

NOVEL HUMAN ASTROVIRUS SEQUENCES FOR DIAGNOSTICS AND VACCINE DEVELOPMENT FOR ENCEPHALITIS AND GASTROENTERITIS

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Technology Description

A team of researchers at Washington University and the Centers for Disease Control discovered, sequenced and patented a novel human astrovirus that can cause encephalitis and gastroenteritis (non-etiologic diarrhea), offering a path to detection and diagnostics.

The virus (Astrovirus VA1, “VA1”, also known as HMO-C, VA1 mastrovirus 9) was first identified from an outbreak of gastroenteritis in a childcare center. Subsequent studies demonstrated that astroviruses (a family of small, single-stranded, positive sense RNA viruses) are an emerging cause of central nervous system (CNS) infection. Furthermore, VA1 is the most prevalent astrovirus in cases of human encephalitis and these infections have a high mortality rate. In addition, the inventors have created the first cell culture system for this virus to facilitate research and development of VA1-based diagnostics and therapeutics. This technology could help fill a diagnostic gap and an unmet medical need for viral gastroenteritis and encephalitis.

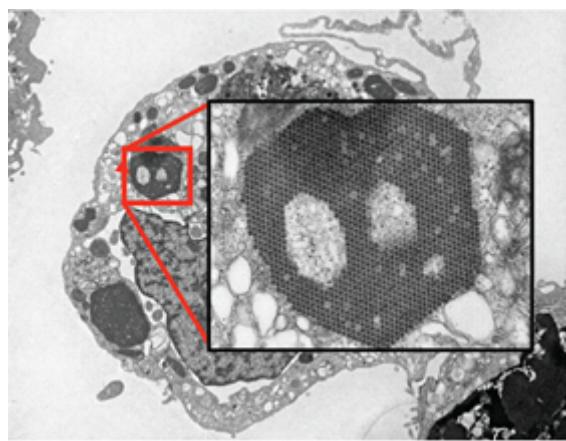


Figure 1. Electron micrograph of astrovirus VA1 infected cell showing crystalline lattice of viral particles.

Stage of Research

Virus identification: After identifying VA1 as the cause of a gastroenteritis outbreak, the inventors sequenced the 6586 nucleotide viral genome and demonstrated that it was highly divergent from all previously described astroviruses.

Cell culture: The inventors have successfully propagated VA1 in multiple human cell lines (Caco2, HEK293T, A549 and SK-N-SH) as well as primary human astrocytes, a necessary tool to facilitate

development of diagnostics, vaccines or anti-viral drugs as well as basic research studies of tropism, pathogenesis, and immune control.

Future studies: The inventors' future work will focus on developing additional cell culture and in vivo models of VA1 CNS infection.

Applications

- **Viral diagnostics:**
 - molecular diagnostics of astrovirus nucleic acid to identify viral agents that cause encephalitis or gastroenteritis
 - cell culture to develop antibody- or antigen-based diagnostics
- **Vaccine development** – astrovirus cell culture to identify critical antigens for vaccine development as well as protective antibodies
- **Research** – basic research into viral pathogenesis including neurotropism and neuropathogenesis
- **Drug screening** – cell culture model may also facilitate high-throughput screens for antiviral agents to treat VA1 infections

Key Advantages

- **Propagated in multiple cell lines** – the inventors have developed cell culture techniques to propagate the virus in cell culture which facilitates research and development of VA1-based products
- **Fills diagnostic gap:**
 - the etiologies of 12-41% of all gastroenteritis outbreaks remain undetermined even after extensive testing; VA1-based diagnostics could be included in diagnostic panels to fill this gap
 - ~65% of encephalitis cases have no known etiology; VA1-based diagnostics could be included in diagnostic panels to fill this gap
- **Unmet medical need** – there is a high mortality rate in patients with VA1-associated encephalitis; therefore, diagnostics, vaccines and anti-viral therapies for VA1 could improve patient outcomes

Publications

- Janowski AB, Klein RS, Wang D, [Differential in vitro infection of neural cells by astroviruses](#). *mBio* 2019 Jul 9;10(4). pii: e01455-19.
- Janowski, A. B., Bauer, I. K., Holtz, L. R., & Wang, D. (2017). [Propagation of astrovirus VA1, a neurotropic human astrovirus, in cell culture](#). *Journal of virology*, 91(19), e00740-17.
- Finkbeiner, S. R., Li, Y., Ruone, S., Conrardy, C., Gregoricus, N., Toney, D., ... & Tong, S. (2009). [Identification of a novel astrovirus \(astrovirus VA1\) associated with an outbreak of acute gastroenteritis](#). *Journal of virology*, 83(20), 10836-10839.

Patents

- [Identification of astrovirus VA1 associated with gastroenteritis in humans](#) (U.S. Patent No. 8,426,574)

Website

- David Wang: [Profile](#) and [Wang Lab](#)