Int J Clin Exp Med 2015;8(11):21407-21413
www.ijcem.com /ISSN:1940-5901/IJCEM0014376

Original Article

Genetic association of G-607C Located at *wnt10b* promoter with *bi-sup* type among Korean cerebral infarction patients

Mi Mi Ko[1], Myeong Soo Lee[2], Min Ho Cha[1]

[1]KM Fundamental Research Division, Korea Institute of Oriental Medicine, 1672 Yuseongdaero, Yuseong-gu, Daejeon, South Korea; [2]Clinical Research Division, Korea Institute of Oriental Medicine, 1672 Yuseongdaero, Yuseong-gu, Daejeon, South Korea

Received August 12, 2015; Accepted October 29, 2015; Epub November 15, 2015; Published November 30, 2015

Abstract: Obesity is a disease threatening health and is known one of risk factors causing chronic disease. In Traditional Korean Medicine, *bi-sup* is casus of obesity. Wnt10b has been indicated as a potential regulator of adipogenesis *in vivo* and *in vitro* models of obesity. To analyze the distribution of wnt10b polymorphism between *bi-sup* group and non-*bi-sup* group in Korean elder subjects with cerebral infarction (CI). The study group was composed of patients with CIwho were admitted to one of the thirteen Korean oriental medical hospitals participating in this study from 2009 to 2010. A total of 670 CI patients, including 416 with *bi-sup* group and 254 with non-*bi-sup* group, participated in this study. Genotype of G-607C was conducted by primer extension using TaqManprobe and five percent of subjects were re-genotyped by direct sequencing to confirm the accuracy of the genotyping. The association of the SNP with the *bi-sup*groupversus non-*bi-sup*group was performed by multiple logistic regression. Frequency of C allele in *bi-sup* was 45.75% which was significantly lower than 56.69% in non-*bi-sup* (P=0.0043, OR=0.628 [0.453-0.864]). Subjects with GC or CC type in *bi-sup* was also 72.36%, that was also small compared with 78.35% in non-*bi-sup* (P=0.0467, OR=0.675 [0.458-0.994]). These results suggest that G-607C might be used as a diagnostic genetic marker for *bi-sup* in stroke patients and in the development of personalized medical care.

Keywords: wnt10b, G-607C, bi-sup, obesity, stroke, cerebral infarction, traditional Korean medicine

Introduction

Obesity is a disease threatening health and is known one of risk factors causing chronic disease such as hypertension, diabetes and atherosclerosis. Obese patients were currently increasing in worldwide. In Korea, adults subjects with obesity (BMI≥25 kg/m^2) is about 30.8% in over 19 aged people at 2010, which was higher than 26% at 1998. Especially, ratio of obesity in man was 36.3%, which is significantly high compared with woman. Because increase of obese subject related with social problems such as raise of disease incidence, decrease of social activity, many efforts is being done to decrease obese population in the world [1].

Particularly, obesity is a risk factor for the onset of stroke [2]. Risk ratio of stroke in man is increasing about 11% whenever BMI increase 1 kg/m^2 [3], and relationship between increase of BMI and onset of ischemic stroke was well known in woman [4]. In *Donguibogam* written at 1610, the relationship between obesity and stroke was described that stroke more occurs in obese subjects than non-obese subjects. It means that obesity is recognized as a risk factor for stroke from old period [5].

In Traditional Korean Medicine (TKM), obese man is defined that shoulder is wide, neck and skin are thick, color of skin is dark, and mouth and lip are large. That also say that *bi-sup* is casus of obese man [6]. The *bi-sup* is a symptom of accumulation of excess waste in body caused by preventing circulation of fat, body fluid, *Qi* and blood, and that occur by erudite and overeating of alcohol, meat and fatty food. That is similar with cause of obesity saying in western medicine [5].

Table 1. Demographic parameters of study subjects

Characteristics	Non-*Bi-Sup*	*Bi-Sup*	*P*
N	254	416	
Sex (M/F)	119/135	150/266	**0.0057**
Age (year)	73 (65, 79)	69 (60, 76)	**<0.0001***
Smoking (none/stop/active)	122/51/81	259/77/80	**0.0003**
Drinking (none/stop/active)	128/38/88	230/50/136	0.3817
TOAST classification			
LAA	79	119	0.6249
CE	21	30	
SVO	135	245	
SOE	7	8	
SUE	11	13	
Medical history			
TIA (Yes, %)	38 (15.08)	49 (11.86)	0.2330
Hypertension (Yes, %)	140 (55.12)	269 (64.66)	**0.014**
Hyperlipidemia (Yes, %)	26 (10.32)	65 (15.7)	**0.0498**
Diabetes (Yes, %)	56 (22.05)	117 (28.26)	0.0751
Heart disease (Yes, %)	16 (6.3)	28 (6.76)	0.8144

All results except age are expressed as frequencies for categorical variables. Age is expressed as Median (25% percentile, 75% percentile). ICH: intracerebral hemorrhage. CI: cerebral infarction. TOAST: Trial of ORG 10172 in Acute Stroke Treatment. LAA: large-artery atherosclerosis. CE: cardioembolism. SVO: small-vessel occlusion. SOE: stroke of other etiology. SUE: stroke of undetermined etiology. TIA: transient ischemic attack. *P*-value of *Bi-Sup* versus *Non-Bi-Sup* using a Student's t-test or Wilcoxon rank-sum test (*) in continuous variables, chi-square test in categorical variables. *P*-values with statistical significance were presented in bold (<0.05).

Table 2. Differences in body characteristics and serum parameters among the study subjects

Characteristics	*Non-Bi-Sup*	*Bi-Sup*	*P*
N	254	416	
Body characteristics			
Weight (kg)	54.99±9.69	65.83±9.82	**<.0001**
BMI (kg/m^2)	21.33±2.48	25.83±2.81	**<.0001**
Waist circumference (cm)	81.24±8.26	92.28±7.45	**<.0001**
WHR	0.95±0.18	0.95±0.08	0.2703
Serum parameter			
GOP (U/ml)	28.45±18.36	25.88±11.94	**0.0199**
GPT (U/ml)	25.3±22.26	24.5±15.89	0.1962
Total cholesterol (mg/dL)	183.0±44.71	189.5±49.31	0.0915
Triglyceride (mg/dL)	139.5±112.1	171.0±122.3	**0.0039**
HDL-cholesterol (mg/dL)	44.78±13.11	42.57±10.20	**0.0181**
Blood sugar (mg/dL)	110.2±48.61	115.7±38.56	0.4012

All of the results are expressed as the mean ± standard deviation. BMI: body mass index. WHR: waist-hip ratio. GOP: glutamate oxaloacetate transaminase. GPT: glutamate pyruvate transaminase. *P*-values were adjusted for sex, age, smoking, hypertension and hyperlipidemiausing a general linear model. *P*-values with statistical significance are presented in bold (<0.05).

Bi-sup of subjects is determined by oriental medical doctor through combination of body, Visage skin thickness etc., and that was some different obese index such as BMI used in western medicine. Previous studies used BMI or waist circumference as indicator of diagnosis of pattern identification instead of *bi-sup*, but the results some different compared with *bi-sup* as index of pattern identification [7-9]. Recently study showed that *bi-sup* was correlated with BMI but not with waist and WHR, an index of abdominal obesity [6], that means western medicine has a limitation to explain the concept of *bi-sup* used in oriental medicine.

Wingless-type MMTV integration sites (WNTs) is signal molecules binding Frizzled receptor and low-density lipoprotein receptor-related protein 5/6 co-receptor and regulate several physical activity [10]. Especially, *wnt10b* is known to inhibit adipogenesis throughout β-catenin pathway [11]. Recent reports showed that singe nucleotide polymorphism in wnt10b promoter region affect obesity, fat mass and abdominal obesity in various population [12-14].

In this study, we elucidated *bi-sup* from ischemic stroke and association between *bi-sup* and SNP of wnt10b gene.

Subjects and methods

Subjects

This study was performed as parts of the project "The Fundamental Study for the Standardization and Objectification of Pattern Identification in TKM for Stroke (SOPI-Stroke)" in the Korean Institute of Oriental Medicine (KIOM) [15]. Patient with ischemic cerebral infarction (CI) and within one month after onset were enrolled from 2009 to 2010 in to 13 Korean oriental medical hospitals. All subjects were confirmed CI by magnetic resonance imaging (MRI) and computerized tomography (CT). Subjects with transient ischemic attack or external hemorrhage were excluded in this study. Subjects to be not recorded ques-

Table 3. Genotype distribution of the G-607C polymorphism in the *Bi-Sup* and *Non-Bi-Sup* group

Model	Genotype	*Non-Bi-Sup*	*Bi-Sup*	†OR [95% CI]	*P*	‡OR [95% CI]	*P*
Allele	G	237 (46.65)	434 (52.16)	0.792 [0.632, 0.991]	**0.0419**	0.779 [0.618, 0.982]	**0.0348**
	C	271 (53.35)	398 (47.84)				
§Do	GG	55 (21.65)	115 (27.64)	0.703 [0.484, 1.022]	0.0649	0.675 [0.458, 0.994]	**0.0467**
	GC+CC	199 (78.35)	301 (72.36)				
§R	GG+GC	182 (71.65)	319 (76.68)	0.764 [0.531, 1.097]	0.1446	0.761 [0.524, 1.104]	0.1506
	CC	72 (28.35)	97 (23.32)				

Data are presented as frequencies (percentages). †ORs after adjustment for sex and age ‡ORs after adjustment for sex, age, smoking, hypertension and hyperlipidemia. *P*-values were calculated by logistic regression analysis. §Do and R denote dominant and recessive models, respectively. *P*-values with statistical significance are presented in bold (<0.05).

Table 4. Association of the G-607C polymorphism with clinical parameters among the study subjects

Variable	Genotype			*P*		
	GG (n=170)	GC (n=331)	CC (n=169)	§Co	§Do	§R
Body characteristics						
Weight (kg)	61.38±11.83	62.63±10.99	60.6±10.42	0.1559	0.4864	0.1450
BMI (kg/m^2)	24.21±3.42	24.28±3.62	23.87±3.16	0.6149	0.8047	0.3258
Waist circumference (cm)	88.07±9.84	88.44±9.62	87.13±8.65	0.4538	0.9648	0.2392
WHR	0.95±0.1	0.95±0.12	0.95±0.18	0.9974	0.9870	0.9428
Serum parameter						
GOP (U/ml)	24.81±10.57	27.36±15.78	27.94±16.09	0.1246	**0.0463**	0.2748
GPT (U/ml)	23.48±16.54	25.38±19.7	24.99±18.14	0.5177	0.2519	0.7489
Total cholesterol (mg/dL)	190.53±51.43	188.4±47.76	181.18±43.15	0.1482	0.2402	0.0618
Triglyceride (mg/dL)	168.84±147.33	160.04±115.06	147.9±94.2	0.3611	0.2553	0.2306
HDL-cholesterol (mg/dL)	43.92±11.08	43.56±11.29	42.41±11.81	0.5200	0.3824	0.3224
Blood sugar (mg/dL)	109.14±29.03	117.11±50.51	111.6±35.64	0.1410	0.1159	0.5475

Data are presented as the mean ± S.D. *P*-values, representing adjusted odds ratios, were adjusted for sex, age, smoking, hypertension and hyperlipidemia using a general linear model. §Co, Do and R denote codominant, dominant and recessive models, respectively. *P*-values with statistical significance are presented in bold (<0.05).

tionnaire by confusion of consciousness or difficult communication were also excluded. Clinical information was collected using questionnaire based on 'Standard of TKM stroke PI' [16]. This study was performed after receiving informed content from each subjects and approval of the Institutional Review Boards of the KIOM.

Diagnosis of bi-sup and patter identification

Determining *bi-sup* from each of subject was diagnosed by two experts of TKM within 24 hours and subjects, which were differently diagnosed by two experts, were excluded in study. 416 subjects with *bi-sup* and 254 without *bi-sup* were enrolled and general characteristics of those were presented in **Table 1**.

Genotyping of G-607C SNP

After agreement of subject, blood were collected and genomic DNA were precipitated using a GeneAll Genomic Isolation Kit (GeneAll, Seoul, Korea) according to manufactual protocol. Genotype of G-607C SNP in wnt10b was determined by PCR and Taqman probe. The primer-set was purchased from Applied Biosystems Inc. (USA), and genotyping were analyzed by Macrogen (Seoul, Korea). To confirm the accuracy of the genotype analysis, five percent of subjects were randomly selected, and the SNP were genotyped by the sequencing method using the ABI 3700 sequencer (ABI Inc. Carlsbad, CA USA). The genotyping agreement between two method was 98% and a kappa value was 0.98 (CI 0.92-1.0), which represents high accuracy. The concordance of G-607C withHardy-Weinberg equilibrium (HWE) was tested using HapAnalyzer software (http://www.genenames.org) [17].

Statistical analysis

All statistical analysis was performed using SAS software version 9.1.3 (SAS Institute Inc.,

Table 5. Demographic parameters of the obese group and non-obese group according to the BMI

Characteristics	Non-Obese	Obese[$]	*P*
N	361	239	
Sex (M/F)	146/215	97/142	0.9722
Age (year)	69.92±10.66	66.23±10.29	**<0.0001**
Smoking (none/stop/active)	187/75/99	154/38/47	**0.0090**
Drinking (none/stop/active)	181/51/129	137/27/75	0.2135
TOAST classification			
LAA	103	68	0.9978
CE	25	16	
SVO	210	141	
SOE	9	5	
SUE	13	9	
Medical history			
TIA (Yes, %)	47 (13.06)	31 (12.97)	0.9759
Hypertension (Yes, %)	200 (55.40)	159 (66.53)	**0.0065**
Hyperlipidemia (Yes, %)	44 (12.26)	42 (17.57)	0.0695
Diabetes (Yes, %)	87 (24.10)	68 (28.57)	0.2214
Heart disease (Yes, %)	27 (7.48)	14 (5.86)	0.4409

All of the results, except age, are expressed as frequencies for the categorical variables. [$]Obese: BMI≥25. ICH: intracerebral hemorrhage. CI: cerebral infarction. TOAST: Trial of ORG 10172 in Acute Stroke Treatment. LAA: large-artery atherosclerosis. CE: cardioembolism. SVO: small-vessel occlusion. SOE: stroke of other etiology. SUE: stroke of undetermined etiology. TIA: transient ischemic attack. *P*-values of Obesegroup versus Non-Obesegroupusing Student's t-test for continuous variables and the chi-square test for categorical variables. *P*-values with statistical significance are presented in bold (<0.05).

NC). The χ^2-test was used to compare the differences between categorical variables. Student t-test or Kruskal-Wallis rank-sum test was used to compare the difference of continuous variables after normality test by a Kolmogorov-Smirnov test. Association of G-607C with *bi-sup* was examined by binary logistic regression model adjusted with sex and age or sex, age, smoking, drinking and hypertension. Effects of G-607C on body characteristics or serum parameter were evaluated using general linear model after adjustment for sex, age, smoking hypertension, hyperlipidemia and diabetes. Statistical significance was determined as P<0.05.

Results

Difference of body characteristics and serum parameters between *bi-sup* and non-*bi-sup* was shown in **Table 2**. Each of BMI and waist circumference in *bi-sup* was 25.83 kg/m^2 and 92.28 cm, which were significantly higher than non-*bi-sup* (P<0.0001). Body weight also increased in *bi-sup*. Among serum parameters, level of triglyceride was significantly high in bi-sup compared with non-*bi-sup* (P=0.0039), but GOP and HDL-cholesterol was lower in *bi-sup* than non-*bi-sup* (P=0.0199 and P=0.0181, respectively).

Table 3 showed allele and genotype distribution of G-607C of wnt10b gene between *bi-sup* and non *bi-sup*. After adjustment for sex, age or sex, age, smoking, drinking, hypertension and hyperlipidemia, frequency of C allele in *bi-sup* was 47.84% which was significantly lower than 53.35% in non-*bi-sup* (P=0.0348, OR=0.779 [0.618-0.982]). Subjects with GC or CC type in *bi-sup* was also 72.36%, that was also small compared with 78.35% in non-*bi-sup* (P=0.0467, OR=0.675 [0.458-0.994]).

Difference of body characteristics and serum parameters among genotypes of G-607C was shown in **Table 4**. Among serum parameters, GOP was increased in subjects with C allele compared with subjects with GG type in dominant model (P=0.0463). BMI and waist circumference in body characteristics and total cholesterol and triglyceride in serum parameters were slightly decreased in subjects with CC type compared with subjects with GG or GC type without significant difference. Previous report showed that G-607C was related with obese phenotypes in Korean female [12], and we also obtained similar results, but not significant (**Tables 5**, **6**).

Previous study reported that obesity was related with Dampness-phlegm in stroke population [18]. Because of relationship between *bi-sup* and obese index, we showed distribution of *bi-sup* in each of pattern identification (**Figure 1**). Ratio of subjects with *bi-sup* was 77.65% in Dampness-phlegm, but 38.67% in Yin-deficiency, 58.64% in Fire/Heat and 50.0% in Qi-deficiency. That means *bi-sup* is major indicator for diagnosing Dampness-phlegm.

Discussion

Obesity doesn't means simple increase of weight, but is serious health problem causing

Table 6. Genotype distribution of the G-607C polymorphism in the obese group and non-obese group according to the BMI

Model	Genotype	Non-Obese	Obese[$]	[†]OR [95% CI]	*P*	[‡]OR [95% CI]	*P*
Allele	G	344 (47.65)	250 (52.30)	0.827 [0.654, 1.045]	0.1121	0.821 [0.645, 1.044]	0.1076
	C	378 (52.35)	228 (47.70)				
[§]Do	GG	85 (23.55)	63 (26.36)	0.842 [0.574, 1.235]	0.3794	0.828 [0.559, 1.227]	0.3472
	GC+CC	279 (76.45)	176 (73.64)				
[§]R	GG+GC	259 (71.75)	187 (78.24)	0.713 [0.483, 1.052]	0.0881	0.710 [0.477, 1.058]	0.0921
	CC	102 (28.25)	52 (21.76)				

Data are presented as frequencies (percentages). [$]Obese: BMI≥25. [†]ORs afteradjustment for age [‡]ORsafter adjustment for age, smoking and hypertension. *P*-values were calculated by logistic regression analysis. [§]Do and R denote dominant and recessive models, respectively.

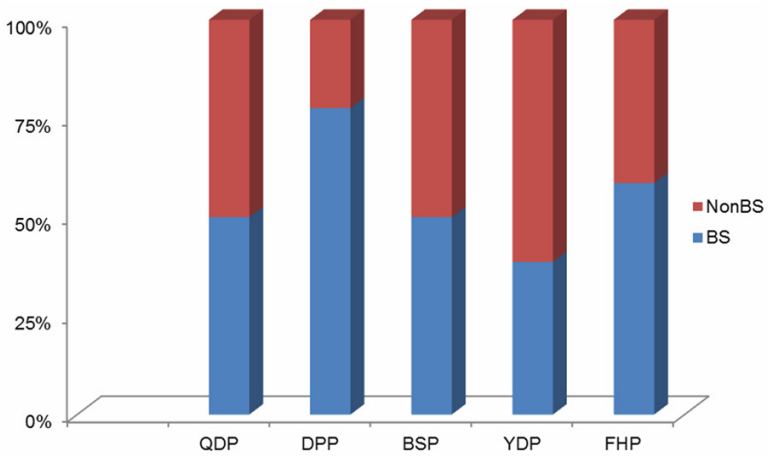

Figure 1. Distribution of patterns in the subjects in the Bi-Sup and Non-Bi-Sup group. Ratio of subjects with Bi-Sup was 77.65% in Dampness-phlegm, but 38.67% in Yin-deficiency, 58.64% in Fire/Heat and 50.0% in Qi-deficiency. QDP: Qi deficiency pattern. DPP: Dampness-phlegm pattern. BSP: Blood stasis pattern. YDP: Yin deficiency pattern. FHP: Fire-heat pattern.

various diseases such as hypertension, disorder of lipid metabolism, diabetes cardiovascular infarction, and stroke [19]. Concept of obese man in TKM is some different with obese subject used in western medicine, in which BMI, waist and WHR is used as standard indices for diagnosing obesity. In TKM, criteria for obesity include body characteristics, features, skin thickness etc. *HuangdiNeijing* explained that obese man has three types, fat, cream and meat, and difference of large or small of appearance, *Qi*, blood, cold and heat pattern. Because of these differences, cause of obesity is distinguished [20]. That means different treatment should be used when the pathogen of obesity is different [5].

Bi-sup is caused by environmental factors such as lifestyle, diet, stress etc., otherwise no impacts of inherent factors such as genetic variation is known until now. But some report suggested that genetic variations might affect *Bi-sup*. Kim et al reported that *bi-sup* co-related with BMI [6], which is same results obtained in this study (**Table 2**). In previous study reported by Ko et al, NPY, a neurotransmitter affecting diet absorbs, is associated with Dampness-phlegm [21]. Dampness-phlegm is major pattern identification represented in subjects with *bi-sup* in this study (**Figure 1**).

TKM categorizes the procedure for determining the pattern of particular patient is called pattern identification. Previous reports have described the pattern identification process for differentiating stroke victims with four TKM types: the Fire-Heat pattern, Dampness-phlegm pattern, Yin deficiency pattern and *Qi*deficiency pattern [14-16, 18].

In this study, we elucidated the association between *bi-sup* and G-607C SNP in Wnt10b among Korean CI patients enrolled from 2009 to 2010. Frequency of C allele and subjects with GC or CC type were significantly lower in *bi-sup* than non-*bi-sup* (**Table 3**).

Wnt10b, one of Wnt's family, is secreted signaling protein and regulate several developmental processes through Wnt/β-catenin signaling pathway [11]. Especially, that is known to decrease obesity. *Wnt10b* inhibited adipogenesis though regulating expression of C/EBP and PPARγ2 [22], and body weight and abdominal

fat mass was significantly decreased in*ob/ob* mice with overexpression of *wnt10b* [23]. Scarda et al also reported that expression of *wnt10b* in muscle and adipocyte was significantly decreased in obese Zucker rat [24]. Recently, Kim et al showed that C allele of G-607C SNP located at promoter region of wnt10b increased wnt10b expression and this SNP was associated with decrease of abdominal fat mass and BMI in Korean woman [12]. This study also showed similar result that the frequency of CC type was lower in obese subjects than non-obese subjects without significant difference (**Table 6**).

In TKM, *Bi-sup* is state accumulating waste in body by preventing circulation of fat, body fluid, *Qi* and blood, and this is caused by strength of tissue function responding digest, absorption and storage or weakness of tissue function performing breathing, blood circulation, energy expenditure and excretion [25]. The disorder of the tissue functions was occurred by environmental factors such as lifestyle aging, stress etc. And, inherent factor might also affect to that.

In this study, we showed association of G-607C of wnt10b with *bi-sup*, and more studies will be need to explain a relation between genetic factors and symptoms of disease in a point of view of TKM.

Acknowledgements

This research was supported by a grant from the Korea Institute of Oriental Medicine (K13-130, K15111) and Korean Food Research Institute (G15060).

Disclosure of conflict of interest

None.

Address correspondence to: Dr. Min Ho Cha, KM Fundamental Research Division, Korea Institute of Oriental Medicine, 1672 Yuseongdaero, Yuseong-gu, Daejeon 305-811, South Korea. Tel: +82-42-869-2768; Fax: +82-42-863-9299; E-mail: mhcha-min@kiom.re.kr

References

[1] Korea Health Statistics2010: Korea National Health and NutritionExamination Survey (KNHANES V-1), Ministry of Health & Welfare.

[2] Boden-Albala B, Sacco RL. Lifestyle factors and stroke risk: Exercise, alcohol, diet, obesity, smoking, drug use, and stress. Curr Atheroscler Rep 2000; 2: 160-166.

[3] Song YM, Sung J, Davey Smith G, Ebrahim S. Body mass index and ischemic and hemorrhagic stroke: aprospective study in Korean men. Stroke 2004; 35: 831-836.

[4] Park JW, Lee SY, Kim SY, Choe H, Jee SH. BMI and stroke risk in Korean women. Obesity 2008; 16: 396-401.

[5] Kim S, Jin SH, Kim TH. A Study on etiological factors, symptoms of a disease, and treatments of obesity based on dong-Yi Bo Gam. J Korean Orient Med Soc 1998; 19: 125-136.

[6] KimSY, Lee JS, Kang BK, Ko MM, Kim JC, Oh DS, Bang OS. Study on the Relationship among *Bi-Su* Type, Obesity Index, and Pattern Identification in Stroke Patients. Korean J Orient Int Med 2009; 30: 550-557.

[7] Choi KH, Lee YK, Lee JG, Son JY, Lee YK, Kang SB, Shin HC. Clinical Studies on Obesity and Right-left of Patients with Bell's palsy. Korean J Orient Physiol Patho 2007; 21: 1619-1623.

[8] Lee HC, Choi YM, Sim WJ. The Study of the Relationship with Abdominal Visceral Fat in Obese Patients Identified as Phlegm Type. Korean J Orient Int Med 2006; 6: 51-59.

[9] Hsia YC, Jung KY, Go HY, Jung H, Baik JW, Yeo HS, Ko MM, Choi YK, Kim DW, Han CH, Cho KH, Bang OS, Park JH, Ko SG, Jun CY. A Study on the Characteristics Linked to Obesity with Acute Stroke Patients. Korean J Orient Int Med 2008; 29: 149-59.

[10] Sugimura R, Li L. NoncanonicalWnt signaling in vertebrate development, stem cells, and diseases. Birth Defects Res C Embryo Today 2010; 90: 243-256.

[11] Cawthorn WP, Bree AJ, Yao Y, Du B, Hemati N, Martinez-Santibañez G, MacDougald OA. Wnt6, Wnt10a and Wnt10b inhibit adipogenesis and stimulate osteoblastogenesis through a β-catenin-dependent mechanism. Bone 2012; 50: 477-489.

[12] Kim IC, Cha MH, Kim DM, Lee H, Moon JS, Choi SM, Kim KS, Yoon Y. A functional promoter polymorphism -607G>C of WNT10B is associated with abdominal fat in Korean female subjects. J Nutr Biochem 2011; 22: 525-258.

[13] Van Camp JK, Beckers S, Zegers D, Verrijken A, Van Gaal LF, Van Hul W. Genetic association between WNT10B polymorphisms and obesity in a Belgian case-control population is restricted to males. Mol Genet Metab 2012; 105: 489-493.

[14] Ko MM, Park TY, Lim JH, Cha MH, Lee MS. WNT10B Polymorphism in Korean Stroke Patients with Yin Deficiency Pattern. Evid Based Complement Alternat Med 2012; 2012: 798131.

[15] Park TY, Lee JA, Cha MH, Kang BK, Moon TW, Choi TY, Ko MM, Choi JA, Lim JH, Lee HY, Lee MS. The fundamental study for the standardization and objectification of pattern identification in Traditional Korean Medicine for stroke (SOPI-Stroke): An overview of phase I. Eur J Integr Med 2012; 4: e125-e131.
[16] Lee JA, Lee JS, Kang BK, Ko MM, Moon TW, Cho KH, Bang OS. Report on the Korean standard pattern identifications for stroke-III. Korean J Orient Int Med 2011; 32: 232-242.
[17] Hedrick PW. Gametic disequilibrium measures: proceed with caution. Genetics 1987; 117: 331-341.
[18] Kim HJ, Bae HS, Park SU, Moon SK, Park JM, Jung WS. Clinical approach to the standardization of oriental medical diagnostic pattern identification in stroke patients. Evid Based Complement Alternat Med 2011; 2011: 768492.
[19] Yim HS, Ko SG. Abdominal Obesity as a Risk Factor of Ischemic Stroke in Case-control study. J Soc Korean Med Obes Res 2002; 2: 25-36.
[20] Chun TK, Hong WS. A study on the type of Bi and Su of Body in 'Yellow Emperior`sNei-Ching'. J Korean Med Classics Med His 1992; 6: 176-188.
[21] Ko MM, Kang BK, Lim JH, Lee MS, Cha MH. Genetic association of NPY gene polymorphismswith Dampness-Phelgm pattern in Korea stroke patients. Evid Based Complement Alternat Med 2012; 2012: 109796.
[22] Ross SE, Hemati N, Longo KA, Bennett CN, Lucas PC, Erickson RL, MacDougald OA. Inhibition ofadipogenesis by Wnt signaling. Science 2000; 289: 950-953.
[23] Wright WS, Longo KA, Dolinsky VW, Gerin I, Kang S, Bennett CN, Chiang SH, Prestwich TC, Gress C, Burant CF, Susulic VS, MacDougald OA. Wnt10b inhibits obesity in ob/ob and agouti mice. Diabetes 2007; 56: 295-303.
[24] Scarda A, Franzin C, Milan G, Sanna M, Dal Prà C, Pagano C, Boldrin L, Piccoli M, Trevellin E, Granzotto M, Gamba P, Federspil G, De Coppi P, Vettor R. Increased adipogenic conversion of muscle satellite cells in obese Zucker rats. Int J Obes (Lond) 2010; 34: 1319-1327.
[25] Unschuld PU, Huang D, Nei J, Su W. Nature, Knowledge, Imagery in an Ancient Chinese Medical Text. Berkeley/Los Angeles, CA: University of California Press; 2003.