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Identification of rare ADCY9 mutations and non-syndromic oral clefts in Puerto Ricans

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Today at the 45th Annual Meeting & Exhibition of the American Association for Dental Research, researcher Carmen Buxó-Martínez, University of Puerto Rico, San Juan, will present a study titled "Identification of Rare ADCY9 Mutations and Non-syndromic Oral Clefts in Puerto Ricans." The AADR Annual Meeting is being held in conjunction with the 40th Annual Meeting of the Canadian Association for Dental Research.

Adenylate cyclase 9 (ADCY9) was recently identified as a new susceptibility locus associated with non-syndromic cleft lip with or without cleft palate (nsCL/P) in China. About 15 babies/10,000 live births are born in Puerto Rico each year with nsCL/P. In this study, researcherers aimed to identify ADCY9 functional variant mutations in Puerto Ricans with nsCL/P.

Puerto Rican children with nsCL/P (n=177), ages 0-14 years, were recruited as cases. Sanger sequencing was carried out using cases' DNA samples to identify ADCY9 variants. Results were confirmed by running sequencing in both directions and by sequencing the parents of cases with variant mutations. The distribution of functional variant mutations seen in case families was compared with variants from controls: 1,000 Genomes Project (1kGP) Exome Variant Server (EVS), and 61K Exomes. The researchers used Sorting Intolerant From Tolerant (SIFT) and Polyphen2 programs to discriminate pathogenic/benign from functional variants.

Eight functional variants of ADCY9 were identified in cases: seven missense and one splice site mutation. Three mutations were found in exon 2, two in exon 7, and one in exons 4, 9 and 11. Missense/probably damaging mutations: rs52791170/K564Q (MAF= 3.6% vs. 1.9% controls) and rs372048350/A811V (MAF= 0.29% vs. 0.01% controls) was reported once and not identified in Puerto Ricans. The rs61731442/T236A (MAF=0.29%) missense mutation predicted as deleterious has not been found in Puerto Ricans and three times (MAF=0.48%) in European Americans (EA). The rs113187435/S661G (MAF=0.29% vs. 0.74% controls) missense mutation predicted as benign/tolerated has not been found in PR and EA. One missense/benign mutation was found in 66 cases (MAF=23% vs. 28% controls).

The researchers conclude that identification of rare mutations in PR and other populations may contribute to the list of variants in ADCY9 related to nsCL/P. Functional variants in ADCY9 should be identified in larger multiethnic case-control studies to determine its role in the etiology of nsCL/P.

More information: This is a summary of oral presentation #0832, "Small Molecule Replacement Therapy to Rescue Craniofacial Defects," which will be presented on Friday, March 18, 2016, 8:15 a.m. - 8:30 a.m. at the Los Angeles Convention Center, room #408B.

Provided by International & American Associations for Dental Research