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ZIKV infection regulates inflammasomes pathway for replication in monocytes

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Abstract

© 2017 The Author(s). ZIKV causes microcephaly by crossing the placental barrier, however, the mechanism of trans-placental dissemination of ZIKV remains unknown. Here, we sought to determine whether monocytes, which can cross tissue barriers, assist ZIKV dissemination to the fetus. We determined this by infecting monocytes with two strains of ZIKV: South American (PRVABC59) and Nigerian (IBH30656) and analyzing viral replication. We found that ZIKV infects and replicates in monocytes and macrophages, which results in the modulation of a large number of cellular genes. Analysis of these genes identified multiple pathways including inflammasome to be targeted by ZIKV, which was confirmed by analyzing the transcript levels of the proteins of inflammasome pathways, NLRP3, ASC, caspase 1, IL-1 and IL-18. Interestingly, IFNα and the IFN inducible gene, MxA were not enhanced, suggesting prevention of innate antiviral defense by ZIKV. Also, inhibition of inflammasome led to an increased transcriptional activity of IFNα, MxA and CXCL10. Based on these results we suggest that ZIKV transcription is regulated by inflammasomes.

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References

[1] MOH. Increase of microcephaly in the northeast of Brazi, http://moh. gov. jm/epidemiological-alert-increase-of-microcephaly-in-thenortheast-of-brazil/ (2015).

[2] Campos, G. S., Bandeira, A. C. & Sardi, S. I. Zika Virus Outbreak, Bahia, Brazil. Emerg Infect Dis 21, 1885-1886, https://doi. org/10. 3201/eid2110. 150847 (2015).

[3] Dowall, S. D. et al. A Susceptible Mouse Model for Zika Virus Infection. PLoS Negl Trop Dis 10, e0004658, https://doi. org/10. 1371/ journal. pntd. 0004658PNTD-D-16-00358 (2016).

[4] Wu, K. Y. et al. Vertical transmission of Zika virus targeting the radial glial cells affects cortex development of offspring mice. Cell Res 26, 645-654, https://doi. org/10. 1038/cr. 2016. 58 (2016).

[5] Li, C. et al. Zika Virus Disrupts Neural Progenitor Development and Leads to Microcephaly in Mice. Cell Stem Cell 19, 120-126, https://doi. org/10. 1016/j. stem. 2016. 04. 017 (2016).

[6] Cugola, F. R. et al. The Brazilian Zika virus strain causes birth defects in experimental models. Nature (2016).

[7] Maestre, A. M. & Fernandez-Sesma, A. Finding Clues for Congenital Zika Syndrome: Zika Virus Selective Infection of Immature Neurons. EBioMedicine 10, 7-8, https://doi. org/10. 1016/j. ebiom. 2016. 07. 026 (2016).

[8] Tang, H. et al. Zika virus infects human cortical neural progenitors and attenuates their growth. Cell Stem Cell 18, 587-590 (2016).

[9] Garcez, P. P. et al. Zika virus impairs growth in human neurospheres and brain organoids. Science 352, 816-818 (2016).

[10] Bayer, A. et al. Type III interferons produced by human placental trophoblasts confer protection against Zika virus infection. Cell host & microbe 19, 705-712 (2016).

[11] Lazear, H. M. et al. A mouse model of Zika virus pathogenesis. Cell host & microbe 19, 720-730 (2016).

[12] Rossi, S. L. et al. Characterization of a novel murine model to study Zika virus. The American journal of tropical medicine and hygiene 94, 1362-1369 (2016).

[13] Cao, W. et al. Rapid differentiation of monocytes into type I IFN-producing myeloid dendritic cells as an antiviral strategy against influenza virus infection. The Journal of Immunology 189, 2257-2265 (2012).

[14] Hamel, R. et al. Biology of Zika Virus Infection in Human Skin Cells. Journal of Virology 89, 8880-8896, https://doi. org/10. 1128/ Jvi. 00354-15 (2015).

[15] Authors' correction for Euro Surveill. 2016;21(26). Euro Surveill 21, https://doi. org/10. 2807/1560-7917. ES. 2016. 21. 31. 30305 30305 (2016).

[16] Gourinat, A. C., O'Connor, O., Calvez, E., Goarant, C. & Dupont-Rouzeyrol, M. Detection of Zika virus in urine. Emerg Infect Dis 21, 84-86, https://doi. org/10. 3201/eid2101. 140894 (2015).

[17] Nicastri, E. et al. Persistent detection of Zika virus RNA in semen for six months after symptom onset in a traveller returning from Haiti to Italy, February 2016. Euro Surveill 21, https://doi. org/10. 2807/1560-7917. ES. 2016. 21. 32. 30314 30314 (2016).

[18] Bingham, A. M. et al. Comparison of Test Results for Zika Virus RNA in Urine, Serum, and Saliva Specimens from Persons with Travel-Associated Zika Virus Disease-Florida, 2016. MMWR Morb Mortal Wkly Rep 65, 475-478, https://doi. org/10. 15585/mmwr. mm6518e2 (2016).

[19] Arias, R. A., Munoz, L. D. & Munoz-Fernandez, M. A. Transmission of HIV-1 infection between trophoblast placental cells and T-cells take place via an LFA-1-mediated cell to cell contact. Virology 307, 266-277, S0042682202000405 [pii] (2003).

[20] Pereira, L., Maidji, E., McDonagh, S., Genbacev, O. & Fisher, S. Human cytomegalovirus transmission from the uterus to the placenta correlates with the presence of pathogenic bacteria and maternal immunity. J Virol 77, 13301-13314 (2003).

[21] McDonagh, S. et al. Viral and bacterial pathogens at the maternal-fetal interface. J Infect Dis 190, 826-834, https://doi. org/10. 1086/422330 JID32235 (2004).

[22] Parekh, F. K., Davison, B. B., Gamboa, D., Hernandez, J. & Branch, O. H. Placental histopathologic changes associated with subclinical malaria infection and its impact on the fetal environment. Am J Trop Med Hyg 83, 973-980, https://doi. org/10. 4269/ ajtmh. 2010. 09-0445 (2010).

[23] Karniychuk, U. U. & Nauwynck, H. J. Pathogenesis and prevention of placental and transplacental porcine reproductive and respiratory syndrome virus infection. Vet Res 44, 95, https://doi. org/10. 1186/1297-9716--4-95 (2013).

[24] Al-Husaini, A. M. Role of placenta in the vertical transmission of human immunodeficiency virus. J Perinatol 29, 331-336, https:// doi. org/10. 1038/jp. 2008. 187 (2009).

[25] Maciejewski, J. P. et al. Infection of hematopoietic progenitor cells by human cytomegalovirus. Blood 80, 170-178 (1992).

[26] Maciejewski, J. P. et al. Infection of mononucleated phagocytes with human cytomegalovirus. Virology 195, 327-336 (1993).

[27] Pirhonen, J., Sareneva, T., Kurimoto, M., Julkunen, I. & Matikainen, S. Virus infection activates IL-1? and IL-18 production in human macrophages by a caspase-1-dependent pathway. The Journal of Immunology 162, 7322-7329 (1999).

[28] Netea, M. G., van de Veerdonk, F. L., van der Meer, J. W. M., Dinarello, C. A. & Joosten, L. A. B. Inflammasome-Independent Regulation of IL-1-Family Cytokines. Annual Review of Immunology 33, 49-77, https://doi. org/10. 1146/annurevimmunol-032414-112306 (2015).

[29] Brough, D. & Rothwell, N. J. Caspase-1-dependent processing of pro-interleukin-1beta is cytosolic and precedes cell death. J Cell Sci 120, 772-781, https://doi. org/10. 1242/jcs. 03377 (2007).

[30] Netea, M. G., van de Veerdonk, F. L., van der Meer, J. W., Dinarello, C. A. & Joosten, L. A. Inflammasome-independent regulation of IL-1-family cytokines. Annu Rev Immunol 33, 49-77, https://doi. org/10. 1146/annurev-immunol-032414-112306 (2015).

[31] Henry, C. M. et al. Neutrophil-Derived Proteases Escalate Inflammation through Activation of IL-36 Family Cytokines. Cell Rep 14, 708-722, https://doi. org/10. 1016/j. celrep. 2015. 12. 072 (2016).

[32] Sims, J. E. & Smith, D. E. The IL-1 family: regulators of immunity. Nat Rev Immunol 10, 89-102, https://doi. org/10. 1038/nri2691 (2010).

[33] Afonina, I. S., Muller, C., Martin, S. J. & Beyaert, R. Proteolytic Processing of Interleukin-1 Family Cytokines: Variations on a Common Theme. Immunity 42, 991-1004, https://doi. org/10. 1016/j. immuni. 2015. 06. 003 (2015).

[34] Dinarello, C. A. Immunological and inflammatory functions of the interleukin-1 family. Annu Rev Immunol 27, 519-550, https:// doi. org/10. 1146/annurev. immunol. 021908. 132612 (2009).

[35] Sakaguchi, S., Yamaguchi, T., Nomura, T. & Ono, M. Regulatory T cells and immune tolerance. Cell 133, 775-787, https://doi. org/10. 1016/j. cell. 2008. 05. 009 (2008).

[36] Ferreri, A. J., Illerhaus, G., Zucca, E. & Cavalli, F. Flows and flaws in primary central nervous system lymphoma. Nat Rev Clin Oncol 7, 10 1038/nrclinonc 20101039-c1031; author reply 1010:1038/nrclinonc 2010 1039-c1032, 10. 1038/nrclinonc. 2010. 9-c1 (2010).

[37] Carson, W. E. et al. Coadministration of interleukin-18 and interleukin-12 induces a fatal inflammatory response in mice: critical role of natural killer cell interferon-gamma production and STAT-mediated signal transduction. Blood 96, 1465-1473 (2000).

[38] Ziegler-Heitbrock, H. W. & Ulevitch, R. J. CD14: cell surface receptor and differentiation marker. Immunol Today 14, 121-125, https://doi. org/10. 1016/0167-5699(93)90212-4 (1993).

[39] Uchide, N., Ohyama, K., Yuan, B., Bessho, T. & Yamakawa, T. Differentiation of monocytes to macrophages induced by influenza virus-infected apoptotic cells. J Gen Virol 83, 747-751, https://doi. org/10. 1099/0022-1317-83-4-747 (2002).

[40] Yang, J., Zhang, L., Yu, C., Yang, X. F. & Wang, H. Monocyte and macrophage differentiation: circulation inflammatory monocyte as biomarker for inflammatory diseases. Biomark Res 2, 1, https://doi. org/10. 1186/2050-7771-2-1 (2014).

[41] Downham, E. et al. A novel mitochondrial ND5 (MTND5) gene mutation giving isolated exercise intolerance. Neuromuscul Disord 18, 310-314, https://doi. org/10. 1016/j. nmd. 2008. 01. 003 (2008).

[42] Ahari, S. E. et al. Investigation on mitochondrial tRNA(Leu/Lys), NDI and ATPase 6/8 in iranian multiple sclerosis patients. Cellular and Molecular Neurobiology 27, 695-700, https://doi. org/10. 1007/s10571-007-9160-2 (2007).

[43] Guo, H. T., Callaway, J. B. & Ting, J. P. Y. Inflammasomes: mechanism of action, role in disease, and therapeutics. Nature Medicine 21, 677-687, https://doi. org/10. 1038/nm. 3893 (2015).

[44] Lu, A. & Wu, H. Structural mechanisms of inflammasome assembly. Febs Journal 282, 435-444, https://doi. org/10. 1111/febs. 13133 (2015).

[45] Maelfait, J. et al. Stimulation of Toll-like receptor 3 and 4 induces interleukin-1? maturation by caspase-8. The Journal of experimental medicine 205, 1967-1973 (2008).

[46] Stetson, D. B. & Medzhitov, R. Type I interferons in host defense. Immunity 25, 373-381 (2006).

[47] Taub, D. D., Longo, D. L. & Murphy, W. J. Human interferon-inducible protein-10 induces mononuclear cell infiltration in mice and promotes the migration of human T lymphocytes into the peripheral tissues and human peripheral blood lymphocytes-SCID mice. Blood 87, 1423-1431 (1996).

[48] Foy, B. D. et al. Probable non-vector-borne transmission of Zika virus, Colorado, USA. Emerg Infect Dis 17, 880-882, https://doi. org/10. 3201/eid1705. 101939 (2011).

[49] Haynes, M. Re: Thomas, L. C. et al. Pre-manipulative testing and the velocimeter. Manual Therapy (2007), 10:1016/j. math. 2006. 11. 003. Man Ther 13, e4; author reply e5-6, doi:S1356-689X(07)00159-2 https://doi. org/10. 1016/j. math. 2007. 09. 008 (2008).

[50] La Morgia, C. et al. Association of the mtDNA m. 4171C > A/MT-ND1 mutation with both optic neuropathy and bilateral brainstem lesions. BMC Neurol 14, 116, https://doi. org/10. 1186/1471-2377-14-116 (2014).

[51] Miao, E. A. et al. Cytoplasmic flagellin activates caspase-1 and secretion of interleukin 1beta via Ipaf. Nat Immunol 7, 569-575, https://doi. org/10. 1038/ni1344 (2006).

[52] Doi, A. et al. Long RP' Tachycardia With Unusual Entrainment Responses: What Is the Mechanism? J Cardiovasc Electrophysiol 27, 1242-1244, https://doi. org/10. 1111/jce. 12987 (2016).

[53] Gabay, C., Lamacchia, C. & Palmer, G. IL-1 pathways in inflammation and human diseases. Nat Rev Rheumatol 6, 232-241, https:// doi. org/10. 1038/nrrheum. 2010. 4 (2010).

[54] Sivakumar, P. V. et al. Interleukin 18 is a primary mediator of the inflammation associated with dextran sulphate sodium induced colitis: blocking interleukin 18 attenuates intestinal damage. Gut 50, 812-820 (2002).

[55] Suptawiwat, O. et al. A simple screening assay for receptor switching of avian influenza viruses. Journal of Clinical Virology 42, 186-189 (2008).

[56] Levy, D. E. & Garc, A. The virus battles: IFN induction of the antiviral state and mechanisms of viral evasion. Cytokine & growth factor reviews 12, 143-156 (2001).

[57] Schmid, S., Mordstein, M., Kochs, G. & García-Sastre, A. Transcription factor redundancy ensures induction of the antiviral state. Journal of Biological Chemistry 285, 42013-42022 (2010).

[58] Haller, O. & Kochs, G. Human MxA protein: an interferon-induced dynamin-like GTPase with broad antiviral activity. Journal of Interferon & Cytokine Research 31, 79-87 (2011).

[59] Yuan, J. et al. CXCL10 inhibits viral replication through recruitment of natural killer cells in coxsackievirus B3-induced myocarditis. Circulation research 104, 628-638 (2009).

[60] Kumar, A. et al. Zika virus inhibits type?I interferon production and downstream signaling. EMBO reports 17, 1766-1775 (2016).