



Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Elsevier hereby grants permission to make all its COVID-19-related research that is available on the COVID-19 resource centre - including this research content - immediately available in PubMed Central and other publicly funded repositories, such as the WHO COVID database with rights for unrestricted research re-use and analyses in any form or by any means with acknowledgement of the original source. These permissions are granted for free by Elsevier for as long as the COVID-19 resource centre remains active.

General Introduction to Volume 1 Emergent and Reemergent Viruses: Modern Important Issues

Moulay Mustapha Ennaji

Laboratory of Virology, Microbiology, Quality, Biotechnologies/Eco-Toxicology and Biodiversity, Faculty of Sciences and Techniques, Mohammedia, University Hassan II of Casablanca, Casablanca, Morocco

DEFINITION OF VIRUS COMES TO AGES

In the late 19th century the work of Ivanovsky and Beijerinck showed that tobacco mosaic virus was able to pass through filters that were known to retain bacteria, and the filtrate was able to cause a disease in new plants. Then, in 1898 Friedrich Loeffler and Paul Frosch applied the filtration criteria to a disease in cattle known as foot and mouth disease (Koonin et al., 2006; Cann, 2001).

The discovery of virus was a luminous start and a new scientific era in microbiology; after decades the definition of virus was concluded as obligate intracellular parasites, since they require living host cells to replicate, or a virus is a small parasite that cannot reproduce by itself. However, most biologists have considered them entities, separate from the realm of life and acting merely as mechanical artifacts that can exchange genes between different organisms. Regarding its heredity matter, DNA or RNA as their genome is enclosed in a protein shell called the capsid. Coded in the DNA or RNA genome of the virus is all the information needed for replication. The agreed idea about virus still

remains abundant, ubiquitous and plays a very important role in the health and evolution of life organisms. The health importance of viruses seems bigger than the definition itself (Castro and Heuschele, 1992; MacLachlan and Dubovi, 2011; White and Fenner, 1994).

BIOINFORMATICS OF VIROLOGY AND VIRAL-GENOME DATABASES

In virology research, virus-related databases and bioinformatic analysis tools are necessary for discerning relationships within complex datasets about viruses and host–virus interactions. The identification of open reading frames, gene prediction, homology searching, sequence alignment, and motif and epitope recognition are the main bioinformatic analyses on viruses. The predictions of transmembrane domains, glycosylation sites, and protein secondary and tertiary structure are also very important fields to analyze the structure–function relationship of proteins encoded in viral genomes. Biochemical pathway analysis can help elucidate information at the biological systems level. Other modern techniques such as microarray analysis can provide methods for high-throughput screening and gene expression profiling. Virus-related databases include viral sequences, taxonomy, and homologous protein families (Yan, 2008). Many general databases and query systems contribute an added value for viral studies. The National Center for Biotechnology Information (NCBI) (<http://www.ncbi.nlm.nih.gov/>) contains major virology resources such as influenza virus resource, retroviruses, and viral genomes. The NCBI is comprehensive with its integrative resources. They are also updated quite frequently and deserve a regular visit. Among other comprehensive databases, Universal Virus Database, specialized for virus classification and nomenclature taxonomy, has been approved by the International Committee on Taxonomy of Viruses (<http://www.ncbi.nlm.nih.gov/ICTVdb/index.htm>). Virus database at University College London (http://www.biochem.ucl.ac.uk/bsm/virus_database/VIDA.html) collects homologous protein families derived from virus genomes, such as Arteriviridae, Coronaviridae, Herpesviridae, Papillomaviridae, and Poxviridae families. The Viral Bioinformatics Resource Center (<http://athena.bioc.uvic.ca/index.php>) provides databases of viral genomes and tools for comparative genomic analyses. Furthermore, it also provides a downloadable database with tools for searching and analyzing the genes, gene families, and genomes of different virus families including Adenoviridae, Arenaviridae, Asfarviridae, Baculoviridae, Bunyaviridae, Coronaviridae, Filoviridae, Flaviviridae, Herpesviridae, Paramyxoviridae, Poxviridae, and Togaviridae (Sbalzarini and Greber, 2018; Xue and Miller-Jensen, 2012).

TUMORS AND VIRUSES RENEWABLE RELATIONS

The tumorigenesis role of viruses has been discussed frequently since decades; during that period, new types of tumors have been discovered and described. Researches continue to explain various tumorigenesis mechanisms, especially when correlated with common cancers such as cervix, liver, stomach, skin cancers, and other types of tumors. Importantly, viruses are associated with a vast majority of known tumors with different degrees of risk. Change of life style increased the complexity of virus–tumor and virus–virus interactions. Vast majority of HPV subtypes, responsible for cervix cancer, are HPV16. HPV is strongly associated with anal, vaginal, anogenital tumor, oropharynx, and oral cavity cancer. It is very strongly observed today that HPV oncoproteins, E6 and E7, inactivate the major tumor suppressors and have been suggested as central mechanism of HPV tumorigenesis. Human immunodeficiency virus (HIV) patients and/or homosexual persons have an elevated risk of cervix and other congenital tumors risk, compared with noninfected individuals. Human T-cell lymphotropic virus HLV-1, Epstein–Barr virus (EBV), HIV, hepatitis C virus, and hepatitis B virus play the role of etiological agents of lymphoma cancers, including an aggressive type of leukemia. Simian virus (SV40) is associated with malignant mesothelioma, brain, and bone cancers. Some cases of gastric adenocarcinoma are associated with EBV. Merkel cell polyomavirus is responsible for causing a vast majority of Merkel cell carcinoma tumors (Haley et al., 2018; Arora et al., 2012; Bosch and De Sanjosé, 2003; Bower et al., 2003; Centers for Disease Control and Prevention (CDC) 2012; Chaturvedi et al., 2009; Fukayama et al., 1994).

WATERBORNE AND FOODBORNE VIRUSES

There are two types of endemically infecting virus: the first one is capable of spreading in the body. These viruses are enteroviruses, hepatitis A virus (HAV), and hepatitis E virus (HEV). The second type of virus is gut inhabitants. These replicate in the intestinal tract; specific symptoms when they occur are those of a gastrointestinal infection—usually diarrhea and vomiting (Carter, 2005). Although there are numerous fecal oral transmitted viruses, most reports of foodborne transmission describe infections with Norwalk-like caliciviruses and HAV, suggesting that these viruses are associated with great risk of foodborne transmission (Koopmans et al., 2002). Several groups of viruses may infect persons after ingestion and then are shed via stool. Of these, the norovirus (NoV) and HAV are currently recognized as the

most important human foodborne pathogens with regard to the number of outbreaks and people affected in the world (Koopmans et al., 2002). HEV is responsible for epidemics and endemics of acute hepatitis in humans, mainly through waterborne, foodborne, and zoonotic transmission relations. It is a single-stranded, positive-sense RNA virus classified in the family of Hepeviridae, which encompasses four known genotypes, at least two new putative genotypes of mammalian HEV and one floating genus of avian HEV. Genotype 1 and 2 HEVs affect only humans, while genotypes 3 and 4 are zoonotic and responsible for sporadic and autochthonous infections in both humans and several other animal species globally (Yugo and Meng, 2013). The same of NoV, a member of the Caliciviridae family, is the most common cause of nonbacterial gastroenteritis worldwide and affects humans in all age groups. Virus transmission is primarily associated with person-to-person spread or the ingestion of contaminated food or water. NoV is highly infectious and causes outbreaks in communities, families, nursing homes, schools, hospitals, and cruise ships (Lysén et al., 2009).

DANGEROUS VIRUSES IN AFRICA

In Africa, a terrified human viral disease, HIV, was found first, in addition to common viral diseases such as human immune deficiency syndrome, hepatitis, measles, yellow fever virus, and monkeypox, which had already been prevailing there. Apart from these, nowadays, several new viral pathogens have also drawn attention. These can be termed modern dangerous: (1) *Lassa virus*—the virus is transmitted by rodents. The cases by this virus can be endemic, which means the virus occurs in a specific region, such as western Africa, and can reoccur there at any time. Approximately 15% of the rodents in western Africa carry the virus. (2) Ebola virus—there are five strains of Ebola, each named on respective countries and regions in Africa: Zaire, Sudan, Tai Forest, Bundibugyo, and Reston. The Zaire Ebola virus is the deadliest among all, with a mortality rate of 90%. It is the strain currently spreading through Guinea, Sierra Leone, Liberia, and many other countries. Flying foxes probably brought the Zaire Ebola virus into cities. The Crimean–Congo fever virus is transmitted by ticks. In the beginning of infection, sufferers present with pin-sized bleedings in the face, mouth, and the pharynx (Purushotham et al., 2019; Oji et al., 2018; Langerak et al., 2019). West Nile fever virus is part of the Flaviviridae family. There are nearly 70 different viruses in this group, formerly termed group B arboviruses, of which nearly half are known to cause illness in humans. The World Health Organization defines arboviruses (arthropod-borne viruses) as a group as those which are maintained in nature principally, or to an important

extent, through biological transmission between susceptible vertebrate hosts by hematophagous arthropods. They multiply and produce viremia in the vertebrates, multiply in the tissues of arthropods, and are passed on to new vertebrates by the bites of arthropods after a period of extrinsic incubation. Research on emerging infectious diseases needs to be identified as a priority in Africa (Petersen et al., 2019; Chemaitelly et al., 2019).

RECENT ADVANCES DISCOVERY OF EMERGENT AND REEMERGENT VIRUS

Emerging viral infections represent a public health risk pointed out by the spreading of pathogens with potential zoonotic risk. The emergent viruses are not new. A change in human behavior has allowed them to spread; the natural hosts for many viruses are animals, but there are some viruses whose natural host is the human (Vonesch et al., 2019). Many of these viruses are isolated in remote areas of the world. With fast travel and more animals being shipped, the viruses can spread to areas where people do not have immunity against them. Normally, the viruses remain unchanged, but often small genetic changes occur, which increase their virulence. A good example for such genetic change occurs frequently within the influenza virus. These changes permit the viruses that reside in animals to infect men. Changing agricultural practices also allow different types of animals to live in new areas, which can also bring new viruses (Culliton, 1990). In 2007 an outbreak of illness characterized by rash, arthralgia, and conjunctivitis was reported on Yap Island in Micronesia, which resulted in 5000 infections estimated among the total population of 6700. Serum samples from patients in the acute phase of illness contained RNA of Zika virus (ZIKV), a flavivirus from the same family like yellow fever, dengue, West Nile, and Japanese encephalitis viruses. This was the first time that ZIKV was detected outside Africa and Asia. Previously, human illness caused by ZIKV was first recognized in Nigeria in 1953. Despite recognizing that ZIKV infection could produce a mild, febrile illness, only 13 naturally acquired cases were reported during the following 57 years (Petersen et al., 2016; Hayes, 2009; Campos et al., 2015). More recent obvious example of emergent viruses is SARS-CoV-like virus (family Coronaviridae) that was found to cause a new, severe acute respiratory syndrome in humans. This virus, named SARS-CoV, is a distant relative of the group 2 coronaviruses that infect rodents, cattle, dogs, pigs, and humans and has been assigned to group 2b. It is distinct from two other coronaviruses, recently identified in bats in southern China. Epidemiologic studies showed that the earliest cases of SARS were associated with the wildlife meat industry. A survey of wildlife in China

found SARS-CoV-like viruses carried by masked palm civets (*Paguma larvata*), raccoon dogs (*Nyctereutes procyonoides*), and hog badgers (*Arctonyx collaris*). Another example is the Ebola virus; Ebola virus (or Marburg virus) is isolated from a wild vertebrate, and experimental infections unambiguously demonstrate that the virus not only persists but also is shed by that animal, and that disease can be transmitted under controlled conditions. Also, viruses in the family of Bunyaviridae can infect a diverse range of hosts, from mosquitoes to marsupials, and thrips to tomatoes. Several of the Bunyaviridae cause serious diseases in humans, and they are recognized as posing an increasing threat to human health and are good examples of the so-called emerging infections (Elliott, 1997; Calisher et al., 2006).

References

- Arora, R., Chang, Y., Moore, P.S., 2012. MCV and Merkel cell carcinoma: a molecular success story. *Curr. Opin. Virol.* 2 (4), 489–498.
- Bosch, F.X., De Sanjosé, S., 2003. Human papillomavirus and cervical cancer—burden and assessment of causality. *JNCI Monogr.* 31, 3–13.
- Bower, M., Powles, T., Nelson, M., Shah, P., Cox, S., Mandelia, S., et al., 2003. HIV-related lung cancer in the era of highly active antiretroviral therapy. *Aids* 17 (3), 371–375.
- Calisher, C.H., Childs, J.E., Field, H.E., Holmes, K.V., Schountz, T., 2006. Bats: important reservoir hosts of emerging viruses. *Clin. Microbiol. Rev.* 19 (3), 531–545.
- Campos, G.S., Bandeira, A.C., Sardi, S.I., 2015. Zika virus outbreak, Bahia, Brazil. *Emerg. Infect. Dis.* 21 (10), 1885.
- Cann, A.J., 2001. *Principles of Molecular Virology*, standard ed. Academic Press.
- Carter, M.J., 2005. Enterically infecting viruses: pathogenicity, transmission and significance for food and waterborne infection. *J. Appl. Microbiol.* 98 (6), 1354–1380.
- Castro, A.E., Heuschele, W.P., 1992. *Veterinary Diagnostic Virology, A Practitioner's Guide*. Mosby-Year Book, Inc, St. Louis, MO.
- Centers for Disease Control and Prevention (CDC), 2012. Human papillomavirus associated cancers—United States, 2004–2008. *MMWR Morb. Mortal. Wkly. Rep.* 61, 258.
- Chaturvedi, A.K., Madeleine, M.M., Biggar, R.J., Engels, E.A., 2009. Risk of human papillomavirus-associated cancers among persons with AIDS. *J. Natl. Cancer Inst.* 101, 1120–1130.
- Chemaitelly, H., Mahmud, S., Kouyoumjian, S.P., Al-Kanaani, Z., Hermez, J.G., Abu-Raddad, L.J., 2019. Who to test for hepatitis C virus in the Middle East and North Africa?: pooled analyses of 2,500 prevalence measures, including 49 million tests. *Hepatol. Commun.* 3 (3), 325–339. Available from: <https://doi.org/10.1002/hep4.1310>. eCollection 2019 Mar. Review. PubMed PMID: 30859146; PubMed Central PMCID: PMC6396361.
- Culliton, B.J., 1990. Emerging viruses, emerging threat. *Science* 247 (4940), 279–281.
- Elliott, R.M., 1997. Emerging viruses: the Bunyaviridae. *Mol. Med.* 3 (9), 572.
- Fukayama, M., Hayashi, Y., Iwasaki, Y., Chong, J., Ooba, T., Takizawa, T., et al., 1994. Epstein-Barr virus-associated gastric carcinoma and Epstein-Barr virus infection of the stomach. *Lab. Invest.* 71 (1), 73–81.
- Haley, C.T., Mui, U.N., Vangipuram, R., Rady, P.L., Tyring, S.K., Human Oncoviruses, et al., 2018. Recent advances in understanding Crimean-Congo hemorrhagic fever virus. *F1000Res.* 29 (7). Available from: <https://doi.org/10.12688/f1000research.16189.1>.

- pii: F1000 Faculty Rev-1715. eCollection 2018. Review. PubMed PMID: 30416710; PubMed Central PMCID: PMC6206615.
- Hayes, E.B., 2009. Zika virus outside Africa. *Emerg. Infect. Dis.* 15 (9), 1347.
- Koonin, E.V., Senkevich, T.G., Dolja, V.V., 2006. The ancient Virus World and evolution of cells. *Biol. Direct* 1 (1), 29.
- Koopmans, M., von Bonsdorff, C.-H., Vinjé, J., de Medici, D., Monroe, S., 2002. Foodborne viruses. *FEMS Microbiol. Rev.* 26 (2), 187–205. Available from: <https://doi.org/10.1111/j.1574-6976.2002.tb00610.x>.
- Langerak, T., Mumtaz, N., Tolk, V.I., van Gorp, E.C.M., Martina, B.E., Rockx, B., et al., 2019. The possible role of cross-reactive dengue virus antibodies in Zika virus pathogenesis. *PLoS Pathog.* 15 (4), e1007640. Available from: <https://doi.org/10.1371/journal.ppat.1007640>. eCollection 2019 Apr. Review. PubMed PMID: 30998804; PubMed Central PMCID: PMC6472811.
- Lysén, M., Thorhagen, M., Brytting, M., Hjertqvist, M., Andersson, Y., Hedlund, K.O., 2009. Genetic diversity among food-borne and waterborne norovirus strains causing outbreaks in Sweden. *J. Clin. Microbiol.* 47 (8), 2411–2418.
- MacLachlan, N., Dubovi, E.J. (Eds.), 2011. *Fenner's Veterinary Virology*. fourth ed. Academic Press, Elsevier Inc, San Diego, CA.
- Oji, M.O., Haile, M., Baller, A., Tremblay, N., Mahmoud, N., Gasasira, A., et al., 2018. Implementing infection prevention and control capacity building strategies within the context of Ebola outbreak in a “Hard-to-Reach” area of Liberia. *Pan. Afr. Med. J.* 12 (31), 107. Available from: <https://doi.org/10.11604/pamj.2018.31.107.15517>. eCollection 2018. PubMed PMID: 31037168; PubMed Central PMCID: PMC6462381.
- Petersen, L.R., Jamieson, D.J., Powers, A.M., Honein, M.A., 2016. Zika virus. *N. Engl. J. Med.* 374 (16), 1552–1563.
- Petersen, E., Kantele, A., Koopmans, M., Asogun, D., Yinka-Ogunleye, A., Ihekweazu, C., et al., 2019. Human monkeypox: epidemiologic and clinical characteristics, diagnosis, and prevention. *Infect. Dis. Clin. North Am.* Available from: <https://doi.org/10.1016/j.idc.2019.03.001>. pii: S0891-5520(19)30017-0. Review. PubMed PMID: 30981594.
- Purushotham, J., Lambe, T., Gilbert, S.C., 2019. Vaccine platforms for the prevention of Lassa fever. *Immunol. Lett.* Available from: <https://doi.org/10.1016/j.imlet.2019.03.008>. pii: S0165-2478(19)30048-3. Review. PubMed PMID: 31026485.
- Sbalzarini, I.F., Greber, U.F., 2018. How computational models enable mechanistic insights into virus infection. *Methods Mol. Biol.* 1836, 609–631. Available from: https://doi.org/10.1007/978-1-4939-8678-1_30. Review. PubMed PMID: 30151595.
- Vonesch, N., Binazzi, A., Bonafede, M., Melis, P., Ruggieri, A., Iavicoli, S., et al., 2019. Emerging zoonotic viral infections of occupational health importance. *Pathog. Dis.* 77 (2), ftz018. Available from: <https://doi.org/10.1093/femspd/ftz018>.
- White, D.E., Fenner, F.J., 1994. *Medical Virology*, fourth ed. Academic Press, San Diego, CA.
- Xue, Q., Miller-Jensen, K., 2012. Systems biology of virus-host signaling network interactions. *BMB Rep.* 45 (4), 213–220. Review. PubMed PMID: 22531130.
- Yan, Q., 2008. Bioinformatics databases and tools in virology research: an overview. In *Silico Biol.* 8 (2), 71–85.
- Yugo, D., Meng, X.J., 2013. Hepatitis E virus: foodborne, waterborne and zoonotic transmission. *Int. J. Environ. Res. Public Health* 10 (10), 4507–4533.