human populations. This genetic variability contributes to the ability of the virus to evade immune responses and to cause periodic outbreaks of illness. Understanding the genome structure of norovirus is crucial for developing diagnostic tests, vaccines, and antiviral therapies [1].

Diagnosis

Diagnosing norovirus infection typically involves a combination of clinical evaluation, symptomatology, and laboratory testing. Here are some key aspects of diagnosing norovirus:

Clinical Evaluation

Healthcare providers assess the patient's symptoms, medical history, and potential exposure to norovirus or contaminated environments. Common symptoms of norovirus infection include sudden onset of vomiting, diarrhea, abdominal pain, nausea, and sometimes fever or headache.

Stool sample analysis

Laboratory testing of stool samples can help confirm the presence of norovirus. Techniques such as reverse transcription-polymerase chain reaction (RT-PCR) are commonly used to detect norovirus RNA in stool specimens. This molecular method is highly sensitive and specific for norovirus detection.

Rapid antigen tests

Rapid antigen tests, which detect norovirus antigens in stool samples, are available for some genotypes of the virus. While these tests provide quick results, they may be less sensitive than molecular methods such as RT-PCR.

Serological testing

Serological assays measure the presence of norovirus-specific antibodies in blood samples. However, serological testing is less commonly used for diagnosing acute norovirus infection and is typically more useful for epidemiological studies or assessing immunity in populations. It's important to note that norovirus diagnosis is primarily based on clinical suspicion and laboratory confirmation, especially during outbreaks or in cases of severe illness. Additionally, norovirus diagnosis may require exclusion of other potential causes of gastroenteritis through differential diagnosis. Prompt and accurate diagnosis of norovirus infection is essential for appropriate patient management, infection control measures, and public health surveillance.

Vaccination Trails

Monovalent and Bivalent Norovirus Virus-like Particle (VLP) Vaccines: These vaccines consist of virus-like particles that mimic the outer shell of norovirus. Monovalent vaccines target specific genotypes of norovirus, while bivalent vaccines aim to provide broader protection against multiple genotypes. Clinical trials have tested the safety, immunogenicity, and efficacy of these VLP vaccines in adults and children. Some trials have shown promising results in terms of immune response, but further research is needed to assess vaccine efficacy in preventing norovirus infection and illness. Recombinant Norovirus GI.1 VLP Vaccine: This vaccine candidate, developed by Takeda Pharmaceuticals, has undergone clinical trials to evaluate its safety and efficacy in preventing norovirus gastroenteritis. Phase IIb trials conducted in adults and elderly individuals demonstrated a reduction in the incidence of acute gastroenteritis caused by

norovirus genotype GI.1. Further development and evaluation of this vaccine are ongoing. Live Attenuated Norovirus Vaccine: Live attenuated vaccines contain weakened forms of the virus that are unable to cause illness but can still stimulate an immune response. Clinical trials of live attenuated norovirus vaccines have been conducted to assess their safety, immunogenicity, and potential efficacy in preventing norovirus infection and illness. Results from these trials have provided insights into the feasibility and challenges of developing live attenuated vaccines for norovirus. These are few examples of vaccine candidates that have been evaluated in clinical trials. Research into norovirus vaccines continues, with ongoing efforts to develop safe and effective vaccines that can provide durable protection against norovirus infection and illness.

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