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Original Article

The association between *phospholipase C epsilon* gene (*PLCE1*) polymorphisms and colorectal cancer risk in a Chinese Han population: a case-control study

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Abstract: Background: Heritable factors contribute to the development of colorectal cancer (CRC). We investigated the association between single nucleotide polymorphisms in *phospholipase C epsilon 1* (*PLCE1*) and CRC susceptibility. Methods: We selected eight tag single nucleotide polymorphisms (tSNPs) and investigated whether they were associated with CRC in Chinese Han population. In this study, we used Sequenom MassARRAY technology and genotyped 276 CRC cases and 385 controls. The effects of the polymorphisms on the risk of CRC were expressed as odds ratios (ORs) with 95% confidence intervals (95% CIs), evaluated by different genetic models using unconditional logistic regression analysis adjusted for age and gender. We also analyzed the risk of the eight *PLCE1* tSNPs in different histology of CRC. Results: Based on x^2 tests, rs753724 (OR = 1.49, 95% CI: 1.10-2.03, *P* = 0.010) and rs10882424 (OR = 1.32, 95% CI: 1.02-1.70, *P* = 0.037) in *PLCE1* were associated with CRC. In genetic model analyses, we found that rs753724 in *PLCE1* may increase CRC risk (OR = 1.48, 95% CI: 1.09-2.03, *P* = 0.013) in the log-additive model, and rs11187842 in *PLCE1* may increase CRC risk (OR = 3.09, 95% CI: 1.17-8.14, *P* = 0.018) in the recessive model. Rs753724 TT (OR = 4.31, *P* = 0.010), rs11187842 TT (OR = 5.78, *P* = 0.003), and rs10882424 GG (OR = 2.64, *P* = 0.022) in *PLCE1* may increase rectal cancer in a recessive model. Conclusions: Our results suggest that *PLCE1* may be associated with CRC in Han Chinese population.

Keywords: Phospholipase C epsilon 1, single nucleotide polymorphism, colorectal cancer, case-control

Introduction

Colorectal cancer (CRC), which includes colon and rectal cancers, is the third most commonly diagnosed cancer in males and the second in females [1, 2]. Although CRC is primarily a disease of high-income countries, there has been a rapid increase in CRC rates in low and middle income countries that have recently transitioned from a relatively low- or middle-income economy, such as Japan, Singapore, and countries in eastern Europe [3]. It has been recognized that CRC is a multifactorial disease caused by complex interactions between environmental and genetic factors [4]. Risk factors for CRC consist of high fat and alcohol intake, obesity, smoking, and lack of physical exercise [5]. Currently, many candidate genes have been identified, including *phospholipase C epsilon 1* (*PLCE1*), which may be implicated in the genesis of CRC [6].

Phospholipase C epsilon 1 (*PLCE1*) is encoded by the *PLCE1* gene on chromosome 10q23 and belongs to the phosphoinositide-specific phospholipase C (PLC) enzyme family. It contains one cell division cycle 25 domain at the N-terminus and two Ras-associating domains at the C-terminus [7, 8]. PLCE1 catalyzes the hydrolysis of polyphosphoinositides such as phosphatidylinositol-4,5-bisphosphate (PtdIns(4,5)P2) to generate the second mes-

Table 1. Clinical and demographic characteristics of Han Chinese patients with CRC and healthy control subjects

Characteristic	Patients with CRC (n = 276)	Healthy control subjects (n = 385)
Sex		
Female	105 (38)	188 (48.8)
Male	171 (62)	197 (51.2)
Age; years	58.20±11.616	50.67±8.425
< 50	58 (21)	191 (49.6)
≥ 50	218 (79)	194 (50.4)
Histology		
Colon	154 (55.8)	
Others	16 (5.8)	
Rectum	106 (38.4)	

Data presented as mean ± SD for age; Other data presented as number (%) of patients or controls.

sengers Ins(1,4,5)P3 and diacylglycerol. These products initiate a cascade of intracellular responses that result in cell growth and differentiation and gene expression [6]. In addition, *PLCE1* activates the small G protein Ras/mitogen-activated protein kinase (MAPK) signaling [9]. Studies have reported that *PLCE1* has a fundamental role in carcinogenesis and the progression of various human cancers, including cancers of the intestine, skin, bladder, and head and neck [10-13]. However, no associations between the potentially functional variants of *PLCE1* and CRC susceptibility have been reported.

Therefore, we performed genotyping analyses of eight tSNPs in *PLCE1* in Chinese populations with a high incidence of CRC and assessed their associations with CRC risk in our case-control study of 276 CRC cases and 385 healthy controls. In addition, we assessed the risk of the eight *PLCE1* tSNPs in different histology of CRC.

Materials and methods

Ethics statement

The use of human tissue and the protocol in this study were strictly conformed to the principles expressed in the Declaration of Helsinki and were approved by the Ethical Committee of Yulin first hospital and the Fourth Hospital of Yulin for approval of research involving human subjects. Signed informed consent was obtained from each participant.

Study population

We conducted a case-control study to assess genetic associations with CRC risk. Patients with newly diagnosed CRC from Yulin first hospital and the Fourth Hospital of Yulin, were enrolled in this study. Control subjects were randomly recruited from health centers of the two hospitals during the same period, and were matched with CRC patients based on age and gender. All cases had histologically confirmed CRC, and controls were newly-diagnosed incident patients. We excluded subjects who underwent radiotherapy or chemotherapy as well as controls with chronic disease. All participants were at least 18 years old and in good mental health. Additionally, all participants were Han Chinese. In total, 385 controls and 276 CRC cases were recruited for this study.

Clinical data and demographic information

Demographic and personal data were collected through an in-person interview using a standardized epidemiological questionnaire, which collected data on age, sex, ethnicity, residential region, diet, education status, family history of cancer, etc. For patients, related information was also collected through consultation with treating physicians or medical chart reviews. All participants signed informed consent forms, and then 5 ml peripheral blood was drawn from each subject.

tSNP selection and genotyping

A total of eight tSNPs from the *PLCE1* gene were selected for our study, each with a minor allele frequency (MAF) greater than 5% in the HapMap Chinese Han Beijing population. Genomic DNA was extracted from peripheral blood using the GoldMag Whole Blood Genomic DNA Extraction kit (GoldMag Co. Ltd. Xi'an, China) according to the manufacturer's instructions. DNA concentrations were measured using the NanoDrop 2000 (Thermo Scientific, Waltham, MA, USA). A Sequenom MassARRAY mass spectrometry analyzer (Sequenom, San Diego, CA, USA) was used for genotyping, and data were managed using Sequenom Typer 4.0 Software (Sequenom).

Statistical analysis

Statistical analyses were performed using Microsoft Excel and SPSS 16.0 statistical pack-

Table 2. Basic information of candidate tSNPs of *PLCE1*

SNP	Gene (s)	Alleles A/B[a]	SNP function	Chromosome	Position	HWE-*p*	ORs (95% CI)	Pearson Chi-Square *p* value
rs753724	*PLCE1*	T/G	Intron 22	10	96051417	0.170	1.49 (1.10-2.03)	0.010*
rs11187842	*PLCE1*	T/C	Intron 22	10	96052511	0.338	1.24 (0.88-1.73)	0.214
rs3818432	*PLCE1*	A/C	Intron 24	10	96064168	0.397	1.31 (1.00-1.71)	0.053
rs11187850	*PLCE1*	G/A	Intron 27	10	96068480	0.236	1.24 (0.95-1.63)	0.114
rs10509671	*PLCE1*	G/T	Intron 27	10	96069054	0.025	1.47 (1.09-1.98)	0.012
rs2077218	*PLCE1*	C/T	Intron 27	10	96071561	0.004	0.91 (0.72-1.14)	0.414
rs12219592	*PLCE1*	T/C	Intron 29	10	96077222	0.010	1.21 (0.83-1.77)	0.326
rs10882424	*PLCE1*	G/T	Intron 32	10	96086078	0.758	1.32 (1.02-1.70)	0.037*

P < 0.05 was considered statistically significant. [a]A/B refers to the major/minor alleles; *indicates statistical significance.

Table 3. Relationship between the *PLCE1* gene and CRC risk (adjusted by sex and age)

Model	rs753724			rs11187842		
	Genotype	OR (95% CI)	*p*-value	Genotype	OR (95% CI)	*p*-value
Codominant	G/G	1	0.032*	C/C	1	0.060
	G/T	1.34 (0.89-1.99)		T/C	0.93 (0.60-1.46)	
	T/T	2.90 (1.16-7.25)		T/T	3.05 (1.15-8.06)	
Dominant	G/G	1	0.039*	C/C	1	0.580
	G/T-T/T	1.49 (1.02-2.17)		T/C-T/T	1.13 (0.74-1.70)	
Recessive	G/G-G/T	1	0.028*	C/C-T/C	1	0.018*
	T/T	2.71 (1.09-6.73)		T/T	3.09 (1.17-8.14)	
Overdominant	G/G-T/T	1	0.240	C/C-T/T	1	0.600
	G/T	1.27 (0.85-1.89)		T/C	0.89 (0.57-1.38)	
Log-additive	---	1.48 (1.09-2.03)	0.013*	---	1.25 (0.89-1.75)	0.190

P < 0.05 was considered statistically significant. *indicates statistical significance.

ages (SPSS, Chicago, IL, USA). All *p* values in this study are two-sided. A *p* value < 0.05 was considered statistically significant. In controls, each tSNP was tested to determine whether it fit Hardy-Weinberg equilibrium (HWE). X^2 tests were used to test the association between gene polymorphisms and CRC [14]. Odds ratio (OR) and 95% confidence intervals (CI) were calculated using unconditional logistic regression analyses adjusted for age and gender [15]. We also divided subjects into subgroups: rectum and colon. The most common control homozygote was used as a reference. Akaike's Information Criterion (AIC) and Bayesian Information Criterion (BIC) were used to choose the best model for each tSNP.

Results

This study included 276 CRC cases (105 females, 171 males; mean age 58.20 years) and 385 controls (188 females, 197 males; mean age 50.67 years). The characteristics of cases and controls are summarized in **Table 1**.

As shown in **Table 2**, three sites (rs10509671, rs2077218, 12219592) did not fit HWE in control subjects. Based on X^2 tests, rs753724 (OR = 1.49, 95% CI: 1.10-2.03, *P* = 0.010) and rs10882424 (OR =1.32, 95% CI: 1.02-1.70, *P* = 0.037) in *PLCE1* were associated with CRC in allele model.

Further model association analyses were performed using logistic tests. As shown in **Table 3**, rs753724 in *PLCE1* may increase CRC risk (OR = 1.48, 95% CI: 1.09-2.03, *P* = 0.013) in the log-additive model, and rs11187842 may increase CRC risk (OR = 3.09, 95% CI: 1.17-8.14, *P* = 0.018) in the recessive model after adjusting for age and sex.

The TT genotype of rs753724 (OR = 4.31, *P* = 0.010), TT genotype of rs11187842 (OR = 5.78,

Table 4. Relationship between *PLCE1* and risk of rectum and colon disease adjusted by sex and age

SNP		Model										
		Co-dominant			Dominant			Recessive			Log-additive	
		Genotype	OR (95% CI)	*p*-value	Genotype	OR (95% CI)	*p*-value	Genotype	OR (95% CI)	*p*-value	OR (95% CI)	*p*-value
rs753724	Rectum	G/G	1	0.026*	G/G	1	0.098	G/G-G/T	1	0.010*	1.63 (1.08–2.46)	0.021*
		G/T	1.26 (0.73–2.19)		G/T-T/T	1.54 (0.93-2.55)		T/T	4.31 (1.45-12.82)			
		T/T	4.56 (1.52-13.67)									
	Colon	G/G	1	0.590	G/G	1	0.480	G/G-G/T	1	0.350	1.20 (0.81–1.76)	0.360
		G/T	1.11 (0.68-1.82)									
		T/T	1.74 (0.57-5.27)		G/T-T/T	1.18 (0.74-1.88)		T/T	1.70 (0.56-5.12)			
rs11187842	Rectum	C/C	1	0.009*	C/C	1	0.540	C/C-T/C	1	0.003*	1.46 (0.94–2.27)	0.099
		T/C	0.83 (0.44-1.59)									
		T/T	5.57 (1.80-17.28)		T/C-T/T	1.19 (0.68–2.09)		T/T	5.78 (1.88-17.81)			
	Colon	C/C	1	0.700	C/C	1	0.670	C/C-T/C	1	0.580	0.96 (0.63–1.49)	0.870
		T/C	0.84 (0.48-1.45)		T/C-T/T	0.90 (0.53-1.50)		T/T	1.43 (0.41-4.91)			
		T/T	1.38 (0.40-4.76)									
rs10882424	Rectum	T/T	1	0.060	T/T	1	0.170	T/T-G/T	1	0.022*	1.45 (1.02–2.07)	0.042*
		G/T	1.17 (0.70-1.93)		G/T-G/G	1.39 (0.87-2.20)		G/G	2.64 (1.17-5.91)			
		G/G	2.78 (1.21-6.36)									
	Colon	T/T	1	0.650	T/T	1	0.410	T/T-G/T	1	0.880	1.11 (0.79–1.55)	0.540
		G/T	1.22 (0.79-1.89)									
		G/G	1.00 (0.41-2.46)		G/T-G/G	1.19 (0.79-1.80)		G/G	0.94 (0.39-2.27)			

P < 0.05 was considered statistically significant. *indicates statistical significance.

P = 0.003), and GG genotype of rs10882424 (OR = 2.64, *P* = 0.022) may increase rectal cancer in a recessive model after adjusting for age and sex (**Table 4**).

Discussion

This hospital-based, case-control study investigated the association between *PLCE1* and the risk of CRC in a Han Chinese population. The current results show that the rs753724 and rs11187842 polymorphisms of *PLCE1* might contribute to CRC risk. To the best of our knowledge, this is the first report evaluating the relationship between the SNPs rs753724 and rs11187842 of *PLCE1* and the risk of CRC. Our results also demonstrate that rs753724, rs11187842, and rs10882424 polymorphisms in the *PLCE1* gene increase the risk of rectum disease, but are not related to colon disease.

PLCE1 is a member of the phospholipase C family of proteins. *PLCE1* functions differently from the other PLC family molecules [16]. It may be related to cellular differentiation and apoptosis via its interaction with the Ras family [17, 18]. Using a gene transfection strategy, Wang et al. showed that *PLCE1* overexpression inhibited tumor cell growth, decreased colony formation, reduced cellular migration, increased apoptosis, reduced tumorigenicity, and arrested cells in the G1 phase. These findings suggest that *PLCE1* overexpression suppresses the aggressive phenotypes of tumor cells [19]. *PLCE1* was observed to regulate GEF activity of CDC25 [20] and is speculated to be a receptor for Ras GTP [21, 22]. Some molecules of the Ras family are associated with cell growth, proliferation, differentiation, and apoptosis. Moreover, several molecules that are either upstream or downstream of Ras have been reported to promote oncogenesis [23].

The SNPs rs753724 (G>T), rs11187842 (C>T), and rs10882424 (T>G) are in noncoding nonpromoter positions within *PLCE1*; therefore, these SNPs are unlikely to directly influence *PLCE1* expression [24, 25]. This phenomenon may be related to sequence variations in regions of the *PLCE1* gene crucial to mRNA processing and may regulate post-transcriptional modifications, protein translation, or activity of the promoter/enhancer cluster. Additionally, two SNPs (rs753724, rs11187842) were located in the core catalytic domains of the PLCε protein, which catalyzes hydrolysis of polyphosphoinositides to generate intracellular secondary messengers, such as diacylglycerol and inositol-1,4,5 trisphosphate, to contribute to intracellular signaling [24]. PLCE1 protein initiates a cascade of intracellular responses that result in cell growth, differentiation, and gene expression. Thus, we speculate that when the two SNPs (rs753724, rs11187842) are mutated, they result in increased expression of cancer genes and uncontrolled cell division, and thus cause cancer.

In previous studies, Duan et al. and Li et al. found no significant association between rs753724 and rs11187842, located on chromosome 10q23, with CRC in the Chinese population [26, 27]. However, our results showed that the rs753724 and rs11187842 polymorphisms of *PLCE1* might contribute to an increased risk of CRC in the Han Chinese population. In addition, the rs753724, rs11187842, and rs10882424 polymorphisms increase the risk of rectum disease, but are not significantly associated with colon disease. There are a number of reasons for these potentially conflicting data. First, our study was a hospital-based study and inherent biases regarding this type of study might lead to unreliable results. Second, our sample size is small and experimental verification of larger samples is necessary. Finally, statistical error might explain these conflicting results.

Conclusions

Our current data show that the genotype distribution of the *PLCE1* rs753724 and rs11187842 polymorphisms differed significantly between patients with CRC and healthy control subjects. Larger population-based studies and in-depth molecular studies are needed to validate our current findings as well as to elucidate the functional roles of rs753724 and rs11187842 in CRC etiology.

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Disclosure of conflict of interest

None.

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References

[1] Li XX, Sun GP, Meng J, Li X, Tang YX, Li Z, Wang MF, Liang GF and Lu XB. Role of toll-like receptor 4 in colorectal carcinogenesis: a meta-analysis. PLoS One 2014; 9: e93904.

[2] Jemal A, Bray F, Center MM, Ferlay J, Ward E and Forman D. Global cancer statistics. CA Cancer J Clin 2011; 61: 69-90.

[3] Kirac I, Sekerija M, Simunovic I, Zgaga L, Velimir Vrdoljak D, Kovacevic D, Kulis T and Znaor A. Incidence and mortality trends of gastric and colorectal cancers in Croatia, 1988-2008. Croat Med J 2012; 53: 124-134.

[4] Mlecnik B, Tosolini M, Charoentong P, Kirilovsky A, Bindea G, Berger A, Camus M, Gillard M, Bruneval P, Fridman WH, Pages F, Trajanoski Z and Galon J. Biomolecular network reconstruction identifies T-cell homing factors associated with survival in colorectal cancer. Gastroenterology 2010; 138: 1429-1440.

[5] Huxley RR, Ansary-Moghaddam A, Clifton P, Czernichow S, Parr CL and Woodward M. The impact of dietary and lifestyle risk factors on risk of colorectal cancer: a quantitative overview of the epidemiological evidence. Int J Cancer 2009; 125: 171-180.

[6] Wang Q, Chen P, Chen D, Liu F and Pan W. Association between phospholipase C epsilon gene (PLCE1) polymorphism and colorectal cancer risk in a Chinese population. J Int Med Res 2014; 42: 270-281.

[7] Bunney TD and Katan M. Phospholipase C epsilon: linking second messengers and small GTPases. Trends Cell Biol 2006; 16: 640-648.

[8] Katan M. New insights into the families of PLC enzymes: looking back and going forward. Biochem J 2005; 391: e7-e9.

[9] Lopez I, Mak EC, Ding J, Hamm HE and Lomasney JW. A novel bifunctional phospholipase c that is regulated by Galpha 12 and stimulates the Ras/mitogen-activated protein kinase pathway. J Biol Chem 2001; 276: 2758-2765.

[10] Li M, Edamatsu H, Kitazawa R, Kitazawa S and Kataoka T. Phospholipase Cepsilon promotes intestinal tumorigenesis of Apc(Min/+) mice through augmentation of inflammation and angiogenesis. Carcinogenesis 2009; 30: 1424-1432.

[11] Bai Y, Edamatsu H, Maeda S, Saito H, Suzuki N, Satoh T and Kataoka T. Crucial role of phospholipase Cepsilon in chemical carcinogen-induced skin tumor development. Cancer Res 2004; 64: 8808-8810.

[12] Ou L, Guo Y, Luo C, Wu X, Zhao Y and Cai X. RNA interference suppressing PLCE1 gene expression decreases invasive power of human bladder cancer T24 cell line. Cancer Genet Cytogenet 2010; 200: 110-119.

[13] Bourguignon LY, Gilad E, Brightman A, Diedrich F and Singleton P. Hyaluronan-CD44 interaction with leukemia-associated RhoGEF and epidermal growth factor receptor promotes Rho/Ras co-activation, phospholipase C epsilon-Ca2+ signaling, and cytoskeleton modification in head and neck squamous cell carcinoma cells. J Biol Chem 2006; 281: 14026-14040.

[14] Adamec C. [Example of the use of the nonparametric test. test x^2 for comparison of 2 independent examples]. Cesk Zdrav 1964; 12: 613-619.

[15] Bland JM and Altman DG. Statistics notes. The odds ratio. BMJ 2000; 320: 1468.

[16] Shibatohge M, Kariya KI, Liao Y, Hu CD, Watari Y, Goshima M, Shima F and Kataoka T. Identification of PLC210, a Caenorhabditis elegansPhospholipase C, as a Putative Effector of Ras. J Biol Chem 1998; 273: 6218-6222.

[17] Harden TK and Sondek J. Regulation of phospholipase C isozymes by ras superfamily GTPases. Annu Rev Pharmacol Toxicol 2006; 46: 355-379.

[18] Ada-Nguema AS, Xenias H, Sheetz MP and Keely PJ. The small GTPase R-Ras regulates organization of actin and drives membrane protrusions through the activity of PLC. J Cell Sci 2006; 119: 1307-1319.

[19] Wang X, Zhou C, Qiu G, Yang Y, Yan D, Xing T, Fan J, Tang H and Peng Z. Phospholipase C epsilon plays a suppressive role in incidence of colorectal cancer. Med Oncol 2012; 29: 1051-1058.

[20] Jin TG, Satoh T, Liao Y, Song C, Gao X, Kariya K, Hu CD and Kataoka T. Role of the CDC25 homology domain of phospholipase Cepsilon in amplification of Rap1-dependent signaling. J Biol Chem 2001; 276: 30301-30307.

[21] Kelley GG, Reks SE, Ondrako JM and Smrcka AV. Phospholipase C(epsilon): a novel Ras effector. EMBO J 2001; 20: 743-754.

[22] Song C, Hu CD, Masago M, Kariyai K, Yamawaki-Kataoka Y, Shibatohge M, Wu D, Satoh T and Kataoka T. Regulation of a novel human phospholipase C, PLCepsilon, through membrane targeting by Ras. J Biol Chem 2001; 276: 2752-2757.

[23] Downward J. Targeting RAS signalling pathways in cancer therapy. Nat Rev Cancer 2003; 3: 11-22.

[24] Cui XB, Chen YZ, Pang XI, Liu W, Hu JM, Li SG, Yang L, Zhang WJ, Liu CX and Cao YW. Multiple polymorphisms within the *PLCE1* are associated with esophageal cancer via promoting the gene expression in a Chinese Kazakh population. Gene 2013; 530: 315-322.

[25] Yuan LJ, Jin TB, Yin JK, Du XL, Wang Q, Dong R, Wang SZ, Cui Y, Chen C and Lu JG. Polymorphisms of tumor-related genes IL-10, PSCA, MTRR and NOC3L are associated with the risk of gastric cancer in the Chinese Han population. Cancer Epidemiol 2012; 36: e366-372.

[26] Duan X, Li X, Lou H, Geng T, Jin T, Liang P, Li S, Long Y and Chen C. Genetic association of PLCE1, C11orf92-C11orf93, and NOC3L with colorectal cancer risk in the Han population. Tumour Biol 2014; 35: 1813-1817.

[27] Li FX, Yang XX, He XQ, Hu NY, Wu YS and Li M. Association of 10q23 with colorectal cancer in a Chinese population. Mol Biol Rep 2012; 39: 9557-9562.