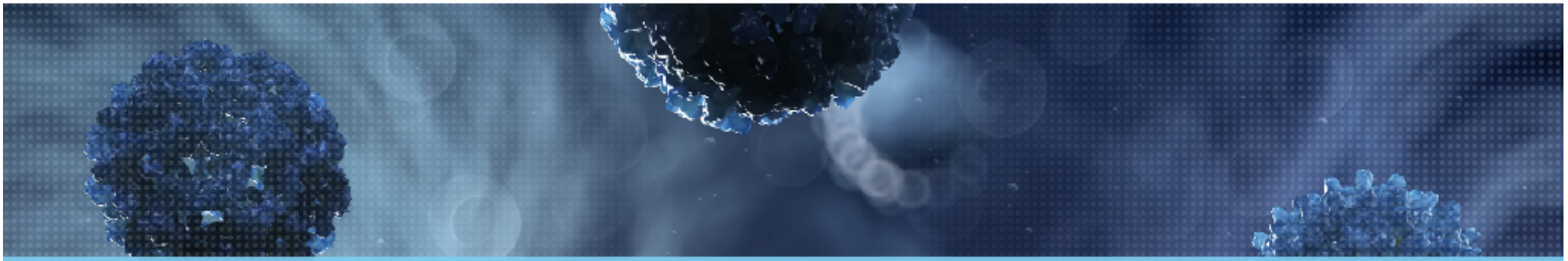
EUROPEAN MANAGEMENT PLATFORM FOR EMERGING AND RE-EMERGING INFECTIOUS DISEASE ENTITIES



Novel (subtypes of) viruses discovered in EMPERIE

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COOPERATION

COORDINATED BY
THE VIROSCIENCE LAB OF Erasmus MC

Within weeks of the first reported cases of the SARS outbreak in 2003, an international network of laboratories identified a novel coronavirus - currently known as SARS-CoV - as the causative agent of SARS. This rapid identification was crucial in containing the further spread of SARS. The successful international collaboration formed the basis of establishing EMPERIE as a network capable of rapidly identifying the causative agent of newly emerging or re-emerging infectious disease outbreaks. To this aim, EMPERIE has established a common virus discovery platform used by the network partners to do just that: identifying viruses in animals and humans from existing samples and samples from humans and high risk animal species - such as bats and birds - collected in key regions across the globe. Testimony to the functioning of this virus discovery platform are the novel viruses discovered in EMPERIE. The platform will be instrumental in the discovery of novel pathogens threatening animals and humans alike. The most well known examples are the identification of the Schmallenberg virus and the Middle East Respiratory Syndrome (MERS) Coronavirus using the EMPERIE virus discovery platform. The table below gives an overview of the novel viruses discovered.

Astrovirus	**A new astrovirus was identified in a patient diagnosed with celiac disease. This expands the geographic range of this virus to include Europe.**	**Smits et al, 2010. *Human Astrovirus Infection in a Patient with New-Onset Celiac Disease.* J. Clin. Microbiol, p. 3416–3418**
	Novel astroviruses were identified in diarrhoea samples from an outbreak of gastrointestinal illness in a Danish population of European roe deer for which no aetiological agent could be identified.	Smits et al, 2010. ***Identification and characterization of deer astroviruses***. J Gen Virol. 91(Pt 11):2719-22.
	Classical human astroviruses and a human MLB1 astrovirus were identified in human faecal samples and novel astroviruses were identified in faecal samples of urban brown rat. Data suggest that the MLB viruses and these novel rat astroviruses may share a common ancestor.	Chu DK, Chin AW, Smith GJ, Chan KH, Guan Y, Peiris JS, Poon LL.2010. ***Detection of novel astroviruses in urban brown rats and previously known astroviruses in humans.*** J. Gen. Virol. 2010 Oct. 91:2457-62.
Henipahvirus	Human Henipavirus infections have been reported in Austrialia and Asia, compatible with the geographic range of Pteropus bats. Novel putative Henipaviruses were identified in African bats, significantly extending the region of potential endemicity of one of the most pathogenic virus genera known in humans.	Drexler et al, 2009. ***Henipavirus RNA in African Bats***. PLoS ONE 4(7): e6367
Picobirnavirus	A new picobirnavirus variant was detected in clinical diarrhea samples for which no etiological agent could be identified. In total, ~20% of clinical diarrhea samples contained human picobirnavirus sequences.	Van Leeuwen et al, 2010. ***Human Picobirnaviruses Identified by Molecular Screening of Diarrhea Samples***, J. Clin. Microbiol. p.1787-1794
	EMPERIE identified group I and new group II porcine picobirnaviruses in the respiratory tract of seemingly healthy pigs. These data show for the first time the presence of picobirnaviruses in the respiratory tract and of group II picobirnaviruses in another species besides humans.	Smits S.L., L.L. Poon, M. van Leeuwen, P.N. Lau, H.K. Perera, J.S. Peiris, J.H. Simon, A.D. Osterhaus (2011). ***Genogroup I and II picobirnaviruses in respiratory tract of pigs.*** Emerg Infect Dis. 17(12):2328-30.
	The identification of new picobirnaviruses in respiratory tract samples from pigs prompted EMPERI**E** to look for the presence of picobirnaviruses in the respiratory tracts of humans. Genogroup I picobirnaviruses could be identified in some of the bronchoalveolar lavage specimens obtained from patients with unexplained respiratory disease in the Netherlands.	Smits S.L., M. van Leeuwen , C.M. Schapendonk, A.C. Schürch, R. Bodewes, B.L. Haagmans, A.D. Osterhaus (2012). ***Picobirnaviruses in the human respiratory tract.*** Emerg Infect Dis. 18(9):1539-40.
Anellovirus	Seasonal hyperacute panuveitis (SHAPU) is a potentially blinding ocular disease occurring in Nepal that principally affects young children. Random amplification of partially purified vitreous fluid (VF)–derived nucleic acid revealed the presence of human anelloviruses in VF of SHAPU patients. The detection of anelloviruses in VF	Smits S.L., A. Manandhar, F. B. van Loenen, M. van Leeuwen, G.S. Baarsma, N. Dorrestijn, A. D.M.E. Osterhaus, T. P. Margolis, G. M.G.M. Verjans (2012). ***High Prevalence of Anelloviruses in Vitreous Fluid of Children With Seasonal***

	samples of uveitis patients, profoundly so in SHAPU patients, is imperative and warrants elucidation of its clinical significance.	***Hyperacute Panuveitis***. *J§ Infect Dis.* Accepted for publication
Bunyavirus	During a surveillance campaign on arthropod-borne infections along anthropogenic disturbance gradients in the tropics, EMPERIE has isolated a novel prototypic bunyavirus, tentatively named Gouléako virus, which most likely represents a novel sixth genus within the family *Bunyaviridae*.	Marklewitz M, Handrick S, Grasse W, Kurth A, Lukashev A, Drosten C, Ellerbrok H, Leendertz FH, Pauli G, Junglen S: ***Gouleako virus isolated from West African mosquitoes constitutes a proposed novel genus in the family Bunyaviridae.*** *Journal of virology* 2011, 85(17):9227-9234.
Nidovirus	EMPERIE discovered the first insect-associated nidovirus, tentatively named Cavally virus, which is likely to represent a novel family within the order *Nidovirales*. Notably, partner 2 UBMC was able to map the spread and genetic evolution of Cavally virus from a pristine rainforest to human settlements.	F Zirkel, A Kurth, P-L Quan, T Briese, H Ellerbrok, G Pauli, FH Leendertz, WI Lipkin, J Ziebuhr, C Drosten, S Junglen. mBIO ***accepted for publication***;.
Novel parvovirus 4	Human parvovirus 4 has been considered to be transmitted only parenterally. However, after novel genotype 3 of parvovirus 4 was found in 2 patients with no parenteral risks, we tested infants in Ghana. A viremia rate of 8.6% over 2 years indicates that this infection is common in children in Africa.	Panning et al, 2010. ***Novel Human Parvovirus 4 Genotype 3 in Infants, Ghana***. Emerging Infectious Diseases. July 2010, p. 1143-1146
Coronaviruses	In an evaluation of Coronaviruses (CoV) in rhinolophid and vespertilionid bat species common in Europe we found that Rhinolophids carried severe acute respiratory syndrome (SARS)-related CoV at high frequencies and concentrations, as well as two Alphacoronavirus clades, one novel and one related to the HKU2 clade. All three clades present in Miniopterus bats in China (HKU7, HKU8, and 1A related) were also present in European Miniopterus bats. An additional novel Alphacoronavirus was detected in Nyctalus leisleri. A close MERS-CoV ancestor was identified in bats from South-Africa and related MERS viruses were found in German hedgehogs .In the Americas 50 novel bat CoVs that were detected. They were unrelated to known human or animal pathogens indicating an absence of recent zoonotic spill-over events.	Drexler et al, 2010. ***Genomic Characterization of Severe Acute Respiratory Syndrome-Related Coronavirus in European Bats and Classification of Coronaviruses Based on Partial RNA-Dependent RNA Polymerase Gene Sequence***. Journal of Virology, p. 11336–11349 Ithete NL, Stoffberg S, Corman VM, Cottontail VM, Richards LR, Schoeman MC, Drosten C, Drexler JF, Preiser W: Close relative of human Middle East respiratory syndrome coronavirus in bat, South Africa. **Emerging infectious diseases** 2013, 19(10):1697-1699. Corman VM, Kallies R, Philipps H, Gopner G, Muller MA, Eckerle I, Brunink S, Drosten C, Drexler JF: Characterization of a novel betacoronavirus related to middle East respiratory syndrome coronavirus in European hedgehogs. **Journal of virology** 2014, 88(1):717-724. Corman VM, Rasche A, Diallo TD, Cottontail VM, Stocker A, Souza BF, Correa JI, Carneiro AJ, Franke CR, Nagy M et al: Highly diversified coronaviruses in neotropical bats. **The**

		Journal of general virology 2013, 94(Pt 9):1984-1994
Wild type 1 polioviruses and enterovirus C strain	Molecular analysis of faecal, throat and cerebrospinal samples identified wildtype 1 poliovirus and an additional enterovirus C strain related to enterovirus 109 as the cause of the 2010 outbreak of flaccid paralysis syndrome in adults in Congo.	G Grard et al, 2010. ***Type 1 wild poliovirus and putative enterovirus 109 in an outbreak of acute flaccid paralysis in Congo***, October-November 2010. Euro Surveillance, Nov. 2010, p1-3;
Human parechoviruses	We determined the complete coding sequences of eight human parechoviruses (HPeV) of types 1, 5 and 6 directly from clinical samples from Brazil. The capsid genes of these strains were not remarkably different from European, North American and Japanese HPeV. Our results support the idea that picornavirus replicative genes acquire capsid proteins introduced by new strains. Under certain epidemiological conditions, replicative genes may be maintained in circumscript geographical regions.	Drexler et al. 2010. ***Full genome sequence analysis of parechoviruses from Brazil reveals geographical patterns in the evolution of non-structural genes and intratypic recombination in the capsid region***. Journal of General Virology, Epub 2010, p. 564-571;
Novel orthobunyavirus "Schmallenberg virus (SBV)"	Based on the intelligent sampling strategy of EMPERIE, the FLI analysed several samples from cattle suffering from fever, decreased milk production, and diarrhea, by metagenomic sequencing. This enabled us to identify the novel orthobunyavirus "Schmallenberg virus (SBV)". This was the first detection ever of an orthobunyavirus of the Simbu serogroup in Europe: Schmallenberg virus.	Hoffmann B, Scheuch M, Höper D, Jungblut R, Holsteg M, Schirrmeier H, et al. ***Novel orthobunyavirus in Cattle***, Europe, 2011. Emerg Infect Dis. 2012;18(3):469-72. Katja V. Goller, Dirk Höper, Horst Schirrmeier, Thomas C. Mettenleiter, Martin Beer. 2012. ***Schmallenberg virus: ancestor of the closely related Shamonda virus?*** Manuscript submitted to Emerg Infect Dis
Calicivirus	To identify unknown human viruses in the enteric tract, we examined 105 stool specimens from patients with diarrhea in Bangladesh. A novel calicivirus was identified in a sample from 1 patient and subsequently found in samples from 5 other patients. Phylogenetic analyses classified this virus within the proposed genus Recovirus.	Smits SL, Rahman M, Schapendonk CME, van Leeuwen M, Faruque ASG, Haagmans BL, et al. ***Calicivirus from novel Recovirus genogroup in human diarrhea, Bangladesh***. Emerg Infect Dis, July 2012
Human picornaviruses	The **pathogenesis of novel human picornaviruses** was studied by analyzing virus prevalence and shedding in adult and pediatric cohorts from Germany and Brazil. Aichi virus fecal transmission and genetic recombination underlined it is a human pathogen that behaves genetically different from most other picornaviruses. Human cardioviruses were detected in CNS specimens of children with meningitis and myocardium of one child who died from sudden infant death syndrome. Cosaviruses were detected at higher rates in Brazilian children without than in patients with gastroenteritis, which	Drexler JF, Baumgarte S, de Souza Luna LK, Eschbach-Bludau M, Lukashev AN, Drosten C: ***Aichi virus shedding in high concentrations in patients with acute diarrhea.*** *Emerging infectious diseases* 2011, 17(8):1544-1548. Lukashev A, Drexler JF, Belalov I, Eschbach-Bludau M, Baumgarte S, Drosten C: ***Genetic variation and recombination in Aichi virus***. *The Journal of general virology* 2012.

	might imply it is not an authentic human pathogen at all.	Drexler JF, Baumgarte S, Eschbach-Bludau M, Simon A, Kemen C, Bode U, Eis-Hubinger AM, Madea B, Drosten C: ***Human cardioviruses, meningitis, and sudden infant death syndrome in children***. *Emerging infectious diseases* 2011, 17(12):2313-2315. Stocker A, Souza BF, Ribeiro TC, Netto EM, Araujo LO, Correa JI, Almeida PS, Peixoto de Mattos A, Ribeiro Hda C, Jr., Pedral-Sampaio DB *et al*: ***Cosavirus Infection in Persons with and without Gastroenteritis, Brazil.*** *Emerging infectious diseases* 2012, 18(4):656-659.
Novel human cyclovirus	We identified a novel human cyclovirus that may be involved in acute meningoencephalitis. Identification of previously unknown pathogens in patients with acute meningoencephalitis remains essential to improve prevention and clinical management of this frequently devastating disease.	LV Tan, van Doorn HR, Nghia HDT, Chau TTH, Tu LTP, de Vries M, Canuti M, Deijs M, Jebbink MF, Baker S, Bryant JE, Tham NT, Chinh NTTB, Boni MF, Loi TQ, Phuong LT, Verhoeven JTP, Crusat M, Jeeninga RE, Schultsz C, Chau NVV, Hien TT, van der Hoek L, Farrar J and de Jong MD. ***Identification of a New Cyclovirus in Cerebrospinal Fluid of Patients with Acute Central Nervous System Infections***. MBio. 2013 Jun 18;4(3):e00231-13. doi: 10.1128/mBio.00231-13 Le VT, de Jong MD, Nguyen VK, Nguyen VT, Taylor W, Wertheim HF, van der Ende A, van der Hoek L, Canuti M, Crusat M, Sona S, Nguyen HU, Giri A, Nguyen TT, Ho DT, Farrar J, Bryant JE, Tran TH, Nguyen VV, van Doorn HR. Limited geographic distribution of the novel cyclovirus CyCV-VN. Sci Rep. 2014 Feb 5;4:3967.
	We also identified a novel cyclovirus commonly presented in serum and CSF of paraplegia patients from Malawi. Our data indicate that cycloviruses may cause systemic infections and are present in multiple organ compartments in humans. Whether cycloviruses play a role in development of paraplegia remains to be determined	Smits SL, Zijlstra EE, van Hellemond JJ, Schapendonk CM, Bodewes R, Schürch AC, Haagmans BL, Osterhaus AD. ***Novel cyclovirus in human cerebrospinal fluid, Malawi, 2010-2011***.**Emerg Infect Dis**. 2013;19(9). doi: 10.3201/eid1909.130404.
Avian coronavirus	Phylogenetic analysis on our newly discovered coronaviruses indicated that	Chu DK, Leung CY, Gilbert M, Joyner PH, Ng EM, Tse TM, Guan Y,

	there are two distinct groups of viruses circulating in wild birds. Based on these observations, these avian coronaviruses are proposed to be classified into two genera (Gammacoronavirus and tentative Deltacoronaviruses). Gammacoronaviruses were found predominantly in Anseriformes birds, whereas deltacoronaviruses could be detected in Ciconiiformes, Pelecaniformes, and Anseriformes birds in this study.	Peiris JS, Poon LL. 2011. ***Avian coronavirus in wild aquatic birds***. J Virol. 85:12815-20.
Avian astroviruses	Characterisation of astrovirus sequences deduced from avian fecal specimens indicated that there is a novel group of astroviruses circulating in wild ducks. In addition, there is evidence of interspecies transmission of astroviruses between different avian species, suggesting the natura reservoir for avian astrovirus might be much larger than previously thought.	Chu DK, Leung CY, Perera HK, Ng EM, Gilbert M, Joyner PH, Grioni A, Ades G, Guan Y, Peiris JS, Poon LL. 2012. ***A novel group of avian astroviruses in wild aquatic birds***. J Virol. 86:13772-8. http://jvi.asm.org/content/86/24/13772.full.pdf+html
parvoviruses	Two novel parvoviruses were identified in two bat species: a *Partetravirus* named Eh-BtPTV-1 in *Eidolon helvum* bats from Ghana and the first member of a new genus detected in *Artibeus jamaicensis* bats from Panama (Aj-BtPV-1)	Canuti M, Eis-Huebinger AM, Deijs M, de Vries M, Drexler JF, Oppong SK, Muller MA, Klose SM, Wellinghausen N, Cottontail VM *et al*: ***Two novel parvoviruses in frugivorous New and Old World bats.*** *PloS one* 2011, 6(12):e29140
Paramyxoviruses	We identified an estimated 66 new paramyxoviruses in a worldwide sample of 119 bat and rodent species (9,278 individuals). Major discoveries included evidence of an origin of Hendra- and Nipah virus in Africa, the identification of a bat virus conspecific with the human mumps virus, the detection of close relatives of respiratory syncytial virus, mouse pneumonia- and canine distemper virus in bats, as well as direct evidence of Sendai virus in rodents.	Drexler JF, Corman VM, Muller MA, Maganga GD, Vallo P, Binger T, Gloza-Rausch F, Rasche A, Yordanov S, Seebens A *et al*: ***Bats host major mammalian paramyxoviruses.*** *Nature communications* 2012, 3:796.
Marburg virus	In a study on Marburg virus in Gabon, local persistence of virus variants in Gabonese *R. aegyptiacus* bats was shown.	Maganga GD, Bourgarel M, Ella GE, Drexler JF, Gonzalez JP, Drosten C, Leroy EM: ***Is Marburg virus enzootic in Gabon?*** *The Journal of infectious diseases* 2011, 204 Suppl 3:S800-803.
Coronaviruses, anello and circovirus-like	We identified ferret enteric coronaviruses at high prevalence in The Netherlands. In addition viral metagenomic analyses in pine marten and European badger resulted in the identification of a pine marten anellovirus that probably belongs to a new genus, a circovirus-like virus from European badger that most likely belongs to a novel virus family, and a new pine marten bocavirus species	Provacia L.B., S.L. Smits, B.E. Martina, V.S. raj, P.V. vand en Doel, G. van Amerongen, H. Moorman-Roest, A.D. Osterhaus, B.L. Haagmans (2011). ***Enteric coronavirus in ferrets***, The Netherlands. Emerg Infect Dis. 17(8):1570-1. van den Brand J.M., M. van Leeuwen, C.M.E. Schapendonk, J.H. Simon, B.L. Haagmans, A.D. Osterhaus, S.L. Smits (2012). ***Metagenomic analysis of the viral flora of pine marten and European badger feces***. J Virol. 86(4):2360-5.
Insect-associated	The first insect-associated nidovirus, tentatively named Cavally virus, which	Zirkel F, Kurth A, Quan PL, Briese T, Ellerbrok H, Pauli G, Leendertz

nidovirus	represents a novel family within the order *Nidovirales* was discovered. The proposed new family was named *Mesoniviridae* as described in an article published in Archives of Virology.	FH, Lipkin WI, Ziebuhr J, Drosten C et al: ***An insect nidovirus emerging from a primary tropical rainfores***t. mBio 2011, 2(3):e00077-00011. Lauber C, Ziebuhr J, Junglen S, Drosten C, Zirkel F, Nga PT, Morita K, Snijder EJ, Gorbalenya AE: ***Mesoniviridae: a proposed new family in the order Nidovirales formed by a single species of mosquito-borne viruses***. *Archives of virology* 2012.
Novel Human Coronavirus in Humans (Middle East Respiratory Syndrome Coronavirus (MERS-CoV)	**P1 EMC, P2 UBMC, P4 HKU, P6 VCB, P11 WTSI and P13 CNB-CSIC**, and others were involved in the identification and characterization of a new coronavirus from the human respiratory tract and follow up studies, which led to a number of publications in 2012 and 2013, among which manuscripts regarding diagnostic assays and receptor identification for the new coronavirus. We investigated possible animal reservoirs of MERS-CoV by assessing specific serum antibodies in livestock. 50 of 50 (100%) sera from Omani camels and 15 of 105 (14%) from Spanish camels had protein-specific antibodies against MERS-CoV spike. Sera from European sheep, goats, cattle, and other camelids had no such antibodies. MERS-CoV neutralising antibody titres varied between 1/320 and 1/2560 for the Omani camel sera and between 1/20 and 1/320 for the Spanish camel sera. There was no evidence for cross-neutralisation by bovine coronavirus antibodies. MERS-CoV or a related virus has infected camel populations. Both titres and seroprevalences in sera from different locations in Oman suggest widespread infection	Zaki AM, van Boheemen S, Bestebroer TM, Osterhaus AD, Fouchier RA.(2012). ***Isolation of a novel coronavirus from a man with pneumonia in Saudi Arabia. N Engl J Med***. 367(19):1814-20 van Boheemen S, de Graaf M, Lauber C, Bestebroer TM, Raj VS, Zaki AM, Osterhaus AD, Haagmans BL, Gorbalenya AE, Snijder EJ, Fouchier RA. (2012). ***Genomic characterization of a newly discovered coronavirus associated with acute respiratory distress syndrome in humans***. MBio. 3(6): e00473-12. Meyer B, Muller MA, Corman VM, Reusken CB, Ritz D, Godeke GJ, Lattwein E, Kallies S, Siemens A, van Beek J et al: Antibodies against MERS coronavirus in dromedary camels, United Arab Emirates, 2003 and 2013. **Emerging infectious diseases** 2014, 20(4):552-559. Reusken CB, Ababneh M, Raj VS, Meyer B, Eljarah A, Abutarbush S, Godeke GJ, Bestebroer TM, Zutt I, Muller MA et al: ***Middle East Respiratory Syndrome coronavirus (MERS-CoV) serology in major livestock species in an affected region in Jordan, June to September*** 2013**. Euro surveillance**: bulletin Europeen sur les maladies transmissibles = European communicable disease bulletin 2013, 18(50):20662. Reusken CB, Haagmans BL, Muller MA, Gutierrez C, Godeke GJ, Meyer B, Muth D, Raj VS, Smits-De Vries L, Corman VM et al***: Middle East respiratory syndrome coronavirus neutralising serum antibodies in dromedary camels: a comparative serological study***. **The Lancet infectious diseases** 2013, 13(10):859-866.

Arenaviruses in boid snakes		Bodewes R, Kik M, Stalin Raj V, Schapendonk C, Haagmans B, Smits SL, Osterhaus A. (2013). ***Detection of novel divergent arenaviruses in boid snakes with inclusion body disease in the Netherlands.*** J Gen Virol. 2013 Jun;94(Pt 6):1206-10. doi: 10.1099/vir.0.051995-0 Bodewes R, Raj VS, Kik MJ, Schapendonk CM, Haagmans BL, et al. (2014***) Updated phylogenetic analysis of arenaviruses detected in boid snakes***. **J Virol** 88: 1399-1400.
Adenovirus		Bodewes R, van de Bildt MW, Schapendonk CM, van Leeuwen M, van Boheemen S, de Jong AA, Osterhaus AD, Smits SL, Kuiken T. (2013). ***Identification and characterization of a novel adenovirus in the cloacal bursa of gulls.*** Virology May 25;440(1):84-8. doi: 10.1016/j.virol.2013.02.011.
Phocine Distemper virus		Bodewes R, D. Morick, M.W.G. van de Bildt, N. Osinga, A. Rubio Garcı´a, G.J. Sa´nchez Contreras, S.L. Smits, L. A.P. Reperant, T. Kuiken, A.D.M.E. Osterhaus. (2013). ***Prevalence of phocine distemper virus specific antibodies: bracing for the next seal epizootic in north-western Europe***. Emerging Microbes and Infections 2(e3): doi:10.1038
Influenza B virus in seals		Bodewes R, D. Morick, G. de Mutsert, N.Osinga, T. Bestebroer, S. van der Vliet, S.L. Smits, T. Kuiken, G.F. Rimmelzwaan, R.A.M. Fouchier, A.D.M.E. Osterhaus (2013). Recurring influenza B virus infections in seals. Emerg Infect Dis. 19(3):511-2.
Novel papillomavirus and novel betaherpes virus in reindeer	We identified a novel papillomavirus and a novel betaherpes virus in eye swabs of reindeer suffering from infectious keratoconjunctivitis, but it remains to be determined whether either virus was causally linked to this disease	Smits SL, Schapendonk CM, van Leeuwen M, Kuiken T, Bodewes R, Stalin Raj V, Haagmans BL, das Neves CG, Tryland M, Osterhaus AD. ***Identification and characterization of two novel viruses in ocular infections in reindeer.*** **PLoS One**. 2013 Jul 16;8(7):e69711.

Entomobirnavirus in mosquitos		Marklewitz M, Gloza-Rausch F, Kurth A, Kümmerer BM, Drosten C, Junglen S. ***First isolation of an Entomobirnavirus from free-living insects***. J Gen Virol. 2012 Nov;93(Pt 11):2431-5. doi: 10.1099/vir.0.045435-0. Epub 2012 Aug 8.
St. Louis encephalitis virus (SLEV) in Culex nigripalpus mosquitoes	**P2 UBMC** discovered an ancestral variant of St. Louis encephalitis virus (SLEV) in Culex nigripalpus mosquitoes in a tropical rainforest in Palenque National Park, Mexico. Knowledge of this virus enabled spatiotemporal reconstruction of the common ancestor of all SLEVs, and how the virus spread from there.	Kopp A, Gillespie TR, Hobelsberger D, Estrada A, Harper JM, Miller RA, Eckerle I, Muller MA, Podsiadlowski L, Leendertz FH et al: ***Provenance and geographic spread of St. Louis encephalitis virus***. mBio 2013, 4(3):e00322-00313.
Hepatitis E viruses	**P2 UBMC** identified novel hepeviruses in bats. These viruses originated from Africa, Europe and Central America and five different bat species. Full genome characterization of one virus confirmed hepevirus taxonomic classification. All bat hepeviruses formed one monophyletic clade, supporting a strict association between hepeviruses and animal hosts. This enabled hypotheses on secondary acquisition of human hepeviruses by peridomestic animals subsequently constituting an animal reservoir of human hepatitis E Testing of anonymized pooled German blood donations, corresponding to 93,955 individual donors, revealed the occurrence of 14 hepevirus sequences by **P2 UBMC**. Eight of the 14 HEV sequences were closely related to viruses detected in wild boars which underlines the role of subclinical infection of donors as a source of contamination of blood products as well as the zoonotic transmission of genotype 3 hepevirus in Germany. We identified a ferret hepatitis E virus, which might allow development of a small animal model for hepatitis E virus infections.	Drexler JF, Seelen A, Corman VM, Fumie Tateno A, Cottontail V, Melim Zerbinati R, Gloza-Rausch F, Klose SM, Adu-Sarkodie Y, Oppong SK, Kalko EK, Osterman A, Rasche A, Adam A, Müller MA, Ulrich RG, Leroy EM, Lukashev AN, Drosten C. ***Bats worldwide carry hepatitis E-related viruses that form a putative novel genus within the family Hepeviridae.*** J Virol. 2012 Sep;86(17):9134-47. doi: 10.1128/JVI.00800-12. Epub 2012 Jun 13. Corman VM, Drexler JF, Eckerle I, Roth WK, Drosten C, Eis-Hübinger AM. ***Zoonotic hepatitis E virus strains in German blood donors***. Vox Sang. 2013 Feb;104(2):179-80. doi: 10.1111/j.1423-0410.2012.01638.x. Epub 2012 Aug 22. Raj VS, Smits SL, Pas SD, Provacia LB, Moorman-Roest H, Osterhaus AD, Haagmans BL. (2012). ***Novel hepatitis E virus in ferrets, the Netherlands***. Emerg Infect Dis. 18(8):1369-70.
Hepaciviruses in rodents	**P2 UBMC** identified novel hepaciviruses in rodents from Africa and Europe, including complete characterization of five full polyproteins, the characterization of distinct rodent hepacivirus serotypes and histopathological analysis of hepatic tropism and inflammation conducted in	Drexler JF, Corman VM, Müller MA, Lukashev AN, Gmyl A, Coutard B, Adam A, Ritz D, Leijten LM, van Riel D, Kallies R, Klose SM, Gloza-Rausch F, Binger T, Annan A, Adu-Sarkodie Y, Oppong S, Bourgarel M, Rupp D, Hoffmann B, Schlegel M, Kümmerer BM, Krüger DH, Schmidt-Chanasit J, Setién AA, Cottontail VM, Hemachudha T,

	cooperation with **P1 EMC**. This study put rodent HCV pathogenesis models plausible and may change conceptions of the origins of HCV.	Wacharapluesadee S, Osterrieder K, Bartenschlager R, Matthee S, Beer M, Kuiken T, Reusken C, Leroy EM, Ulrich RG, Drosten C. ***Evidence for novel hepaciviruses in rodents.*** **PLoS Pathog**. 2013;9(6):e1003438. doi: 10.1371/journal.ppat.1003438. Epub 2013 Jun 20.
Hepadnaviruses in Bats	**P2 UBMC** detected novel hepadnaviruses in bats from Central America and Africa. The viruses were recovered in vitro and used to show that one of them can infect human hepatocytes, using the same cellular receptor as HBV. HBV vaccine-induced antibodies in human sera could not confer protection against this virus. The analysis of hepatic tropism and inflammation was done in cooperation with **P1 EMC**.	Drexler JF, Geipel A, Konig A, Corman VM, van Riel D, Leijten LM, Bremer CM, Rasche A, Cottontail VM, Maganga GD et al: ***Bats carry pathogenic hepadnaviruses antigenically related to hepatitis B virus and capable of infecting human hepatocytes***. **PNAS 2013**, 110(40):16151-16156.
Parvovirus 4	A retrospective study by **P2 UBMC** in Ghana investigated the prevalence of Parvovirus 4 (PARV4) in children. PARV4 DNA was detected in 8 (0.83%) of 961 nasal samples and 5 (0.53%) of 943 fecal samples from 1,904 children in Ghana. Virus concentrations ≤ 6-7 log(10) copies/mL suggest respiratory or fecal-oral modes of PARV4 transmission.	Drexler JF, Reber U, Muth D, Herzog P, Annan A, Ebach F, Sarpong N, Acquah S, Adlkofer J, Adu-Sarkodie Y, Panning M, Tannich E, May J, Drosten C, Eis-Hübinger AM. ***Human parvovirus 4 in nasal and fecal specimens from children, Ghana.*** Emerg Infect Dis. 2012 Oct;18(10):1650-3. doi: 10.3201/eid1810.111373.
Merkel cell polyomavirus	We used unbiased amplification and deep sequencing on a hair follicle of a 70-year old male patient who had small, folliculocentric, coarse, yellowish spicules located on his face, chest, and lower arms. We demonstrated the presence of Merkel cell polyomavirus in this hair follicle by NGS.	van Boheemen S, Jones T, Muhlemann B, Feltkamp MC, Fouchier RA, and Hajdarbegovic E. ***Cidofovir Gel as Treatment of Follicular Spicules in Multiple Myeloma***. JAMA dermatology, In press
Multiple novel viruses in Red Fox	Red foxes (Vulpes vulpes) are the most widespread members of the order of Carnivora. Since they often live in (peri)urban areas, they are a potential reservoir of viruses that transmit from wildlife to humans or domestic animals. Here we evaluated the fecal viral microbiome of 13 red foxes by random PCR in combination with next-generation sequencing. Various novel viruses, including a parvovirus, bocavirus, adeno-associated virus, hepevirus, astroviruses, and picobirnaviruses, were identified	Bodewes R, van der Giessen J, Haagmans BL, Osterhaus AD, Smits SL. ***Identification of multiple novel viruses, including a parvovirus and a hepevirus, in feces of red foxes***. **J Virol.** 2013 Jul;87(13):7758-64. doi: 10.1128/JVI.00568-13. Epub 2013 Apr 24.
Novel B19-Like Parvovirus in the Brain of a Harbor Seal	Using random PCR in combination with next-generation sequencing, a novel parvovirus was detected in the brain of a young harbor seal (Phoca vitulina) with chronic non-suppurative meningo-encephalitis. In addition, two novel	Bodewes R, Rubio García A, Wiersma LC, Getu S, Beukers M, Schapendonk CM, van Run PR, van de Bildt MW, Poen MJ, Osinga N, Sánchez Contreras GJ, Kuiken T, Smits SL, Osterhaus AD. ***Novel b19-***

	viruses belonging to the family Anelloviridae were detected in the lungs of this animal.	***like parvovirus in the brain of a harbor seal.*** **PLoS One**. 2013 Nov 5;8(11):e79259. doi: 10.1371/journal.pone.0079259.
Novel Rhabdovirus in white-beaked dolphin	We identified a novel rhabdovirus (a virus family including rabies virus) in a white-beaked dolphin. This virus may derive from fish rhabdoviruses and possibly cycles between fishes and marine mammals	Siegers JY, van de Bildt MW, van Elk CE, Schürch AC, Tordo N, Kuiken T, Bodewes R, Osterhaus AD. ***Genetic relatedness of dolphin rhabdovirus with fish rhabdoviruses***. **Emerg Infect Dis**. 2014 Jun;20(6):1081-2.
Mosquito-associated Flavi-, Bunya-, and Nidoviruses	Highly diversified novel mosquito-associated viruses (Flavi-, Bunya-, Nidoviruses) were detected including the discovery of a sylvatic ancestor of St. Louis encephalitis virus (SLEV)	Kopp A, Gillespie TR, Hobelsberger D, Estrada A, Harper JM, Miller RA, Eckerle I, Muller MA, Podsiadlowski L, Leendertz FH et al: ***Provenance and geographic spread of St. Louis encephalitis virus***. **mBio** 2013, 4(3):e00322-00313
Torque teno mini virus	A novel genotype of torque teno mini virus was identified in injecting drug users with extremely low B-cell counts.	Jazaeri Farsani SM, Jebbink MF, Deijs M, Canuti M, van Dort KA, Bakker M, Grady BP, Prins M, van Hemert FJ, Kootstra NA, van der Hoek L. ***Identification of a new genotype of Torque Teno Mini virus.*** **Virol J.** 2013 Oct 30;10:323. doi: 10.1186/1743-422X-10-323.)
Pestivirus "Bungowannah virus"	The novel and emerging pestivirus "Bungowannah virus" was further characterized for a better understanding of the broad host range, which is atypical for pestiviruses. It could be shown that despite a low sequence homology to other pestiviruses, the Bungowannah virus Npro protein also is a very strong inhibitor of the interferon alpha response . Furthermore, it could be demonstrated that Bungowannah virus has the broadest cell tropism of all know pestiviruses, infecting bovine, ovine and porcine cell cultures but also human cell lines like HEK and HUH7, murine cells and also VERO cells.	Richter, M., P. König, I. Reimann, and M. Beer. 2014. ***Npro of Bungowannah virus exhibits the same antagonistic function in the IFN induction pathway than that of other classical pestiviruses***. **Vet Microbiol** 168:340-347. Maria Richter, Ilona Reimann, Horst Schirrmeier, Peter D. Kirkland, Martin Beer. ***The viral envelope is not sufficient to transfer the unique broad cell tropism of Bungowannah virus to a related pestivirus.*** **Journal of General Virology**, *in revision.*