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RESEARCH ARTICLE

GENETIC POLYMORPHISM OF *XRCC1* AND *XRCC3* GENES AND RISK OF CERVICAL CANCER IN SENEGALESE POPULATION

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Abstract

X-ray repair cross complementing 1 and 3 (*XRCC1* and *XRCC3*) gene plays a key role in DNA repair, genetic instability and tumorigenesis. We hypothesized that single nucleotide polymorphisms (SNPs) in *XRCC1* and *XRCC3* gene might affect its expression and/or function which have an influence on the development of cervical cancer. The aim of our study was to assess the association of four polymorphisms was carried out in the following DNA repair genes: *XRCC1* (Arg399Gln, Arg194Trp) (rs25487, rs1799782), *XRCC3* (C241T and A316G) (rs861539, rs1799794). The study group included 505 Senegalese individuals (313 cervical cancer patients, and 192 healthy controls). From the cancer patients and controls, genomic DNA was extracted from blood and tissues samples. Genotype was carried out for four SNPs using Taqman genotyping assay method. A significant association was found between *XRCC1* 194C>T and cervical cancer (OR= 2.696; 95% CI= 1.181-6.154; p= 0.018, using an additive model), (OR=2.989; 95% CI= 1.078-8.283; p= 0.035, using dominant model), while there is no significant association between Arg399Gln polymorphisms and cervical cancer. Also, no association was found between *XRCC3* Thr241Met genotype and expressed risk of susceptibility to both cervical cancer in Senegalese population. This study indicates that variant types of DNA repair genes play an important role in modifying individual susceptibility to cervical cancer.

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Background

Cervical cancer (CC) is one of the most common genital tract carcinomas which has become an exigent health concern and the first leading cause of cancer related death among women world over with more than 570 000 new cases and 311 365 deaths (Bray et al., 2018). Among these, 85% of the cervical cancer cases occur in developing countries (Jemal et al., 2011).

Infection with high-risk types of human papillomavirus (HPV) is the main causative factor for developing cervical intraepithelial neoplasia (CIN) which is a precursor lesion for cervical cancer (Ahn et al., 2003). While, not all women who are infected with HPV will certainly progress into cervical cancer, suggesting that there are still other factors playing a role in the pathogenesis of cervical cancer such as genetic and environmental factors (Shi et al., 2016). In human body, DNA repair genes are considerable factors in the prevention of genomic injury and sequential carcinogenesis. Previous studies have shown that genomic instability is a crucial event in HPV associated cancers, with a significant increase in single and double strand breaks (Udumudi et al., 1998; Cortés-Gutiérrez et al., 2012).

DNA damage may contribute to both genetic instability and carcinogenesis, which could occur through different pathways (exogenous carcinogens, endogenously produced reactive oxygen metabolites). DNA damage repair systems play vital roles in maintaining normal physiological functions, particularly for sustaining genome integrity in humans (Pan et al., 2014).

Exposure to different endogenous and exogenous mutagens and carcinogens can result in various types of DNA damages. These alterations, if not repaired, can cause genetic instability, mutagenesis and cancer (Goode et al., 2002). Importantly, to counteract the deleterious consequences of the DNA-damaging agents, evolution has moulded a number of DNA repair systems that as a whole take care of most of the insults inflicted on a cell's vital genetic information. The repairing of different types of DNA damages is important for safeguarding genomic integrity (Smith et al., 2003). There are six DNA repair pathways: direct repair (Eker et al., 2009), base excision repair (BER) (Robertson et al., 2009), nucleotide excision repair (NER) (Diderich et al., 2011), mismatch repair (MMR) (Hsieh and Yamane, 2008), double-strand breaks repair

(DSBR) (Khanna and Jackson, 2001; Scott, 2004) and ribonucleotide excision repair (RER) (Wallace and Williams, 2014).

Among the main DNA maintenance mechanisms operating in humans, the base excision repair (BER) pathway is the primary defence against lesions and responsible for repairing the DNA single-strand breaks caused by oxidative stress (such as reactive oxygen species, ROS), thereby maintaining genomic integrity. Impaired BER pathways are considered the major cause of cervical cancer (Jiricny and Marra, 2003).

The double-strand break DNA repair pathway, including *XRCC3* genes, is implicated in maintaining genomic stability and therefore could affect the cancer risk (Tambini et al., 2010; Yuan et al., 2014). Genetic polymorphisms in homologous recombination repair (HRR) genes, which can lead to protein haploinsufficiency, have been associated with increased cancer risk (Areeshi, 2013).

We have selected two DNA repair genes, representing two different repair pathways, for this study: the X-ray repair cross-complementing group 1 (*XRCC1*) and the X-ray repair cross complementing group 3 (*XRCC3*) genes.

XRCC1 gene, located on chromosome 19 (19q13.2–13.3) is a key mediator of single-strand break DNA repair, including nucleotide excision repair (NER) and base excision repair (BER) (Fan and Wilson, 2005; Al Zoubi, 2015). *XRCC1* serves as the scaffold protein in the BER pathway, which recognizes DNA breaks and interacts with polynucleotide kinase enzyme, DNA polymerase β , PARP1 and DNA ligase III α (Caldecott et al., 1995; Pramanik et al., 2011). There are three most common polymorphisms in *XRCC1*, contributing to amino acid substitutions in *XRCC1* at codon 194 (exon 6, base C to T, amino acid Arg to Trp), codon 280 (exon 9, base G to A, amino acid Arg to His), and codon 399 (exon 10, base G to A, amino acid Arg to Gln). Moreover, these variants eventually alter *XRCC1* function.

The associations of SNPs in DNA repair genes and various types of cancer and tumors have been extensively described. However, the evidence is frequently confusing, with some SNPs increasing the risk of certain types of cancer, but decreasing the risk of others.

Many studies have demonstrated that *XRCC1* polymorphisms (rs1799782, Arg194Trp; rs25489, Arg280His; and rs25487, Arg399Gln) could alter *XRCC1* function and result in altered efficiency of the protein, eventually increased risk of development of oesophageal squamous cell carcinoma (Yun et al., 2015), lung cancer (Fan and Xiu, 2015), pancreatic cancer (Hou et al., 2016), breast cancer (Zheng et al., 2013), colorectal cancer (Nissar et al., 2015), gastric cancer (Zhao et al., 2013) and cervical cancer risk (Niwa et al., 2005; Huang et al., 2007; Alsbeih et al., 2013).

XRCC3 gene, located at chromosome 14q32.3 is one of the central protein, playing an important role in HRR (homologous recombinational repair) pathway. *XRCC3* interacts, stabilizes RAD51 and involves in HRR for DNA DSBs (double strand breaks of DNA) and cross-link repair in mammalian cells (Kurumizaka et al., 2001; Zhao et al., 2013). *XRCC3* is a paralog of RAD51, it is essential for genetic stability (Brenneman et al., 2002).

XRCC3 polymorphism was associated with the risks of numerous types of cancer, such as ovarian cancer, breast cancer, head and neck cancer, colorectal cancer (Yin et al., 2012; He et al., 2012; Yuan et al., 2014; Nissar et al., 2015) and cervical cancer is inconclusive (Settheetham-Ishida et al., 2011; Wang and Yang, 2010).

Thus, our hereby was to investigate the relationship between *XRCC1* and *XRCC3* polymorphisms in women with cervical cancer and healthy controls. Then, we genotyped 4 variants of the two DNA repair genes *XRCC1* (C194T and G399A) and *XRCC3* (C241T and A316G), and assessed their contributions to cervical cancer susceptibility, and their association with other epidemiological risk factors in a Senegalese woman.

Materials and Methods

Study population

The Ethical and Scientific committee of Cheikh Anta Diop of Dakar University approved the study under the number 0197/2016/CER/UCAD. Blood samples and tissues were obtained from patients attending at the center of cancerology Aristide le Dantec hospital (Joliot Curie center) and Gaspard Camara Health Center, from 313 cervical cancer patients (include 127 tissue and 186

blood samples) and 192 healthy controls (blood samples).

All included cases were newly and histopathologically diagnosed with cervical cancer. None of the patients had received chemotherapy or radiotherapy prior to enrolment.

Blood controls patients enrolled in this study were obtained from the Yeumbeul Health Center. All controls were age matched and recruited following physical examinations after diagnostic exclusion of cancer and who were histologically confirmed to have a normal cervix. Demographic data and clinical data of the patients were collected from their files, after obtaining informed and written consent from each patient (Table 1).

DNA isolation

DNA was extracted from both whole blood and cervical tissue using Qiagen kit and based on the manufacturer's instructions (Qiagen, Germantown, Maryland, USA). Quantification of DNA was carried out by measuring absorbance using NanoDrop Lite Spectrophotometer (Thermo Scientific, USA) and were stored at -20°C until used for genotyping.

Single-nucleotide polymorphisms (SNP) genotyping

The SNPs included in this study were selected based on previous studies that demonstrated their association with cervical cancer (rs1799782, rs25487 of *XRCC1* gene and rs861539, rs1799794 of *XRCC3* gene). The polymorphisms were genotyped using a TaqMan SNP genotyping assay (Applied Biosystems, Foster City, CA, USA) and a 96-well ABI 7500HT real-time PCR system (Applied Biosystems, Foster City, CA, USA). The final volume for each reaction was 10 μL , containing 5 μL Quanta Mix, 0.5 μL TaqMan probe mix, 2.5 μL DNase/RNase-Free distilled water (Bio Basic Inc. CA) and 2 μL genomic DNA. The real-time PCR steps included an initial activation step at 95°C for 10 min, followed by 40 cycles of 95°C for 15 sec, and 60°C for 1 min. To validate results from real-time PCR, around five percent of assays were repeated. Eventually, the frequencies of genotype or allele of *XRCC1* and *XRCC3* polymorphisms were determined based on the allelic discrimination plots. To ensure the accuracy of the results, 10% of samples were randomly chosen for repeated assays, and no inconsistent results

were found.

Statistical analysis

The comparison of two groups of categorical variables was performed using Student test or Fisher's exact test. Hardy–Weinberg equilibrium analysis was performed for each SNP. The statistical analysis was performed using multivariate logistic regression in the additive, dominant, recessive and genotypic model, adjusted for age, marital status, gestity, parity and oral contraceptive. Linkage disequilibrium (LD) was computed for each pair of polymorphisms. $P < 0.05$ was considered statistically significant. All statistical analyses were carried out using the PLINK software <http://zzz.bwh.harvard.edu/plink/>.

Results

Characteristics of the study population

A total of 313 women diagnosed with cervical cancer (include 127 tissue and 186 blood samples) and 192 controls were included in this study. The demographic and clinical characteristics of cervical cancer patients and normal controls are summarized in [Table 1](#).

From the 186 blood cervical cancer patients (CCB), 8 (4.3%) were IB stage, 24 (12.9%) were IIA stage, 47 (25.27%) were IIB stage, 41 (22.04%) were IIIA stage, 19 (10.21%) IIIB stage, 31 (16.67%) IVA stage and 16 (8.6%) IVB stage. Of the 127 tissues cervical cancer patients (CCT), 37 (29.13%) were IIA stage, 13 (10.23%) were IIB stage, 40 (31.50%) were IIIA stage, 16 (12.60%) IIIB stage, 10 (7.87%) IVA stage and 1 (0.8%) IVB stage.

At all, 110 (59.14%) of women were polygamous among CCB and 106 (83.46%) among CCT while 114 (59.37%) were monogamous among controls.

The median ages of the cervical cancer patients (CCB and CCT) and control women were 53.1 (range 24–80), 49.84 (range 27–85), and 38.76 (range 20–64),

respectively. The subjects more than 45 years old in cervical cancer CCB, CCT and control group were 140 (75.27%), 78 (61.42%), and 67 (34.9%), while the subjects less than 45 years old in cervical cancer CCB, CCT and control group were 41 (22.04%), 42 (33.07%), and 52 (27.08%), respectively.

The oral contraceptive in CCB, CCT, and control group were 38 (20.43%), 96 (75.59%) and 66 (34.38%) respectively. Women with more than 5 children from the CCB, CCT and controls were 137 (73.66%), 94 (74.01%) and 56 (29.17%), while the patients with less than 5 children were from the CCB, CCT and controls were 37 (19.89%), 22 (17.32%) and 118 (61.46%).

There was significant difference in age between controls and patients with CCB and CCT. Similarly, significant differences between the cases and controls were found in parity, gestity, oral contraception and the marital status. However, the smoking status, alcohol consumption was not significantly associated with cervical cancer risk.

XRCC1 and XRCC3 gene variations and structure in Senegalese population

In the present study, the polymorphism of the *XRCC1* and *XRCC3* gene were analysed in a population of 505 Senegalese, including 127 CCT, 186 CCB and 192 CTR individuals. The SNPs rs25487 and rs1799782 are in linkage disequilibrium (LD) with $D' = 1$ and $r^2 = 0.006$ in according to the 1000 Genomes African populations, while rs861539 and rs1799794 are not in linkage disequilibrium (LD) with $D' = 0.54$ and $r^2 = 0.008$.

[Table 2](#) summarizes the frequency of each polymorphism in the CCB, CCT and CTR groups. Allelic frequencies obtained in our study are similar to the data provided by 1000Genomes database with regard to African populations except rs861539.

Table 1: Frequency distribution analysis of selected demographic and risk factors in cervical cancer cases and controls

	CTR	CCB		CCT	
Variables	(n=192) no.(%)	(n=186) no.(%)	p-value	(n=127) no.(%)	p-value
Tumor stage (FIGO)					
IB		8 (4.3)		0	
IIA		24 (12.9)		37 (29.13)	
IIB		47 (25.27)		13 (10.23)	
IIIA		41 (22.04)		40 (31.50)	
IIIB		19 (10.21)		16 (12.60)	
IVA		31 (16.67)		10 (7.87)	
IVB		16 (8.6)		1 (0.8)	
unknown		0		10 (7.87)	
Age (years)					
Median (range)	38.76 (20–64)	53.1 (24–80)		49.84 (27–85)	
<35	73 (38.02)	5 (2.69)	8.09e ^{-27a}	7 (5.51)	7.47e ^{-15a}
35-45	52 (27.08)	41 (22.04)		42 (33.07)	
>45	67 (34.90)	140 (75.27)		78 (61.42)	
Marital status					
Polygamy	48 (25)	110 (59.14)	3.31 e ^{-8b}	106 (83.46)	1.62 e ^{-20b}
Monogamy	114 (59.38)	76 (40.86)		21 (16.54)	
Unmarried	30 (15.62)	0		0	
Tobacco smoking					
Yes	5 (2.6)	0	0.06 ^b	0	0.16 ^b
No	187 (97.40)	186 (100)		127 (100)	
Alcohol consumption					
Yes	1 (0.5)	0	1 ^b	0	1 ^b
No	191 (99.5)	186 (100)		127 (100)	
Oral Contraceptive					
Yes	66 (34.37)	38 (20.43)	0.002 ^b	96 (75.59)	3.14 e ^{-13b}
No	126 (65.63)	148 (79.57)		31 (24.41)	
Gestity					
<5	118 (61.46)	37 (19.89)	8.04e ^{-21a}	22 (17.32)	4.18e ^{-16a}
>5	74 (38.54)	149 (80.11)		105 (82.68)	
Parity					
<5	136 (70.83)	49 (26.34)	7.1e ^{-24a}	33 (25.98)	6.32e ^{-20a}
>5	56 (29.17)	137 (73.66)		94 (74.02)	
HIV	0	3		0	

^a Student test; ^b Fischer exact test; Cervical cancer blood (CCB), cervical cancer tissues (CCT), Controls (CTR)

Table 2: Allele frequencies and Hardy–Weinberg estimations of SNPs in the study population

Genes		MAF (A1 frequency)						HWE p-value	Allele A1 African (1000Genomes)	Allele A1 European (1000Genomes)
	dbSNP number	A1	A2	CCB	CCT	CTR	GP			
XRCC1	rs25487	A	G	0.92	0.91	0.90	0.91	0.56	0.89	0.63
	rs1799782	T	C	0.05	0.06	0.02	0.04	0.61	0.07	0.05
XRCC3	rs861539	T	C	0.09	0.09	0.08	0.09	0.41	0.19	0.39
	rs1799794	G	A	0.23	0.20	0.21	0.21	0.41	0.20	0.21

Cervical cancer blood (CCB), cervical cancer tissues (CCT), Controls (CTR), group GP (global population), HWEp, Hardy–Weinberg in global group, Minor Allele frequency (MAF)

Association of the *XRCC1* and *XRCC3* gene polymorphisms with CCB susceptibility

We found no significant association between the *XRCC1* and *XRCC3* polymorphism with the risk of cervical cancer in all the subjects in the multivariate logistic regression analyses (Table 3).

Association of the *XRCC1* and *XRCC3* gene polymorphism with CCT susceptibility

In the dominant genetic model, the SNP *XRCC1* rs1799782 Arg194Trp had an increased risk of CC (OR=2.989; 95% CI= 1.078-8.283; p= 0.035) when adjusted for age, parity, gestity, oral contraception and marital status. The effect was more clear when the additive model was applied (OR= 2.696; 95% CI=

1.181-6.154; p= 0.018) Table 4. Similarly, the frequency of Arg194Trp (rs1799782) genotypes in CCB were 160 (86%) for CC, 19 (10%) for CT and 0% for TT while in CCT cases the frequencies were 108 (85%) for CC, 16 (13%) for CT and 0% for TT. However, the C allele was associated with cervical cancer risk in CCT (OR= 2.579; 95% CI= 1.151-5.78; p= 0.017). while it was not associated in CCB (OR= 2.096; 95% CI= 0.9612-4.571; p= 0.057).

Similarly, by comparing 17 identical patients with blood and tumour we found that there is a mutation from the T allele in the blood to the C allele (3%) in the tumour and for the other patients they are homozygous (CC) in the blood and tumour.

Table 3: Genotype frequency distribution of XRCC1 and XRCC3 gene polymorphisms and risk associated with CCB

SNP	CCB (n= 186) (%)	CTR (n= 192) (%)	OR ^a (95% CI)	P value
XRCC1-399^b (rs25487)				
GG	156 (84)	157 (82)	1.00 (ref)	
GA	30 (16)	33 (17)	1 (0.5-2)	0.900
AA	0	2 (1)	-	-
additive			0.8 (0.4-1.3)	0.446
XRCC1-194^b (rs1799782)				
CC	160 (86)	182 (95)	1.00 (ref)	
CT	19 (10)	10 (5)	1.5 (0.5-4.3)	0.432
TT	0	0	-	-
additive			2.1 (0.9-4.7)	0.057
XRCC3-241^b (rs861539)				
CC	143 (77)	154 (80)	1.00 (ref)	
CT	30 (16)	33 (17)	1.5 (0.7- 3)	0.193
TT	2	0	-	-
additive			1.1 (0.6-1.8)	0.673
XRCC3-316^b (rs1799794)				
AA	103 (56)	114 (59)	1.00 (ref)	
AG	66 (35)	68 (35)	0.8 (0.4-1.3)	0.456
GG	8 (4)	7 (4)	0.3 (0.08-1.5)	0.172
additive			1 (0.7-1.5)	0.624

Table 4: Genotype frequency distribution of XRCC1 and XRCC3 gene polymorphisms and risk associated with CCT

SNP	CCT (n= 127) (%)	CTR (n= 192) (%)	OR ^a (95% CI)	P value
XRCC1-399^b (rs25487)				
GG	105 (83)	157 (82)	1.00 (ref)	
GA	20 (16)	33 (17)	0.9 (0.4-1.8)	0.801
AA	0	2 (1)	-	-
additive			0.8 (0.4-1.4)	0.547
XRCC1-194^b (rs1799782)				
CC	108 (85)	182 (95)	1.00 (ref)	
CT	16 (13)	10 (5)	2.9 (1-8.2)	0.035
TT	0	0	-	-
additive			2.6 (1.1-6.1)	0.018
XRCC3-241^b (rs861539)				
CC	95 (75)	154 (80)	1.00 (ref)	
CT	22 (17)	33 (17)	0.8 (0.4-1.8)	0.722
TT	0	0	-	-
additive			1.1 (0.6-2)	0.685
XRCC3-316^b (rs1799794)				
AA	58 (46)	114 (59)	1.00 (ref)	
AG	30 (24)	68 (35)	0.8 (0.4-1.6)	0.703
GG	4 (3)	7 (4)	0.8 (0.1- 3.7)	0.803
additive			0.9 (0.6-1.4)	0.773

CI: confidence interval; OR: odds ratio; CCB: Cervical cancer blood; CTR: Controls; ref: Reference; CCT: Cervical cancer tissues; Bold values indicate statistical significance.

^aAdjusted for age, parity, gestity, marital status and use of oral contraceptive.

^bGenotypic frequencies [N (%)].

Discussion

Cervical cancer is still the leading cause of cancer-related deaths among women. Carcinogenic compounds play an important role in causing direct or indirect DNA alteration. DNA repair is responsible for maintaining genomic stability in response to the assault of environmental carcinogens that causes DNA damage (Friedberg, 2003). If left unrepaired, such DNA damage could cause mutation fixation and initiation of carcinogenesis. Polymorphisms, which have an effect

on the regulation of gene expression, can contribute to the differences between individuals in the susceptibility to a disease and its severity (Choi and Kim, 2007).

There are many opinions about influence of *XRCC1* (X-ray repair complementing defective repair in Chinese hamster cells 1) and *XRCC3* (X-ray repair complementing defective repair in Chinese hamster cells 3) genes on different cancer types. These genes participate in excision repair of bases and repair of single and double strand breaks. In our study, we

conducted a study to investigate the XRCC1 Arg194Trp, Arg399Gln and XRCC3 Thr241Met, A316G polymorphisms and development of cervical cancer.

The previous studies also point out to the relation of XRCC1 (Arg399Gln, Arg194Trp) and XRCC3 Thr241Met polymorphisms with colorectal cancer, skin cancer, lung cancer (Cui et al., 2012; Zheng et al., 2013), and others. There are data confirming the participation of XRCC1 genes polymorphism to cervical cancer (Li et al., 2012).

In the present analysis, we demonstrated that the XRCC1 Arg194Trp polymorphism is associated with an increased risk of cervical cancer in CCT, while there is no significant association between Arg399Gln polymorphisms and cervical cancer in CCT and CCB.

Interestingly, that Barbisan et al., (2011) have made a conclusion, that Arg194Trp polymorphism may be associated with cervical cancer risk, Arg399Gln polymorphism might be a low penetrant risk factor for cervical cancer only at Asians, which is confirmed by (Shuai et al., 2012). The meta-analysis of 16 studies (Li et al., 2012) found out that there were no obvious associations of XRCC1 Arg399Gln polymorphism with cervical cancer risk. But in the subgroup analyses by ethnicity/country, a significantly increased risk was observed among Asian, especially among Chinese. We found out that XRCC1 Arg194Trp polymorphism had been associated with cervical cancer in Kazakhstan population, but indifferent manner.

Different from previous studies (Huang et al., 2007; Roszak et al., 2011; Wen-peng et al., 2011), by pooling all available data from included studies, we found that only Arg194Trp polymorphism was associated with increased risk of cervical cancer.

Regarding the XRCC1 Arg399Gln polymorphism our results did not find significant association between XRCC1 Gln399Gln genotype carriers which is confirmed by other (Bajpai et al., 2016).

Published data on the relationship of XRCC3 Thr241Met polymorphism with cancer risk are inconsistent (Au et al., 2003; Konstantinos and Theodoros, 2010; Settheetham-Ishida et al., 2011). However, the most studies show the association of XRCC3 241Met allele. But XRCC3 241Met allele did not increase the risk of cervical cancer development in the Chinese population (He et al., 2008; Cao et al., 2017) and among Thai women (Settheetham-Ishida et al., 2011). Our data confirm the no association between

XRCC3 Thr241Met genotype and expressed risk of susceptibility to both cervical cancer in Senegalese population.

However, significant differences between the cases and controls were found in parity, gestity, oral contraception and the marital status. These factors have previously been reported as risk factors for HPV infection, or co-factors for cervical cancer (Munoz et al., 2003; Hinkula et al., 2004; Kim et al., 2012; Vessey and Yeates, 2013). Long-term use of oral contraceptive could be a cofactor that increases the risk of cervical carcinoma by up to four-fold in women who are positive for cervical HPV DNA ((Moreno et al., 2002). We found a significant number of oral contraceptive users in CCB (20%) and CCT (24%) compared with only 34% among the controls. However, oral contraceptive use was not correlated with the disease in CCB and CCT.

High parity, as evident in studies by (Jensen et al., 2013), seems to increase the risk of SCC of the cervix among HPV positive women. In our study, high parity was also associated significantly with CCB and CCT cases. Our study assessed the difference in age in cervical cancer cases and controls. There was a significant difference between cervical cancer cases and controls, whereas the difference in age was associated statistically significant with CCB and CCT cases.

Our study also showed that both blood and tumor samples can act as sources to detect polymorphism in DNA repair genes as findings of both blood and tissue samples matched 100%. Therefore, this interesting finding of a complete correlation between tissue and blood samples suggests that gene polymorphism in blood may be used as a non-invasive method to evaluate the risk of cervical cancer.

The identification of polymorphisms in many genes and the determination of their functional importance in cervical cancer will enable the design of susceptibility risk models for de-novo and therapy-related disease.

Conclusion

In conclusion, the research of the relationship of XRCC1 and XRCC3 polymorphisms and cervical cancer is very popular but conflicting at present. This is the first molecular epidemiological study on XRCC1 (rs1799782, rs25487), XRCC3 (rs861539, rs1799194) polymorphism and cervical cancer risk in Senegalese. Our study suggests that XRCC1 Arg194Trp polymorphism may be associated with cervical cancer

risk, while XRCC1 Arg399Gln and XRCC3 polymorphism didn't show an association with cervical cancer risk.

List of Abbreviations

HPV: Human Papilloma Virus; CIN: Cervical Intraepithelial Neoplasia; CC: Cervical Cancer; CTR: Control; CCB: Cervical Cancer Blood; CCT: Cervical Cancer Tissue; HRR: homologous recombination repair; PARP1: Poly (ADP-Ribose) Polymerase 1; DSBs: double strand breaks; HWE: Hardy–Weinberg equilibrium; MAF: Minor Allele frequency; BER: base excision repair; NER: nucleotide excision repair; MMR: mismatch repair; RD: Direct Reversion; DSB: double-strand breaks repair; RER: Ribonucleotide Excision Repair; FIGO: International Federation of Gynecology and Obstetrics; ROS: reactive oxygen species

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Consent and Approval

We declare no conflicts of interest associated with this publication.

All patients and their families signed the informed consent form that was approved by the Ethical and Scientific committees.

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