BabyNEXT

INFORMATION ABOUT NEWBORN SCREENING TEST BY DNA ANALYSIS

A. About BabyNEXT™ test

BabyNEXT™ Test is a highly accurate newborn screening test that analyses baby's DNA for more than **200 conditions**, as well as providing personalized genetic information on the metabolism of more than **30 medications.**

BabyNEXT™ is a **genetic test** and it only screens for conditions that can be treated with medication, dietary modification, or other therapies.

Early screening with BabyNEXT™ test can help parents and pediatrician to know whether to take proactive steps, sooner, to care for baby's health.

There are two types of Test:

Standard – It analyses 86 genes for 87 diseases (including 34 conditions of the Recommended Uniform Screening Panel RUSP) and 12 genes for more than 30 medications.

Extended – It analyses 220 genes for 222 diseases (including 34 conditions of the Recommended Uniform Screening Panel RUSP) and 12 genes for more than 30 medications.

B. What is newborn screening

Almost every child is screened for certain medical conditions shortly after birth. Commonly known as newborn screening, this public health program helps identify babies who may be at an increased risk for serious, but treatable, inherited conditions soon after birth or in childhood.

Most babies who are born with these conditions appear healthy at first. Without early screening, a condition may not be discovered until symptoms appear and it may be too late to prevent serious health consequences. Proactive screening can help parents and pediatricians to identify conditions early in life, so that treatment can be started immediately.

Newborn screening is currently performed only for selected conditions which can be analyzed by biochemical assays from blood, and for which treatment options exist[1]. Each country determines which conditions babies will be screened for, so different countries may test for different conditions. In general, most countries screen for 34 conditions that are recommended. This is also known as the Recommended Uniform Screening Panel (RUSP) [2,3]. BabyNEXT™ is a more extensive newborn screen. It screens for every condition on the RUSP and all state panels, as well as 188 additional conditions that can benefit from early detection.

The newborn screening covered by the National Health System (NHS) primarily uses biochemical analysis to look at analytes and markers in the blood. BabyNEXT™ is a genetic test that analyzes DNA to check for variations, or changes, that may cause certain diseases. Since many diseases cannot be detected via biochemical blood analysis, BabyNEXT™ is able to screen for a wider range of conditions than current NHS newborn screening.

C. BabyNEXT™ test results

"POSITIVE"

Pathogenic / Likely Pathogenic mutation(s) detected

Indicates that a well characterized disease-causing mutation(s) was identified. This result can indicate the best way to treat the disease.

Only **known pathogenic** and **likely pathogenic** mutations are reported

"NEGATIVE"

NO Pathogenic / Likely Pathogenic mutation(s) detected

Indicates that no disease causing mutations have been detected in the target genes screened.

A negative test result reduces, but doesn't eliminate, a child's risk of being affected by these genetic conditions or any other genetic conditions not covered by this test.

BabyNEXT™ is only intended to identify mutations in DNA that are very likely to cause genetic conditions (pathogenic or likely pathogenic). Variants of uncertain clinical significance (VOUS), i.e. findings with insufficient evidence available for unequivocal determination of clinical significance, are not reported with BabyNEXT™ test.

No single genetic test can detect all of the possible gene variants that could cause a condition. Parental DNA is only analyzed using targeted testing if indicated by the child's test results. A separate report will not be issued to the parent.

D. BabyNEXT™ test procedure

The DNA isolated from cells collected by a buccal swab is then amplified by PCR. Through a state-of-the-art technological process, named massive parallel sequencing (MPS), which uses Next Generation Sequencing (NGS) techniques with ILLUMINA sequencing instruments, genes included in BabyNEXT™ panels are completely sequenced (exons and adjacent intronic regions, ± 5 nucleotides) at high read depth. The resulting genetic sequences are analysed via an advanced bioinformatics analysis, to check the presence of potential mutations in the genes under investigation.

E. Test limitations

This examination analyses only the genetic diseases and the genes selected. The test does not detect other genetic diseases or genes that were not specifically targeted.

Moreover, the test cannot detect:

- Mutation located into intronic regions beyond +/- nucleotides from the breakpoints.
- Deletions, inversions or duplications of more than 20 bps.
- Germline mosaicism (i.e. mutations occurring only in the gametes)

The intrinsic limitation of the NGS methodology is the lack of coverage uniformity of each examined genetic region. Quantity and quality of the DNA extracted from samples is one of the potential causes of such lack of uniformity, which may lead to the lack of detection of gene mutations. Due to this limitation, NGS tests may not detect specific genetic mutations in the selected genes.

Some of these variations may not be identified or validated yet by the scientific community and, therefore, may not be classified as pathogenic variations at the time of analysis. For a correct interpretation of results, we need to have accurate information on the health of the patient and any pathology in the clinical history of the couple and their relatives. This information allows our geneticists to have a better interpretation of genetic results.

F. Results turnaround times

The test results will be available in about 15 working days. However, these terms can extend in case of test repetitions, diagnostic in-depth analyses or interpretative doubts.

G. Bibliography

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4. Fuller M, Meikle PJ, Hopwood JJ. Epidemiology of lysosomal storage diseases: an overview. In: Mehta A, Beck M, Sunder-Plassmann G, editors. Fabry Disease: Perspectives from 5 Years of FOS. Oxford: Oxford PharmaGenesis; 2006.
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