

Frontiers in Microbiology, 2018, vol.9, NSEP

---

## History of ZIKV infections in India and management of disease outbreaks

Khaiboullina S., Uppal T., Martynova E., Rizvanov A., Baranwal M., Verma S.  
*Kazan Federal University, 420008, Kremlevskaya 18, Kazan, Russia*

---

### Abstract

© 2007-2018 Frontiers Media S.A. All Rights Reserved. Zika virus (ZIKV) is an emerging arbovirus infection endemic in multiple countries spread from Asia, Africa to the Americas and Europe. Previously known to cause rare and fairly benign human infections, ZIKV has become a major international public health emergency after being linked to unexpected neurological complications, that includes fetal brain damage/death and microcephaly in babies born to infected mothers and Guillain-Barre syndrome (GBS) in adults. It appears that a single genetic mutation in the ZIKV genome, likely acquired during explosive ZIKV outbreak in French Polynesia (2013), made virus causing mild disease to target fetus brain. The Aedes mosquitoes are found to be the main carrier of ZIKV, passing the virus to humans. Originally isolated from patients in Africa in 1954 (African lineage), virus disseminated to Southeast Asia (Asian lineage), establishing new endemic foci, including one in India. Numerous cases of ZIKV infection have been reported in several locations in India and neighboring countries like Pakistan and Bangladesh since mid of the last century, suggesting that the virus reached this part of Asia soon after it was first discovered in Uganda in 1947. Although, the exact means by which ZIKV was introduced to India remains unknown, it appears that the ZIKV strain circulating in India possibly belongs to the "Asian lineage, " which has not yet been associated with microcephaly and other neurological disorders. However, there still exists a threat that the contemporary ZIKV virulent strain from South America, carrying a mutation can return to Asia, posing a potential crisis to newborns and adult patients. Currently there is no specific vaccine or antiviral medication to combat ZIKV infection, thus, vector control and continuous monitoring of potential ZIKV exposure is essential to prevent the devastating consequences similar to the ones experienced in Brazil. However, the major obstacle faced by Indian healthcare agencies is that most cases of ZIKV infection have been reported in rural areas that lack access to rapid diagnosis of infection. In this review, we attempt to present a comprehensive analysis of what is currently known about the ZIKV infection in India and the neighboring countries.

<http://dx.doi.org/10.3389/fmicb.2018.02126>

---

### Keywords

ADEs, Aedes aegypti, Emerging infections, Epidemiology, India, Zika virus (ZIKV)

### References

- [1] Amraoui, F., Atyame-Nten, C., Vega-Rua, A., Lourenco-de-Oliveira, R., Vazeille, M., and Failloux, A. B. (2016). Culex mosquitoes are experimentally unable to transmit Zika virus. *Eur. Surveill.* 21: 30333. Doi: 10.2807/1560-7917.ES.2016.21.35

- [2] Balmaseda, A., Stettler, K., Medialdea-Carrera, R., Collado, D., Jin, X., Zambrana, J. V., et al. (2017). Antibody-based assay discriminates Zika virus infection from other flaviviruses. *Proc. Natl. Acad. Sci. U.S.A.* 114, 8384-8389. Doi: 10.1073/pnas.1704984114
- [3] Baronti, C., Piorowski, G., Charrel, R. N., Boubis, L., Leparç-Goffart, I., and de Lamballerie, X. (2014). Complete coding sequence of zika virus from a French polynesia outbreak in 2013. *Genome Announc.* 2: e00500-14. Doi: 10.1128/genomeA.00500-14
- [4] Bhattacharya, S. (2005). "Mosquito-borne diseases and vector diversity in Kolkata 604 with special reference to malaria, " in *Perspectives in Environmental Health-605 Vector and Water-Borne Diseases*, eds A. Mukhopadhyay and A. K. De (Delhi: Books for All), 53-70.
- [5] Bhattacharya, S., and Basu, P. (2016). The southern house mosquito, *Culex quinquefasciatus*: profile of a smart vector. *J. Entomol. Zool. Stud.* 4, 73-81.
- [6] Bogoch, I. I., Brady, O. J., Kraemer, M. U. G., German, M., Creatore, M. I., Brent, S., et al. (2016). Potential for Zika virus introduction and transmission in resource-limited countries in Africa and the Asia-Pacific region: a modelling study. *Lancet Infect. Dis.* 16, 1237-1245. Doi: 10.1016/S1473-3099(16)30270-5
- [7] Boyer, S., Calvez, E., Chouin-Carneiro, T., Diallo, D., and Failloux, A. B. (2018). An overview of mosquito vectors of Zika virus. *Microbes Infect.* [Epub ahead of print]. Doi: 10.1016/j.micinf.2018.01.006
- [8] Burt, A. (2003). Site-specific selfish genes as tools for the control and genetic engineering of natural populations. *Proc. Biol. Sci.* 270, 921-928. Doi: 10.1098/rspb.2002.2319
- [9] Cao-Lormeau, V. M., Blake, A., Mons, S., Lastere, S., Roche, C., Vanhomwegen, J., et al. (2016). Guillain-Barre syndrome outbreak associated with Zika virus infection in French Polynesia: a case-control study. *Lancet* 387, 1531-1539. Doi: 10.1016/S0140-6736(16)00562-6
- [10] Cao-Lormeau, V. M., Roche, C., Teissier, A., Robin, E., Berry, A. L., Mallet, H. P., et al. (2014). Zika virus, French polynesia, South Pacific, 2013. *Emerg. Infect. Dis.* 20, 1085-1086. Doi: 10.3201/eid2006.140138
- [11] Carrio, A., Sampedro, C., Sanchez-Lopez, J. L., Pimienta, M., and Campoy, P. (2015). Automated low-cost smartphone-based lateral flow saliva test reader for drugs-of-abuse detection. *Sensors (Basel.)* 15, 29569-29593. Doi: 10.3390/s151129569
- [12] Cauchemez, S., Besnard, M., Bompard, P., Dub, T., Guillemette-Artur, P., Eyrolle-Guignot, D., et al. (2016). Association between Zika virus and microcephaly in French Polynesia, 2013-15: a retrospective study. *Lancet* 387, 2125-2132. Doi: 10.1016/S0140-6736(16)00651-6
- [13] Cerbino-Neto, J., Mesquita, E. C., Souza, T. M., Parreira, V., Wittlin, B. B., Durovni, B., et al. (2016). Clinical manifestations of Zika virus infection, Rio de Janeiro, Brazil, 2015. *Emerg. Infect. Dis.* 22, 1318-1320. Doi: 10.3201/eid2207.160375
- [14] Chakraborty, S., Bhattacharya, S., and Hati, A. K. (1986). Bait preference pattern of *Culex vishnui* mosquito in rural West Bengal. *Bull. Cal. Sch. Trop. Med.* 34, 15-17.
- [15] Choi, J. R., Yong, K. W., Tang, R., Gong, Y., Wen, T., Yang, H., et al. (2017). Lateral flow assay based on paper-hydrogel hybrid material for sensitive point-of-care detection of Dengue Virus. *Adv. Healthcare Mater.* 6, 2192-2659. Doi: 10.1002/adhm.201600920
- [16] Coelho, A. V. C., and Crovella, S. (2017). Microcephaly prevalence in infants born to Zika virus-infected women: a systematic review and meta-analysis. *Int. J. Mol. Sci.* 18: E1714. Doi: 10.3390/ijms18081714
- [17] Darwish, M. A., Hoogstraal, H., Roberts, T. J., Ahmed, I. P., and Omar, F. (1983). A sero-epidemiological survey for certain arboviruses (Togaviridae) in Pakistan. *Trans. R. Soc. Trop. Med. Hyg.* 77, 442-445. Doi: 10.1016/0035-9203(83)90106-2
- [18] de Oliveira, W. K., de Franca, G. V. A., Carmo, E. H., Duncan, B. B., de Souza Kuchenbecker, R., and Schmidt, M. I. (2017). Infection-related microcephaly after the 2015 and 2016 Zika virus outbreaks in Brazil: a surveillance-based analysis. *Lancet* 390, 861-870. Doi: 10.1016/S0140-6736(17)31368-5
- [19] Dejnirattisai, W., Supasa, P., Wongwiwat, W., Rouvinski, A., Barba-Spaeth, G., Duangchinda, T., et al. (2016). Dengue virus sero-cross-reactivity drives antibody-dependent enhancement of infection with Zika virus. *Nat. Immunol.* 17, 1102-1108. Doi: 10.1038/ni.3515
- [20] Dick, G. W., Kitchen, S. F., and Haddow, A. J. (1952). Zika virus, I. Isolations and serological specificity. *Trans. R. Soc. Trop. Med. Hyg.* 46, 509-520. Doi: 10.1016/0035-9203(52)90042-4
- [21] Duffy, M. R., Chen, T. H., Hancock, W. T., Powers, A. M., Kool, J. L., Lanciotti, R. S., et al. (2009). Zika virus outbreak on Yap Island, Federated States of Micronesia. *N. Engl. J. Med.* 360, 2536-2543. Doi: 10.1056/NEJMoa0805715
- [22] Dupont-Rouzeyrol, M., O'Connor, O., Calvez, E., Daures, M., John, M., Grangeon, J. P., et al. (2015). Co-infection with Zika and dengue viruses in 2 patients, new Caledonia, 2014. *Emerg. Infect. Dis.* 21, 381-382. Doi: 10.3201/eid2102.141553
- [23] ECDC (2016). Mosquito Maps: New Information About Areas with *Aedes albopictus* and *Aedes aegypti* in Europe. Available at: <https://ecdc.europa.eu/en/news-events/mosquito-maps-new-information-about-areas-aedes-albopictus-and-aedes-aegypti-europe>
- [24] European Centre for Disease Prevention and Control (2016). Epidemiological Update: Outbreaks of Zika virus and Complications Potentially Linked to the Zika virus Infection, 6 November 2016. Solna: European Centre for Disease Prevention and Control.
- [25] Ferreira-de-Brito, A., Ribeiro, I. P., Miranda, R. M., Fernandes, R. S., Campos, S. S., Silva, K. A., et al. (2016). First detection of natural infection of *Aedes aegypti* with Zika virus in Brazil and throughout South America. *Mem. Inst. Oswaldo Cruz* 111, 655-658. Doi: 10.1590/0074-02760160332
- [26] Gantz, V. M., Jasinskiene, N., Tatarenkova, O., Fazekas, A., Macias, V. M., Bier, E., et al. (2015). Highly efficient Cas9-mediated gene drive for population modification of the malaria vector mosquito *Anopheles stephensi*. *Proc. Natl. Acad. Sci. U.S.A.* 112, E6736-E6743. Doi: 10.1073/pnas.1521077112
- [27] Gatherer, D., and Kohl, A. (2016). Zika virus: a previously slow pandemic spreads rapidly through the Americas. *J. Gen. Virol.* 97, 269-273. Doi: 10.1099/jgv.0.000381
- [28] Gong, Z., Gao, Y., and Han, G. Z. (2016). Zika virus: two or three lineages? *Trends Microbiol.* 24, 521-522. Doi: 10.1016/j.tim.2016.05.002
- [29] Gubler, D. J. (1989). *Aedes aegypti* and *Aedes aegypti*-borne disease control in the 1990s: top down or bottom up, Charles Franklin Craig LECTURE. *Am. J. Trop. Med. Hyg.* 40, 571-578. Doi: 10.4269/ajtmh.1989.40.571
- [30] Guedes, D. R., Paiva, M. H., Donato, M. M., Barbosa, P. P., Krokovsky, L., Rocha, S., et al. (2017). Zika virus replication in the mosquito *Culex quinquefasciatus* in Brazil. *Emerg. Microbes Infect.* 6: e69. Doi: 10.1038/emi.2017.59

- [31] Guerbois, M., Fernandez-Salas, I., Azar, S. R., Danis-Lozano, R., Alpuche-Aranda, C. M., Leal, G., et al. (2016). Outbreak of Zika virus infection, Chiapas State, Mexico, 2015, and first confirmed transmission by *Aedes aegypti* mosquitoes in the Americas. *J. Infect. Dis.* 214, 1349-1356. Doi: 10.1093/infdis/jiw302
- [32] Guo, X. X., Li, C. X., Deng, Y. Q., Xing, D., Liu, Q. M., Wu, Q., et al. (2016). *Culex pipiens quinquefasciatus*: a potential vector to transmit Zika virus. *Emerg. Microbes Infect.* 5: e102. Doi: 10.1038/emi.2016.102
- [33] Halstead, S. B. (2003). Neutralization and antibody-dependent enhancement of dengue viruses. *Adv. Virus Res.* 60, 421-467. Doi: 10.1016/S0065-3527(03)60011-4
- [34] Hammond, A. M., and Galizi, R. (2017). Gene drives to fight malaria: current state and future directions. *Pathog. Glob Health* 111, 412-423. Doi: 10.1080/20477724.2018.1438880
- [35] James P., and Collins, E. H. (ed.) (2016). *Committee on Gene Drive Research in Non-Human Organisms: Recommendations For Responsible Conduct*. Washington, DC: National Academies Press.
- [36] Kalra, N. L., Kaul, S. M., and Rastogi, R. M. (1997). *Prevalence of Aedes aegypti and Aedes albopictus Vectors of Dengue Haemorrhagic Fever in North, North-East and Central India*. New Delhi: WHO Regional Office for South-East Asia.
- [37] Kouri, G., Guzman, M. G., Valdes, L., Carbonel, I., del Rosario, D., Vazquez, S., et al. (1998). Reemergence of dengue in Cuba: a 1997 epidemic in Santiago de Cuba. *Emerg. Infect. Dis.* 4, 89-92. Doi: 10.3201/eid0401.980111
- [38] Kumari, R., Kumar, K., and Chauhan, L. S. (2011). First dengue virus detection in *Aedes albopictus* from Delhi, India: its breeding ecology and role in dengue transmission. *Trop. Med. Int. Health* 16, 949-954. Doi: 10.1111/j.1365-3156.2011.02789.x
- [39] Kuno, G., and Chang, G. J. (2007). Full-length sequencing and genomic characterization of Bagaza, Kedougou, and Zika viruses. *Arch. Virol.* 152, 687-696. Doi: 10.1007/s00705-006-0903-z
- [40] Lee, D., Shin, Y., Chung, S., Hwang, K. S., Yoon, D. S., and Lee, J. H. (2016). Simple and highly sensitive molecular diagnosis of Zika virus by lateral flow assays. *Anal. Chem.* 88, 12272-12278. Doi: 10.1021/acs.analchem.6b03460
- [41] Macias, V. M., Ohm, J. R., and Rasgon, J. L. (2017). Gene drive for mosquito control: where did it come from and where are we headed? *Int. J. Environ. Res. Public Health* 14: E1006. Doi: 10.3390/ijerph14091006
- [42] Magambo, K. A., Kalluvya, S. E., Kapoor, S. W., Seni, J., Chofle, A. A., Fitzgerald, D. W., et al. (2014). Utility of urine and serum lateral flow assays to determine the prevalence and predictors of cryptococcal antigenemia in HIV-positive outpatients beginning antiretroviral therapy in Mwanza, Tanzania. *J. Int. AIDS Soc.* 17: 19040. Doi: 10.7448/IAS.17.1.19040
- [43] Manni, M., Guglielmino, C. R., Scolari, F., Vega-Rua, A., Failloux, A. B., Somboon, P., et al. (2017). Genetic evidence for a worldwide chaotic dispersion pattern of the arbovirus vector, *Aedes albopictus*. *PLoS Negl. Trop. Dis.* 11: e0005332. Doi: 10.1371/journal.pntd.0005332
- [44] Marchette, N. J., Garcia, R., and Rudnick, A. (1969). Isolation of Zika virus from *Aedes aegypti* mosquitoes in Malaysia. *Am. J. Trop. Med. Hyg.* 18, 411-415. Doi: 10.4269/ajtmh.1969.18.411
- [45] Martin-Acebes, M. A., Saiz, J. C., Jimenez, and de Oya, N. (2018). Antibody-dependent enhancement and Zika: real threat or phantom menace? *Front. Cell Infect Microbiol.* 8: 44. Doi: 10.3389/fcimb.2018.00044
- [46] Martines, R. B., Bhatnagar, J., Keating, M. K., Silva-Flannery, L., Muehlenbachs, A., Gary, J., et al. (2016). Notes from the Field: evidence of Zika Virus infection in brain and placental tissues from two congenitally infected newborns and two fetal losses-brazil, 2015. *MMWR Morb. Mortal. Wkly. Rep.* 65, 159-160. Doi: 10.15585/mmwr.mm6506e1
- [47] Moghadam, S. R. J., Bayrami, S., Moghadam, S. J., Golrokhi, R., Pahlaviani, F. G., and Alinaghi, S. A. S. (2016). Zika virus: a review of literature. *Asian Pac. J. Trop. Biomed.* 6, 989-994. Doi: 10.1016/j.apjtb.2016.09.007
- [48] Mohamed, M., Gonzalez, D., Fritchie, K. J., Swansbury, J., Wren, D., Benson, C., et al. (2017). Desmoplastic small round cell tumor: evaluation of reverse transcription-polymerase chain reaction and fluorescence in situ hybridization as ancillary molecular diagnostic techniques. *Virchows Arch.* 471, 631-640. Doi: 10.1007/s00428-017-2207-y
- [49] Moreno, M. L., Cebolla, A., Munoz-Suano, A., Carrillo-Carrion, C., Comino, I., Pizarro, A., et al. (2017). Detection of gluten immunogenic peptides in the urine of patients with coeliac disease reveals transgressions in the gluten-free diet and incomplete mucosal healing. *Gut* 66, 250-257. Doi: 10.1136/gutjnl-2015-310148
- [50] Mukhopadhyay, A. K., and Hati, A. K. (1978). Man-biting activity of *Anopheles stephensi* in Calcutta. *Bull. Cal. Sch. Trop. Med.* 26, 5-7.
- [51] Muraduzzaman, A. K. M., Sultana, S., Shirin, T., Khatun, S., Islam, M., and Rahman, M. (2017). Introduction of Zika virus in Bangladesh: an impending public health threat. *Asian Pac. J. Trop Med.* 10, 925-928. Doi: 10.1016/j.apjtm.2017.08.015
- [52] Olson, J. G., Ksiazek, T. G., Suhandiman, and Triwibowo. (1981). Zika virus, a cause of fever in Central Java, Indonesia. *Trans. R. Soc. Trop. Med. Hyg.* 75, 389-393. Doi: 10.1016/0035-9203(81)90100-0
- [53] Padmanabha, H., Durham, D., Correa, F., Diuk-Wasser, M., and Galvani, A. (2012). The interactive roles of *Aedes aegypti* super-production and human density in dengue transmission. *PLoS Negl. Trop. Dis.* 6: e1799. Doi: 10.1371/journal.pntd.0001799
- [54] Pettersson, J. H., Eldholm, V., Seligman, S. J., Lundkvist, A., Falconar, A. K., Gaunt, M. W., et al. (2016). How did Zika virus emerge in the Pacific islands and Latin America? *MBio* 7: e00386-18. Doi: 10.1128/mBio.01239-16
- [55] Pierson, T. C., and Kielian, M. (2013). Flaviviruses: braking the entering. *Curr. Opin. Virol.* 3, 3-12. Doi: 10.1016/j.coviro.2012.12.001
- [56] Plourde, A. R., and Bloch, E. M. (2016). A literature review of Zika virus. *Emerg. Infect. Dis.* 22, 1185-1192. Doi: 10.3201/eid2207.151990
- [57] Pocquet, N., Milesi, P., Makoundou, P., Unal, S., Zumbo, B., Atyame, C., et al. (2013). Multiple insecticide resistances in the disease vector *Culex p. quinquefasciatus* from Western Indian Ocean. *PLoS One* 8: e77855. Doi: 10.1371/journal.pone.0077855
- [58] Polonio, C. M., de Freitas, C. L., Zanluqui, N. G., and Peron, J. P. S. (2017). Zika virus congenital syndrome: experimental models and clinical aspects. *J. Venom Anim. Toxins Incl. Trop. Dis.* 23: 41. Doi: 10.1186/s40409-017-0131-x131
- [59] Priyamvada, L., Quicke, K. M., Hudson, W. H., Onlamoon, N., Sewatanon, J., Edupuganti, S., et al. (2016). Human antibody responses after dengue virus infection are highly cross-reactive to Zika virus. *Proc. Natl. Acad. Sci. U.S.A.* 113, 7852-7857. Doi: 10.1073/pnas.1607931113
- [60] Public Health England (2017). *Clinical Advice on Zika: Assessing Pregnant Women Following Travel; Symptoms, Transmission (Includes Sexual Transmission)*, Epidemiology. London: Public Health England.

- [61] Quick, J., Grubaugh, N. D., Pullan, S. T., Claro, I. M., Smith, A. D., Gangavarapu, K., et al. (2017). Multiplex PCR method for MinION and Illumina sequencing of Zika and other virus genomes directly from clinical samples. *Nat. Protoc.* 12, 1261-1276. Doi: 10.1038/nprot.2017.066
- [62] Reiter, P., and Gubler, D. J. (1997). *Surveillance and Control of Urban Dengue Vectors*. London: CAB International.
- [63] Rocklöv, J., Quam, M.B., Sudre, B., German, M., Kraemer, M.U.G., Brady, O., et al. (2016). Assessing seasonal risks for the introduction and mosquito-borne spread of Zika virus in Europe. *EBioMed.* 9, 250-256. Doi: 10.1016/j.ebiom.2016.06.009
- [64] Roth, A., Mercier, A., Lepers, C., Hoy, D., Duituturaga, S., Benyon, E., et al. (2014). Concurrent outbreaks of dengue, chikungunya and Zika virus infections—An unprecedented epidemic wave of mosquito-borne viruses in the Pacific 2012-2014. *Eur. Surveill.* 19: 20929. Doi: 10.2807/1560-7917.ES2014.19.41.20929
- [65] Roundy, C. M., Azar, S. R., Rossi, S. L., Huang, J. H., Leal, G., Yun, R., et al. (2017). Variation in *Aedes aegypti* mosquito competence for Zika virus transmission. *Emerg. Infect. Dis.* 23, 625-632. Doi: 10.3201/eid2304.161484
- [66] Russell, J. A., Campos, B., Stone, J., Blosser, E. M., Burkett-Cadena, N., and Jacobs, J. L. (2018). Unbiased strain-typing of arbovirus directly from mosquitoes using nanopore sequencing: a field-forward biosurveillance protocol. *Sci. Rep.* 8: 5417. Doi: 10.1038/s41598-018-23641-7
- [67] Saiz, J. C., Vazquez-Calvo, A., Blazquez, A. B., Merino-Ramos, T., Escribano-Romero, E., and Martin-Acebes, M. A. (2016). Zika virus: the latest newcomer. *Front. Microbiol.* 7: 496. Doi: 10.3389/fmicb.2016.00496
- [68] Sapkal, G. N., Yadav, P. D., Vegad, M. M., Viswanathan, R., Gupta, N., and Mourya, D. T. (2018). First laboratory confirmation on the existence of Zika virus disease in India. *J. Infect.* 76, 314-317. Doi: 10.1016/j.jinf.2017.09.020
- [69] Sarno, M., Sacramento, G. A., Khouri, R., do Rosario, M. S., Costa, F., Archanjo, G., et al. (2016). Zika virus infection and stillbirths: a case of hydrops fetalis, hydranencephaly and fetal demise. *PLoS Negl. Trop. Dis.* 10: e0004517. Doi: 10.1371/journal.pntd.0004517
- [70] Schuler-Faccini, L., Ribeiro, E. M., Feitosa, I. M., Horovitz, D. D., Cavalcanti, D. P., Pessoa, A., et al. (2016). Possible association between Zika virus infection and microcephaly—Brazil, 2015. *Morbidity and Mortality Weekly Report (MMWR)* 65, 59-62. Doi: 10.15585/mmwr.mm6503e2
- [71] Smithburn, K. C., Kerr, J. A., and Gatne, P. B. (1954). Neutralizing antibodies against certain viruses in the sera of residents of India. *J. Immunol.* 72, 248-257
- [72] Stettler, K., Beltramello, M., Espinosa, D. A., Graham, V., Cassotta, A., Bianchi, S., et al. (2016). Specificity, cross-reactivity, and function of antibodies elicited by Zika virus infection. *Science* 353, 823-826. Doi: 10.1126/science.aaf8505
- [73] Sukupolvi-Petty, S., Austin, S. K., Purtha, W. E., Oliphant, T., Nybakken, G. E., Schlesinger, J. J., et al. (2007). Type- and subcomplex-specific neutralizing antibodies against domain III of dengue virus type 2 envelope protein recognize adjacent epitopes. *J. Virol.* 81, 12816-12826. Doi: 10.1128/JVI.00432-07
- [74] Tognarelli, J., Ulloa, S., Villagra, E., Lagos, J., Aguayo, C., Fasce, R., et al. (2016). A report on the outbreak of Zika virus on Easter Island, South Pacific, 2014. *Arch. Virol.* 161, 665-668. Doi: 10.1007/s00705-015-2695-5
- [75] Triunfol, M. (2016). Microcephaly in Brazil: confidence builds in Zika connection. *Lancet Infect. Dis.* 16, 527-528. Doi: 10.1016/S1473-3099(16)30015-9
- [76] van den Pol, A. N., Mao, G., Yang, Y., Ornaghi, S., and Davis, J.N. (2017). Zika virus targeting in the developing brain. *J. Neurosci.* 37, 2161-2175. Doi: 10.1523/JNEUROSCI.3124-16.2017
- [77] van der Eijk, A. A., van Genderen, P. J., Verdijk, R. M., Reusken, C. B., Mogling, R., van Kampen, J. J., et al. (2016). Miscarriage associated with Zika virus infection. *N. Engl. J. Med.* 375, 1002-1004. Doi: 10.1056/NEJMc1605898
- [78] Wang, A., Thurmond, S., Islas, L., Hui, K., and Hai, R. (2017). Zika virus genome biology and molecular pathogenesis. *Emerg. Microbes Infect.* 6: e13. Doi: 10.1038/emi.2016.141
- [79] Wang, J., Moore, N. E., Deng, Y. M., Eccles, D. A., and Hall, R. J. (2015). MinION nanopore sequencing of an influenza genome. *Front. Microbiol.* 6: 766. Doi: 10.3389/fmicb.2015.00766
- [80] Weger-Lucarelli, J., Ruckert, C., Chotiwan, N., Nguyen, C., Garcia Luna, S. M., Fauver, J. R., et al. (2016). Vector competence of American mosquitoes for three strains of Zika virus. *PLoS Negl. Trop. Dis.* 10: e0005101. Doi: 10.1371/journal.pntd.0005101
- [81] Windbichler, N., Menichelli, M., Papathanos, P. A., Thyme, S. B., Li, H., Ulge, U. Y., et al. (2011). A synthetic homing endonuclease-based gene drive system in the human malaria mosquito. *Nature* 473, 212-215. Doi: 10.1038/nature09937
- [82] World Health Organization (2016). *Zika Situation Report: Neurological Syndrome and Congenital Anomalies*. Geneva: World Health Organization
- [83] Zander, C. (2016). Denmark Reports First Case of Zika virus. Patient, Currently Hospitalized, Had Been Traveling in Latin America. Available at: <http://www.wsj.com/articles/denmark-reports-first-case-of-zika-virus-1453895642>
- [84] Zhu, Z., Gorman, M. J., McKenzie, L. D., Chai, J. N., Hubert, C. G., Prager, B. C., et al. (2017). Zika virus has oncolytic activity against glioblastoma stem cells. *J. Exp. Med.* 214, 2843-2857. Doi: 10.1084/jem.20171093