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Genetic Testing for Rhizomelic Chondrodysplasia Punctata

Clinical Features:

Rhizomelic Chondrodysplasia Punctata (RCDP) is a peroxisomal disorder characterized by disproportionately short stature primarily affecting the proximal parts of the extremities, congenital contractures, characteristic ocular involvement, severe intellectual disability and spasticity. Characteristic facial features include broad nasal bridge, epicanthus, high-arched palate, dysplastic external ears and micrognathia. RCDP presents in the neonatal period and most affected individuals die in the first decade of life, although milder forms of RCDP can present with variable growth and developmental delays and survival into adulthood (1).

Molecular Genetics:

Mutations in *PEX7* [OMIM#601757] account for more than 90% of patients with RCDP1 [OMIM#215100] (2). The finding of a deficiency of plasmalogens in red blood cells, increased plasma concentration of phytanic acid, and normal plasma concentration of very long chain fatty acids is consistently identified in individuals with PEX7 mutations (1). *PEX7* is one of sixteen *PEX* genes that are involved in mammalian peroxisome assembly.

Mutations in *GNPAT* [OMIM#222765] and *AGPS* [MIM#600121] account of less than 10% of patients with RCDP2 [OMIM#222765] and RCDP3 [OMIM#60012] respectively (2). PEX7 transports AGPS into the peroxisome, where AGPS and GNPAT partner on the luminal membrane surface.

Inheritance:

RCDP follows an autosomal recessive inheritance pattern. Therefore, parents of an affected child are most likely obligate carriers. Recurrence risk for carrier parents is 25%. The prevalence of RCDP1 is estimated to be less than 1 in 100,000.

Test methods:

Our RCDP panel includes full gene sequencing for the *PEX7, GNPAT* and *AGPS* genes. Our RCDP series employs testing of *PEX7, GNPAT* and *AGPS* genes in a sequential manner. Tier 1 is sequencing of *PEX7* followed by Tier 2 sequencing of *GNPAT* and *AGPS.* We offer mutation analysis of all 10 coding exons and intron/exon boundaries of *PEX7*, all 16 coding exons and intron/exon boundaries of *GNPAT,* and all 20 coding exons and intron/exon boundaries of *AGPS* by direct sequencing of amplification products in both the forward and reverse directions.

Rhizomelic Chondrodysplasia Punctata Sequencing Panel (*PEX7, GNPAT* and *AGPS* sequencing)

Sample specifications:	3 to10 cc of blood in a purple top (EDTA) tube
Cost:	$2650
CPT codes:	81407
Turn-around time:	4 weeks

Rhizomelic Chondrodysplasia Punctata Series

Sample specifications:	3 to10 cc of blood in a purple top (EDTA) tube
Cost:	$1200 – $3850
CPT codes:	see below
Turn-around time:	4 weeks (per Tier)

Tier		CPT codes	Cost
1	*PEX7* sequencing	81405	$1200
2	*GNPAT* and *AGPS* sequencing	81407	$2400

Results:

Results, along with an interpretive report, will be faxed to the referring physician. Additional reports will be provided as requested. All abnormal results will be reported by telephone.

References:

1. Braverman NE, D'Agostino MD, Maclean GE. Peroxisome biogenesis disorders: Biological, clinical and pathophysiological perspectives. Dev Disabil Res Rev 2013: 17: 187-196.
2. Itzkovitz B, Jiralerspong S, Nimmo G et al. Functional characterization of novel mutations in GNPAT and AGPS, causing rhizomelic chondrodysplasia punctata (RCDP) types 2 and 3. Hum Mutat 2012: 33: 189-197.