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LETTER TO THE EDITOR

An overview of the current medical literature on *Zika virus*

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Abstract
Zika virus is a member of the family of *Flaviviridae*, which is primarily spread to humans by mosquito bites. It has been linked to microcephaly in neonates, and as such, it poses a significant risk to human pregnancy. *Zika virus* infection is also implicated in other severe neurological disorders such as Guillain-Barre syndrome. There is currently no vaccine available to treat *Zika virus* disease, and as such, it represents a serious challenge to public health. Antigenic similarities between Zika and dengue can suggest artificially high infection rates of Zika within specific population groups. Here, we review recent literature and provide an update on the status of the Zika outbreak, including a description of available medical countermeasure options and current diagnosis methodology.

Keywords Zika · Dengue · Flavivirus · Mosquitos · Microcephaly · Aedes aegypti

Introduction

Zika virus is able to infect humans and other mammals and was first discovered in the Uganda Zika Forest in 1947 (Dick 1952). *Zika virus* is a member of the family *Flaviviridae* and was first isolated from the blood of sentinel rhesus macaques in 1948 (Macnamara 1954). Zika antibody was first detected in humans in 1964 in Africa (Wikan and Smith 2016). It is challenging to detect *Zika virus*-specific antibodies because of their cross-reactivity to other related *Flavivirus* such as dengue and this is especially so in patients previously vaccinated against other flaviviruses (Cao-Lormeau et al. 2014). The first severe Zika outbreak was reported in Yap Island in 2007, where 73% of the population was infected with the *Zika virus* within 4 months (Zanluca et al. 2015). In 2013, there was a second major outbreak in French Polynesia (Malone et al. 2016). Since then the *Zika virus* has spread throughout the western hemisphere causing a massive epidemic in the continent of South America, with localised outbreaks in Argentina, Brazil, Venezuela, Paraguay, El Salvador, Columbia Southern United States, and Singapore (Culjat et al. 2016; Fontanet et al. 2016; Hoen et al. 2018; Kostyuchenko et al. 2016; Parola and Musso 2020). The list of countries with an elevated risk of Zika infections is shown in Table 1.

Zika virus infection of pregnant mothers has been shown to produce neurological defects in the foetus at a case rate of 7% (Simpson 1964). *Zika virus* infection can additionally cause congenital syndrome (congenital disabilities) in infants, which includes a spectrum of defects (Campos et al. 2015). Recent studies suggested that the *Zika virus* directly causes neuronal tissue damage (Kikuti et al. 2018). However it is not presently understood why not all *Zika virus* infections produce brain abnormalities during embryonic development. Within the *Flavivirus* family, there are structural similarities between the Zika, and dengue viruses and the antibody raised against one of the viruses frequently cross-react with the other virus (Li et al. 2018). This cross-reactivity phenomenon has led to mistaken assessments of the degree of epidemic infection levels (Sirohi et al. 2016a).

It has been suggested that the binding of human dengue antibodies to the *Zika virus* does not neutralise the *Zika virus*, but it instead enhances Zika infection in cell clusters (Reina et al. 2020).

Composition and structure of the *Zika virus*

Zika virus genome is a single-stranded positive RNA with a single open reading frame located within two RNA-structural 5′ and 3′ untranslated regions (Bhargava et al. 2019). As

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Table 1 *Zika virus*: countries specific risk (WHO 2020)

Angola	Bonaire	Cuba	French Guiana	Mexico	Grenadines
Anguilla	Brazil	Curacao	Gabon	Nigeria	Samoa
Antigua	Cambodia	Costa Rica	Grenada	Panama	Senegal
Argentina	Cameroon	Cote D'Ivoire	Guatemala	Papua New Guinea	Saint Martin
Aruba	Cape Verde	Cuba	Guyana	Paraguay	Turks and Caicos Islands
American Samoa	Cayman Islands	Curacao	Haiti	Philippines	Uganda
Angola	African Republic	Dominica	Honduras	Puerto Rico	Thailand
Bahamas	Texas	Dominican Republic	India	Saba	Tonga
Bangladesh	Colombia	Ecuador	Indonesia	Saint Barthelemy	Trinidad and Tobago
Barbados	Cape Verde	El Salvador	Jamaica	Saint Kitts and Nevis	Venezuela
Belize	Costa Rica	Ethiopia	Malaysia	Saint Lucia	Vietnam
Bolivia	Cote D'Ivoire	Fiji	Maldives	Saint Martin	Virgin Islands (British)

described in the literature, the genome codes for three structural proteins and seven non-structural proteins involved in replication, assembly, and mediating the innate host responses to infection (Cox et al. 2015). Recent studies found that *Zika virus* surfaces share similar protein structure to other flaviviruses like DENV (Dengue viruses is a positive single-stranded RNA virus of family *Flaviviridae*) and WNV (West Nile virus is a single-stranded RNA virus of the family *Flaviviridae*) (Simpson 1964). This virus has 180 copies of protein E, which associates with protein M (Cai et al. 2017) to form the viral capsid. Protein E copies are assembled into an icosahedral symmetry which is formed by 90 dimers at a pH of 7.4 and anchored in the lipid bilayer (Zhang et al. 2013). According to Lin et al. (2018), protein E lies in parallel with the viral membrane (Figure 1).

Early filtration studies indicated that the size of *Zika virus* was in the range of 30–45 nm in diameter (Campos et al. 2015). Electron transmission microscopy (ETM) analysis reveals that virions are spherical and approximately 40–43 nm in diameter (Coelho et al. 2017). Zika particles can be inactivated at a pH of 6.2 by using potassium permanganate either at temperature 58 °C for 30 min or 60 °C for 15 min (Conte et al. 2017). The structure of both proteins (E and M) has been determined by the cryo-electron microscopy (cryoEM) (Faye et al. 2014; Rubin et al. 2016; Valente and Moraes 2019). The smaller M proteins reside underneath, the more abundant protein E binding to the cellular transmembrane domain (Cao-Lormeau and Musso 2014; Rathore et al. 2019). From X-ray crystallography, the structure of the NS1 protein was found to be similar to the corresponding protein in dengue but has a different distribution of electrical charge on its surface (Sirohi and Kuhn 2017). *Zika virus* surface composites are both positively and negatively charged central regions and negatively charged towards the distal ends (Ramharack and Soliman 2018; Wikan and Smith 2016).

The *Zika virus* genome is 10.7 kb and, aside from proteins E and M, encodes several non-structural proteins such as NS1, NS2A, NS2B, NS3, NS4A, NS4B, and NS5. *Zika virus* encoding genome and proteins is described in Table 2 (Marquez-Jurado et al. 2018).

Both the structure of *Zika virus* and knowledge of its pathogenesis are essential for the rapid development of vaccines and therapeutics (Sirohi et al. 2016b) (Fig. 2)

Transmission and life cycle of *Zika virus*

At the population level, *Zika virus* transmission involves both sylvatic and urban cycles and is facilitated by a variety of *Aedes* genera mosquito species (Gabaglia 2017). *Zika virus* is transmitted from the bite of infected female *Aedes aegypti* mosquito. After a human receives such a bite, the *Zika virus*

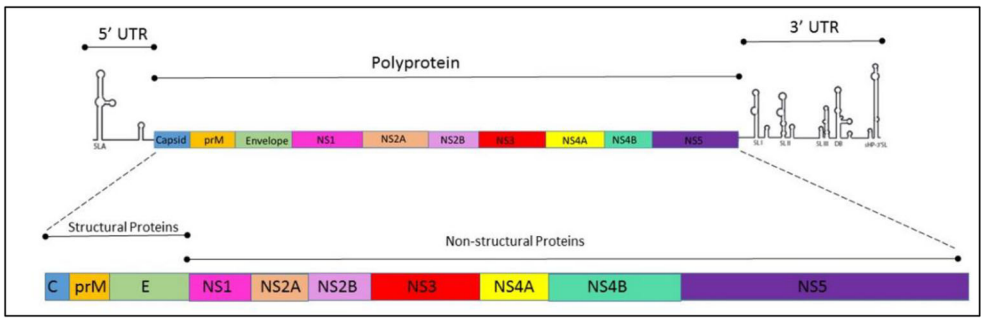

Fig. 1 Schematic representation of the *Zika virus* genome, 11 kb *Zika virus* genome, including the 5′ and 3′ untranslated region (Zhang et al. 2013).

Table 2 Characterisation of structural and non-structural *Zika virus* proteins (Houa et al. 2017)

Name	Size: Aa (kDa)	Cellular distribution	Subcellular location
C	122 (14)	Cyto.& Nuc.	Golgi apparatus,LD,and nucleoli
PrM	168 (19)	Cyto.	Endoplasmic reticulum, centrosome
Env	504 (54)	Cyto.	Endoplasmic reticulum
NS1	352 (40)	Cyto.& Nuc.	Autophagosome
NS2a	226 (24)	Cyto.	Endoplasmic reticulum
NS2b	1.30 (14)	Cyto.	Golgi apparatus
NS3	617 (69)	Cyto.	Co-localize with Tubulin, centrosome
NS4a	127 (14)	Cyto.	Golgi apparatus
NS4b	251 (27)	Cyto.	Early endosome
NS5	903 (103)	Nuc.	Co-localize with SC35

spreads into the lymphatic system concentrating at the nodes (Simpson 1964). At these regions, the virus is amplified after which it then disseminates through the bloodstream to the peripheral tissue and visceral organs (Craig et al. 2016). The first symptoms following infection typically occur after 3 to 12 days (Kostyuchenko et al. 2016). Recent studies suggest that male-to-female sexual transmission constitutes a significant route of *Zika virus* infection, but female-to-male sexual transmission has not been observed (Zhang et al. 2013). It is not yet clear whether mosquitos or other mammals serve as an amplifying reservoir; however, Zika is maintained in nature in a sylvatic cycle transmission between non-human primates (NHP) and the forest-dwelling mosquitos (Peters and Stevenson 2019; Wikan and Smith 2016). Zika transmission through breastfeeding has not been demonstrated, but this may represent another significant infection route because milk has been shown to contain a high viral load (Javed et al. 2018). To prevent further spread of the *Zika virus*, it is critical to

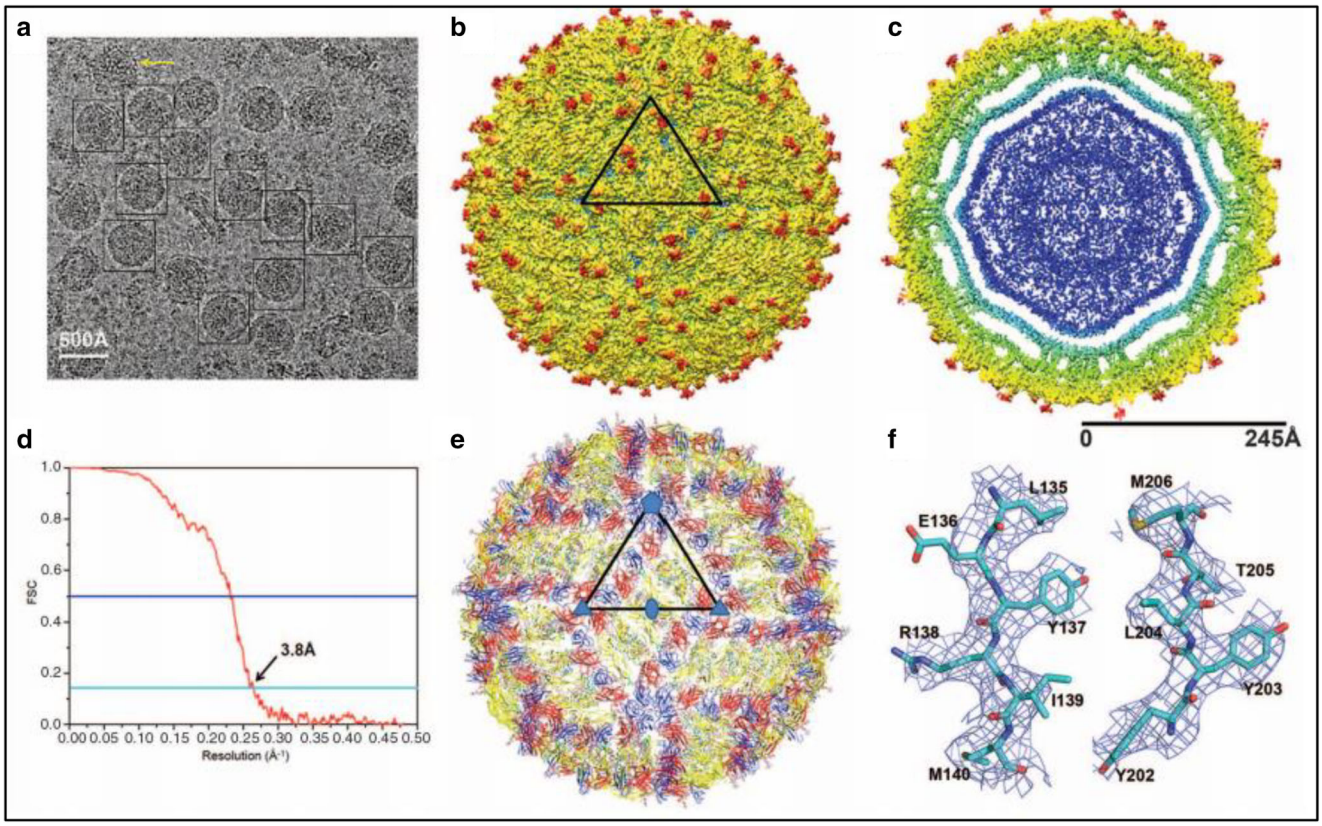

Fig. 2 The cyro-EM structure of *Zika virus* at 3.8 A° (Sirohi et al. 2016b). (A) Represents cryo-EM of frozen-hydrated *Zika virus*. (B) A surface shaded depth cued of *Zika virus*, (C) The radial density distribution colour coding of *Zika virus*. (D) Plot of Fourier shell correlation. (E) The backbone of E and M proteins. (F) Cryo-EM electron density of amino acids of E protein

understand and reveal the amplifying reservoirs of the *Zika virus* (Figure 3).

Zika virus entry into the host cells requires a low-pH step to trigger fusion of the viral envelope with the endosome membrane. It will then release the nucleocapsid into the cytosol through the receptor protein of human cells. The role of the acidic pH for *Zika virus* infection of T98G cell is very well described in (Li et al. 2020). The acidification will result in a viral fusion with the endosomal membrane and releases the viral RNA into the cytoplasm. Entry to the cells is mostly mediated by the viral protein E. Proteolytic maturation results in highly complex and dynamic infection particles; this offers various possibilities to receptor interaction sites (Agrelli et al. 2019). However, the exact mode of entry is not yet understood. The virus spreads to the lymph and blood nodes, and it replicates in the cytoplasm (Li et al. 2020).

The *Zika virus* entry process depends on the protein pattern expressed in viral particle lattice, and it appears to rely on the degree of proteolytic maturation of the particles (Perera-Lecoin et al. 2013). Cell types also play a significant role in this process, and the cellular receptors such as T cell and receptor tyrosine kinases and those receptor families can recognise lipids in the viral membrane and mediate *Zika virus* entry (Hamel et al. 2015); (Perera-Lecoin et al. 2013). The ability of *Zika virus* to infect human cells has been extensively described in cell culture studies (Hamel et al. 2015). In the process of receptor binding and recognition, multiple molecules are used in combination of infectious entries (Kaufmann and Rossmann 2012). The *Zika virus* can produce ensemble structures with different virions circulating in an organism able to exhibit different tissue tropisms. *Zika virus* may use apoptotic mimicry as an entry mechanism, which further enables it to increase the range of *Zika virus* susceptible cells (Agrelli et al. 2019). Thus, the degree of viral particle maturations and the amount of proteins M, E, and NS1 exposed at the capsid surface help to regulate the *Zika virus* entry mechanism (Agrelli et al. 2019).

Symptoms

Some of the most detailed case notes accompanying *Zika virus* infection are due to reports associated with the disease of scientists and medics who have contracted the virus during either laboratory or fieldwork (Simpson 1964). The majority of those who have been infected by the *Zika virus* have minimal symptoms during a mild and short-lived 2–7-day illness (Zorrilla et al. 2016). As mentioned, *Zika virus* infection in a woman during pregnancy causes congenital brain abnormalities in the foetus, which includes microcephaly (Faye et al. 2014). Typically, the majority of patients do not get seriously ill, and therefore, their infection occurs without hospital admission (Campos et al. 2015). Once infected, the affected person is more likely to be protected from future infections (Rubin et al. 2016).

Microcephaly

Perhaps the most alarming aspect of recent outbreaks has been the high prevalence of congenital malformations, including foetal microcephaly, in babies born to infected mothers (Coelho et al. 2017). *Zika virus*-induced neurodevelopmental disorder results in abnormally formed brain and head (Sirohi et al. 2016a). *Zika virus* has been shown to attenuate the growth of human neural progenitor cells (Simpson 1964). It is not yet clear what type of exposure and whether symptomatic display during infection necessarily indicates a higher risk to the developing foetus (Sirohi et al. 2016a). In addition, the other malformations reported in foetus and newborn babies with congenital *Zika virus* infections include brain atrophy, arthrogryposis, and foetal abnormalities (Kikuti et al. 2018).

Diagnosis and test for *Zika virus*

Zika virus can be detected from human blood within the first 10 days of infection with viral loads peaking at the onset of

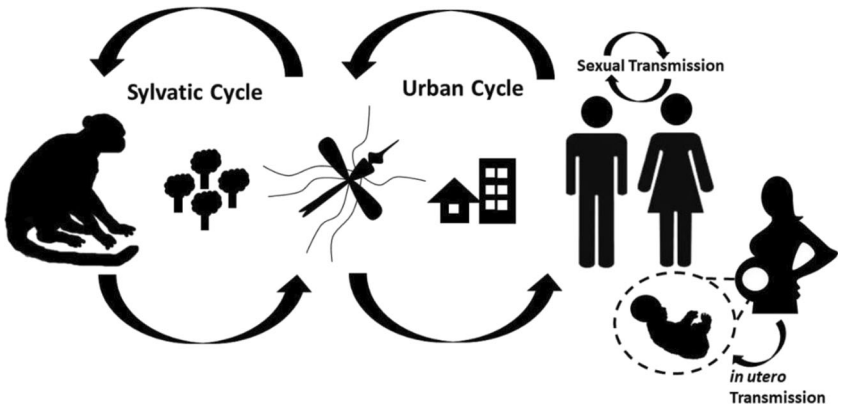

Fig. 3 Routes of *Zika virus* transmission (Basu and Tumban 2016)

symptoms based on the nucleic acid amplification test (Gabaglia 2017). *Zika virus* diagnosis typically requires the presence of fever with arthralgia or with arthritis, and no associated purulent conjunctivitis (Malone et al. 2016). The first stage test involves a conjunction of symptoms with the identification of anti-*Zika virus* IgM antibodies (Sumita et al. 2016). Secondary confirmation requires a PCR-based laboratory test to detect the presence of *Zika virus* RNA (Sumita et al. 2016). As mentioned, it is difficult to distinguish between Zika-infected patients and patients previously infected with, or vaccinated against, other related *Flavivirus* (Zhang et al. 2013).

Conclusion

Currently, there is no anti-*Zika virus* vaccine available, and important challenges remain for developing this clinical vaccine (Zhang et al. 2013). However, typically the *Zika virus* infection is mild, and the standard treatment for the majority of non-seriously ill patients involves the provision of supporting nurse care for symptom relief (Simpson 1964). With this study, I note the following points. *Zika virus* outbreak has been declared as a public health threat in many countries (Fontanet et al. 2016; Zanluca et al. 2015). Countries with a significant risk level of *Zika virus* infection are presented in Table 1 (as judged by the WHO (2020)**)**. As the virus is currently endemic to several areas (Barnard et al. 2018), the risk of its further international spread is likely. Locations with suitable mosquito vectors facilitate virus transmission.

Zika virus vectors, epidemiology, and pathology remain uncertain. Diagnosis remains subjective, and laboratory diagnostics are not widely available. The commercial test of the *Zika virus* is limited to these, including molecular assays and lateral flow tests (Sumita et al. 2016). In some cases, similar tests/assays for chikungunya and dengue viruses are used, thereby reducing specificity and increasing the number of false-positive detections (Mardekian and Roberts 2015). According to the World Health Organization (WHO), the prevention measures of vector control are a current priority (Campos et al. 2015). As discussed, current diagnosis methods are not optimal. There is a need for cheap, fast, and reliable testing methods for *Zika virus* diagnosis. It is hoped that this review can act as a quick primer of recent research (and recent outbreaks) related to the *Zika virus*.

References

Agrelli A, de Moura RR, Crovella S, Brandao LAC (2019) Zika virus entry mechanisms in human cells. Infect Genet Evol 69:22–29

Barnard TR, Rajah MM, Sagan SM (2018) Contemporary Zika virus isolates induce more dsRNA and produce more negative-strand intermediate in human astrocytoma cells. Viruses 10

Basu R, Tumban E (2016) Zika virus on a spreading spree: what we now know that was unknown in the 1950's. Virol J 13:165

Bhargava S, Patel T, Gaikwad R, Patil UK, Gayen S (2019) Identification of structural requirements and prediction of inhibitory activity of natural flavonoids against Zika virus through molecular docking and Monte Carlo based QSAR simulation. Nat Prod Res 33:851–857

Cai L, Sun Y, Song Y, Xu L, Bei Z, Zhang D, Dou Y, Wang H (2017) Viral polymerase inhibitors T-705 and T-1105 are potential inhibitors of Zika virus replication. Arch Virol 162:2847–2853

Campos GS, Bandeira AC, Sardi SI (2015) Zika virus outbreak, Bahia, Brazil. Emerg Infect Dis 21:1885–1886

Cao-Lormeau VM, Musso D (2014) Emerging arboviruses in the Pacific. Lancet 384:1571–1572

Cao-Lormeau VM, Roche C, Teissier A, Robin E, Berry AL, Mallet HP, Sall AA, Musso D (2014) Zika virus, French Polynesia, South Pacific, 2013. Emerg Infect Dis 20:1085–1086

Coelho SVA, Neris RLS, Papa MP, Schnellrath LC, Meuren LM, Tschoeke DA, Leomil L, Vercoza BRF, Miranda M, Thompson FL, da Poian AT, Souza TML, Carneiro FA, Damaso CR, Assuncao-Miranda I, de Arruda LB (2017) Development of standard methods for Zika virus propagation, titration, and purification. J Virol Methods 246:65–74

Conte FP, Martins RS, Cajaraville A, Nascimento HJ, Jurgilas PB, de Lima SMB, Missailidis S, Arissawa M (2017) Production of monoclonal antibody that recognizes Zika virus and other flaviviruses in serum-free conditions. Monoclon Antib Immunodiagn Immunother 36:264–271

Cox BD, Stanton RA, Schinazi RF (2015) Predicting Zika virus structural biology: challenges and opportunities for intervention. Antivir Chem Chemother 24:118–126

Craig AT, Paterson BJ, Durrheim DN (2016) Commentary: Zika virus: the latest newcomer. Front Microbiol 7:1028

Culjat M, Darling SE, Nerurkar VR, Ching N, Kumar M, Min SK, Wong R, Grant L, Melish ME (2016) Clinical and imaging findings in an infant with Zika embryopathy. Clin Infect Dis 63:805–811

Dick GW (1952) Zika virus. II. Pathogenicity and physical properties. Trans R Soc Trop Med Hyg 46:521–534

Faye O, Freire CC, Iamarino A, Faye O, de Oliveira JV, Diallo M, Zanotto PM, Sall AA (2014) Molecular evolution of Zika virus during its emergence in the 20(th) century. PLoS Negl Trop Dis 8:e2636

Fontanet A, Cao-Lormeau VM, Dub T, Mallet HP, Ghawche F (2016) Association between Guillain-Barre syndrome and Zika virus infection – Authors' reply. Lancet 387:2600

Gabaglia CR (2017) Zika virus and diagnostics. Curr Opin Pediatr 29:107–113

Hamel R, Dejarnac O, Wichit S, Ekchariyawat P, Neyret A, Luplertlop N, Perera-Lecoin M, Surasombatpattana P, Talignani L, Thomas F, Cao-Lormeau VM, Choumet V, Briant L, Despres P, Amara A, Yssel H, Misse D (2015) Biology of Zika virus infection in human skin cells. J Virol 89:8880–8896

Hoen B, Schaub B, Funk AL, Ardillon V, Boullard M, Cabie A, Callier C, Carles G, Cassadou S, Cesaire R, Douine M, Herrmann-Storck C, Kadhel P, Laouenan C, Madec Y, Monthieux A, Nacher M, Najioullah F, Rousset D, Ryan C, Schepers K, Stegmann-Planchard S, Tressieres B, Volumenie JL, Yassinguezo S, Janky E, Fontanet A (2018) Pregnancy outcomes after ZIKV infection in French territories in the Americas. N Engl J Med 378:985–994

Houa W, Cruz-Cosme R, Armstrong N, Obwolo LA, Wen F, Hu W, Luo M-H, Tang Q (2017) Molecular cloning and characterization of the genes encoding the proteins of Zika virus. Gene 628:116–128

Javed F, Manzoor KN, Ali M, Haq IU, Khan AA, Zaib A, Manzoor S (2018) Zika virus: what we need to know? J Basic Microbiol 58:3–16

Kaufmann B, Rossmann MG (2012) Molecular mechanisms involved in the early steps of Flavivirus cell entry. Microbs Infect 13:1–9

Kikuti M, Cardoso CW, Prates APB, Paploski IAD, Kitron U, Reis MG, Mochida GH, Ribeiro GS (2018) Congenital brain abnormalities during a Zika virus epidemic in Salvador, Brazil, April 2015 to July 2016. Euro Surveill:23

Kostyuchenko VA, Lim EX, Zhang S, Fibriansah G, Ng TS, Ooi JS, Shi J, Lok SM (2016) Structure of the thermally stable Zika virus. Nature 533:425–428

Li M, Santpere G, Imamura Kawasawa Y, Evgrafov OV, Gulden FO, Pochareddy S, Sunkin SM, Li Z, Shin Y, Zhu Y, Sousa AMM, Werling DM, Kitchen RR, Kang HJ, Pletikos M, Choi J, Muchnik S, Xu X, Wang D, Lorente-Galdos B, Liu S, Giusti-Rodriguez P, Won H, de Leeuw CA, Pardinas AF, Brainspan C, Psych EC, Psych EDS, Hu M, Jin F, Li Y, Owen MJ, O'Donovan MC, Walters JTR, Posthuma D, Reimers MA, Levitt P, Weinberger DR, Hyde TM, Kleinman JE, Geschwind DH, Hawrylycz MJ, State MW, Sanders SJ, Sullivan PF, Gerstein MB, Lein ES, Knowles JA, Sestan N (2018) Integrative functional genomic analysis of human brain development and neuropsychiatric risks. Science 362

Li M, Zhang D, Li C, Zheng Z, Fu M, Ni F, Liu Y, Du T, Wang H, Griffin GE, Zhang M, Hu Q (2020) Characterization of Zika virus endocytic pathways in human glioblastoma cells. Front Microbiol 11:242

Lin HH, Yip BS, Huang LM, Wu SC (2018) Zika virus structural biology and progress in vaccine development. Biotechnol Adv 36:47–53

Macnamara FN (1954) Zika virus: a report on three cases of human infection during an epidemic of jaundice in Nigeria. Trans R Soc Trop Med Hyg 48:139–145

Malone RW, Homan J, Callahan MV, Glasspool-Malone J, Damodaran L, Schneider ADB, Zimler R, Talton J, Cobb RR, Ruzic I, Smith-Gagen J, Janies D, Wilson J, Zika Response Working Group (2016) Zika virus: medical countermeasure development challenges. PLoS Negl Trop Dis 10:e0004530

Mardekian SK, Roberts AL (2015) Diagnostic options and challenges for dengue and chikungunya viruses. Biomed Res Int 2015:834371

Marquez-Jurado S, Nogales A, Avila-Perez G, Iborra FJ, Martinez-Sobrido L, Almazan F (2018) An alanine-to-valine substitution in the residue 175 of Zika virus NS2A protein affects viral RNA synthesis and attenuates the virus in vivo. Viruses 10

Parola P, Musso D (2020) Zika, dengue, chikungunya and yellow fever infections in Europe? - Winter is over, warm days are coming - so hedge your bets. Travel Med Infect Dis:101614

Perera-Lecoin M, Meertens L, Carnec X, Amara A (2013) Flavivirus entry receptors: an update. Viruses 6:69–88

Peters R, Stevenson M (2019) Zika virus diagnosis: challenges and solutions. Clin Microbiol Infect 25:142–146

Ramharack P, Soliman MES (2018) Zika virus NS5 protein potential inhibitors: an enhanced in silico approach in drug discovery. J Biomol Struct Dyn 36:1118–1133

Rathore APS, Saron WAA, Lim T, Jahan N, St John AL (2019) Maternal immunity and antibodies to dengue virus promote infection and Zika virus-induced microcephaly in fetuses. Sci Adv 5:eaav3208

Reina J, Lopez de Bilbao C, Riera M (2020) Prevalence of influenza B Yamagata lineage in adults in the 2017-2018 flu season. Med Clin (Barc) 154:29–30

Rubin EJ, Greene MF, Baden LR (2016) Zika Virus and Microcephaly. N Engl J Med 374:984–985

Simpson DI (1964) Zika Virus Infection in Man. Trans R Soc Trop Med Hyg 58:335–338

Sirohi D, Kuhn RJ (2017) Zika virus structure, maturation, and receptors. J Infect Dis 216:S935–S944

Sirohi D, Chen Z, Sun L, Klose T, Pierson TC, Rossmann MG, Kuhn RJ (2016a) The 3.8 A resolution cryo-EM structure of Zika virus. Science 352:467–470

Sirohi D, Chen Z, Sun L, Klose T, Pierson TC, Rossmann MG & Kuhn RJ (2016b) The 3.8 Å resolution cryo-EM structure of Zika virus EVOLUTIONARY GENETICS, 352, 467

Sumita LM, Rodrigues JP, Ferreira NE, Felix AC, Souza NC, Machado CM, Junior HF (2016) Detection of human anti-Zika virus IgG by ELISA using an antigen from in vitro infected vero cells: preliminary results. Rev Inst Med Trop Sao Paulo 58:89

Valente AP, Moraes AH (2019) Zika virus proteins at an atomic scale: how does structural biology help us to understand and develop vaccines and drugs against Zika virus infection? J Venom Anim Toxins Incl Trop Dis 25:e20190013

WHO (2020) *Zika Virus* [Online]. Available: https://www.who.int/news-room/fact-sheets/detail/zika-virus. Accessed 29 Feb 2020

Wikan N, Smith DR (2016) Zika virus: history of a newly emerging arbovirus. Lancet Infect Dis 16:e119–e126

Zanluca C, Melo VC, Mosimann AL, Santos GI, Santos CN, Luz K (2015) First report of autochthonous transmission of Zika virus in Brazil. Mem Inst Oswaldo Cruz 110:569–572

Zhang X, Sheng J, PLEVKA P, Kuhn RJ, Diamond MS, Rossmann MG (2013) Dengue structure differs at the temperatures of its human and mosquito hosts. Proc Natl Acad Sci U S A 110:6795–6799

Zorrilla CD, Mosquera AM, Rabionet S, Rivera-Vinas J (2016) HIV and Zika in pregnancy: parallel stories and new challenges. Obstet Gynecol Int J 5