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Meridian Bioscience Malaria Assay Shines as Screening Tool in Multiple ECCMID Studies

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VIENNA (GenomeWeb) – Five independent studies presented at the European Congress of Clinical Microbiology and Infectious Disease (ECCMID) here this week provide the most compelling data to date regarding the accuracy, speed, and ease of use of Meridian Bioscience's molecular malaria assay.

The presentations, which also coincide with World Malaria Day today, provide further support for the test, Illumigene Malaria, as a tool for routine screening of travelers in non-endemic areas of the world who are returning from high-burden disease regions.

The new data also follow on the heels of a study published in November in Scientific Reports showing the value of Illumigene Malaria for detecting malaria parasites in patients in remote, endemic areas of the world, although the company has additional hurdles to clear before further penetrating this market.

Meridian developed Illumigene Malaria in house using proprietary sample prep methods and loop-mediated isothermal amplification (LAMP) technology, which is the cornerstone for all of the company's molecular tests. The test consists of primers targeting regions of the mitochondrial genome common to all species of Plasmodium, the parasite species that causes malaria, and therefore can be used to detect multiple species but not distinguish between them.

The company actually markets two tests, Illumigene Malaria and Illumigene Malaria Plus, with the former being slightly simpler and quicker to run (about 2 minutes of hands-on time as opposed to 5 minutes) and the latter being slightly more sensitive (showing a limit of detection of 0.2 parasites per microliter of blood versus 2 parasites per microliter). Both tests were CE marked last year, and both are run using a simple, inexpensive heating block combined with a turbidimetric readout.

The advantages of LAMP technology over more commonly used qPCR approaches — speed, ease of use, and relatively low cost — are well documented, and as such, it is attractive as a molecular alternative to more commonly used malaria diagnosis methods such as microscopy and immunoassays. However, isothermal amplification methods have also generally lagged behind qPCR in terms of sensitivity.

But this is not the case for Illumigene Malaria, which in the new ECCMID studies demonstrated nearly 100 percent sensitivity and specificity when compared with multiple alternative testing methods including microscopy, which remains the gold standard, and so-called rapid diagnostic tests (RDTs) such as Alere's BinaxNOW immunochromatographic test.

In one featured study presented today, a team led by Tom van Gool of the Academic Medical Center in Amsterdam used Illumigene Malaria to test 205 samples collected from

patients in 11 laboratories in The Netherlands and Belgium. The samples had previously been tested using the gold standard of microscopy, as well as with the BinaxNOW assay.

According to the gold standard, 85 patients were positive and 120 patients negative for malaria, with all five human Plasmodium species present as confirmed by qPCR. The sensitivity of Illumigene Malaria, Illumigene Malaria Plus, and BinaxNOW were respectively 99 percent, 100 percent and 89 percent, with specificities of 100 percent for Illumigene Malaria and Malaria Plus and 99 percent for BinaxNOW.

In a second study, researchers from the Laboratoire de Parasitologie at Hôpital Bichat Claude-Bernard in Paris and Université Paris Descartes tested 145 patient specimens, 85 of which were negative and 60 positive by microscopy and RDT. Of these, 44 were P. falciparum (73.4 percent), 11 were P. ovale (18.3 percent), three were P. vivax (5 percent) and two were P. malariae (3.3 percent).

Illumigene Malaria was negative for 100 percent of negative cases and positive for 100 percent of positive samples. Meanwhile, RDT sensitivity was 83.6 percent for all studied samples. The researchers concluded that Illumigene demonstrated "excellent performance in the context of an initial diagnosis of malaria, to exclude malaria infection for all negative samples and to confirm the diagnosis of malarial infection, regardless of species ... and for inframicroscopic and high parasitemia. These performances are superior to those of RDTs routinely performed in the laboratory."

The researchers further noted that the test "offers the advantage of not requiring any special training for its implementation nor for the use of its dedicated equipment." Further, they wrote, "the absence of amplicon production and the completion of the entire reaction in a closed tube avoids the risks of contamination."

In another study a team from Hospital Center Regional University De Lille in France used Illumigene to test 60 of 94 suspected malaria cases that were also tested with a French commercial rapid immunoassay called Palutop+4 Optima as well as smear microscopy. They found that Illumigene confirmed 100 percent of negative cases and allowed diagnosis of one case which microscopy could not. Illumigene also provided an earlier diagnosis in 5.5 percent of cases.

These researchers noted that Illumigene Malaria testing is currently decided in their laboratory on a case-by-case basis and is performed only if a patient returns from an endemic area, shows a negative RDT result, or when there is discordance between RDT and microscopy. "In the future, a test allowing discrimination between species as P. falciparum would certainly change the current strategy and would place the LAMP technique in first line," the researchers concluded.

Finally, similar separate studies by groups from the Amedeo di Savoia Hospital in Italy and the University of Bonn in Germany also demonstrated 100 percent sensitivity for Illumigene Malaria compared to microscopy when testing travelers returning from endemic countries and immigrants.

The ECCMID studies add to the burgeoning data supporting the use of Illumigene Malaria as a routine screening test in settings where malaria incidence is relatively low but it is still important to quickly and simply identify negative patients.

"All present data available today suggest that the Illumigene tests are useful and reliable as screening tests for malaria in travelers," AMC's van Gool said. "Because the tests were only introduced in 2016, more studies can add evidence about its performance. The Illlumigene

tests always should be part of a diagnostic package of the laboratory which should also include microscopic diagnostic methods."

Van Gool added that the test "[definitely] has the potential to change and improve diagnosis of malaria in many laboratories. This is quite an achievement because the last important improvements in this field came from the introduction of the rapid diagnostic test for malaria" some 15 years ago.

Indeed, since Meridian launched the test commercially in regions recognizing CE mark, it has garnered around 100 customers, said Slava Elagin, executive vice president of research and product development at Meridian Bioscience. And as positive data continues to mount, Meridian expects this number to grow.

"It's one thing for us to say this test is great or perfect, but it's different when your customers on the front line of malaria diagnostics will testify the same," Elagin said.

"A number of independent studies … have demonstrated 100 percent negative predictive value, and near perfect sensitivity levels whenever they encounter a positive," added Richard Hughes, associate director for marketing at Meridian. "That, in addition to the peer-reviewed publications, provides a pretty burgeoning level of evidence."

Meridian's test could also have a big impact in regions affected by malaria. In 2015, the Bill and Melinda Gates Foundation and the UN released a report summarizing how malaria could realistically be eradicated by 2040, and noted that inexpensive, easy-to-use, and accurate diagnostic tests are a key component of that plan.

"The most important question that will come: How can we diagnose asymptomatic carriers — people who are reservoirs for malaria who need to be treated, which will lead to elimination of malaria," Elagin said. "And this test, with the given sensitivity, provides a perfect tool which is field deployable and very sensitive."

In one pivotal peer-reviewed study conducted last year, Meridian and its collaborators put the test in the hands of a remote laboratory in Senegal, where it was performed by a relatively unskilled technician. The test still yielded high accuracy and was as easily implemented in that setting as it has been in advanced diagnostic labs.

But, as always with diagnostic tests, especially molecular diagnostics, the considerations are different in the low-resource, high-burden areas of the world. Meridian's Hughes said that about 95 percent of Meridian's customers so far are in non-endemic areas, although the company hopes that can change.

Despite the fact that it runs on a relatively simple and inexpensive instrument, Illumigene still requires electricity. Furthermore, although it is cheaper than real-time PCR, the test is a long way off from approaching the low cost of RDTs.

Van Gool noted that the issue of deploying Illumigene Malaria in high-burden, low-resource settings "still deserves more study. There are probably locations where it can and will suit very well, but in remote areas the test does have limitations. A major factor which will influence introduction and use will of course [be] the [price] of the assays in these settings."

"This is a very complex question when you start to compare yourself to rapid tests, which in some cases can [cost as little as] 50 cents," Elagin said. But, he added, comparisons are also not straightforward because many of these tests lack the accuracy or quality standards of Illumigene.

Hughes said that in the EU, the typical price for an Illiumigene test is around €20, but there is flexibility in that price depending on the volume of tests.

"I think we're still exploring the cost in the high-burden sub-Saharan African region," Hughes said. "We're still having discussions of what that needs to be. Part of the success of deploying and getting large-scale implementation and scale-up in [these areas] will depend on the funding mechanism that supports this. We've started some of those discussions already, and it's looking promising in some of the early work in Africa so far."