BECAUSE LIFE BEGINS TODAY

CentoICU®
Who should consider CentoICU®?

- Parents and physicians providing treatment to newborns and children under 24 months admitted to the ICU and presenting with unclear symptomatology which can be part of a genetic condition, i.e.:
  - Bleeding Dyathesis
  - Blood Abnormalities (Anemia)
  - Bone Fragility
  - Failure to Thrive
  - Heart Abnormality/Arrhythmia
  - Hepatosplenomegaly
  - Hypotonia
  - Ichthyosis/Epidermolysis Bullosa
  - Metabolic Abnormalities
  - Microcephaly
  - Neutropenia
  - Abnormal Newborn Screening Results
  - Respiratory Failure
  - Skeletal Abnormalities/Craniosynostosis
  - Skin Fragility
  - Unclear Seizures

Why choose CentoICU®?

CentoICU® is our comprehensive NGS panel for the earliest and fastest diagnosis of critically ill newborns and children in intensive care units of hospitals. It offers:

- Short TATs: 15 days (CentoICU®) or 10 days (CentoICU® FAST)
- Add-on option of CentoArrayCyto® possible to complement copy number analysis with high density array
- Exhaustive coverage of the coding regions within more than 800 targeted genes
- Specialized technology that allows us to target genes that are clinically linked to the ACMG-recommended newborn screening conditions as well as conditions that have been nominated for the list
- Earlier detection of these conditions can also result in less invasive and lower cost treatments for patients
- Can be performed on as little as 1 CentoCard® (10 drops of blood), 1 mL EDTA blood, and 1 μg DNA

References:

1 Abnormal Acylcarnitine Profile, Amino Acidemia/Urea, Hyperbilirubinemia, Hyper-/Hypoinsulinism, Persistent Hypoglycemia, Organic Acidemia/Urea
2 CentoICU® includes genes to cover all ACMG core panel phenotypes for newborn screening except hearing loss
3 We recommend to complement CentoICU® with CentoArrayCyto® for increased sensitivity for genome wide structural variants, wherever analysis of structural variants may have a significant bearing on the phenotype.
Genetic testing for newborns or children <24 months admitted to the ICU

Severe genetic disorders encompass diseases with complex phenotypic presentations and severe disease courses. A precise diagnosis of the underlying condition is especially important in serious and life-threatening situations as found in the intensive care setting.

Newborns and children presenting severe metabolic, neurologic, gastrointestinal, or urogenital conditions need a fast and precise diagnosis to ensure rapid and efficient further diagnostic and therapeutic initiation. Up to one third of all babies and children admitted to the intensive care unit (ICU) have a genetic disease. For many of them early identification can make the difference for their immediate and later health.

CentoICU® is a comprehensive NGS panel that includes more than 800 genes, explicitly selected for the genetic testing of critically ill newborns and children under 24 months. CentoICU® is designed to address multiple genetic conditions that may present in the newborn or first childhood period, many with overlapping phenotypes and immediate implications for treatment initiation. It allows clinicians to utilize just one single test to provide an accurate diagnosis of newborn-related diseases.

Statistics on genetic disorders in newborns admitted to the ICU

› About 3-4% of newborns will be born with a genetic disease or major birth defect
› Approximately 1% of all babies will be born with a chromosomal abnormality which can cause physical problems and intellectual disabilities
› More than 20% of infant deaths are caused by birth defects or genetic conditions (e.g. congenital heart defects, abnormalities of the nervous system, or chromosomal abnormalities)
› 11.1% of pediatric hospital admissions are for children with genetic disorders and 18.5% are children with other congenital anomalies
› Approximately 10% of all adults and 30% of children in hospitals are there due to genetically related problems; 12% of adult hospital admissions are for genetic causes

Every moment counts.

CentoICU® FAST enables you to get your results within 10 days.

"We offer NGS sequencing of all targeted genes in CentoICU® with exhaustive coverage of the coding regions."
What genes are included in CentoICU®?

CentoICU® is designed for analysis of more than 800 genes and more than 100 associated conditions/phenotypes. The list of included genes has been developed by our expert medical team based on several selection criteria, i.e.:

- Early onset
- Severe disease
- ICU related symptomatology
- Diseases/syndromes of differential diagnostic value

**DISORDERS WITH POTENTIAL DIRECT THERAPEUTIC CONSEQUENCES**

<table>
<thead>
<tr>
<th>DISEASE</th>
<th>GENE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alagille syndrome</td>
<td>NOTCH2, JAG1</td>
</tr>
<tr>
<td>Alpha-Thalassemia</td>
<td>HBA1, HBA2</td>
</tr>
<tr>
<td>Arginase deficiency</td>
<td>ARG1</td>
</tr>
<tr>
<td>Beta-Thalassemia</td>
<td>HBB</td>
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<tr>
<td>Biotin-thiamine-responsive basal ganglia disease</td>
<td>SLC19A3</td>
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<tr>
<td>Biotinidase deficiency</td>
<td>BTD</td>
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<tr>
<td>Carnitine deficiency</td>
<td>SLC22A5</td>
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<tr>
<td>Cystic Fibrosis</td>
<td>CFTR</td>
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<tr>
<td>Dystonia DOPA responsive</td>
<td>GCH1</td>
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<tr>
<td>Factor VII deficiency</td>
<td>F7</td>
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<tr>
<td>Glucose transporter 1 deficiency</td>
<td>SLC2A1</td>
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<tr>
<td>Glutaric acidemia Type 1</td>
<td>GCDH</td>
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<tr>
<td>Hemophilia A</td>
<td>F8**</td>
</tr>
<tr>
<td>Hemophilia B</td>
<td>F9</td>
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<tr>
<td>Hereditary Fructose intolerance</td>
<td>ALDOB</td>
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<tr>
<td>Holocarboxylase synthetase deficiency</td>
<td>HLCS</td>
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<tr>
<td>MSUD</td>
<td>BCKDHA, BCKDHB, DBT</td>
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<tr>
<td>Non ketotic hyperglicinemia</td>
<td>GLDC</td>
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<tr>
<td>Phenylketonuria</td>
<td>PAH</td>
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<tr>
<td>Pompe disease</td>
<td>GAA</td>
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<tr>
<td>Primary coenzyme Q10 deficiency</td>
<td>COQ8A</td>
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<tr>
<td>Pyridoxamine 5 phosphate oxidase deficiency</td>
<td>PNPO</td>
</tr>
<tr>
<td>Pyridoxine-dependent epilepsy</td>
<td>ALDH7A1</td>
</tr>
<tr>
<td>Pyruvate carboxylase deficiency</td>
<td>PC</td>
</tr>
<tr>
<td>Tuberous sclerosis complex</td>
<td>TSC1</td>
</tr>
<tr>
<td>Tuberous sclerosis complex</td>
<td>TSC2</td>
</tr>
<tr>
<td>Tyrosinemia Type I</td>
<td>FAH</td>
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<tr>
<td>VLCAD deficiency</td>
<td>ACADVL</td>
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</tbody>
</table>

* List does not include all disorders covered by our panel
* This panel does not detect intronic inversions for F8.

What type of test results can you expect?

**POSITIVE RESULT**

Indicates that a well characterized and certain disease-causing mutation was identified. This result can help to assess the risk of experiencing certain symptoms and indicate the best way to treat the disease. A positive result may also identify family members who are at risk of having the mutation, therefore carrier testing may be recommended.

**INCONCLUSIVE RESULT**

Indicates a change in the DNA, but this change has not been proven thus far to be associated with any disorder. To clarify the clinical significance of the variant, testing of other family members may be helpful.

**NEGATIVE RESULT**

Does not necessarily rule out a disorder; the patient should be managed according to clinical symptoms. Further testing may be recommended.

For the full list of genes, please visit:

www.centogene.com/diagnostics/medical-reporting

For ordering, please visit:

www.centoportal.com
Your partner of choice

For further information and support, please contact our closest representative or our customer support team, easily accessible by phone or email.

[www.centogene.com](http://www.centogene.com)

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