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Association between rs3833912/rs16944 haplotypes and risk for Cerebral Palsy in Mexican children

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Background: Perinatal asphyxia in the neonatal brain triggers a robust inflammatory response in which nitric oxide (NO) generation plays a hazardous role. Increased levels of NO can be maintained by the activity of inducible NO synthase (NOS2A) on its own or activated by IL-1beta (IL-1 β) gene transcription and positive back stimulation of the NOS2 (CCTTT)n microsatellite by IL-1 β , thus potentiating brain injury after ischemic perinatal asphyxia. We investigated whether the risk for cerebral palsy (CP) increases when an expansion of the -2.5 kb (CCTTT)n microsatellite in the NOS2A gene and a single nucleotide polymorphism (SNP) in -C511T of the IL- IL-1 β gene promoter occurs in patients after perinatal hypoxic-ischemic encephalopathy.

Methods: Genomic DNA was purified from peripheral leukocytes of 48 patients with CP and of 57 healthy control children. IL-1 β SNP genotypes were established using a real-time PCR technique and fluorogenic probes and were validated by restriction fragment length polymorphism (RFLP) analysis using the Aval restriction enzyme. The length of the CCTTTn microsatellite in the NOS2 gene promoter was determined by automated sequencing.


Results: The 14-repeat long allele of the CCTTTn NOS2A microsatellite was present in 27% of CP patients vs 12.3 % of controls, showing an odds ratio (OR)=2.6531 and 95 % confidence interval (CI)= 0.9612–7.3232, P<0.0469. The -511 TT genotype frequency showed an OR = 2.6325 (95% CI = 1.1348–6.1066), P = 0.0189. Interestingly, the haplotype CCTTT14/TT showed an OR =9.561; 95 %, CI = 1.1321–80.753; P = 0.0164.

Conclusions: The haplotype (CCTTT)14/TT, formed by the expansion of the -2.5 kb (CCTTT)n microsatellite in the NOS2A gene promoter and the -511 C α T SNP of the IL-1 β gene promoter, might be a useful marker to identify patients who are at high risk for developing CP after hypoxic ischemic encephalopathy.

Speaker Biography

Juan Antonio Gonzalez Barrios is a highly professional Medical Doctor, Cellular and Molecular Neurobiologist and a Health System Manager at Mexico. He completed his bachelor's degree in National Polytechnic Institute, Mexico City, Mexico. He completed his MSc. Degree and PhD. Degree in Cellular and Molecular Neurobiology at Center for Research and Advances Studies, Mexico City, Mexico. He completed his Master's in Health System Management at National Autonomous University of Mexico, Mexico City, Mexico. He is currently serving as Head of Genomic Medicine Laboratory, Regional Hospital "October 1st, Mexico City, Mexico.

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