

## ExomeNext-*Rapid* Provides Accurate and Fast Diagnosis

HIGH DIAGNOSTIC YIELD AND SHORT TURNAROUND TIME ENABLES  
IMPROVED CLINICAL DECISION MAKING IN THE NICU



A recent study published in *Genetics in Medicine* demonstrates how testing with Ambry's ExomeNext-*Rapid* led to early diagnosis and effective treatment decisions in critically ill newborn infants in the NICU.

### WHY THIS MATTERS TO YOU

A rapid, accurate genetic diagnosis for critically ill newborn infants is vital for both prognosis and clinical decision making. Ambry's ExomeNext-*Rapid*, with a high diagnostic yield and low turnaround time (8 days average in this study), can be superior to traditional genetic testing approaches when assessing neonatal patients with suspected genetic conditions.

### BACKGROUND

Neonatal patients are particularly appropriate for utilization of diagnostic exome sequencing (DES), as many Mendelian genetic diseases are known to present in this period of life but often with complex, heterogeneous features. This renders traditional genetic testing, which often requires a clinical or differential diagnosis, less useful.

In this collaborative study conducted with researchers from University of Pittsburgh Medical Center, we performed DES in a diverse neonatal population (from birth to 1 month of age at the time of testing), and demonstrated that roughly 38% of the patients were found to have pathogenic or likely pathogenic mutations. Our study highlights the life-saving potential for the use of DES in the diagnosis and treatment of an affected neonate within the first month of life.

As such, findings from this study support the use of DES, such as ExomeNext-*Rapid*, in the NICU for critically ill newborn infants when an early diagnosis is critical to guide the clinical management of these vulnerable patients.

### POINTS FOR YOUR PRACTICE

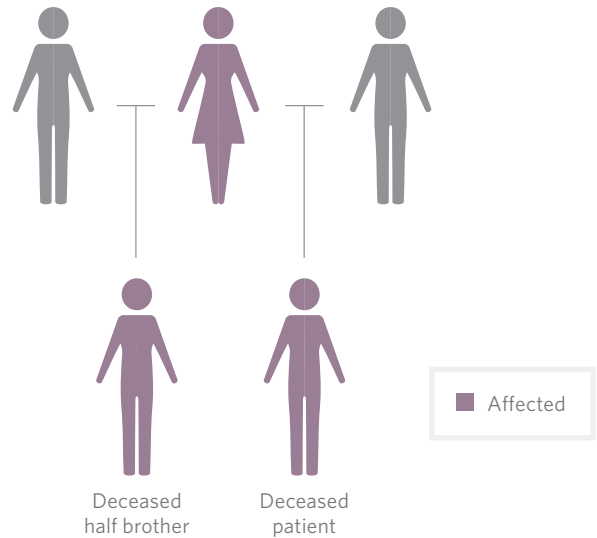
- The option for rapid testing with results in 8 days gives the medical provider information that can potentially improve outcomes for this vulnerable population.
- Ambry's ExomeNext-*Rapid* has a 38% diagnostic yield in this vulnerable population. All findings were in characterized genes, with the exception of one novel candidate gene finding.
- Diagnostic exome sequencing in neonates may be considered as the first-line test for diagnosing critically ill newborns.

## CASE REPORT

Male proband was delivered via cesarean section at 38 5/7 weeks after a pregnancy complicated by intrauterine growth restriction and decreased movements

At birth, baby presented with low respiratory response and very limited spontaneous movement

Baby had high arched palate and persistently elevated hemidiaphragm; however imaging studies were normal



## DES Testing and Results

## Findings

- Likely pathogenic *SOX10* alteration, c.523C>T (p.P175S), was identified
  - Alteration associated with peripheral demyelinating neuropathy, central dysmyelination, Waardenburg syndrome with or without Hirschsprung disease
  - Alteration is located in a mutation hot spot where similar amino-acid changes have been observed.<sup>2</sup>

## Clinical Decision

- Previous reported cases of *SOX10* alterations noted patients having respiratory depressions without any recovery of function
- Given the poor prognosis and expected outcome, family made the difficult decision to withdraw ventilator support

## Follow-up

- Based on the information obtained in this pregnancy via whole-exome sequencing, prenatal testing was conducted in a subsequent pregnancy, confirming a healthy fetus
- A healthy baby boy was delivered at 37 weeks

## REFERENCES

1. Powis, Z *et al.* Exome sequencing in neonates: diagnostic rates, characteristics, and time to diagnosis. *Genet Med.* 2018 [Epub ahead of print.]
2. Wissmuller S, *et al.* The high-mobilitygroup domain of Sox proteins interacts with DNA-binding domains of many transcription factors. *Nucleic Acids Res.* 2006;34:1735-1744.