

# Hepatitis E virus in the virome of water and animals

Akademisk avhandling

Som för avläggande av medicine doktorexamen vid Sahlgrenska akademien, Göteborgs universitet kommer att offentlig försvaras i Mikrobiologens föreläsningssal, vån 3, Guldhedsgatan 10A, Göteborg, fredag den 13 December 2019, klockan 13.00

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## Avhandlingen baseras på följande delarbeten

- I. **Hao Wang**, Raquel Castillo-Contreras, Fredy Saguti, Jorge R López-Olvera, Marie Karlsson, Gregorio Mentaberre, Magnus Lindh, Jordi Serra-Cobo, Heléne Norder, Genetically similar hepatitis E virus strains infect both humans and wild boars in the Barcelona area, Spain, and Sweden. *Transboundary and Emerging Diseases*, 2019, 66, (2), 978-985.
- II. **Hao Wang**, Marie Karlsson, Maria Lindberg, Kristina Nyström, Heléne Norder, Hepatitis E virus strains infecting Swedish domestic pigs are unique for each pig farm and remain in the farm for at least 2 years. *Transboundary and Emerging Diseases*, 2019, 66, (3), 1314-1323.
- III. **Hao Wang**, Per Sikora, Carolin Rutgersson, Magnus Lindh, Tomas Brodin, Berndt Björleinius, D.G. Joakim Larsson, Heléne Norder, Differential removal of human pathogenic viruses from sewage by conventional and ozone treatments. *International Journal of Hygiene and Environmental Health*, 2018, 221, (3), 479-488.
- IV. **Hao Wang**, Inger Kjellberg, Per Sikora, Henrik Rydberg, Magnus Lindh, Olof Bergstedt, Heléne Norder, Hepatitis E virus genotype 3 strains and a plethora of other viruses detected in raw and still in tap water. *Water Research*, 2019, 168, 115141.
- V. **Hao Wang**, Julianna Neyvaldt, Lucica Enache, Per Sikora, Ann Mattsson, Anette Johansson, Magnus Lindh, Olof Bergstedt, Heléne Norder, One year seasonal variations of enteric viruses in incoming and treated water at a wastewater plant. Manuscript.

# Hepatitis E virus in the virome of water and animals

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## ABSTRACT

This thesis was aimed to investigate viruses in different animals and water to get some understanding of viruses that disseminate into the environment. Next generation sequencing (NGS) was used to explore the virome from raw to treated water at two Swedish drinking water treatment plants (DWTP) and in tap water. The amount of viruses was lowered with 3-4 log<sub>10</sub> after the treatments. The viral diversity was reduced from 26 different virus families in raw water to 12 in tap water. Hepatitis E virus (HEV), subtypes HEV3c/i and HEV3a, were identified in most water samples, with 10-130 International Units of HEV RNA/mL tap water. The viral diversity was also investigated in incoming and treated wastewater at two Swedish wastewater treatment plants (WWTP) in Knivsta, Stockholm, and Gryaab in Gothenburg. Ozone treatment was used after conventional treatment before the release of the treated wastewater from Knivsta WWTP. At least 327 virus species, belonging to 25 known virus families were detected in the raw wastewater. The virus concentration was reduced by 1-6 log<sub>10</sub> for 21 human related viruses, with lowest removal efficiency for adenovirus. At Gryaab WWTP, seasonal differences in presence and concentration of 13 human viruses in raw and treated wastewater were investigated during one year. Twelve of the viruses were detected throughout the year in influent and effluent wastewater by either qPCR or NGS. HEV was found in effluents when released into the Göta River. The concentrations of all viruses in influent were reduced by 3-4 log<sub>10</sub> in the effluents. Since HEV was identified in most water samples, its prevalence among their major hosts, wild boars and pigs, was investigated. HEV in Spanish and Swedish wild boars were compared. HEV RNA was found in 20% in Spanish wild boars vs. 15% in Swedish wild boars, while anti-HEV was significantly higher among Spanish wild boars (59% vs. 8%). Most Swedish and some Spanish wild boars were infected by subtype HEV3f, while several Spanish wild boars were infected by divergent HEV3c/i strains, indicating regional differences in infecting HEV strains. The Swedish wild boar strains were similar to strains from infected Swedes and Swedish domestic pigs. These wild boars were also infected with at least 27 different viruses, identified by NGS on liver samples. HEV3 was identified in 22% of piglets from 77% of 30 investigated pig farms sampled twice with more than one year apart. Most piglets were infected with HEV3f or HEV3e. Each pig farm had a unique HEV strain, and several strains were similar to human HEV3 strains.

These studies showed that viruses are disseminated into the environment both from raw water, treated wastewater and animals, and may be found in tap water. The HEV3 strains identified in drinking water were different from those isolated from Swedish pigs and wild boars, and similar to strains from humans with unknown source of infection, indicating waterborne transmission also for HEV3.

**Keywords:** pig, wild boar, wastewater, tap water, enteric virus, NGS