Genetic variants in S-adenosyl-methionine synthesis pathway and nonsyndromic cleft lip with or without cleft palate in Chile

Por: Salamanca, C (Salamanca, Carlos)[1,2,3]; Gonzalez-Hormazabal, P (Gonzalez-Hormazabal, Patricio)[4]; Recabarren, AS (Recabarren, Andrea S.)[1]; Recabarren, PA (Recabarren, Pamela A.)[1]; Pantoja, R (Pantoja, Roberto)[5,6]; Leiva, N (Leiva, Noemi)[7]; Pardo, R (Pardo, Rosa)[8,9,10]; Suazo, J (Suazo, Jose)[1]

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Abstract

Background TheS-adenosyl-methionine (SAM) availability is crucial for DNA methylation, an epigenetic mechanism involved in nonsyndromic cleft lip with or without cleft palate (NSCL/P) expression. The aim of this study was to assess the association between single-nucleotide polymorphisms (SNPs) of genes involved in SAM synthesis and NSCL/P in a Chilean population. Methods In 234 cases and 309 controls, 18 SNPs inAHCY,MTR,MTRR, andMAT2Awere genotyped, and the association between them and the phenotype was evaluated based on additive (allele), dominant, recessive and haplotype models, by odds ratio (OR) computing. Results Three deep intronic SNPs ofMTRshowed a protective effect on NSCL/P expression: rs10925239 (OR 0.68;p = 0.0032;q = 0.0192), rs10925254 (OR 0.66;p = 0.0018;q = 0.0162), and rs3768142 (OR 0.66;p = 0.0015;q = 0.0162). Annotations in expression database demonstrate that the protective allele of the three SNPs is associated with a reduction ofMTRexpression summed to the prediction by bioinformatic tools of its potentiality to modify splicing sites. Conclusions The protective effect against NSCL/P of these intronicMTRSNPs seems to be related to a decrease in MTR enzyme expression, modulating the SAM availability for proper substrate methylation. However, functional analyses are necessary to confirm our findings. Impact

SAM synthesis pathway genetic variants are factors associated to NSCL/P. This article adds new evidence for folate related genes in NSCL/P in Chile. Its impact is to contribute with potential new markers for genetic counseling.

Palabras clave

KeyWords Plus:FOLATE METABOLISM; ASSOCIATION; POLYMORPHISMS; METHYLATION; CLONING; INHERITANCE; DISCOVERY; REDUCTASE; FAMILIES; RISKS

Información del autor

Dirección para petición de copias: Suazo, J (corresponding author)

Univ Chile, Sch Dent, Inst Res Dent Sci, Santiago, Chile.

Direcciones:

[1] Univ Chile, Sch Dent, Inst Res Dent Sci, Santiago, Chile

[2] Univ La Frontera, Res Ctr Dent Sci CICO, Dent Sch, Santiago, Chile

[3] Univ Adventista Chile, Chillan, Chile

[4] Univ Chile, Sch Med, Inst Biomed Sci, Human Genet Program, Santiago, Chile

[5] Hosp Clin San Borja Arriaran, Unit Oral & Maxillofacial Surg, Santiago, Chile

[6] Univ Chile, Sch Dent, Dept Oral & Maxillofacial Surg, Santiago, Chile

[7] Univ Chile, Sch Dent, Unit Maxillofacial Malformat, Santiago, Chile

[8] Univ Chile, Sect Genet, Hosp Clin, Santiago, Chile

[9] Univ Chile, Unit Neonatol, Hosp Clin, Santiago, Chile

[10] Hosp Dr Sotero del Rio, Unit Genet, Santiago, Chile

Direcciones de correo electrónico:jsuazo@odontologia.uchile.cl

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