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An Overview of Coffin Siris Syndrome and ARID1B-Related Disorders

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Coffin Siris Syndrome is a rare inherited genetic disorder that is characterized by intellectual disability, developmental delays, cardiac anomalies, feeding difficulties, underdeveloped or absent fifth fingernails, sparse scalp hair, hearing and vision loss, frequent infections, and distinct facial features (Schrier Vergano et al., 1993). This condition was first described in 1970 by Dr. Coffin and Dr. Siris when three unrelated girls presented with similar findings including sparse scalp hair, absent fifth fingernails, distinct facial features, and developmental delays (Coffin, 1970). Since the initial description of Coffin-Siris syndrome we have been able to better understand the condition, genetic etiology, and management for these individuals. The further description of ARID1B-related disorder helped to identify individuals who were presenting similarly to Coffin Siris syndrome but were on the milder and more variable scale (Vergano et al., 1993). Coffin Siris syndrome and ARID1B-related disorder are both highly variable in their clinical presentation meaning individuals may only have a few of the described characteristics in different combinations (Schrier Vergano et al., 1993).

Coffin Siris syndrome was diagnosable based on clinical findings alone before we understood the genetic basis of the condition. Now we are able to do genetic testing in patients with suggestive clinical findings in order to confirm the diagnosis. There are 12 genes that have been identified as being associated with Coffin Siris syndrome when a pathogenic variant occurs in the gene (Schrier Vergano et al., 1993). These genes are responsible for encoding the BAF chromatin remodeling complex subunits which impact chromatin structure and gene expression (MedlinePlus, 2021). Chromatin helps to package DNA into chromosomes and can change gene expression as well (MedlinePlus, 2021). Among those genes ARID1B is the most common gene for individuals with Coffin Siris to have a pathogenic variant (MedlinePlus, 2021). The ARID1B gene is located on the chromosome 6 q arm and is responsible for the ARID1B-related disorder as well (Unique Rare Chromosome Disorder Support Group, 2014). An estimated 40% of individuals with Coffin Siris syndrome have an unknown genetic etiology (Schrier Vergano et al., 1993).

Coffin Siris syndrome and ARID1B-related disorder are inherited in an autosomal dominant manner (Schrier Vergano et al., 1993). Typically, individuals inherit half of their genetic information from their biological mother and half from their biological father resulting in two sets of genetic information. It only takes a pathogenic variant in one of two copies of the gene for an individual to be affected with the syndrome. This results in a 50% chance that an individual with this syndrome would pass down their non-working copy to offspring. Most individuals have a pathogenic variant as a result of a new mutation that has occurred for the first time in that person and was not inherited by their parents.

Management for individuals with Coffin Siris syndrome and ARID1B-related disorder is tailored to the individuals needs and clinical presentation. They may need to follow with multiple different medical specialties and therapies. Early intervention therapies like speech therapy, feeding therapy, ABA therapy, occupational therapy, and physical therapy can help these individuals improve on developmental

delays (Unique Rare Chromosome Disorder Support Group, 2014). Individuals will need to receive routine audiology and optometry evaluations to ensure hearing and vision loss is not occurring. Some individuals may need to be followed by cardiology, gastroenterology, and immunology depending on their needs and clinical symptoms.

Identifying individuals with Coffin Siris syndrome and ARID1B-related disorder is important so they can receive the surveillance and management necessary for health concerns they may be at risk for. Ensuring these patients and families receive genetic counseling can help them to understand the condition, risks, and management they may be facing down the road as well as getting necessary resources.

Coffin Siris syndrome and ARID1B-related disorder are very rare, complex, and highly variable genetic conditions. These patients may be very different from one another and may require different interventions. Identifying these individuals helps us to better treat them as well as deepen our understanding of the conditions. More research is needed for these two overlapping conditions in order to better understand their needs, differences, and treatment options.

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About the RCPU:

The Raymond C. Philips Research and Education Unit began in 1978 when the legislature established section 393.20, F.S., of what is now known as the "prevention" legislation. It is named after Raymond C. Philips, who was the Superintendent of Gainesville's Tacachale (formerly Sunland) Center for 38 years, and was an acknowledged state and national leader in services for mentally retarded persons. The Unit is located on the Tacachale campus and is funded through a contract with the Department of Children and Families and the Department of Health.

The purpose of the R.C.P.U. is to treat, prevent, and/or ameliorate disorders of intellectual disability through medical evaluations, education and research. The unit provides direct evaluations and counseling to families and promotes service, education, and prevention projects. Some of the conditions currently under study at the RCPU involve Angelman, Velo-Cardio-Facial, Prader-Willi, Fragile X, Williams and Smith-Lemli-Opitz syndromes.

The R.C. Philips Unit is a resource for all Floridians interested in the diagnosis, treatment and prevention of mental retardation. Staff members are available for consultation and for educational programs for health.

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