Measles Virus Genotype A RT-qPCR (MeVA RT-qPCR)

Background:

Circulation of measles virus in the United States has been interrupted as a result of high vaccine coverage. However, importations occur from regions of the world where measles is still circulating, as highlighted by the continued occurrence of measles outbreaks in the United States. During a measles outbreak, vaccination is an important component of the public health response to limit the spread of the virus.

Approximately 5% of individuals vaccinated with a measles-containing vaccine develop fever and rash that can be clinically indistinguishable from measles infection. While individuals with vaccine reactions are not contagious, suspicion for wild-type measles may be high, especially if vaccine was administered as part of an outbreak response.[1] Serologic assays and currently used diagnostic measles virus RT-qPCR assays (MeV assay) cannot distinguish between vaccine reactions and infections with wild-type virus. However, rapid differentiation of vaccine reactions from infections with virus is critical for guiding the public health response to outbreaks by preventing unnecessary isolation of patients and reducing the direct and indirect costs of an outbreak. A recent study found that total costs associated with responding to a single case of measles ranged between $18,423 and $49,769, as well as 435 to 756 hours of personnel time.[2]

Purpose and Description of Test:

Vaccine reactions can be laboratory confirmed by detecting measles vaccine virus in respiratory secretions or urine followed by sequencing to determine genotype. Sequencing typically takes 24-72 hours to complete. We have developed a RT-qPCR assay for specific detection of measles vaccine strains that is a more rapid alternative to genotyping and can discriminate between vaccine reactions and wild-type measles infections within hours instead of days.[3] This assay (MeVA test) detects regions of the nucleoprotein gene that are specific to and conserved among measles vaccine strains, which are genotype A. Global virologic surveillance has shown that wild-type genotype A measles viruses are no longer circulating, so detection of genotype A is consistent with a vaccine reaction.

Intended Use:

The MeVA test should be performed only on specimens collected from patients with a suspected vaccine reaction, (i.e. a febrile rash illness occurring within 21 days after vaccination with a measles-containing vaccine) in a person <u>also</u> potentially exposed to wild-type measles virus, e.g., in an outbreak setting. The MeVA test can be informative in situations when vaccination history is available; it should not be used as a stand-alone test. The MeVA test should be performed in parallel with a CLIA-validated measles RT-qPCR assay (MeV test) or as a reflex test following the MeV test. The same specimen should be tested in both assays. Results from MeVA and MeV tests should always be reported together for each specimen.

Interpretation:
A positive result in the MeV test indicates the detection of measles virus RNA, but cannot distinguish between vaccine-associated symptoms or infection with wild-type measles virus. A positive result in both the MeV and MeVA RT-qPCR assays for the same specimen indicates that the patient's symptoms were likely due to a recent vaccination. Results from all specimens that test positive by the MeVA test should be confirmed by genotyping. The sequencing data generated from this effort will provide an independent multi-site verification of MeVA test performance.

A negative result in the MeVA test accompanied by a positive result in the MeV test is consistent with infection with wild-type measles virus, in which case the specimen should be submitted for genotyping. However, due to the lower analytical sensitivity of the MeVA RT-qPCR test, this assay may not detect all vaccine-associated reactions. Therefore, a negative result in the MeVA test from a specimen with a very high Ct value in the MeV test should be interpreted with caution. If either the MeV or the MeVA RT-qPCR test return an indeterminate result, the specimen must be re-tested in both assays. If amplification is observed only in the MeVA assay, the test is inconclusive.

Reporting:
The following language is suggested for reporting of results from the MeVA RT-qPCR test. "This sample was tested using two measles RT-qPCR assays – one which detects both wild-type and vaccine measles strains and one which is specific for the measles vaccine strain (genotype A). Detection of a measles vaccine strain indicates that this patient's symptoms were likely due to vaccine reaction following recent vaccination. The specimen will be genotyped to confirm the result of the PCR testing."

For more information, please contact:

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References:
1. Berggren KL, Tharp M, Boyer KM. 2005. Vaccine-associated "wild-type" measles. Pediatr Dermatol. 22: 130-132.

2. Marx GE, Chase J, Jasperse J, Stinson K, McDonald CE, Runfola JK, Jaskunas J, Hite D, Barnes M, Askenazi M, Albanese B. 2017. Public health economic burden associated with two single measles case investigations – Colorado, 2016-2017. MMWR. 66(46): 1272-1275.

3. Roy F, Mendoza L, Hiebert J, McNall RJ, Bankamp B, Connolly S, Ludde A, Friedrich N, Mankertz A, Rota PA, Severini A. 2017. Rapid identification of measles virus vaccine genotype by real time PCR. J Clin Microbiol. 55: 735-743.