



**PROGRAMA DE PÓS-GRADUAÇÃO EM CIÊNCIAS BIOLÓGICAS –
EDITAL COPG/PRPPG 001/2017**

PROVA DE CONHECIMENTOS DE LÍNGUA INGLESA – 31/07/2017

Número de Inscrição: ___ ___ ___ Assinatura: _____

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- 1) As questões da prova deverão ser respondidas à caneta, cor azul ou preta, exclusivamente nas folhas de respostas fornecidas pela comissão de seleção.
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- BOA PROVA!**

**Zika Grabs Neural Stem Cell Protein to Cause Damage:
The new findings, obtained from cell culture experiments, could explain the link between
infection with the virus during pregnancy and infant microcephaly.**

By Jef Akst for The scientist, June 1st, 2017

When the Zika virus enters neural stem cells, a protein called Musashi-1 (MSI1) latches on to the virus's RNA genome, somehow promoting viral replication. Almost all MSI1 protein in the developing embryo is produced in the neural stem cells that will eventually develop into the baby's brain, which could explain why these cells are so vulnerable to Zika. Blocking the cells' ability to produce MSI1 significantly inhibits Zika's ability to reproduce, according to an *in vitro* study published in *Science*.

Researchers from the University of Cambridge studied a variety of cell lines, including human neural stem cells, to investigate how Zika virus infection can lead to microcephaly. They suspected that MSI1 - an RNA binding protein - might be important in this process because it is involved in regulating the pool of neural stem cells that are required for normal brain development.

They show that when the Zika virus enters these stem cells, it hijacks MSI1 for its own replication and damages the cells in at least two ways. Firstly, MSI1 binds to the Zika virus genome allowing it to replicate and making the cells more vulnerable to virus-induced cell death. Secondly, they showed that MSI1 also disrupts the normal development programme of neural stem cells. In cells infected with Zika virus MSI1 binds to the virus genome in favour of its normal targets in the cell. The virus essentially prevents MSI1 from working correctly and alters the expression of many genes involved in neuronal development. In both of these scenarios, neural stem cells, which are crucial for normal neural development, are lost, leading to microcephaly.

The results provide clues as to how Zika causes microcephaly in fetuses whose mothers were infected while pregnant. Indeed, the team also found that a rare type of inherited microcephaly called autosomal recessive primary microcephaly is associated with mutations in MSI1. "We've shown for the first time this interaction between Zika and MSI1—with MSI1 getting exploited by the virus for its own destructive life cycle, turning MSI1 into the enemy within," says coauthor Fanni Gergely from the University of Cambridge. "We hope that in the future this discovery could lead to ways of generating potential Zika virus vaccines."

"This is the first study to show a clear link between a specific protein, the Zika virus, and microcephaly," adds Mike Turner, head of Infection and Immunobiology at the Wellcome Trust, which partly funded the study. "This new finding really helps to explain why neural stem cells are so vulnerable to Zika infection and I hope this can be a first step in determining how we could stop this interaction and disease."

Original article: "Neurodevelopmental protein Musashi 1 interacts with the Zika genome and promotes viral replication," Chavali et al. *Science* (2017). vol 357: 83. doi:10.1126/science.aam9243

