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Absence of the E2 allele of apolipoprotein in Amerindians

Abstracts

Determination of the ApoE allele distribution in five South American Amerindian tribes revealed absence of the ApoE2 allele, accompanied by high ApoE3 and low ApoE4 allele frequencies for most tribes, a distribution only previously reported for the Inuit Eskimo from Greenland.

A determinação da distribuição do alelo ApoE em cinco tribos de índios sulamericanos revelou ausência do alelo ApoE2, acompanhada por freqüência alta do alelo ApoE3 e baixa do alelo ApoE4 na maioria das tribos, uma distribuição previamente relatada apenas para os esquimós Inuit da Groenlândia.

SHORT COMMUNICATION

Absence of the E2 allele of apolipoprotein in Amerindians

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ABSTRACT

Determination of the ApoE allele distribution in five South American Amerindian tribes revealed absence of the ApoE2 allele, accompanied by high ApoE3 and low ApoE4 allele

frequencies for most tribes, a distribution only previously reported for the Inuit Eskimo from Greenland.

INTRODUCTION

Apolipoprotein E (apoE) plays a central role in lipoprotein metabolism thus affecting lipid homeosta-3sis in many tissues (Mahley, 1988). Three common isoforms have been described (apoE2, E3 and E4) encoded by the alleles e2, e3 and e4, respectively (Utermann *et al*., 1977; Davignon *et al*., 1988; Hallman *et al*., 1991). Recent studies have linked the e2 allele to type III hyperlipidemia (Utermann, 1987), and the e4 variant to coronary heart disease (CHD) (Cumming and Robertson, 1984; Davignon *et al*., 1988) and Alzheimer's disease (AD) (Strittmatter *et al*., 1993; Saunders *et al*., 1993). Consequently, the frequency of apoE genotypes has been determined in several populations such as Caucasians. Blacks, Asians and North American Indians (Kamboh *et al*., 1990, 1991; Hallman *et al*., 1991; Kao *et al*., 1995; Sandholzer *et al*., 1995; Scheer *et al*., 1995; Benkmann *et al*., 1996; Kataoka *et al*., 1996). We determined the apoE allele distribution in five Amerindian tribes from the Brazilian Amazon region, and found that it differed from all other populations thus far studied, except for the Inuit Eskimo (Gerdes *et al*., 1996).

SUBJECTS AND METHODS

Populations sampled

The Amerindian sample comprised 121 individuals from five Brazilian Amazonian tribes: 23 Yanomami, 25 Wayana-Apalai, 26 Wayampi, 21 Arara and 26 Kayapo. The individuals studied were apparently unrelated, except for the Wayampi and the Arara among whom there are high inbreeding levels, making it difficult to select only unrelated individuals.

DNA analysis

DNA samples were obtained from leukocytes by phenol-chloroform extraction and ethanol precipitation and then PCR amplified, using primers and conditions described by Hixson and Vernier (1990). Genotypes were determined by restriction fragment length polymorphism (RFLP) analysis after disgestion with *Hha*I restriction enzyme and polyacrylamide gel electrophoresis. ApoE allele frequencies were determined by gene counting.

RESULTS AND DISCUSSION

The frequencies of apoE alleles obtained for the Amerindians are compared with other populations in Table I. ApoE3 alelle had the highest frequency (0.8306), which is in accordance with frequencies described for Tyroleans, French Canadian Caucasians, Chinese and Alaskan natives (Hallman *et al*., 1991; Kao *et al*., 1995; Scheer *et al*., 1995; Robitaille *et al*., 1996). ApoE4 allele had a lower frequency among the Amerindians when compared to South African Khoi San, Papua-New Guineans, Australian aborigines and African blacks (Nigerians, Sudanese) (Kamboh *et al*., 1990, 1991; Hallman *et al*., 1991; Sandholzer *et al*., 1995; Benkmann *et al*., 1996) who are known to have high ApoE4 frequencies. The ApoE2 allele was absent in the Amazonian Amerindian populations, a fact that has also been described for an Inuit population residing in Greenland's southeast coast (Gerdes *et al*., 1996), while a low ApoE2 frequency (0.02) has been found in Alaskan natives (Scheer *et al*., 1995). ApoE allele frequencies were homogeneous between the different tribes (Table II) except for the Wayampi, where the ApoE4 variant exhibited a frequency (0.423) compared to the highest reported for any human ethnic group to date

(Kamboh *et al*., 1990, 1991; Hallman *et al*., 1991; Sandholzer *et al*., 1995; Benkmann *et al*., 1996). This difference cold be explained by isolation and genetic drift. A heterogeneous distribution of genetic polymorphic markers has been observed in these populations when studying other genetic systems, such as the a-globin gene haplotypes and several variable number of tandem repeats (VNTRs) (Zago *et al*., 1995, 1996).

Table I

- Distribution of ApoE alleles in different human populations.

Table II

- Distribution of ApoE alleles in five Amerindian populations (No. = number of chromosomes).

The frequencies of ApoE alleles in a population may have implications regarding CHD and AD prevalence. The ApoE2 allele is usually associated with lower total cholesterol (TC) and low density lipoprotein (LDL) levels and higher high density lipoprotein (HDL) levels, whereas the ApoE4 allele is usually linked to effects opposite to those described for the ApoE2 allele besides being associated with AD in several populations (Cumming and Robertson, 1984; Davignon *et al*., 1988; Hallman *et al*., 1991; Saunders *et al*., 1993; Strittmatter *et al*., 1993). Therefore, the absence of the ApoE2 allele as well as the high ApoE4 frequency among the Wayampi could play a role in the prevalence of these diseases in this population, a point which should be further investigated.

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RESUMO

A determinação da distribuição do alelo ApoE em cinco tribos de índios sulamericanos revelou ausência do alelo ApoE2, acompanhada por freqüência alta do alelo ApoE3 e baixa do alelo ApoE4 na maioria das tribos, uma distribuição previamente relatada apenas para os esquimós Inuit da Groenlândia.

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Benkmann, H.G., Agarwal, D.P., Vasisht, S., Srivastava, L.M. and **Goedde, H.W.** (1996). Distribution of apolipoprotein E genotypes in Asian Indians, Hungarians, and Papua New Guineans. *Anthropol. Anz. 54*: 31-34.

Cumming, A.M. and **Robertson, F.R.** (1984). Polymorphism at the apoprotein-E locus in relation to risk of coronary disease. *Clin. Genet. 25*: 310-313.

Davignon, J., Gregg, R.E. and **Sing, C.F.** (1988). Apoliprotein E polymorphism and atherosclerosis. *Artherosclerosis 8*: 1-21.

Gerdes, L.U., Gerdes, C., Hansen, P.S., Klausen, I.C., Faergeman, O. and **Dyerberg, J.** (1996). The apolipoprotein E polymorphism in Greenland Inuit in its global perspective. *Hum. Genet. 98*: 546-550.

Hallman, D.M., Boerwinkle, E., Saha, N., Sandholzer, C., Menzel, H., Császár, A. and **Utermann, G.** (1991). The apolipoprotein E polymorphism: a comparison of allele frequencies and effects in nine populations. *Am. J. Hum. Genet. 49*: 338-349.

Hixson, J.E. and **Vernier, D.T.** (1990). Restriction isotyping of human apolipoprotein E by gene amplification and cleavage with Hhal. *J. Lipid Res. 31*: 545-548.

Kamboh, M.I., Bhatia, K.K. and **Ferrel, R.E.** (1990). Genetic studies of human apoliproteins: XII. Population genetics of apolipoproteins in Papua New Guinea. *Am. J. Hum. Biol. 2*: 17-23.

Kamboh, M.I., Serjeanston, S.W. and **Ferrel, R.E.** (1991). Genetic studies of human apolipoproteins. XVIII. Apolipoprotein polymorphism in Australian Aborigines. *Hum. Biol. 63*: 179-186.

Kao, J.T., Tsai, K.S., Chang, C.J. and **Huang, P.C.** (1995). The effects of apolipoprotein E polymorphism on the distribution of lipids and lipoproteins in the Chinese population. *Atherosclerosis 114*: 55-59.

Kataoka, S., Robbins, D.C., Cowan, L.D., Go, O., Yeh, H.L., Devereux, R.B., Fabsitz, R.R., Lee Welty, T.K. and **Howard, B.V.** (1996). Apolipoprotein E polymorphism in American Indians and its relation to plasma lipoproteins and diabetes. The Strong Heart Study. *Arterioscler. Thromb. Vasc. Biol. 16*: 918-925.

Mahley, R.W. (1988). Apoliprotein E: cholesterol transport protein with expanding role in cell biology. *Science 240*: 622-633.

Robitaille, N., Cormier, G., Couture, R., Bouthillier, D., Davigson, J. and **Perusse, L.** (1996). Apolipoprotein E polymorphism in a French Canadian population of northeastern Quebec: allele frequencies and effects on blood lipid and lipoprotein levels. *Hum. Biol. 68*: 357-370.

Sandholzer, C., Delport, R., Vermaak, H. and **Utermann, G.** (1995). High frequency of the apo E4 allele in Khoi San from South Africa. *Hum. Genet. 95*: 46-48.

Saunders, A.M., Strittmatter, W.J., Schmechel, D., St. George-Hyslop, P.H., Pericak-Vance, M.A., Joo, S.H., Rosi, B.L., Gusella, J.F., Crapper-MacLachlan, D.R., Alberts, M.H., Hulette, C., Crain, B., Goldgaber, D. and **Roses, A.D.** (1993). Association of apolipoprotein E (allele E4) with late-onset familial and sporadic Alzheimer's disease. *Neurology 43*: 1467-1472.

Scheer, W.D., Boudreau, D.A., Malcon, G.T. and **Middaugh, J.P.** (1995). Apoliprotein E and atherosclerosis in Alaska Natives. *Atherosclerosis 114*: 197-202.

Strittmatter, W.J., Weisgraber, K.H., Huang, D.Y., Dong, L.-M., Salvesen, G.S., Pericak-Vance, M., Schmechel, D., Saunders, A.M., Goldgaber, D. and **Roses, A.D.** (1993). Binding of human apolipoprotein E to synthetic amyloid beta peptide: isoform-specific effects and implications for late-onset Alzheimer disease. *Proc. Natl. Acad. Sci. USA 90*: 8098-8102.

Utermann, G. (1987). Apolipoprotein E polymorphism in health and disease. *Am. Heart J. 113*: 433-440.

Utermann, G., Hess, M. and **Steinmetz, A.** (1977). Polymorphism of apolipoprotein E and occurrence of dysbetalipoproteinemia in man. *Nature 269*: 604-607.

Zago, M.A., Santos, E.J.M., Clegg, J.B., Guerreiro, J.F., Martinson, J.J., Norwich, J. and **Figueiredo, M.S.** (1995). a-Globin gene haplotypes in South American Indians. *Hum. Biol. 67*: 535-546.

Zago, M.A., Silva, W.A., Tavella, M.H., Santos, S.E.B., Guerreiro, J.F. and **Figueiredo, M.S.** (1996). Interpopulational and intrapopulational genetic diversity of Amerindians as revealed by six variable number of tandem repeats. *Hum. Hered. 46*: 274-289.

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