RNU4-2 Gene Sequencing

ReNU syndrome:

The RNU4-2 gene encodes U4 snRNA, a small nuclear RNA which forms a splicesosome complex along with other snRNAs and proteins to carry out splicing of RNA transcripts. De novo heterozygous variants within an 18 base-pair critical region of RNU4-2, in particular a recurrent insertion variant, n.64_65insT, have been reported in association with RNU4-2 syndromic neurodevelopmental disorder. Also known as ReNU syndrome (PMID: 38991538, 38821540), this condition is characterized by developmental delays, intellectual disability, unique facial features, gait differences, short stature, hypotonia, and seizures. It is estimated to account for up to 0.4% of individuals with neurodevelopmental disorders (PMID: 39358183).

Indications:

- Unexplained developmental delays or clinical findings that overlap with ReNU syndrome, such as intellectual disability, unique facial features, gait differences, short stature, hypotonia, and seizures
- Confirmation of diagnosis in a symptomatic individual
- Pre-symptomatic testing for at-risk relatives
- Prenatal diagnosis in families with an identified RNU4-2 variant

Methodology:

PCR-based Sanger sequencing of the single non-coding exon of the RNU4-2 gene

Clinical Sensitivity:

All previously reported RNU4-2 variants are detectable by Sanger sequencing.

Results:

Results can be positive, uncertain, or negative. Each test report includes a detailed interpretation of the genetic findings, the clinical significance of the result, and specific recommendations for clinical management and additional testing, if warranted. Results will be reported to the referring physician or health care provider as specified on the test requisition form.

Specimen:

- **Blood**: At least 3 mL whole blood in a lavender top (EDTA) tube
- **Saliva**: Saliva collected in an Oragene saliva kit. Please call 513-636-4474 for a free saliva collection kit.
- **Prenatal**: At least 20 mL of amniotic fluid or at least 30 mg chorionic villi or 2 flasks of cultured cells is needed. 3 mL of maternal blood in lavender top (EDTA) tube is needed for maternal cell contamination studies.
- **Skin fibroblast**: at least 0.5cm x 0.5cm x 0.5 cm (100 mg) tissue sample placed in a sterile container containing tissue transport media, RPMI solution, or sterile saline. Culturing of skin fibroblasts is done at an additional charge.
- **DNA**: 1 mcg of DNA extracted by a CLIA certified lab may be submitted.

Label the container with the patient's name, birth date, and date of collection. Ship all sample types at room temperature for overnight delivery.

Cincinnati Children's®
changing the outcome together

Genetics and Genomics Diagnostic Laboratory
CLIA#: 36D0656333
Phone: (513) 636-4474
Fax: (513) 636-4373
Email: LabGeneticCounselors@cchmc.org
www.cincinnatichildrens.org/genetics

Turnaround Time:

- 28 days

CPT Code:

- RNU4-2 sequence analysis: 81479

Please call 1-866-450-4198 for current pricing, insurance preauthorization or with any billing questions.

Shipping Instructions:

Please enclose test requisition with sample. **All information must be completed before sample can be processed.**

Place samples in styrofoam mailer and ship at room temperature by overnight Federal Express to arrive Monday through Saturday*.

Ship to:

Genetics and Genomics Diagnostic Laboratory
3333 Burnet Avenue NRB 1042
Cincinnati, OH 45229
513-636-4474

*For Saturday deliveries only: Please add "Dock 5" to the address and select the Saturday delivery check box on the shipping label (if applicable).

References:

Burns, V. F., & Radford, E. J. (2024). ReNU syndrome - a newly discovered prevalent neurodevelopmental disorder. Trends in genetics : TIG, 40(11), 914–916.

Chen, Y., et al. (2024). De novo variants in the RNU4-2 snRNA cause a frequent neurodevelopmental syndrome. Nature, 632(8026), 832–840.

Greene, D., et al. (2024). Mutations in the U4 snRNA gene RNU4-2 cause one of the most prevalent monogenic neurodevelopmental disorders. Nature medicine, 30(8), 2165–2169.