Polymorphisms in DNA Repair Gene *XRCC1* (Arg194Trp) and (Arg399Gln) and their Role in the susceptibility of Bacterial Meningitis

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and 30 s for codon 194 and of 2 min for codon 399 (temperatures given in Table 2), elongation for 1 min at 72°C and a final extension step of 10 min at 72°C. PCR products were run on a 1% agarose gels and visualized with SYBR green. The amplified fragments were digested with appropriate restriction endonucleases *PvuII* and *NciI* for SNPs *XRCC1* Arg194Trp and Arg399Gln, respectively (Table 2) and the resulting cleavage products were separated by electrophoresis on 8% polyacrylamide gel for 1 h at 100 V and detected with silver staining according to the protocol described by Sanguinetti et al. [22].

Genetic Polymorphism	Exon	Primer sequence	Annealing Temp. (0°C)	Restriction enzyme	Genotype	Fragments (bp)
XRCC1 Arg194Trp (rs1799782)	6	F 5'GTTCCGTGTGAAGGAGGAGGA3' R 5'CGAGTCTAGGTCTCAACCCTACTCACT3' (138 pb)	58.7°C	*PvuII*	Arg/Arg Arg/Trp Trp/Trp	138 138+75+63 75+63
XRCC1 Arg399Gln (rs 25487)	10	F 5'CAGTGGTGCTAACCTAATC3' R 5'AGTAGTCTGCTGGCTCTGG3' (871 pb)	58°C	*NciI*	Arg/Arg Arg/Gln Gln/Gln	461+278+132 593+461+278+132 593+278

Table 2: SNPs in DNA repair genes, primers and conditions used for genotyping.

Detection of FPG sensitive sites

The genomic DNA from patients was submitted to treatment with formamidopyrimidine DNA glycosylase (FPG) (New England Biolabs) as described by da Silva et al. [6]. This

Measurement of cytokines and chemokines in patients with BM

T e main cytokines and chemokines involved in the BM in f ammatory response were examined in the CSF samples from patients. BM patients carrying *XRCC1* Gln allele did not showed statistical di f erence in the cytokines and chemokines levels (Figure 2). For SNP *XRCC1* Arg194Trp, no statistical di f erence was also observed in the concentration of cytokines and chemokines (data not shown).

Discussion

Bacterial meningitis has been known to be an important cause of mortality and morbidity. T e disease evolution is mainly in f uenced by the host immune response determined by several genes that regulate the intensity of the in f ammatory response to infection [8-11].

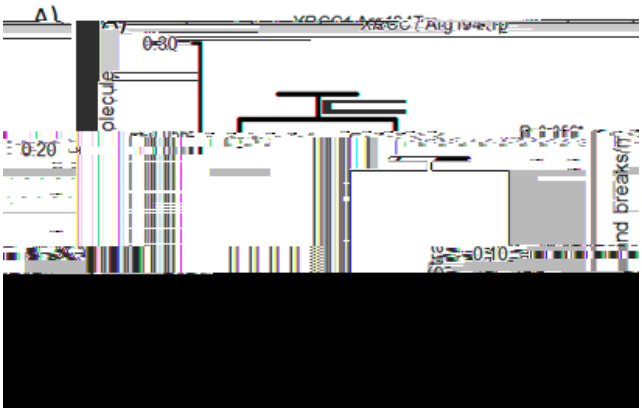

Figure 1A: FPG sensitive sites in genomic DNA in relation to *XRCC1*

diference

women with a family history of breast cancer from Rio de Janeiro. Genet Mol Biol 32:255-259.

27. Yang SF, Xu YJ, Xie JG, Zhang ZX (2009) h*OGG1* Ser326Cys and XRCC1 Arg399Gln polymorphisms associated with chronic obstructive pulmonary disease. Chin Med J (Engl) 122: 960-966.

28. Dogru-Abbasoglu S, Aykac-Toker G, Hanagasi HA, Gurvit H, Emre M, Uysal M (2007) T e Arg194Trp polymorphism in DNA repair gene XRCC1 and the risk for sporadic late-onset Alzheimer's disease. Neurol Sci 28: 31-34.

29. Jiang J, Liang X, Zhou X, Huang R, Chu Z, et al. (2010) DNA repair gene X-ray repair cross complementing group 1 Arg194Trp polymorphism on the risk of lung cancer: a meta-analysis on 22 studies. J T orac Oncol 5: 1741-1747.

30. Ginsberg G, Angle K, Guyton K, Sonawane B (2011) Polymorphism in the DNA repair enzyme XRCC1: utility of current database and implications for human health risk assessment. Mutat Res 727: 1-15.

31. Wu K, Su D, Lin K, Luo J, Au WW (2011) XRCC1 Arg399Gln gene polymorphism and breast cancer risk: a meta-analysis based on case-control studies. Asian Pac J Cancer Prev 12: 2237-2243.

32. Gencer M, Dasdemir S, Cakmakoglu B, Cetinkaya