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Start Codon Polymorphism in the Vitamin D Receptor is Associated with Colorectal Cancer

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The expression of the nuclear vitamin D receptor (*VDR*) gene involved in regulating cell growth and proliferation may contribute to the development of the pathogenesis of colorectal cancer. The *VDR*has the start codon (*Fok*I) polymorphism (ATG to ACG) in exon 2, the C allele at the second of two potential translation initiation sites, which is effective in transactivation of 1,25(OH)2D3 signal, and a T1056C polymorphism (*Taq*I) in exon 9. This study evaluated the *VDR* germline mutation was responsible for colorectal cancer. Polymorphisms (*Fok*I and *Taq*I) of the *VDR*gene were analyzed by the PCR-RFLP in 203 colorectal cancer and 222 controls. The **C/*C* genotype frequency of the start codon polymorphism was significantly higher in colorectal cancer (**C/*C*, 49.3%; **C/*T*, 42.8%; **T/*T*, 7.9%) than controls (**C/*C*, 33.3%; **C/*T*, 50.0%; **T/*T*, 16.7%) (p=0.0009; OR=1.9; 95% CI=1.3-2.9) while the T1056C polymorphism was not different between colorectal cancer (**T/*T*, 87.7%; **T/*C*, 12.3%; **C/*C*, 0.0%) and controls (**T/*T*, 92.8%; **T/*C*, 7.2%; **C/*C*, 0.0%). The C allele (start codon), the short VDR transcript, interacts more efficiently binding to the basal transcription factor TF?B, and provides a mechanism for greater transactivation potency of the *VDR*gene. There is evidence that a high level of VDR expression is associated with prognosis of colorectal cancer. These results show that the *VDR* start codon polymorphism is associated with an increased risk for colorectal cancer.

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Single Nucleotide Polymorphisms of the Matrix Metalloproteinase 1, 3, 7, 9 and 12 in Koreans

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The matrix metalloproteinases (MMPs) are a large family of proteolytic enzymes, which cleave extracellular matrix and non -matrix substrates. Increased MMPs expression has been reported in tumor invasion and metastasis. And *MMP* promoter variants have been known to be different from an effect of the MMPs transcriptional activities, such as *MMP1 -1607GG*, *MMP9-1562T*, and *MMP12-82A* allele increased transcription or *MMP3-11716A*and *MMP7-181A* allele decreased transcription. Analysis of the *MMP* promoter *MMP1*, *MMP3*, *MMP7*, *MMP9*, and *MMP12* single nucleotide polymorphisms were performed by PCR-RFLP using *Alu*I, *Xmn*I, *Eco*RI, *Sph*I, and *Pvu*II, respectively, in 219 unrelated Koreans. The genotype and allele frequency of five genes were compatible with the Hardy-Weinberg equilibrium. The allele frequencies of the *MMP1-1607*GG*, *MMP3-1171*6A*, *MMP7 -181*A*, *MMP9-1562*C*, and *MMP 12-82*A* were 0.724, 0.893, 0.932, 0.868, and 0.984, respectively. The allele frequencies of the *MMP1* and *MMP3* polymorphisms were different among ethnic distributions. The frequency of the *MMP1-1607*GG* was different among Oriental (0.613-0.724), Caucasians (0.482-0.527), and Blacks (0.570). The allele frequency of the *MMP3-1171*6A*was different between Orientals (0.803-0.893) and Caucasians (0.464-0.590). The haplotypes of the *MMP7*, *MMP12*, *MMP1*, and *MMP3* on 11q21-23 were detected in 16 types. The common haplotypes were the *MMP7A-181A*, *MMP12A-82A*, *MMP1GG-1607GG*, *MMP36A-11716A* (35.1%), *MMP7A-181A*, *MMP12A-82A*, *MMP1G-1607GG*, *MMP36A -11716A* (27.8%), and *MMP7A-181A*, *MMP12A-82A*, *MM P1G-1607GG*, *MMP35A-11716A*(7.8%). These results suggest that single nucleotide polymorphisms of the *MMP* promoters may influence the expression of MMPs.

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Genotypes of Mannose-binding Lectin in Behcet's Disease

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Mannose-binding lectin (MBL) is an acute phase protein of the innate immune response which participates in complement activation by binding to many pathogens surfaces. It has been well known that *MBL*exon and promoter polymorphisms affect MBL levels. We investigated the *MBL* polymorphism in 195 Behcet's disease (BD) and 200 healthy controls in Koreans. The genomic DNA analyzed the promoter region at *G-550C*(H/L variants), and *G-221C*(Y/X variants) and three missense mutations at codon 52 (C223T, *Arg52Cys*, A/D variants), 54 (G230A, *Gly54Asp*, A/B variants), and 57 (G239A, *Gly57Glu*, A/C variants) in exon 1 of the *MBL* gene by PCR-RFLP, SDM-PCR RFLP, and PCR-SSP. The difference was not found in exon 1 variants between BD and controls, the allele frequency of the *MBL54*Gly* was 0.754 and 0.774 in BD and controls, respectively. No variants were found in *MBL52*Cys* and in *MBL57*Glu* either in BD and in controls, but only one *MBL52*Arg/*Cys* was found in controls. However *-550G*(H) allele was significantly higher in the BD patients than that in the controls (0.582 *vs.* 0.473, p=0.003, *OR*=2.3, 95% CI=1.32-4.09). *G-221C*(Y/X) was similar in BD patients and in contorls. In the promoter region, high-MBL producing haplotype H.Y in the BD was significantly higher than that in the controls (58.0% vs. 47.3%, p=0.0026, OR=1.5 95% CI=1.16-2.04). We did not detect the H.X haplotype either in BD or in controls. High MBL concentration influence to complement activation consequently it may increase susceptibility to inflammatory disorders, including BD. These results suggest that the MBL -550G,-221G (H,Y) haplotype, high-MBL producing haplotype may contribute to BD susceptibility.

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Characterization of P Element Insertion Mutant Lines Screened by otd Expression in *Drosophila* Central Nervous System

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All complex nervous systems comprise two equally important cell types: neurons and glial cells. Glial cells play crucial roles in nervous system development, axonal guidance and fasciculation, and shaping of neuropilar structures. In order to find the genes involved in the gliogenesis, we screened the P enhancer trap lines which was primarily screened by the abnormal otd(orthodenticle) expression. 6 enhancer trap mutant lines out of 11 original lines affected the expression of gcm(glial cell missing), repo(reverse polarity), and pros(prospero)t hat are involved in gliogenesis. As glial cells are known to regulate the differentiation process of axons, these lines wereexamined on the expression of FasII and BP102 that are markers on the central nervous system. These enhancer trap lines affected the expression of FasII and BP102. As gcm, a master gene in gliogenesis, is also involved in the hematopoiesis, the expressionof Crq (croquemort) gene was investigated in these lines. croquemort is a marker of plasmatocyte. These lines also affected the expression of croquemort. Our results indicates that the screened lines are involved in gliogenesis, neuronal development process and hematopoiesis.