Rhizomelic Chondrodysplasia Punctata: Sequencing Panel

Test Code: MM610
Turnaround time: 6 weeks
CPT Codes: 81479 x1

Condition Description

Rhizomelic chondrodysplasia punctata (RCDP) is a group of peroxisomal disorders that affects many parts of the body. Characteristic features include disproportionate shortening of bones of the upper arms and thighs (rhizomelia), specific bone changes seen on X-ray (punctate calcifications in cartilage), congenital cataracts, growth deficiency, distinctive facial features, and severe intellectual disability and developmental delay. Additionally, most children with this condition have respiratory tract infections, seizures, and may not live past the first decade of life. Some individuals may present with less severe symptoms that constitute a milder form of RCDP.

There are three different types of Rhizomelic Chondrodysplasia Punctata; type one is the most common. Types one, two, and three are caused by mutations in the \textit{PEX7}, \textit{GNPAT} (\textit{DHAPAT}), and \textit{AGPS} genes, respectively. RCDP is inherited in an autosomal recessive pattern and is estimated to affect less than 1 in 100,000 people.

References:

3. OMIM (Type 1): [http://www.omim.org/entry/215100](http://www.omim.org/entry/215100)
   - OMIM (Type 2): [http://www.omim.org/entry/222765](http://www.omim.org/entry/222765)
   - OMIM (Type 3): [http://www.omim.org/entry/600121](http://www.omim.org/entry/600121)

Genes

\textit{AGPS, GNPAT, PEX7}

Indications

This test is indicated for:

- Confirmation of a clinical diagnosis of Rhizomelic Chondrodysplasia Punctata.

Methodology

**Next Generation Sequencing:** In-solution hybridization of all coding exons is performed on the patient's genomic DNA. Although some deep intronic regions may also be analyzed, this assay is not meant to interrogate most promoter regions, deep intronic regions, or other regulatory elements, and does not detect single or multi-exon deletions or duplications. Direct sequencing of the captured regions is performed using next generation sequencing. The patient's gene sequences are then compared to a standard reference sequence. Potentially causative variants and areas of low coverage are Sanger-sequenced. Sequence variations are classified as pathogenic, likely pathogenic, benign, likely benign, or variants of unknown significance. Variants of unknown significance may require further studies of the patient and/or family members.

Detection

**Next Generation Sequencing:** Clinical Sensitivity: Unknown. Pathogenic variants in the promoter region, some pathogenic variants in the introns and other regulatory element mutations cannot be detected by this analysis. Large deletions/duplications will not be detected by this analysis. Results of molecular analysis should be interpreted in the context of the patient's clinical/biochemical phenotype.

Analytical Sensitivity: \textasciitilde 99%.

Specimen Requirements

Submit both of the following specimens

* Preferred specimen type: Whole Blood

**Type: Whole Blood**

Specimen Requirements:
In EDTA (purple top) tube:

- Infants (<2 years): 2-3 ml
- Children (>2 years): 3-5 ml
- Older Children & Adults: 5-10 ml

Specimen Collection and Shipping: Ship sample at room temperature with overnight delivery.

**Type: Isolated DNA**

Specimen Requirements:

- In microtainer: 60 ug

Isolation using the Qiagen™ Puregene kit for DNA extraction is recommended.

Specimen Collection and Shipping: Refrigerate until time of shipment in 100 ng/ul of TE buffer. Ship sample at room temperature with overnight delivery.

**Related Tests**

- Individual sequencing is available for **PEX7**, **GNPAT**, and **AGPS**.