Clinical Genetics

AB093. Report of a *SMARCA4* variant identified in a patient with Coffin-Siris syndrome

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Background: Coffin-Siris syndrome (CSS, OMIM 614609) is a rare condition that affects multiple body systems. Hallmarks of this condition include developmental disability, abnormalities of the fifth fingers or toes, and characteristic facial features. Here, the case of a 4-year-old Chinese boy with lateral flaring and thick eyebrows, long eyelashes, coarse facies, left single palmar crease, absent of both fifth toenails, posterior cleft palate, umbilical hernia and congenital nystagmus is presented. The boy also has bilateral developmental dysplasia of the hip, which has not been reported in CSS.

Methods: Genomic DNA was extracted from peripheral blood samples collected from the patient and parents. Targeted next generation sequencing of the patient sample was performed on the Illumina MiSeq system using the TruSight One panel that covers >4,800 clinically relevant genes. Alignment and variant calling was carried out using the on-instrument MiSeq Reporter software, and the VCF file generated was annotated and filtered using WANNOVAR. The presence of the variant and the *de novo* status was confirmed by Sanger sequencing of patient and parental samples.

Results: A heterozygous c.3127C>T variant was detected in exon 23 of the *SMARCA4* gene in the patient. It was not present in his parents. The *de novo* variant is predicted to cause a p. (Arg1043Trp) missense substitution of a highly conserved amino acid in the SNF2-related domain of the SMARCA4 protein, and can be classified as likely pathogenic for CSS based on the ACMG/AMP 2015 guidelines. This variant is not in the Exome Sequencing Project, 1000 Genomes Project and Exome Aggregation Consortium databases, although it has been reported previously in a patient with CSS.

Conclusions: The *SMARCA4* gene encodes the ATP-hydroxylase containing subunits of the BAF complex and variants are expected to influence the ATP-hydrolase activity and affect downstream processes such as DNA packaging and gene expression.

Keywords: *SMARCA4*; Coffin-Siris syndrome (CSS); *de novo*; dominant; heterozygous

doi: 10.21037/atm.2017.s093

Cite this abstract as: Loke MF, Jamuar SS, Lim EC, Tan EC. Report of a SMARCA4 variant identified in a patient with Coffin-Siris syndrome. Ann Transl Med 2017;5(Suppl 2):AB093. doi: 10.21037/atm.2017.s093