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Original Article

Association between interleukin-32 polymorphisms and ovarian cancer in the Chinese Han population

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Abstract: Interleukin-32 (IL-32) as a pro-inflammatory cytokine participates in the progression of inflammation and cancer. Ovarian cancer (OC) accounts for a considerable mortality rate, but research on IL-32 and OC is almost nil. Our study aims to explore the association between IL-32 and the progression as well as prognosis of OC initially. This hospital-based case-control study enrolled 147 OC patients and 337 healthy controls, and we used the polymerase chain reaction-restriction fragment length polymorphism (PCR-RFLP) method to distribute the genotypes. The results showed that the homozygous genotype (TT) of rs28372698 SNP was significantly higher in patients compared to controls (12.9% vs. 6.2%, $P = 0.018$, OR (95% CI) = 2.23 (1.16-4.29)). This revealed that TT genotype might be a risk factor in OC progression. This present study indicates that *IL-32* gene polymorphism relates to an increased OC susceptibility, and IL-32 may be a marker for OC progression.

Keywords: Interleukin-32, ovarian cancer, susceptibility, progression

Introduction

Ovarian cancer (OC), as one of the three major malignant gynecologic tumors, is a leading cause of tumor-associated mortality. Moreover, the incidence and mortality of ovarian cancer are increasing [1, 2]. According to the data from International Agency for Research on Cancer in 2018, the incidence and mortality number for ovarian cancer are 295,414 and 184,799 worldwide, and Chinese patients account for 17.9% and 16.7% respectively [3]. Furthermore, most ovarian cancer patients have been diagnosed at an advanced stage, and the prognosis and five-year survival rate are disappointing after treatment [4]. OC is a polygenic genetic disease [5, 6], and research has pointed out some biomarkers for the development of OC, including TP53 and BRCA1/2 [7, 8]. Thus, more specific and precise markers for OC screening are needed. Furthermore, additional markers for the development and prognosis of OC are needed.

Interleukin-32 (IL-32) is encoded by *IL-32* gene located on the human chromosome 16p13.3, and it consists of eight exons [9]. IL-32 has nine splice variants: IL-32α, IL-32β, IL-32γ, IL-32δ, IL-32ε, IL-32θ, IL-32ζ, IL-32η, and IL-32small (IL-32sm). It is mainly produced by T cells, NK cells, and monocytes [10-12]. Several studies have indicated an association between IL-32 and rheumatoid arthritis [13], chronic obstructive pulmonary disease [14], and cancers [15-17].

Recently, Wang et al. and Yu et al. have demonstrated a relationship between the single nucleotide polymorphism (SNP) rs28372698 (T/A) of IL-32 with lung cancer and endometrial cancer [18, 19]. However, no relationship has been established so far between IL-32 and OC. Thus, we chose the rs28372698 (T/A) of IL-32 to

Table 1. Characteristics of the individuals

Characteristic	Patients	Controls	*P*
Sample size	147	337	
Age at first diagnosis (mean ± SD)	49.93±10.13	48.88±17.86	0.51
Clinical histology			
Serous	77 (52.4%)	-	
Mucinous	10 (6.80%)	-	
Endometrioid	9 (6.1%)	-	
Clear cell	21 (14.3%)	-	
Others	30 (20.4%)	-	
FIGO stage			
I	34 (23.1%)	-	
II	11 (7.5%)	-	
III	95 (64.6%)	-	
IV	7 (4.8%)	-	
Tumor grade			
Low grade	100 (68.0%)	-	
Middle grade	20 (13.6%)	-	
High grade	7 (4.8%)	-	
NA	20 (13.6%)	-	

Table 2. Primer sequences for genotyping the SNP in *IL-32* gene

SNP ID	Primer sequence	Restriction Enzyme	Allele (bp)
rs28372698	F: 5'-GTCAGAAGGACCTGGTCAGC-3'	Hpy188III	A (115)
	R: 5'-GTTGGAGGGGTGGCTAGTC-3'		T (21+94)

explore an association between IL-32 and OC in the Chinese Han population.

Materials and methods

Subjects

This study enrolled 337 healthy controls and 147 ovarian cancer patients from the West China Second University Hospital of Sichuan University in 2007 to 2012, and all of the participants provided informed consent. The study was approved by the hospital ethics committee. The clinical characteristics were collected from the medical records and follow-up data were abstracted every 6 months for 5 years by telephone calls. The diagnosis of tissue from resected specimens was confirmed by histologic examination. This study excluded the individuals with borderline ovarian tumors, two or more different malignancies, autoimmune and infectious diseases, and metastatic cancer from other origins. The International Federation of Gynecology and Obstetrics ovarian cancer staging criteria (FIGO, 2014) were used to clarify the tumor stage [20], and the clinical characteristics are summarized in **Table 1**. All of the participants were genetically unrelated individuals of the Han population living in Sichuan province of China.

DNA & genotyping

As shown in **Table 2**, the SNP polymerase chain reaction (PCR) primers were designed by the software Primer 3 web version 4.1.0. (http://primer3.ut.ee/) [21]. Individuals' genetic DNA was extracted from a 200 μL EDTA-anticoagulated peripheral blood sample by the DNA isolation kit from BioTeke (Peking, China). The polymerase chain reaction-restriction fragment length polymorphism (PCR-RFLP) was used for genotyping. The DNA fragments that contain the polymorphisms were amplified in a volume of 10 μL, and the volume contained 100 ng extracted genomic DNA, 2.7pico mole primers, and 5 μL 2x power Taq PCR Master Mix (BioTeke, Peking, China). The PCR annealing temperature was 60°C for 30 s. After the termination of PCR, the products were digested by restriction enzyme Hpy188III, and the digested fragments were totally separated by a 6% polyacrylamide gel and stained with 1.5 g/L argent nitrate. Finally, DNA sequencing analysis was used to confirm the genotypes, and about 10% of the randomly selected samples were 100% in agreement with the results after performing repeated assays.

Statistical analysis

Genotypic association was performed by SNPstats online analysis software, and it consisted of the codominant, dominant, recessive, and over-dominant genetic models [22]. The Hardy-Weinberg equilibrium was calculated by chi- square test. The effects of different genotypes and alleles were evaluated by odds ratio

Table 3. Distribution of SNPs in *IL-32* among patients and controls and their association with ovarian cancer risk

Model	Genotype	rs28372698			
		Patients *N* (%)	Controls *N* (%)	OR (95% CI)	*P*
Codominant	AA	70 (47.6%)	162 (48.1%)	1.00 (reference)	
	AT	58 (39.5%)	154 (45.7%)	0.87 (0.58-1.32)	0.048
	TT	19 (12.9%)	21 (6.2%)	2.09 (1.06-4.14)	
Dominant	AA	70 (47.6%)	162 (48.1%)	1.00 (reference)	
	AT/TT	77 (52.4%)	175 (51.9%)	1.02 (0.69-1.50)	0.93
Recessive	AA/AT	128 (87.1%)	316 (93.8%)	1.00 (reference)	
	TT	19 (12.9%)	21 (6.2%)	2.23 (1.16-4.29)	0.018
Over-dominant	AA/TT	89 (60.5%)	183 (54.3%)	1.00 (reference)	
	AT	58 (39.5%)	154 (45.7%)	0.77 (0.52-1.15)	0.20
Allele	A	198 (67.3%)	478 (70.9%)	1.18 (0.88-1.59)	0.27
	T	96 (32.7%)	196 (29.1%)		

N corresponds to the number of individuals. Boldfaced values indicate a significant difference at the 5% level.

(OR) and respective 95% confidence intervals (95% CI). Cox regression multivariate survival analysis model were used to estimate the patients' outcomes. The level of significance was set at $P < 0.05$.

Results

Susceptibility to OC according to IL-32 genotypes

The genotype distributions of rs28372698 were in agreement with the Hardy-Weinberg equilibrium ($P > 0.05$) in this study. The effects of *IL-32* genotypes and allele susceptibility on OC patients are presented in **Table 3**. For rs28372698 SNP, the homozygous genotype (TT) in the recessive genetic model was significantly higher in the patient group compared with control group (12.9% vs. 6.2%, $P = 0.018$, OR (95% CI) = 2.23 (1.16-4.29)), which indicates an increased OC susceptibility. Moreover, in codominant model, compared with AA and AT genotypes, TT genotype was significantly higher in OC patients than controls ($P = 0.048$, OR (95% CI) = 2.09 (1.06-4.14)).

Clinical outcome

In this study, all of the 147 OC patients took part in the follow-up program. At the end of the study, 26 patients (17.7%) had died and 28 patients (19.0%) had relapsed. Based on these data, we conducted Multivariate Cox survival analyses adjusted by age, histology type, FIGO stage and tumor grade, and the final associations between *IL-32* SNP and OC patients' outcome are summarized in **Table 4**. However, no significant relationship was detected for the rs28372698 and OC patients' outcome ($P > 0.05$).

Discussion

IL-32 rs28372698 T/A genetic variant is located on the 5'-UTR in the promoter region, which might affect the regulation of IL-32 protein expression. The results of Shamoun et al. indicate the SNP rs28372698 seems to modulate the expression of IL-32 protein in colorectal carcinoma tissues through the interaction with IL-6, TNFα, and VEGF agree with the above opinion [23]. In the present study, we demonstrated that the distribution of SNP rs28372698 significantly showied a difference between OC patients and healthy controls. The TT homozygous genotype carriers presented an increased risk of OC susceptibility compared with AA/AT genotype carriers, which indicated the IL-32 A to T genetic variant might play a critical role in OC progression. This result was similar to that in endometrial cancer (EC) by Yu et al. which elaborated that TT genotype and T allele of rs28372698 represented a high risk of EC progression, and it even related to clinical stage as well as cervical invasion [19].

Substantial research on the rs28372698 of *IL-32* and the prognosis of cancer patients has been reported. It is reported that the T allele of rs28372698 is related to lower differentiation and poor prognosis in moderate and well-differentiated lung cancer [18]. However, in this study, we detected no significant association between rs28372698 and OC patients' prognosis. Limited sample size might be one of the reasons. IL-32 as a pro-inflammatory cytokine can induce many key cytokines to participate in inflammation or tumor progression [10, 24-26], and it consists of nine splice variants that occu-

Table 4. Association between SNPs in *IL-32* and patients' outcome

SNP/genotype	Ovarian Cancer Patients' Outcome					
	Alive/dead, *N*	HR (95% CI)[a]	*P*	Recurrence/Non-recurrence	HR (95% CI)[a]	*P*
rs28372698						
AA	59/11			14/56		
AT	45/13			10/48		
TT	17/2			4/15		
Codominant		0.97 (0.58-1.62)	0.90		1.17 (0.72-1.89)	0.53
Dominant		1.16 (0.54-2.49)	0.71		1.05 (0.51-2.13)	0.90
Recessive		0.66 (0.21-2.01)	0.46		1.63 (0.67-3.93)	0.28
Over-dominant		1.44 (0.68-3.06)	0.35		0.76 (0.36-0.63)	0.48

N corresponds to the number of individuals. [a]Adjusted by age, clinical histology, FIGO stage, and tumor grade.

py various protein functions and pathways in different tissues [27-29]. Therefore, our results need further large size studies to dialectically confirm.

In conclusion, the present study is the first one to detect an association between IL-32 SNP and OC. Our data showed that rs28372698 of *IL-32* is a significant risk factor to OC susceptibility. Thus IL-32 may be a marker of OC progression. However, because of the limitations in our study, such as sample size shortage, lack of variety on SNPs and research on expression level of IL-32 in participants, the present results need confirmation. Thus, further studies with a larger sample size, various IL-32 SNP genetic variants, and different populations are required to explore the role and mechanism of IL-32 in OC progression and prognosis.

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Disclosure of conflict of interest

None.

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References

[1] Huang Z, Zheng Y, Wen W, Wu C, Bao P, Wang C, Zhong W, Gao YT, Jin F, Xiang YB, Shu XO and Beeghly-Fadiel A. Incidence and mortality of gynaecological cancers: secular trends in urban Shanghai, China over 40 years. Eur J Cancer 2016; 63: 1-10.

[2] Dubeau L. The cell of origin of ovarian epithelial tumors and the ovarian surface epithelium dogma: does the emperor have no clothes? Gynecol Oncol 1999; 72: 437-42.

[3] Ferlay ISJ, Ervik M, et al. Globocan 2012 v1.0, Cancer incidence and mortality worldwide: Iarc CancerBase no. 11, international agency for research on cancer. http://globocan.Iarc.Fr.

[4] Jammal MP, Martins-Filho A, Silveira TP, Murta EF and Nomelini RS. Cytokines and prognostic factors in epithelial ovarian cancer. Clin Med Insights Oncol 2016; 10: 71-76.

[5] Jones MR, Kamara D, Karlan BY, Pharoah PDP and Gayther SA. Genetic epidemiology of ovarian cancer and prospects for polygenic risk prediction. Gynecol Oncol 2017; 147: 705-713.

[6] Kar SP, Berchuck A, Gayther SA, Goode EL, Moysich KB, Pearce CL, Ramus SJ, Schildkraut JM, Sellers TA and Pharoah PDP. Common genetic variation and susceptibility to ovarian cancer: current insights and future directions. Cancer Epidemiol Biomarkers Prev 2018; 27: 395-404.

[7] Kuchenbaecker KB, Ramus SJ, Tyrer J, Lee A, Shen HC, Beesley J, Lawrenson K, McGuffog L, Healey S, Lee JM, Spindler TJ, Lin YG, Pejovic T, Bean Y, Li Q, Coetzee S, Hazelett D, Miron A, Southey M, Terry MB, Goldgar DE, Buys SS,

Janavicius R, Dorfling CM, van Rensburg EJ, Neuhausen SL, Ding YC, Hansen TV, Jønson L, Gerdes AM, Ejlertsen B, Barrowdale D, Dennis J, Benitez J, Osorio A, Garcia MJ, Komenaka I, Weitzel JN, Ganschow P, Peterlongo P, Bernard L, Viel A, Bonanni B, Peissel B, Manoukian S, Radice P, Papi L, Ottini L, Fostira F, Konstantopoulou I, Garber J, Frost D, Perkins J, Platte R, Ellis S; EMBRACE, Godwin AK, Schmutzler RK, Meindl A, Engel C, Sutter C, Sinilnikova OM; GEMO Study Collaborators, Damiola F, Mazoyer S, Stoppa-Lyonnet D, Claes K, De Leeneer K, Kirk J, Rodriguez GC, Piedmonte M, O'Malley DM, de la Hoya M, Caldes T, Aittomäki K, Nevanlinna H, Collée JM, Rookus MA, Oosterwijk JC; Breast Cancer Family Registry, Tihomirova L, Tung N, Hamann U, Isaccs C, Tischkowitz M, Imyanitov EN, Caligo MA, Campbell IG, Hogervorst FB; HEBON, Olah E, Diez O, Blanco I, Brunet J, Lazaro C, Pujana MA, Jakubowska A, Gronwald J, Lubinski J, Sukiennicki G, Barkardottir RB, Plante M, Simard J, Soucy P, Montagna M, Tognazzo S, Teixeira MR; KConFab Investigators, Pankratz VS, Wang X, Lindor N, Szabo CI, Kauff N, Vijai J, Aghajanian CA, Pfeiler G, Berger A, Singer CF, Tea MK, Phelan CM, Greene MH, Mai PL, Rennert G, Mulligan AM, Tchatchou S, Andrulis IL, Glendon G, Toland AE, Jensen UB, Kruse TA, Thomassen M, Bojesen A, Zidan J, Friedman E, Laitman Y, Soller M, Liljegren A, Arver B, Einbeigi Z, Stenmark-Askmalm M, Olopade OI, Nussbaum RL, Rebbeck TR, Nathanson KL, Domchek SM, Lu KH, Karlan BY, Walsh C, Lester J; Australian Cancer Study (Ovarian Cancer Investigators); Australian Ovarian Cancer Study Group, Hein A, Ekici AB, Beckmann MW, Fasching PA, Lambrechts D, Van Nieuwenhuysen E, Vergote I, Lambrechts S, Dicks E, Doherty JA, Wicklund KG, Rossing MA, Rudolph A, Chang-Claude J, Wang-Gohrke S, Eilber U, Moysich KB, Odunsi K, Sucheston L, Lele S, Wilkens LR, Goodman MT, Thompson PJ, Shvetsov YB, Runnebaum IB, Dürst M, Hillemanns P, Dörk T, Antonenkova N, Bogdanova N, Leminen A, Pelttari LM, Butzow R, Modugno F, Kelley JL, Edwards RP, Ness RB, du Bois A, Heitz F, Schwaab I, Harter P, Matsuo K, Hosono S, Orsulic S, Jensen A, Kjaer SK, Hogdall E, Hasmad HN, Azmi MA, Teo SH, Woo YL, Fridley BL, Goode EL, Cunningham JM, Vierkant RA, Bruinsma F, Giles GG, Liang D, Hildebrandt MA, Wu X, Levine DA, Bisogna M, Berchuck A, Iversen ES, Schildkraut JM, Concannon P, Weber RP, Cramer DW, Terry KL, Poole EM, Tworoger SS, Bandera EV, Orlow I, Olson SH, Krakstad C, Salvesen HB, Tangen IL, Bjorge L, van Altena AM, Aben KK, Kiemeney LA, Massuger LF, Kellar M, Brooks-Wilson A, Kelemen LE, Cook LS, Le ND, Cybulski C, Yang H, Lissowska J, Brinton LA, Wentzensen N, Hogdall C, Lundvall L, Nedergaard L, Baker H, Song H, Eccles D, McNeish I, Paul J, Carty K, Siddiqui N, Glasspool R, Whittemore AS, Rothstein JH, McGuire V, Sieh W, Ji BT, Zheng W, Shu XO, Gao YT, Rosen B, Risch HA, McLaughlin JR, Narod SA, Monteiro AN, Chen A, Lin HY, Permuth-Wey J, Sellers TA, Tsai YY, Chen Z, Ziogas A, Anton-Culver H, Gentry-Maharaj A, Menon U, Harrington P, Lee AW, Wu AH, Pearce CL, Coetzee G, Pike MC, Dansonka-Mieszkowska A, Timorek A, Rzepecka IK, Kupryjanczyk J, Freedman M, Noushmehr H, Easton DF, Offit K, Couch FJ, Gayther S, Pharoah PP, Antoniou AC and Chenevix-Trench G; Consortium of Investigators of Modifiers of BRCA1 and BRCA2. Identification of six new susceptibility loci for invasive epithelial ovarian cancer. Nat Genet 2015; 47: 164-171.

[8] Rechsteiner M, Zimmermann AK, Wild PJ, Caduff R, von Teichman A, Fink D, Moch H and Noske A. TP53 mutations are common in all subtypes of epithelial ovarian cancer and occur concomitantly with KRAS mutations in the mucinous type. Exp Mol Pathol 2013; 95: 235-41.

[9] Dahl CA, Schall RP, He HL and Cairns JS. Identification of a novel gene expressed in activated natural killer cells and T cells. J Immunol 1992; 148: 597-603.

[10] Kim SH, Han SY, Azam T, Yoon DY and Dinarello CA. Interleukin-32: a cytokine and inducer of TNFalpha. Immunity 2005; 22: 131-142.

[11] Sohn DH, Nguyen TT, Kim S, Shim S, Lee S, Lee Y, Jhun H, Azam T, Kim J and Kim S. Structural characteristics of seven IL-32 variants. Immune Netw 2019; 19: e8.

[12] Sloot YJE, Smit JW, Joosten LAB and Netea-Maier RT. Insights into the role of IL-32 in cancer. Semin Immunol 2018; 38: 24-32.

[13] Joosten LA, Netea MG, Kim SH, Yoon DY, Oppers-Walgreen B, Radstake TR, Barrera P, van de Loo FA, Dinarello CA and van den Berg WB. IL-32, a proinflammatory cytokine in rheumatoid arthritis. Proc Natl Acad Sci U S A 2006; 103: 3298-3303.

[14] Calabrese F, Baraldo S, Bazzan E, Lunardi F, Rea F, Maestrelli P, Turato G, Lokar-Oliani K, Papi A, Zuin R, Sfriso P, Balestro E, Dinarello CA and Saetta M. IL-32, a novel proinflammatory cytokine in chronic obstructive pulmonary disease. Am J Respir Crit Care Med 2008; 178: 894-901.

[15] Suga H, Sugaya M, Miyagaki T, Kawaguchi M, Fujita H, Asano Y, Tada Y, Kadono T and Sato S. The role of IL-32 in cutaneous T-cell lymphoma. J Invest Dermatol 2014; 134: 1428-1435.

[16] Guenin S, Mouallif M, Hubert P, Jacobs N, Krusy N, Duray A, Ennaji MM, Saussez S and Delvenne P. Interleukin-32 expression is associated with a poorer prognosis in head and

neck squamous cell carcinoma. Mol Carcinog 2014; 53: 667-73.
[17] Kang YH, Park MY, Yoon DY, Han SR, Lee CI, Ji NY, Myung PK, Lee HG, Kim JW, Yeom YI, Jang YJ, Ahn DK, Kim JW and Song EY. Dysregulation of overexpressed IL-32alpha in hepatocellular carcinoma suppresses cell growth and induces apoptosis through inactivation of NF-kappaB and Bcl-2. Cancer Lett 2012; 318: 226-33.
[18] Wang Y, Yang Y, Zhu Y, Li L, Chen F and Zhang L. Polymorphisms and expression of IL-32: impact on genetic susceptibility and clinical outcome of lung cancer. Biomarkers 2017; 22: 165-170.
[19] Yu X, Zhou B, Zhang Z, Gao Q, Wang Y, Song Y, Pu Y, Chen Y, Duan R, Zhang L and Xi M. Significant association between IL-32 gene polymorphisms and susceptibility to endometrial cancer in Chinese Han women. Tumour Biol 2015; 36: 5265-72.
[20] Mutch DG and Prat J. 2014 FIGO staging for ovarian, fallopian tube and peritoneal cancer. Gynecol Oncol 2014; 133: 401-404.
[21] Untergasser A, Cutcutache I, Koressaar T, Ye J, Faircloth BC, Remm M and Rozen SG. Primer3--new capabilities and interfaces. Nucleic Acids Res 2012; 40: e115.
[22] Sole X, Guino E, Valls J, Iniesta R and Moreno V. SNPStats: a web tool for the analysis of association studies. Bioinformatics 2006; 22: 1928-1929.
[23] Shamoun L, Kolodziej B, Andersson RE and Dimberg J. Protein expression and genetic variation of il32 and association with colorectal cancer in Swedish patients. Anticancer Res 2018; 38: 321-328.
[24] Sunaga N, Imai H, Shimizu K, Shames DS, Kakegawa S, Girard L, Sato M, Kaira K, Ishizuka T, Gazdar AF, Minna JD and Mori M. Oncogenic KRAS-induced interleukin-8 overexpression promotes cell growth and migration and contributes to aggressive phenotypes of non-small cell lung cancer. Int J Cancer 2012; 130: 1733-1744.
[25] Sullivan NJ, Sasser AK, Axel AE, Vesuna F, Raman V, Ramirez N, Oberyszyn TM and Hall BM. Interleukin-6 induces an epithelial-mesenchymal transition phenotype in human breast cancer cells. Oncogene 2009; 28: 2940-2947.
[26] Li Y, Wang L, Pappan L, Galliher-Beckley A and Shi J. IL-1beta promotes stemness and invasiveness of colon cancer cells through Zeb1 activation. Mol Cancer 2012; 11: 87.
[27] Oh JH, Cho MC, Kim JH, Lee SY, Kim HJ, Park ES, Ban JO, Kang JW, Lee DH, Shim JH, Han SB, Moon DC, Park YH, Yu DY, Kim JM, Kim SH, Yoon DY and Hong JT. IL-32gamma inhibits cancer cell growth through inactivation of NF-kappaB and STAT3 signals. Oncogene 2011; 30: 3345-59.
[28] Park JS, Choi SY, Lee JH, Lee M, Nam ES, Jeong AL, Lee S, Han S, Lee MS, Lim JS, Yoon DY, Kwon Y and Yang Y. Interleukin-32beta stimulates migration of MDA-MB-231 and MCF-7cells via the VEGF-STAT3 signaling pathway. Cell Oncol (Dordr) 2013; 36: 493-503.
[29] Yousif NG, Al-Amran FG, Hadi N, Lee J and Adrienne J. Expression of IL-32 modulates NF-kappaB and p38 MAP kinase pathways in human esophageal cancer. Cytokine 2013; 61: 223-227.