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Viral infection

Reliably detecting dengue fever

Tiger mosquitoes are indigenous to Africa and Asia. However, they are increasingly being found around the Mediterranean and are bringing the dengue virus with them. Up to now, there's been no sure-fire antibody test for detecting this virus. Researchers have now developed such a test, creating a cost-effective and fail-safe way to diagnose dengue.

Eeeeeee... the high-pitched whine homes in on your ear. That mosquitoes keep us awake is bad enough, but infinitely worse is the fact that they can carry serious diseases – among them dengue fever. Some 20,000 people die from this disease every year, with hot areas such as Africa and Asia being the worst hit. And now thanks to climate change and globalization, tiger mosquitoes are also discovering other countries around the Mediterranean. Several cases of people being infected with dengue virus have already been reported in the south of France and in Croatia.

Until now, it's been rather difficult to say for sure whether someone is suffering from dengue fever or whether they've contracted another flavivirus, such as yellow fever, West Nile virus or TBEV (tick-borne encephalitis virus). There are already tests on the market, but none of them can tell the difference between these individual flaviviruses. If a definitive diagnosis is required, a sample of the patient's blood has to be sent to a high-security laboratory for analysis. Since each country has only a handful of these labs, it's not practical to test everyone. What's more, the high cost makes it practically impossible for developing countries, in particular, to conduct tests at all.

Test distinguishes between dengue and other flaviviruses

"We've succeeded in developing the first ever antibody test for dengue infections that is capable of distinguishing between dengue and other flaviviruses," says Dr. Sebastian Ulbert, Head of the Working Group on Vaccine Technologies at the Fraunhofer Institute for Cell Therapy and Immunology IZI. "Since our test is also based on detecting antibodies, it's just as cheap and easy to run as its conventional counterparts." In short: The new method can easily be integrated into existing test setups – and at no extra cost to manufacturers.

Conventional antibody tests are performed as follows: First, the doctor draws the patient's blood. If infected with the dengue virus, the blood will contain specific antibodies produced by the body to attack the intruder. The doctor then applies the

Editorial Notes

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blood to a test platform with dengue antigens that systematically bind with these antibodies. If, after a set reaction time, antibodies are found on the platform, the doctor will assume that the patient has been infected with the dengue virus. The catch is that, although the antigens bind with the antibodies according to the lock and key principle, they almost always do so at the same site as all other flaviviruses. This means that, even when the test is positive, no one can say for sure that it is actually a case of dengue. "This is why, for our test, we produced special antigens – using certain point mutations, we altered the area of the antigens that is the same for all flaviviruses, effectively shutting it off. Antibodies are then unable to bind at these now non-specific sites, with the exception of the dengue-specific antibodies that would otherwise have been masked by the crowd," Ulbert explains. So now, if the test comes back positive, we can be 100 percent sure that the patient has been infected with the dengue virus.

Next step: differentiating between the four strains of the virus

Demand for such a system is massive: dengue fever is one of the most commonly occurring diseases in the world, with some two-thirds of all people living in dengue danger zones. The researchers hope that their test will hit the market around one year from now. In a further step, they are working on ways to differentiate between the four strains of the dengue pathogen. This could be an important breakthrough: Anyone who has survived a dengue-related illness has then acquired immunity against that specific pathogen, but when it comes to the other three strains, that person is at even greater risk. This is because the antibodies they produced to combat the first bout of dengue fever actually help the new virus to spread and make it much harder for that person to recover. "Our test system has the potential to differentiate between the four viral strains," says Ulbert. "We now want to put this theory into practice."

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Facts about the tiger mosquito

- Tiger mosquitoes carry diseases such as dengue fever, West Nile virus and chikungunya fever.
- In 1990, they were brought from the U.S. state of Georgia to Genoa, Italy in a shipment of used tires. The tiger mosquito went on to take up home across almost all of Italy and also spread to other Mediterranean countries.
- In August 2014, one was found in the Waldsee area of Freiburg im Breisgau, Germany. Follow-up investigations discovered larva, pupae and eggs. This was the first time all development stages had been found in Germany beyond the flight range of highways.
- Up to 600 cases of dengue fever are reported in Germany every year, but all cases have been the result of bites received abroad.

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Researchers have developed a novel test to detect dengue fever. © Fraunhofer IZI | Picture in color and printing quality: www.fraunhofer.de/en/press