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Study finds potential link between Zika virus and various neurological disease



A research group identified, in cells infected with Zika, the expression of proteins common to schizophrenia, Alzheimer's, Parkinson's and autism, among other diseases

November 23, 2018 - By Camila Raposo

It is known that the Zika virus infection is related to a series of neurological complications, such as microcephaly and Guillain-Barré syndrome. A study published in October 2018 in the journal Molecular Neurobiology, however, describes a potential link between Zika's infection and several other brain diseases, such as Alzheimer's, autism, amyotrophic lateral sclerosis (ALS), schizophrenia, and Parkinson's. Started in 2017, the research was carried out at the Federal University of Rio Grande do Sul (UFRGS) and the Hospital of Clinics of Porto Alegre (HCPA) and counted with the collaboration of the Institute of Cardiology of Rio Grande do Sul and the American research institutes Sanford Burnham Prebys Medical Discovery Institute and Scripps Research.

For this study, the scientists experimentally infected human stem cells with the Zika virus and evaluated the differential gene expression resulting from the infection. Gene expression refers to the process by which information encoded by a given gene is decoded into a functional gene product, such as proteins or RNA. In the case of this investigation, the researchers identified $% \left(1\right) =\left(1\right) \left(1\right) \left($ and quantified the proteins expressed by the infected cells and compared



Zika is transmitted by the mosquito Aedes Aegypti - Photo: Stephen Ausmus / US Department of Agriculture

them with those of a set of uninfected cells. "By quantifying the proteins, we can determine which genes are more or less expressed because of Zika's infection. By evaluating this differential proteome (protein pool), we were able - with the aid of bioinformatics tools - to identify molecular processes and metabolic pathways that were being altered by the infection in this cellular model," says the Professor of the Faculty of Pharmaceutical Sciences of UFRGS Walter O. Beys da Silva, one of the authors of the study.

It was when we noticed that the infection of the virus in human stem cells results in a drastic change in the expression of the proteins of that cell type. All the proteins identified in this process were compared with the information from a specific database of human pathologies, in order to find matches to other neurological diseases. Scientists searched for correlations with 30 different disorders, and identified 74 proteins implicated in 16 neuropathologies (of which six were already associated with Zika infection, such as microcephaly and epilepsy). The highest number of proteins attributed to pathologies already associated with this virus was found in microcephaly, with 13 proteins in common. Among the diseases not previously related to that infection, we identified amyotrophic lateral sclerosis, with 23 proteins, followed by schizophrenia (14), Alzheimer's disease (7) and Parkinson's disease (7).

According to Silva, finding the possible association between the virus and other neurological diseases of great clinical impact - such as Alzheimer's, autism, amyotrophic lateral sclerosis, schizophrenia, and Parkinson's disease – proved to be the true big discovery. "Zika had already been linked to epilepsy, multiple sclerosis, Guillain-Barré and other conditions, but our research findings are the first to bring evidence to these four. As they are diseases of slow development, confirming their occurrence probability is an important contribution to the preventive clinical screening, as well as for further studies to see if these outcomes can actually be associated with Zika infection," explains the professor.

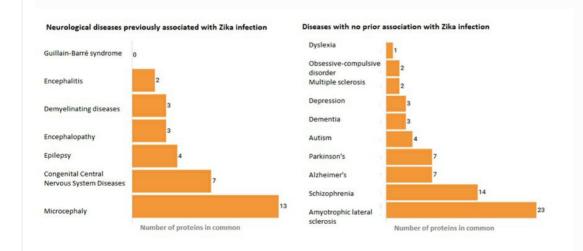
Despite being preliminary, the results point to new targets for this infection and may contribute to the prevention and diagnosis of these neurological conditions and to the treatment of individuals who have been infected with Zika. "In addition, this molecular link can support a preventive clinical screening of infected individuals, not only children but also adults. Many people, especially children born after 2015 and who have been infected by Zika during pregnancy, are currently being monitored for evaluation of the extent of still unknown neurological damage," savs Silva.

About the Zika virus

The recent Zika virus epidemic in Brazil was first associated with the outbreak of microcephaly in newborns in 2015, mainly in the Northeast region. Subsequently, the World Health Organization (WHO) declared a state of global emergency with the finding of the rapid spread of this virus and the growing report of congenital neurological problems in several countries around the world. With the intensification of research studies, other neurological complications, such as Guillain-Barré syndrome and epilepsy, were identified to be associated to the infection of this virus, transmitted mainly through the bite of the mosquito Aedes Aegypti.

Research group

The research group responsible for the study, which is coordinated by the professor of the Department of Biochemistry of UFRGS Diogo Souza, works on different fronts to improve understanding about Zika and its consequences. The research project, which aims to characterize the infection by Zika in a multidisciplinary and translational way, has funding from the Brazilian Ministry of Health, Capes and CNPq. "We have involved research groups from HCPA, departments of microbiology, genetics, biochemistry, School of Pharmacy, Institute of Cardiology of Rio Grande do Sul and other national and foreign institutions. Aspects related to prevention, epidemiology, pathogenesis, neurochemistry and molecular impact, among others, are being studied. Specially on the results found in the published work, we are evaluating other experimental models and deepening the correlation found with these diseases," says Silva.



Translated by Fernanda Cristina Cestari, under the supervision and translation revision of Professor Elizamari R. Becker (P.h.D.) – IL/UFRGS.

