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GM mosquitoes may help fight dengue virus

WASHINGTON, PTI: Scientists have for the first time genetically engineered Aedes aegypti mosquitoes to develop increased resistance against dengue virus, an advance that may help combat the deadly infection.

When a mosquito bites someone infected with dengue virus (DENV), the virus needs to complete its lifecycle in the mosquito's gut, eventually infecting its salivary glands, before it can infect another person.

Previous studies have shown that mosquitoes rely on a molecular pathway dubbed JAK/STAT to try to fight DENV infection and stop this cycle.

Proteins known as Dome and Hop are involved in turning on the JAK/STAT when the mosquito is infected with DENV.

Researchers from Johns Hopkins University in the US genetically engineered Aedes aegypti mosquitoes to turn on expression of either Dome or Hop in the fatbody tissue earlier in infection – immediately after ingesting blood – and make more of the proteins.

Mosquitoes with engineered versions of Dome or Hop that were then infected with DENV had 78.18% (Dome) and 83.63% (Hop) fewer copies of the virus in their guts, as well as significantly less virus in their salivary glands.

Mosquitoes with the altered genes had normal lifespans, but produced fewer eggs than normal mosquitoes.

Unique to DENV

When the researchers repeated the experiments with Zika virus and chikungunya virus, no impact was seen on infection, suggesting that the importance of the JAK/STAT pathway in the fatbody tissue is unique to DENV.

"It may be possible to achieve improved or total resistance to dengue and other viruses by expressing additional transgenes in multiple tissues that block the virus through different mechanisms," said the researchers.

"Recently developed powerful mosquito gene-drive systems, that are under development, are likely to make it possible to spread pathogen resistance in mosquito populations in a self-propagating fashion, even at a certain fitness cost," they said.

After decades of research and countless control attempts, dengue fever – a mosquito-borne viral disease – continues to infect an estimated 390 million people around the world each year.

THE NEW INDIAN EXPRESS

Multiregional brain-on-a-chip to study disorders

HARVARD researchers have developed a multiregional brain-on-a-chip that models the connectivity between three distinct regions of the brain and allows studying how diseases like schizophrenia impact different brain areas simultaneously.

The chip could be useful for studying any number of neurological and psychiatric diseases, including drug addiction, post traumatic stress disorder, and traumatic brain injury, researchers said.

The in vitro model was used to extensively characterise the differences between neurons from different regions of the brain and to mimic the system's connectivity.

"The brain is so much more than individual neurons," said Ben Maoz, postdoctoral fellow at Harvard University's John A Paulson School of Engineering and Applied Sciences (SEAS).

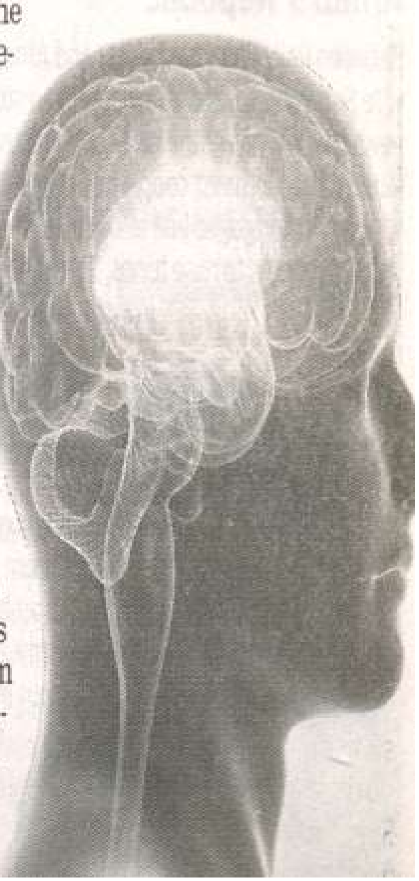
> It's no surprise that neurons in distinct regions of the brain are different but it is surprising just how different they are
>
> Stephanie Dauth, former postdoctoral fellow in Disease Biophysics

"It 's about the different types of cells and the connectivity between different regions of the brain. When modelling the brain, you need to be able to recapitulate that connectivity because there are many different diseases that attack those connections," Maoz said. Researchers modelled three regions of the brain most affected by schizophrenia - the amygdala, hippocampus and prefrontal cortex.

They began by characterising the cell composition, protein expression, metabolism, and electrical activity of neurons from each region in vitro. "It's no surprise that neurons in distinct regions of the brain are different but it is surprising just how different they are," said Stephanie Dauth, former postdoctoral fellow in the Disease Biophysics Group at SEAS.

"We found that the cell-type ratio, the metabolism, the protein expression and the electrical activity all differ between regions in vitro. This shows that it does make a difference which brain region's neurons you are working with," Dauth said.

The team also looked at how these neurons change when they are communicating with one another. They cultured cells from each region independently and then let the cells establish connections via guided pathways embedded in the chip. The researchers then measured cell composition and electrical activity again and found that the cells dramatically changed when they were in contact with neurons from different regions. To demonstrate the chip's efficacy in modelling disease, the team doped different regions of the brain with the drug Phencyclidine hydrochloride - commonly known as PCP - which simulates schizophrenia. The brain-on-a-chip allowed the researchers for the first time to look at both the drug's impact on the individual regions as well as its downstream effect on the interconnected regions in vitro.



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