PORCINE SAPELOVIRUS

Swine Health Information Center

The mission of the Swine Health Information Center is to protect and enhance the health of the United States swine herd through coordinated global disease monitoring, targeted research investments that minimize the impact of future disease threats, and analysis of swine health data.

September 2015 | Updated June 2021

SUMMARY

IMPORTANCE

- Porcine sapelovirus (PSV) is an enteric picornavirus of swine.
- It has been detected in healthy pigs and pigs with diarrhea. The virus is also associated with neurological, reproductive, and respiratory disease.
- Co-infection with other infectious agents is common, and to date, the importance of PSV as a swine pathogen remains unclear.

PUBLIC HEALTH

- PSV does not infect humans.

INFECTION IN SWINE

- PSV infections are often subclinical. However, PSV is also associated with gastrointestinal, neurological, reproductive, and respiratory disease. Co-infection with other enteric pathogens often occurs.
- Experimentally, PSV has been shown to cause diarrhea in pigs.

TREATMENT

- There is no treatment for pigs infected with PSV.

CLEANING AND DISINFECTION

- PSV is stable in the environment, and resistant to elevated temperatures and acid pH.
- Sodium hypochlorite is an effective disinfectant for PSV. Experimentally, peracetic acid, hydrogen peroxide, and acetic acid also inactive PSV.

PREVENTION AND CONTROL

- Many farm environments are likely contaminated with PSV. To prevent infection with PSV, cleaning and disinfection protocols should be in place. Additionally, sick pigs should be isolated to minimize disease spread.
- There are no specific control measures for PSV. However, standard biosecurity practices should be in place on all swine premises.

TRANSMISSION

- PSV transmission is mainly fecal-oral.
- Fomites may also play a role, and vertical transmission is suspected.

PATHOGENESIS

- The pathogenesis of PSV is not well understood. Receptors in the intestinal tract may include α2,3-linked sialic acid on glycolipids. PSV enters cells through caveolae/lipid raft-mediated endocytosis.

DIAGNOSIS

- PSV can be cultured in many different cell lines. Virus can be identified via immunohistochemistry, in situ hybridization, and immunofluorescence. However, reverse-transcriptase polymerase chain reaction (RT-PCR) assays are most often used to detect PSV. Most assays target the 5'UTR or VP1 region.
- A VP2-VP1-based indirect enzyme-linked immunosorbent assay (ELISA) has been described for use with serum and oral fluids.

EPIDEMIOLOGY

- Domestic and wild swine are the only known hosts for PSV. Sapelo-like picornaviruses have been identified in pigs, bats, rodents, dogs, cats, birds, sea lions, and Tasmanian devils.
- PSV has been detected in Australia, Brazil, Spain, Italy, Hungary, the Czech Republic, France, China, Korea, Japan, India, Zambia, the United Kingdom, and the United States.
- Prevalence estimates vary, but the virus has been detected in healthy pigs and pigs with diarrhea. In the United States, 32% of fecal samples from diarrheic pigs were PSV-positive.
- An outbreak of polioencephalomyelitis occurred in U.S. swine, with reported morbidity and case fatality rates of 20% and 30%, respectively. Intravaginal and intrauterine inoculation of gilts at day 30 of gestation leads to 94% fetal mortality.

ETIOLOGY

- PSV is an RNA virus belonging to the genus *Sapelovirus* in the family *Picornaviridae.* PSV is closely related to members of the genera *Teschovirus* and *Enterovirus* and has previously been known as porcine enterovirus 8 (PEV-8).
- Until recently, there were three species within the genus *Sapelovirus* genus: simian, avian and porcine (sapelo: simian, avian, and porcine entero-like viruses). PSV contains a single serotype, while simian sapelovirus (*Sapelovirus B*), has three. Avian sapelovirus has been moved to the genus *Anativirus*.
- Some PSVs seem to be mostly neurotropic, while others are diarrheic. However, there are strains that cause disease in more than one body system.
- Evidence of recombination exists between different PSV strains.

HISTORY IN SWINE

- PSVs, formerly known as porcine enteroviruses, are linked to cases of neurological disease, reproductive failure, pneumonia, and diarrhea dating back to the 1950s.

IMMUNITY

- It is unclear whether maternal antibodies are protective against PSV infection.
- There are no sapelovirus vaccines.

GAPS IN PREPAREDNESS

- The role of PSV as a pathogen, and more specifically as a cause of polioencephalomyelitis, is unclear. PSV is commonly isolated from the intestinal tract of healthy swine, and it is often found with other enteric pathogens.
- More research is needed to determine its importance as a primary pathogen, and vaccine development should be explored.
- Additionally, PSV is hardy and likely persists in swine environments. Further information is needed on biosecurity practices, including cleaning and disinfection, to prevent PSV infection.

LITERATURE REVIEW: PORCINE SAPELOVIRUS

IMPORTANCE

Porcine sapelovirus (PSV) is an enteric picornavirus of swine. It has been detected in healthy pigs and pigs with diarrhea. The virus is also associated with neurological, reproductive, and respiratory disease. Co-infection with other infectious agents is common, and to date, the importance of PSV as a primary pathogen remains unclear. PSV has been found nearly worldwide.

PUBLIC HEALTH

PSV does not infect humans.

INFECTION IN SWINE

While subclinical infection is common, PSV also causes gastrointestinal, neurological, reproductive, and respiratory disease. PSV has been found in feces from healthy pigs and pigs with diarrhea (see *Morbidity and Mortality*). In addition, co-infection with other enteric pathogens often occurs.[1-10] Significant PSV-associated outbreaks include the following:

- Polioencephalomyelitis, gastroenteritis, and respiratory distress were associated with PSV on a commercial farm in China.[11] Pigs 50–60 days old at two nearby breeding farms showed similar signs. Only PSV was isolated from affected pigs.[11]

- Polioencephalomyelitis was reported in pigs 3–4 weeks post-weaning in the United Kingdom. Pigs developed front and hind limb ataxia, progressing to generalized weakness and lateral recumbency. Affected pigs died 2–3 days after the onset of clinical signs, and PSV was detected in the spinal cord.[12]

- An outbreak of atypical neurological disease in 11-week-old pigs in the southern United States was attributed to PSV. Affected pigs developed ataxia, incoordination, paresis, paralysis, and decreased responsiveness to environmental stimuli. The observed morbidity and case fatality rates were 20% and 30%, respectively.[10] Histologically, severe lymphoplasmacytic and necrotizing polioencephalomyelitis were observed. Additionally, retrospective analysis of neurological cases submitted to the Iowa State University Veterinary Diagnostic Laboratory (ISU-VDL) found evidence of PSV infection alone and in combination with porcine teschovirus (PTV) and porcine epidemic diarrhea virus (PEDV).[10]

Only a few studies have described experimental infection with PSV.

- In the 1960s, PSV was associated with SMEDI syndrome (stillbirth [S], mummified fetus [M], embryonic death [E.D.], infertility [I]).[13] Experimental PSV infection of pregnant sows caused fetal infection.[14] Intravaginal inoculation with PSV on day 15 of gestation led to early embryonic death and complete resorption. Infection on day 30 of gestation resulted in a significant increase in fetal death.[14]

- After isolating PSV from an outbreak, pigs 50–60 days old were inoculated with PSV-csh. Two developed diarrhea and respiratory distress at two days post-infection (dpi). Polioencephalomyelitis syndrome, characterized by ataxia and limb paralysis, was observed at seven dpi.[11] PSV was isolated from feces and lung tissue, and PSV-induced lesions were found in the intestines, lungs, and brain.[11]

- A porcine intestinal epithelial cell line (IPEC-J2) was infected in vitro with PSV-csh to demonstrate the pathogenicity of PSV. IPEC-J2 cells began to shrink at 24 hours post-infection (hpi), rupture at 60 hpi spontaneously, and slough at 72 hpi. Viral load was highest at 48 hpi, prior to cell rupture.[15]

- In 3-day-old piglets orally inoculated with a Korean PSV, diarrhea and fecal shedding occurred from 1–5 dpi. Intestinal lesions were documented, including severe villous atrophy.[16] PSV was isolated from feces and serum. Chicks inoculated with PSV did not become ill.[16]

- In two colostrum-deprived neonatal piglets orally inoculated with PSV, watery diarrhea developed at four dpi.[17] Fecal shedding occurred from 2–4 dpi, and pigs were euthanized at five dpi due to severe illness. PSV RNA was detected in various tissues, with the highest levels found in the cecum, colon, rectum, tonsil, inguinal lymph nodes, and bladder.[17]

Lesions seen with PSV-induced polioencephalomyelitis are consistent with other neurotropic viral infections, such as PTV. In the CNS, punctate hemorrhages and hyperemia are present in the dura mater.[11] Polio-encephalomyelitis is usually subacute, multifocal, and non-suppurative.[12] Neuronal vacuolization and perivascular cuffing are commonly observed.[11] In the small intestine congestion is apparent, with pronounced loss of villi and hemorrhages in the lamina propria.[11] In cases of PSV-induced pneumonia, consolidation and multifocal hemorrhages are seen in the lung lobes. Histologically, erythrocytes are pervasive in the interstitium and alveoli, and prominent alveolar ectasia with wall thinning can be observed. Some alveoli rupture to form large cysts.[11]

TREATMENT

There is no treatment for pigs infected with PSV.

CLEANING AND DISINFECTION

SURVIVAL

PSVs are very stable in the environment. Isolates are resistant to elevated temperatures and acid pH.[18] PSV is inactivated by heating to 54°C for six minutes,[17] 60°C for 10 minutes, or 65°C for five minutes.[19]

Using PSV as a surrogate for swine vesicular disease virus (SVDV), Dee et al. showed that PSV maintained infectivity under conditions simulating transport between continents.[20] Specifically, viable PSV was detected in soybean meal (conventional and organic), soy oilcake, lysine, vitamin D, and pork sausage casings, as well as dog and cat food.[20]

DISINFECTION

Heat, lipid solvents, and some disinfectants do not destabilize picornaviruses. Sodium hypochlorite is an effective disinfectant.[19] Experimentally, picornaviruses can also be inactivated by peracetic acid, hydrogen peroxide, and acetic acid.[21]

Inactivation of PSV has been assessed in spray-dried porcine plasma (SDPP). Hulst and colleagues found that the virus was undetectable in citrate-treated porcine plasma spiked with PSV1 at pH 7.5. No infectious PSV was re-isolated from plasma and SDPP samples in cell culture.[22] Citrate has also been observed to inactive foot-and-mouth disease virus, another picornavirus.[23]

PREVENTION AND CONTROL

DISEASE REPORTING

PSV is not an OIE-listed disease. There are no restrictions for importation of animals from countries or zones affected by PSV. Any suspicious clinical or necropsy findings should always be reported to the USDA and your State Animal Health Official.

DISEASE PREVENTION

PSV prevalence can be high (see *Morbidity and Mortality*), and many farm environments are likely contaminated with PSV. To prevent infection with PSV, cleaning and disinfection protocols should be in place. Additionally, sick pigs should be isolated to minimize disease spread.

DISEASE CONTROL

There are no specific control measures for PSV. However, standard biosecurity practices should be in place on all swine premises.

TRANSMISSION

Transmission of PSV is mainly fecal-oral. A longitudinal study of PSV, PTV, and enterovirus G (EV-G) excretion showed that pigs did not shed virus during the suckling period; however, 50% of fecal samples from weaned pigs were positive for PSV and either PTV or EV-G.[7]

PSV is hardy in the environment, and fomites may play a role in transmission.[24] PSV causes viremia, and extra-intestinal infection occurs in the central nervous system, reproductive system, and respiratory system. Virus has also been found in the intestinal contents of stillborn pigs, raising the possibility of vertical transmission.[25]

PATHOGENESIS

The pathogenesis of PSV is not well understood. Replication occurs mainly in the intestinal tract. Possible receptor sites include α2,3-linked sialic acid on glycolipids (GD1a).[26] Endocytosis of PSV does not involve clathrin or micropinocytosis pathways like some other picornaviruses. Rather, PSV entry depends on caveolae/lipid raft-mediated endocytosis; it is pH-dependent and requires dynamin (a regulatory GTPase) and P13K (phosphatidy-linositide 3-kinases).[27]

DIAGNOSIS

TESTS TO DETECT NUCLEIC ACIDS, VIRUS, OR ANTIGENS

PSV can be cultured in many cell lines, including porcine kidney cells (PK-15) and IB-RS-2 cells;[11, 28 29] BHK-21 cells;[17, 30] human 293 T cells;[17] and PLC/PRF/5, HepG2/C3A, Vero E6, and primary green monkey kidney cells.[19] In cell culture, PSV can interrupt the growth of other enteric viruses. Therefore, an infection-resistant cell line (N1380) has been developed to isolate non-PSV pathogens from PSV-positive samples.[31]

Immunohistochemistry has been used to demonstrate PSV in the brain and spinal cord,[12] and the large and small intestine.[32] In situ hybridization has been described for detection of PSV in the central nervous system.[10] Additionally, cultured PSV can be identified by immunofluorescence antibody (IFA) assays.[33] Nowadays, reverse transcriptase polymerase chain reaction (RT-PCR) assays are most commonly employed to detect PSV. Some of the assays that have been developed include:

- RT-PCR and nested RT-PCR targeting the 5' UTR[10, 28, 34-36]
- RT-PCR targeting VP1[33]
- RT-loop-mediated isothermal amplification (RT-LAMP) targeting the 5’ UTR[37]
- Real-time RT-PCR (qRT-PCR) targeting the 5' UTR; described with a Taqman probe[38] and a minor groove-binding Taqman probe[16, 39]
- Duplex RT-PCR (PTV, PSV) targeting the 5' UTR[40]
- Triplex RT-PCR (PEDV, PSV, porcine sapovirus) targeting the 5' UTR[41]
- Modified arbitrarily primed PCR (AP-PCR, generates a genomic fingerprint that can compare RNAs simultaneously)[9, 42]

TESTS TO DETECT ANTIBODY

Cultured PSVs have been serotyped using virus neutralization.[28] A VP2-VP1-based indirect enzyme-linked immunosorbent assay (ELISA) assay has been described for detection of PSV in serum and oral fluids.[43]

SAMPLES

PSV has been isolated from feces, intestinal contents, and the intestines. Preferred CNS samples include the spinal cord and brain. PSV has not been successfully isolated from stillborn or mummified fetuses.[14] Use of oral fluids with an ELISA has been described.[43]

EPIDEMIOLOGY

SPECIES AFFECTED

Pigs are the only known hosts for PSV. The virus has been detected in both domestic pigs (see *Infection in Swine*) and feral swine.[1, 2, 44-46] A sapelo-like porcine picornavirus was identified in the feces of healthy and diarrheic pigs in Japan.[47] Additionally, sapelo-like viruses have been detected in bats,[48-50] rodents,[51, 52] dogs,[53] cats,[54] birds,[55, 56] sea lions,[57] and Tasmanian devils.[58]

GEOGRAPHIC DISTRIBUTION

PSV has been detected in Australia,[59] Brazil,[3, 7, 8, 60] Spain,[4, 61, 62] Italy,[28, 63-65] Hungary,[46, 66, 67] the Czech Republic,[2] France,[68] China,[9, 11, 17, 69] Korea,[5, 16, 33] Japan,[19, 47, 70] India,[29] Zambia,[42] the United Kingdom,[12] and the United States.[71]

MORBIDITY AND MORTALITY

Numerous studies have attempted to document the extent of PSV in swine. Estimates for PSV prevalence include:

- 7% of fecal samples from healthy pigs in India[29]
- 9% of fecal samples from healthy pigs in Spain[61]
- 6% of fecal samples from wild boar in Spain[1]
- 36% and 94% of fecal samples from suckling and fattening pigs, respectively, in Zambia[42]
- 32% in diarrheic feces from pigs in the United States[72]
- 46% in feces and intestinal contents from healthy pigs and pigs with diarrhea in Hunan, China, with the highest prevalence in nursery and fattening pigs[69]
- 41% in fecal samples from healthy pigs and pigs with diarrhea in China[17]
- 51% in feces, serum, and rectal and nasal swabs from healthy pigs and pigs with neurological signs in Hungary[67]
- 98% in fecal samples from young growers and 14% in fecal samples from sows in Italy[64]

At least one study has shown no difference in PSV prevalence in diarrheic vs. non-diarrheic pigs.[5] However, others have demonstrated higher PSV prevalence in pigs with diarrhea compared to healthy pigs.[17, 73]

Little information on mortality is available. Experimentally, intravaginal and intrauterine inoculation of gilts with PSV at day 30 of gestation resulted in 94% fetal mortality.[14] Arruda et al. reported morbidity and case fatality rates of 20% and 30%, respectively, in 11-week-old finishers with atypical neurological disease.[10]

ETIOLOGY

CHARACTERISTICS OF PICORNAVIRUSES

Sapeloviruses are members of the family *Picornaviridae*. Picornaviruses are small (30 nm), round, single-stranded positive-sense RNA viruses. They contain a large open reading frame (ORF) translated into a polyprotein containing a leader (L) protein, four structural capsid proteins (V1–4), and seven nonstructural proteins (2A–2C, 3A–3D).[24, 74, 75] Additionally, picornaviruses have one of five internal ribosome entry sites (IRESs) involved in ribosome recruitment and initiation of translation. Type IV IRES is found in PSV.[76]

The family *Picornaviridae* currently contains 68 genera and 158 species.[77] Additionally, picornavirus "supergroups" have been proposed based on phylogenetic clustering. Sapeloviruses belong to SG3, which includes the genera *Enterovirus, Rabovirus*, and *Sapelovirus*.[76] Picornaviruses that infect pigs are found in the genera *Kobuvirus*, *Aphthovirus, Cardiovirus, Cosavirus, Enterovirus, Pasivirus, Parechovirus, Sapelovirus, Senecavirus,* and *Teschovirus*.[24]

CHARACTERISTICS OF SAPELOVIRUSES

Enteric picornaviruses were formerly known as "porcine enteroviruses" (PEVs).[24] Research has since shown that PEVs include teschoviruses and true enteroviruses (EV–G1 to EV–G20) as well as sapeloviruses.[24] Previously, PSV was named porcine enterovirus 8 (PEV-8) and classified in the species *Porcine enterovirus A*.[24, 77]

The name sapelovirus comes from the three original species, simian, avian, and porcine (sapelo: simian, avian, and porcine entero-like viruses).[18] Sapeloviruses must have <30% divergence in the polyprotein aa sequence, <36% divergence in the P1 aa sequence, and <30 divergence in the 2C + 3CD aa sequence, plus similar genome base composition and a common genome organization.[18]

As of 2020, PSV belongs to the genus *Sapelovirus*, species *Sapelovirus A*.[77] PSV has a single serotype, porcine sapelovirus 1 (PSV-1). The genus holds a second species, *Sapelovirus B*, containing simian sapelovirus (SSV) and its three serotypes.[77] A third species, avian sapelovirus, was recently moved to the genus *Anativirus* and renamed *Anativirus A*.[77]

Numerous PSV isolates have been characterized. Neurotropic strains include PSV-csh (China, Shanghai)[11] and PSV- G5 (United Kingdom).[12] PSV-csh also caused diarrhea and respiratory distress prior to the onset of polioencephalomyelitis in infected animals.[11] Diarrheic strains include Korean PSVs KS0515, KS04105, and KS055217[33] and Chinese PSV YC2011.[78] The U.S. strain PSV USA/IA33375/2015 was isolated from a pig with diarrhea and is most similar to Asian PSVs.[72]

The PSV capsid protein VP1 is often used to assess phylogeny.[17] Although there is only one PSV serotype, recombination between strains has been documented in China,[9] Japan,[70] Hungary,[67] and France.[68]

HISTORY IN SWINE

Formerly known as porcine enteroviruses, PSVs are linked to cases of neurological disease, reproductive failure, pneumonia, and diarrhea dating back to the 1950s.[13, 14, 59, 79-81]

IMMUNITY

POST-EXPOSURE

Little is known about PSV immunity. In cell culture, infection with PSV leads to changes in innate immunity pathways. The humoral response to PSV has been primarily characterized by IgA early in infection.[15]

It is unclear whether maternal antibodies are protective. In seropositive gilts, intrauterine and intravaginal PSV inoculation results in embryonic and fetal infection.[14] On some PSV-infected farms, shedding and illness have been seen in post-weaning pigs but not in suckling pigs.[7, 12]

VACCINES
There are no sapelovirus vaccines.

CROSS-PROTECTION
No information was found on cross-protection between PSV strains.

GAPS IN PREPAREDNESS
PSV is commonly isolated from the intestinal tract of healthy swine, and it is often found with other enteric pathogens. More research is needed to determine its importance as a primary pathogen, and vaccine development should be explored. Additionally, PSV is hardy and likely persists in swine environments. Further information is needed on biosecurity practices, including cleaning and disinfection, to prevent PSV infection.

REFERENCES

1. Cano-Gómez C, García-Casado MA, Soriguer R, Palero F, Jiménez-Clavero MA. Teschoviruses and sapeloviruses in faecal samples from wild boar in Spain. *Vet Microbiol*. Jul 2013;165(1-2):115-22. doi:10.1016/j.vetmic.2012.11.022
2. Prodělalová J. The survey of porcine teschoviruses, sapeloviruses and enteroviruses B infecting domestic pigs and wild boars in the Czech Republic between 2005 and 2011. *Infect Genet Evol*. Oct 2012;12(7):1447-51. doi:10.1016/j.meegid.2012.04.025
3. Donin DG, de Arruda Leme R, Alfieri AF, Alberton GC, Alfieri AA. First report of porcine teschovirus (PTV), porcine sapelovirus (PSV) and enterovirus G (EV-G) in pig herds of Brazil. *Trop Anim Health Prod*. Mar 2014;46(3):523-8. doi:10.1007/s11250-013-0523-z
4. Vilar MJ, Peralta B, Garcia-Bocanegra I, et al. Distribution and genetic characterization of Enterovirus G and Sapelovirus A in six Spanish swine herds. *Virus Res*. Apr 2 2016;215:42-9. doi:10.1016/j.virusres.2016.01.019
5. Bak GY, Kang MI, Son KY, et al. Occurrence and molecular characterization of Sapelovirus A in diarrhea and non-diarrhea feces of different age group pigs in one Korean pig farm. *J Vet Med Sci*. Jan 10 2017;78(12):1911-1914. doi:10.1292/jvms.16-0237
6. Chen Q, Wang L, Zheng Y, et al. Metagenomic analysis of the RNA fraction of the fecal virome indicates high diversity in pigs infected by porcine endemic diarrhea virus in the United States. *Virol J*. May 25 2018;15(1):95. doi:10.1186/s12985-018-1001-z
7. Leme RA, Silva DR, Lorenzetti E, Moraes DA, Alfieri AF, Alfieri AA. Longitudinal survey of teschovirus A, sapelovirus A, and enterovirus G fecal excretion in suckling and weaned pigs. *Braz J Microbiol*. Jan 2019;50(1):321-327. doi:10.1007/s42770-018-0018-1
8. Hammerschmitt ME, de Almeida PR, de Cecco BS, et al. Swine polioencephalomyelitis in Brazil: identification of teschovirus A, sapelovirus A, and enterovirus G in a farm from Southern Brazil. *Braz J Microbiol*. May 22 2021. doi:10.1007/s42770-021-00509-z
9. Yang T, Li R, Peng W, et al. First isolation and genetic characteristics of porcine sapeloviruses in Hunan, China. *Arch Virol*. Jun 2017;162(6):1589-1597. doi:10.1007/s00705-017-3264-x
10. Arruda PH, Arruda BL, Schwartz KJ, et al. Detection of a novel sapelovirus in central nervous tissue of pigs with polioencephalomyelitis in the USA. *Transbound Emerg Dis*. Apr 2017;64(2):311-315. doi:10.1111/tbed.12621
11. Lan DL, Ji WH, Yang SX, et al. Isolation and characterization of the first Chinese porcine sapelovirus strain. *Arch Virol*. Sep 2011;156(9):1567-1574. doi:10.1007/s00705-011-1035-7
12. Schock A, Gurrala R, Fuller H, et al. Investigation into an outbreak of encephalomyelitis caused by a neuroinvasive porcine sapelovirus in the United Kingdom. *Vet Microbiol*. Aug 2014;172(3-4):381-9. doi:10.1016/j.vetmic.2014.06.001
13. Dunne HW, Gobble JL, Hokanson JF, Kradel DC, Bubash GR. Porcine reproductive failure associated with a newly identified "SMEDI" group of picornaviruses. *Am J Vet Res*. Nov 1965;26(115):1284-97.
14. Huang J, Gentry RF, Zarkower A. Experimental infection of pregnant sows with porcine enteroviruses. *Am J Vet Res*. Apr 1980;41(4):469-73.

15. Lan D, Tang C, Yue H, et al. Microarray analysis of differentially expressed transcripts in porcine intestinal epithelial cells (IPEC-J2) infected with porcine sapelovirus as a model to study innate immune responses to enteric viruses. *Arch Virol*. Jul 2013;158(7):1467-75. doi:10.1007/s00705-013-1638-2
16. Kim DS, Kang MI, Son KY, et al. Pathogenesis of Korean SapelovirusA in piglets and chicks. *J Gen Virol*. Oct 2016;97(10):2566-2574. doi:10.1099/jgv.0.000571
17. Li Y, Du L, Jin T, et al. Characterization and epidemiological survey of porcine sapelovirus in China. *Vet Microbiol*. May 2019;232:13-21. doi:10.1016/j.vetmic.2019.02.017
18. International Committee on Virus Taxonomy (ICTV). Genus: Sapelovirus. Accessed June 25, 2021. https://talk.ictvonline.org/ictv-reports/ictv_online_report/positive-sense-rna-viruses/w/picornaviridae/701/genus-sapelovirus
19. Bai H, Liu J, Fang L, et al. Characterization of porcine sapelovirus isolated from Japanese swine with PLC/PRF/5 cells. *Transbound Emerg Dis*. Jun 2018;65(3):727-734. doi:10.1111/tbed.12796
20. Dee SA, Bauermann FV, Niederwerder MC, et al. Survival of viral pathogens in animal feed ingredients under transboundary shipping models. *PLoS One*. 2018;13(3):e0194509. doi:10.1371/journal.pone.0194509
21. Spickler A. Teschovirus Encephalomyelitis and Porcine Teschovirus Infections. Center for Food Security and Public Health (CFSPH),. Accessed June 25, 2021. https://www.cfsph.iastate.edu/Factsheets/pdfs/enterovirus_encephalomyelitis.pdf
22. Hulst MM, Heres L, Hakze-van der Honing RW, Pelser M, Fox M, van der Poel WHM. Study on inactivation of porcine epidemic diarrhoea virus, porcine sapelovirus 1 and adenovirus in the production and storage of laboratory spray-dried porcine plasma. *J Appl Microbiol*. Jun 2019;126(6):1931-1943. doi:10.1111/jam.14235
23. Hong JK, Lee KN, You SH, et al. Inactivation of foot-and-mouth disease virus by citric acid and sodium carbonate with deicers. *Appl Environ Microbiol*. Nov 2015;81(21):7610-4. doi:10.1128/aem.01673-15
24. Alexandersen S, Knowles N, Graham J, et al. Picornaviruses. In: Zimmerman J, Karriker L, Ramirez A, Schwartz K, Stevenson G, eds. *Diseases of Swine*. 11th ed. John Wiley & Sons; 2019:587-620:Chap 40.
25. Kumari S, Ray PK, Singh R, Desingu PA, Varshney R, Saikumar G. Pathological and molecular investigation of porcine sapelovirus infection in naturally affected Indian pigs. *Microb Pathog*. Feb 2019;127:320-325. doi:10.1016/j.micpath.2018.12.006
26. Kim DS, Son KY, Koo KM, et al. Porcine sapelovirus uses α 2,3-linked sialic acid on GD1a ganglioside as a receptor. *J Virol*. Apr 2016;90(8):4067-4077. doi:10.1128/jvi.02449-15
27. Zhao T, Cui L, Yu X, Zhang Z, Shen X, Hua X. Porcine sapelovirus enters PK-15 cells via caveolae-dependent endocytosis and requires Rab7 and Rab11. *Virology*. Mar 2019;529:160-168. doi:10.1016/j.virol.2019.01.009
28. Sozzi E, Barbieri I, Lavazza A, et al. Molecular characterization and phylogenetic analysis of VP1 of porcine enteric picornaviruses isolates in Italy. *Transbound Emerg Dis*. Dec 2010;57(6):434-442. doi:10.1111/j.1865-1682.2010.01170.x
29. Ray PK, Desingu PA, Kumari S, et al. Porcine sapelovirus among diarrhoeic piglets in India. *Transbound Emerg Dis*. Feb 2018;65(1):261-263. doi:10.1111/tbed.12628
30. Kumari S, Singh R, Desingu PA, Ray PK, Taru Sharma G, Saikumar G. Immunocytochemistry assay in BHK-21 cell line infected with porcine sapelovirus. *Cytotechnology*. Jun 2019;71(3):751-755. doi:10.1007/s10616-019-00315-4
31. Zhang W, Kataoka M, Yen Doan H, et al. Isolation and characterization of mammalian orthoreoviruses using a cell line resistant to sapelovirus infection. *Transbound Emerg Dis*. Nov 2020;67(6):2849-2859. doi:10.1111/tbed.13655
32. Kumari S, Saikumar G, Desingu PA, Das T, Singh R. Immunohistochemical detection of naturally occurring porcine sapelovirus infection in Indian pigs. *J Immunoassay Immunochem*. 2019;40(6):676-684. doi:10.1080/15321819.2019.1675695
33. Son KY, Kim DS, Kwon J, et al. Full-length genomic analysis of Korean porcine sapelovirus strains. *Plos One*. Sep 2014;9(9):11. e107860. doi:10.1371/journal.pone.0107860
34. Zell R, Krumbholz A, Henke A, et al. Detection of porcine enteroviruses by nRT-PCR: differentiation of CPE groups I-III with specific primer sets. *J Virol Methods*. Aug 2000;88(2):205-18.

35. Harmon K. Validation of a Real-Time Reverse Transcription PCR Assay for Detection of Porcine Sapelovirus. Swine Health Information Center (SHIC),. Accessed June 26, 2021. https://www.swinehealth.org/wp-content/uploads/2020/02/SHIC-diagnostic-assay-catalog-20Feb2020.pdf
36. Krumbholz A, Wurm R, Scheck O, et al. Detection of porcine teschoviruses and enteroviruses by LightCycler real-time PCR. *J Virol Methods*. Oct 2003;113(1):51-63.
37. Wang CY, Yu DY, Cui L, et al. Rapid and real-time detection of porcine sapelovirus by reverse transcription loop-mediated isothermal amplification assay. *J Virol Meth*. Jul 2014;203:5-8. doi:10.1016/j.jviromet.2014.03.011
38. Kumari S, Ray PK, Singh R, Desingu PA, Sharma GT, Saikumar G. Development of a Taqman-based real-time PCR assay for detection of porcine sapelovirus infection in pigs. *Anim Biotechnol*. Jun 2020;31(3):264-267. doi:10.1080/10495398.2018.1549561
39. Chen J, Chen F, Zhou Q, et al. Development of a minor groove binder assay for real-time PCR detection of porcine Sapelovirus. *J Virol Methods*. Mar 2014;198:69-74. doi:10.1016/j.jviromet.2013.12.003
40. Palmquist JM, Munir S, Taku A, Kapur V, Goyal SM. Detection of porcine teschovirus and enterovirus type II by reverse transcription-polymerase chain reaction. *J Vet Diagn Invest*. Nov 2002;14(6):476-80.
41. Jiang C, He H, Zhang C, et al. One-step triplex reverse-transcription PCR detection of porcine epidemic diarrhea virus, porcine sapelovirus, and porcine sapovirus. *J Vet Diagn Invest*. Nov 2019;31(6):909-912. doi:10.1177/1040638719883834
42. Harima H, Kajihara M, Simulundu E, et al. Genetic and biological diversity of porcine sapeloviruses prevailing in Zambia. *Viruses*. Feb 5 2020;12(2). doi:10.3390/v12020180
43. Bai J, Palinski R. Development and Validation of ELISA to Detect IgA, IgM, IgG in Serum and Oral Fluids to Porcine Sapelovirus. Swine Health Information Center (SHIC),. Accessed June 26, 2021. https://www.swinehealth.org/wp-content/uploads/2020/02/SHIC-diagnostic-assay-catalog-20Feb2020.pdf
44. Hause BM, Padmanabhan A, Pedersen K, Gidlewski T. Feral swine virome is dominated by single-stranded DNA viruses and contains a novel Orthopneumovirus which circulates both in feral and domestic swine. *J Gen Virol*. Sep 2016;97(9):2090-5. doi:10.1099/jgv.0.000554
45. Abe M, Ito N, Sakai K, et al. A novel sapelovirus-like virus isolation from wild boar. *Virus Genes.* Oct 2011;43(2):243-8. doi:10.1007/s11262-011-0628-2
46. Boros A, Nemes C, Pankovics P, et al. Characterization of a novel porcine enterovirus in wild boars in Hungary. *Arch Virol*. May 2012;157(5):981-6. doi:10.1007/s00705-012-1255-5
47. Masuda T, Sunaga F, Naoi Y, et al. Whole genome analysis of a novel picornavirus related to the *Enterovirus/Sapelovirus* supergroup from porcine feces in Japan. *Virus Res*. Sep 15 2018;257:68-73. doi:10.1016/j.virusres.2018.09.003
48. Lau SK, Woo PC, Lai KK, et al. Complete genome analysis of three novel picornaviruses from diverse bat species. *J Virol*. Sep 2011;85(17):8819-28. doi:10.1128/JVI.02364-10
49. Yinda CK, Conceicao-Neto N, Zeller M, et al. Novel highly divergent sapoviruses detected by metagenomics analysis in straw-colored fruit bats in Cameroon. *Emerg Microbes Infect.* May 24 2017;6(5):e38. doi:10.1038/emi.2017.20
50. Lukashev AN, Corman VM, Schacht D, et al. Close genetic relatedness of picornaviruses from European and Asian bats. *J Gen Virol*. May 2017;98(5):955-961. doi:10.1099/jgv.0.000760
51. Phan TG, Kapusinszky B, Wang C, Rose RK, Lipton HL, Delwart EL. The fecal viral flora of wild rodents. *PLoS Pathog*. Sep 2011;7(9):e1002218. doi:10.1371/journal.ppat.1002218
52. Du J, Lu L, Liu F, et al. Distribution and characteristics of rodent picornaviruses in China. *Sci Rep*. Sep 2016;6:34381. doi:10.1038/srep34381
53. Woo PC, Lau SK, Choi GK, et al. Complete genome sequence of a novel picornavirus, canine picornavirus, discovered in dogs. *J Virol*. Mar 2012;86(6):3402-3. doi:10.1128/JVI.07228-11
54. Lau SK, Woo PC, Yip CC, et al. Identification of a novel feline picornavirus from the domestic cat. *J Virol*. Jan 2012;86(1):395-405. doi:10.1128/JVI.06253-11
55. Wille M, Shi M, Klaassen M, Hurt AC, Holmes EC. Virome heterogeneity and connectivity in waterfowl and shorebird communities. *ISME J*. 10 2019;13(10):2603-2616. doi:10.1038/s41396-019-0458-0

56. Kofstad T, Jonassen CM. Screening of feral and wood pigeons for viruses harbouring a conserved mobile viral element: characterization of novel Astroviruses and Picornaviruses. *PLoS One*. 2011;6(10):e25964. doi:10.1371/journal.pone.0025964
57. Li L, Shan T, Wang C, et al. The fecal viral flora of California sea lions. *J Virol*. Oct 2011;85(19):9909-17. doi:10.1128/jvi.05026-11
58. Chong R, Shi M, Grueber CE, et al. Fecal viral diversity of captive and wild Tasmanian devils characterized using virion-enriched metagenomics and metatranscriptomics. *J Virol*. 06 2019;93(11). doi:10.1128/JVI.00205-19
59. Forman AJ, Pass DA, Connaughton ID. The characterization and pathogenicity of porcine enteroviruses isolated in Victoria. *Aus Vet J*. 1982;58(4):136-142.
60. Donin DG, Leme RD, Alfieri AF, Alberton GC, Alfieri AA. Molecular survey of porcine teschovirus, porcine sapelovirus, and enterovirus G in captive wild boars (*Sus scrofa scrofa*) of Parana state, Brazil. *Pesq Vet Bras*. May 2015;35(5):403-408.
61. Buitrago D, Cano-Gómez C, Agüero M, Fernandez-Pacheco P, Gómez-Tejedor C, Jiménez-Clavero MA. A survey of porcine picornaviruses and adenoviruses in fecal samples in Spain. *J Vet Diagn Invest*. Sep 2010;22(5):763-6.
62. Cano-Gómez C, Palero F, Buitrago MD, et al. Analyzing the genetic diversity of teschoviruses in Spanish pig populations using complete VP1 sequences. *Infect Genet Evol*. Dec 2011;11(8):2144-50. doi:10.1016/j.meegid.2011.09.014
63. La Rosa G, Muscillo M, Di Grazia A, Fontana S, Iaconelli M, Tollis M. Validation of RT-PCR assays for molecular characterization of porcine teschoviruses and enteroviruses. *J Vet Med B Infect Dis Vet Public Health*. Aug 2006;53(6):257-265. doi:10.1111/j.1439-0450.2006.00955.x
64. Chelli E, De Sabato L, Vaccari G, Ostanello F, Di Bartolo I. Detection and characterization of porcine sapelovirus in Italian pig farms. *Animals (Basel)*. Jun 2 2020;10(6). doi:10.3390/ani10060966
65. Tassoni L, Zamperin G, Monne I, Beato MS. Nearly complete genome sequence of a sapelovirus A strain identified in swine in Italy. *Microbiol Resour Announc*. Jul 18 2019;8(29). doi:10.1128/mra.00481-19
66. Boros Á, Pankovics P, Reuter G. Characterization of a novel porcine enterovirus in domestic pig in Hungary. *Infect Genet Evol*. Jul 2011;11(5):1096-102. doi:10.1016/j.meegid.2011.04.003
67. Boros Á, László Z, Pankovics P, et al. High prevalence, genetic diversity and a potentially novel genotype of Sapelovirus A (*Picornaviridae*) in enteric and respiratory samples in Hungarian swine farms. *J Gen Virol*. Jun 2020;101(6):609-621. doi:10.1099/jgv.0.001410
68. Piorkowski G, Capai L, Falchi A, et al. First identification and genomic characterization of a porcine sapelovirus from Corsica, France, 2017. *Microbiol Resour Announc*. Sep 2018;7(11). doi:10.1128/mra.01049-18
69. Yang T, Yu X, Yan M, et al. Molecular characterization of Porcine sapelovirus in Hunan, China. *J Gen Virol*. Oct 12 2017. doi:10.1099/jgv.0.000951
70. Sunaga F, Masuda T, Ito M, et al. Complete genomic analysis and molecular characterization of Japanese porcine sapeloviruses. *Virus Genes*. Apr 2019;55(2):198-208. doi:10.1007/s11262-019-01640-8
71. Shan TL, Li LL, Simmonds P, Wang CL, Moeser A, Delwart E. The fecal virome of pigs on a high-density farm. *J Virol*. Nov 2011;85(22):11697-11708. doi:10.1128/jvi.05217-11
72. Chen Q, Zheng Y, Guo B, et al. Complete genome sequence of porcine sapelovirus strain USA/IA33375/2015 identified in the United States. *Genome Announc*. Sep 29 2016;4(5). doi:10.1128/genomeA.01055-16
73. Zhang B, Tang C, Yue H, Ren Y, Song Z. Viral metagenomics analysis demonstrates the diversity of viral flora in piglet diarrhoeic faeces in China. *J Gen Virol*. Jul 2014;95(Pt 7):1603-1611. doi:10.1099/vir.0.063743-0
74. Khamrin P, Maneekarn N, Okitsu S, Ushijima H. Epidemiology of human and animal kobuviruses. *Virusdisease*. 2014;25(2):195-200. doi:10.1007/s13337-014-0200-5
75. Reuter G, Boros A, Pankovics P. Kobuviruses - a comprehensive review. *Rev Med Virol*. Jan 2011;21(1):32-41. doi:10.1002/rmv.677
76. Zell R. Picornaviridae-the ever-growing virus family. *Arch Virol*. Feb 2018;163(2):299-317. doi:10.1007/s00705-017-3614-8

77. International Committee on Virus Taxonomy (ICTV). Virus Taxonomy: 2020 Release. Accessed June 17, 2021. https://talk.ictvonline.org/taxonomy/
78. Chen J, Chen F, Zhou Q, et al. Complete genome sequence of a novel porcine Sapelovirus strain YC2011 isolated from piglets with diarrhea. *J Virol*. Oct 2012;86(19):10898. doi:10.1128/JVI.01799-12
79. Dilovski M, Ognianov D. [Isolation and identification of a virus causing abortions and stillbirths in swine (Preliminary report)]. *Vet Med Nauki*. 1975;12(8):52-3.
80. Dunne HW, Wang JT, Ammerman EH. Classification of North American porcine enteroviruses: a comparison with European and Japanese strains. *Infect Immu*. 1971;4(5):619-631.
81. Lamont PH, Betts AO. Enteroviruses in the pig. *Nature*. Aug 30 1958;182(4635):608-9. doi:10.1038/182608a0