GOLDnatal®: non-invasive, high-sensitivity prenatal screening test

With the non-invasive prenatal test (NIPT) GOLDnatal® (Illumina® method), the foetal DNA circulating in the maternal venous blood undergoes the following tests:

- Chromosome anomalies:
Trisomies 21, 18 and 13

- Sex Chromosome or gonosomal aneuploidies
Monosomy X (Turner syndrome)
Triple-X syndrome
Klinefelter syndrome (XXY)
Jacobs syndrome (XYY)

- Gender test

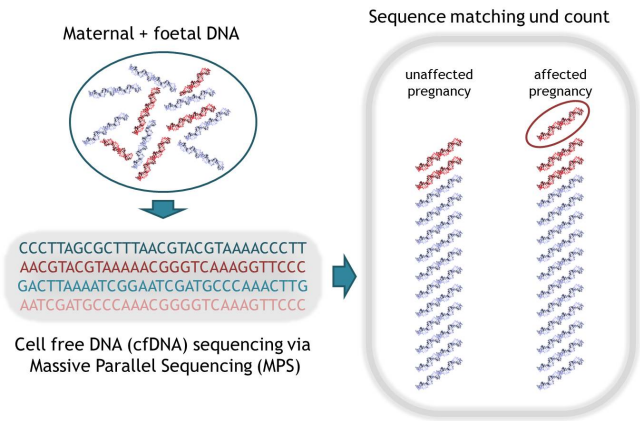
GOLDnatal® can be carried out from the 10th week of pregnancy (9+0 WOP), and is also suitable for twin and IVF pregnancies.
The standard test does not include micro-deletion screening, but this option is additionally available upon request.

Analytics

Method

The blood of a pregnant woman mainly contains maternal DNA. A small part of it, however, comes from the foetus. The more advanced the pregnancy is, the more foetal DNA is found in the maternal blood. To isolate as much foetal cell-free DNA (cfDNA) as possible, the mother's DNA is prevented from being released from the blood cells by means of a stabiliser inside the Streck® vacutainers.
Using *genome-wide massive parallel sequencing* (MPS), all fragments of the cfDNA so obtained are multiplied and sequenced (*Fig. 1*).

Fig. 1 Isolation, sequencing and screening of foetal, cell-free DNA from the maternal blood.



The isolated sequences are compared using bioinformatics algorithms with a reference genome and the number of copies per chromosome is determined. Using the Verinata® method, a *Normalized Chromosome Value* is calculated for each screened chromosome. In this way, any fluctuations during the runs are reduced so that a higher level of precision can be achieved.

Reliability and limitations

Reliability

Like all NIPTs, GOLDnatal® is a screening procedure, not a diagnostic test.

According to recently published studies [*1,2*], GOLDnatal® has a very high level of specificity (>99%), i.e. there is a low incidence rate of false positive results. The sensitivity (percentage of correctly recognized positive results) is currently 99.49% to 100% for trisomy 21, 97.23% for trisomy 18, and 97.98% for trisomy 13. For sex chromosome aneuploidies (monosomy X, trisomy X, and Klinefelter syndrome) the sensitivity is somewhat lower at 95%. Sensitivity and specificity are, however, much higher than with a first trimester test (*Fig. 2*).

Fig. 2: Sensitivity comparisons between cfDNA-NIPT and first trimester screening methods for trisomy 21, 18 and 13. The data source is a prospective clinical study by M. Norton *et. al.* (2015)

Twin and multiple pregnancies

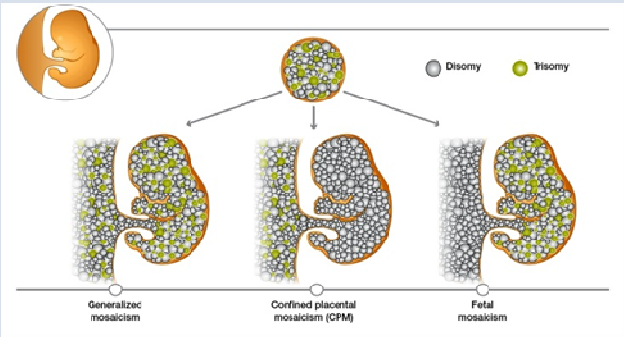
GOLDnatal® is suitable for twin pregnancies for the diagnosis of autosomal trisomies, but not for sex chromosome or gonosomal aneuploidies. For twin pregnancies, GOLDnatal® can only determine whether both foetuses are girls or at least one of them is a boy.

GOLDnatal® has not been validated for pregnancies with a foetal resorption (vanishing twin) nor for triplets or higher multiple pregnancies.

Mosaics

The foetal cfDNA in the mother's blood mainly comes from trophoblasts from the placenta. Around 1% to 2% of all pregnancies are affected by autosomal or gonosomal mosaics, which occur as a result of a defect during the mitotic processes. In most cases, the chromosome aberration is limited to the placenta, and the foetus is healthy. In rare cases, the segregation of the chromosomes or chromatids or a defective cell division can lead to monosomy or trisomy. Mosaics are difficult to detect and can lead to false positives or negative results (*Fig. 3*) in GOLDnatal®.

Fig. 3: Mosaics occur in various forms and can lead to false positives and false negatives in NIPTs.
[*Source: Illumina®-verifi®*]



Results

As already mentioned, GOLDnatal® is a screening test. By analyzing data, the results are classified as a high or low risk for each syndrome tested for. If the results appear to show an anomaly, a conclusive test using an invasive diagnostic tool is strongly advised.

Notification of results

If the results show any anomalies, the health care provider will be called in addition to receiving a written report.
Upon request, the patient will be sent a copy of the results without the gender information (please mark the corresponding option on the request form).

Repetition rate

In rare cases (<1%), in which GOLDnatal® does not produce a reliable result, it is possible to repeat the test without incurring any extra charge.

The test only screens for the described numeric chromosome anomalies; micro-deletions are not part of the standard test. These anomalies can, however, be analyzed upon request at extra charge. The predictive value for micro-deletions is considerably lower than for the standard anomalies because of their low prevalence and of the sub-chromosomal size.

How long does it take to get the results?

DNA sequencing is carried out twice a week in our laboratory. This means the average total processing time is between 4 working days.

Blood sample, advice

Blood sample collection and genetic advice are carried out by the health care provider.

Information

The laboratory can be contacted at any time for questions and information.

Literature/References

1. D.W. Bianchi *et al.*, Obstet. Gynecol. **2012;** 119:*890-901*
2. P.A Taneja *et al.*, Prenat. Diagn. **2016**; 26:*238-243*
3. M. Schmid *et al.*, Ultraschall in Med **2015**; 36:*507-510*
4. D.W. Bianchi *et al.*, Obstet. Gynecol. **2015;** 125:*375-382*
5. M.E. Norton et al., N. Engl. J. Med. **2015;** *372;17*

Analytic

Profile: 9547 **Price:** CHF 510.-	**GOLDnatal® Trisomy 21, 18, 13**
Profile: 9543 **Price**: CHF 610.-	**GOLDnatal® Trisomy 21, 18, 13, gonosomal aneuploidies**
Profile: 9545 **Price:** CHF 840.-	**GOLDnatal® Trisomy 21, 18, 13, gonosomal aneuploidies, microdeletion screening**

Material: 2 Streck® vacutainers, special sample test (order no. M7495)