V World Congress on Mountain Medicine and High Altitude Physiology

Congreso Mundial de Medicina de Montaña
VIII Congreso SEMAM

Barcelona, April 18-22, 2002

Late Abstracts & Additional Information

2002, the International Year of the Mountains

shifted to rightward within the range of that equation. These phenomena may offer a clue for solving the mechanism of high altitude acclimatization.

161. MITOCHONDRIAL DNA HAPLOGROUP B PREDOMINANCE IN THE AYMARA POPULATION LIVING IN THE ANDES

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The objective of this study was to know whether there are genetic markers in the amerindian Aymara population living in the Andes that would predispose this population to a better adaptation to the high altitude prevailing in this area. The mitochondrial DNA (mtDNA) was analyzed in populations that were born and are still living around 3,800 m of altitude, either in La Paz (45 subjects) or in rural areas of the altiplano (90 subjects). Four mtDNA haplogroups, A, B, C and D have been defined to characterize the amerindian populations. In the Aymara population, the prevalence of the B haplogroup was impressing: about 85% in the urban area and more than 95% in the rural area. This predominance could be related either to a founder effect or to a selection over the years, due to a better adaptation of this haplogroup to altitude. Sequencing the D-loop hypervariable mtDNA region revealed several differences among the analyzed subjects. This favors the hypothesis of a better adaption that might have induced a selection over the generations. Whether or not and if so, how, the differences in mtDNA sequence might interfere in this adaptation remains to be determined.

164. ACTIVIDAD ATPasa EN ANIMALES DE ALTURA Y DE NIVEL DEL MAR

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Objetivos: Comparar la actividad de ATPasa, y la relación ADP:O (P:O), Control respiratorio (RCR) en cobayos de altura Morococha (4,540 m.s.n.m.) y de nivel del mar (150m.s.n.m.) y observar si existe alguna diferencia por efecto de la altura. **Metodología:** El estudio se realizó en 60 cobayos machos con un peso promedio de 400 a 450 gramos. Las mitocondrias de corazón fueron obtenidas por centrifugación diferencial a 4° C de un homogeneizado de tejido: la relación P:O y Control Respiratorio (RCR) fueron medidos polarográficamente por el método de Tyler, la concentración de ATPasa se midió por el método de Holton et al. **Resultados:** Los valores promedios obtenidos para los 60 cobayos fueron:

	Altura (n=30)		Nivel del mar (n=30)	
	P:O	RCR	P:O	RCR
Glutamato + Malato (μmol $O_2 \cdot mg^{-1}$ prot $\cdot h^{-1}$)	2.93	6.0	2.90	6.02
Piruvato + Malato (μmol $O_2 \cdot mg^{-1}$ prot $\cdot h^{-1}$)	2.70	4.80	2.60	5.0
Actividad ATPasa (μmol P$\cdot mg^{-1}$ prot $\cdot h^{-1}$)	64.50		57.50	

Conclusiones: Los resultados sugieren que los cobayos de altura han desarrollado la habilidad de realizar la fosforilación oxidativa en forma mas eficiente y el ligero incremento observado en la actividad ATPasa nos indica que tal vez se realizan pequeños ajustes para mantener el equilibrio dentro del medio ambiente mitocondrial.

POSTER 161

2002

Mitochondrial DNA Haplogroup B predominance in the Aymara Population living in the ANDES

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INTRODUCTION

The objective of this study is to know whether there are genetic markers in the amerindian Aymara population living in the Andes around the city of La Paz that would predispose this population to an easier adaptation to the high altitude prevailing in this area (3,800 to 4,200 m). The studied subjects were born and are still living in the Altiplano in the La Paz region.

Since mitochondrial DNA contains genes coding for essential respiratory chain subunits responsible for most oxygen consumption in the cell, we have analyzed mtDNA diversity in this population.

Contemporary Ameridian mtDNA lineages are characterized by four mtDNA markers that define haplogroups A, B, C and D (Ballinger et al, 1992) in the human mtDNA genome (figure 1). We have first determined the mtDNA haplogroups of the selected subjects. We have then sequenced their mtDNA control region that is representative of population diversity.

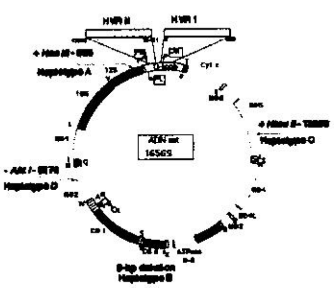


Figure 1 : Human mtDNA genome, showing the approximate location of the four mtDNA markers that delineate the Ameridian haplotypes A, B, C and D and the hypervariable regions (HVR I and II).

SUBJECTS

Two types of collection campaign have been performed for this study :

- In the city of La Paz : 46 medical students from the San Andres medicine faculty. No special selection related to their birth origin was made.

- In small Altiplano communities in the vicinity of La Paz : 18 samples from subjects originated from Tuni and 42 from Viacha.
- 126 samples from the rural area of Ventilla.

All blood samples were obtained as part of medical examinations carried out by bolivian physicians in joint programe with the French government.

Since mtDNA is only transmitted by the mother, only one descent of the same mother was taken into consideration and retained for the mtDNA analysis.

METHODS

Samples of 10-20 ml of whole blood per person was collected in sodium heparin anticoagulant tubes. Total genomic DNA was extracted by standard techniques.

Four mtDNA fragments were amplified between the following mtDNA positions :
- nucleotides 563 to 727 for haplotype A,
- nucleotides 8195 to 8316 for haplotype B,
- nucleotides 13209 to13364 for haplotype C,
- nucleotides 5100 to 5275 for haplotype D

The size of amplicons prepared for identification of haplotype B was directly analyzed on 3% NuSieve™ agarose gel electrophoresis. Other amplicons were treated according to the manufacturer instructions by restriction enzymes : *HaeIII*, *HincII* or *AluI* for the haplotypes A, C and D, respectively and analyzed by gel electrophoresis (fig. 2).

Templates encompassing the mtDNA hypervariable segments of the control region were amplified as double-stranded PCR segments between mtDNA positions 4 and 406 or 15498 and 16401, respectively. Each one was sequenced in both directions.

Sequence alignments and comparisons to the Cambridge reference sequence (CRS) were performed using the Clustal W program :
(NPS@npsa-pbil.ibcp.fr/CLUSTALW)

HAPLOGROUP ANALYSIS

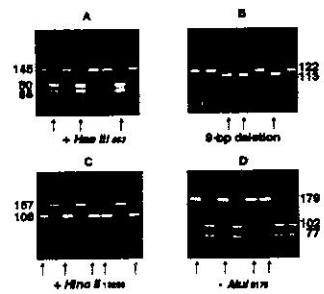
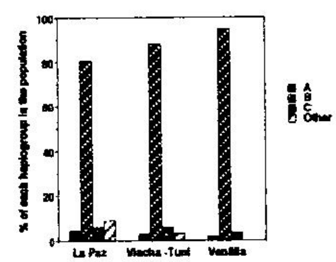


Figure 2 : Gel electrophoresis of amplicons treated with the indicated restriction enzymes. The arrows indicate samples characteristic for the studied haplotype. The numbers on both sides indicate the fragment sizes.

HAPLOGROUP FREQUENCY



HVR-I SEQUENCE VARIABILITY IN THE ALTIPLANO BOLIVIAN POPULATION

	MtDNA number																							
	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1			
	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6			
HVS-I	0	0	0	0	1	1	1	1	1	2	2	2	2	2	2	2	2	3	3	3	3			
Seq N°	5	5	5	8	1	8	8	9	9	1	2	4	5	6	9	9	9	1	2	5	6			
	0	1	5	0	1	3	9	2	3+	7	3	5	8	6	0	2	8	9	5	7	2			
CRS	T	A	A	A	C	A	T	C	_	T	C	C	A	C	C	C	T	G	T	T	T	Haplogroup	Haplotype	N
BOL 73					T						T			T	T			A			C	A	1	4
BOL 4									C	C												B	2	6
BOL 45						C	C			C						T						B	3	11
BOL 49						C	C		C	C												B	4	25
BOL 56						C	C	T		C		T										B	5	5
BOL 60									C	C												B	6	5
BOL 66						C	C			C												B	7	28
BOL 67							C		C	C						T						B	8	4
BOL 18											T						C		C			C or V	11	1

DISCUSSION - CONCLUSIONS

The predominance of the haplotype B is striking in all communities. However it is the highest in the Ventilla community that is the most remote from the city of La Paz. The D-loop sequence confirms the difference between B and non-B haplogroups. Among the B haplogroups, there are two dominant haplotypes (hapolypes 4 and 7). Although some mutations may have occurred recently, the variability in the D-loop suggests that the population originated from several founders.

Acknowledgements

This work was supported by the CNRS, by the French Ministry of Foreign affairs and by the Rhône Alpes Region.
Thanks are due to Dr Favier, Dr Nigon, G. Buznet, Dr Crognier, Dr Dugoujon and all the colleagues from the IBBA for their participation in collecting the samples.

PERSPECTIVES - QUESTIONS

In which respect, the haplogroup B predominance may be an advantage to adapt to the high altitude?

Are haplogroup B or some specific control region haplotypes in the Haplogroup B less prone to the Monge disease ?

Is there any relationship between these mtDNA haplotypes and the lower incidence of prenatal problems in women living in La Paz than in other high altitude countries (Moore et al, 2001)?

References

Ballinger SW, Schurr TG, Torroni A, Gan YY, Hodge JA, Hassan K, Chen K-H, and Wallace DC (1992) genetics 130, 139.

Armaza F, Vargas E. and Moore L. (2001) High Altitude Medicine and Biology 2, 92.