

Supplement. Location of seven VEGFA promoter SNPs and haplotypes of alleles contained in TFBS. (+/-) is the DNA strand location of the TFBS. TSS denotes the base pair distance from the transcriptional start site. TFBS in **bold** are only present for the given allele.

Haplotypes	TSS	(-)2578bp	(-)2548bp	(-)1203	(-)1190bp	(-)1179	(-)1154bp	(-)634BP	Study group haplotype frequency			
	SNP	rs699947	rs34357231 rs35569394	rs79469752	rs13207351	rs28357093	rs1570360	rs2010963	Han	AMS	NT	CMS
1	C	D	C	G	A	G	C	0.341	0.307	0.441	0.483	
	GATA2 (+) GATA3 (-) HIF1A:ARNT (-) TAL1:TCF3 (+) Tcfcp2l1 (-) Tcfcp2l1 (+)	AP1 (+) CREB1 (-) NFIC (+) NR4A2 (-) RUNX1 (-) TFAP2A (+) Zfx (-)	Bsap (-) NFIC (-) Pax5 (-) TFAP2A (-) Zfx (+)	NFIC (+) Tcfcp2l1 (-) Tcfcp2l1 (+) Zfx (-)	RUNX1 Zfx (-) Zfx (+)	Klf4 (+) MZF1_1-5-13 (+) SP1 (-) ZNF354C (-)	GABPA (+) IRF2 (+) IRF1 (+) Pax2 (-)					
2	C	D	C	G	A	G	G	0.218	0.148	0.18	0.138	
							Pax2 (-) SP1 (-) SP1 (-)					
3	A	I	C	A	A	A	G	0.176	0.113	0.079	0.114	
	GATA2 (+) NFIC (-) Tcfcp2l1 (-) Tcfcp2l1 (+)	AP1 (+) CREB1 (-) ETS1 (+) GATA3 (-) MZF1_1-4 (-) NFATC2 (+) Nkx3-2 (-) RUNX1 (-) RUNX1 (-) SP1 (+) SPL1 (-) TFAP2A (-) TFAP2A (+) Zfx (-)		MIZF (+) Nkx3-2 (-) Zfx (-)		ETS1 (-) SP1 (-) SPIB (+) ZNF354C (-)						
4	C	D	C	A	A	G	C		0.037	0.057	0.029	
5	A	I	C	A	A	G	G	0.088	0.05	0.055	0.081	

6	C	D	C	G	C	G	C			0.043
					TFAP2A (-) Zfx (+)					
	C	D	C	G	C	G	G	0.096	0.082	0.035
7	A	I	C	G	A	G	G	0.021		0.042
8	C	D	C	A	A	A	C			0.041
9	A	I	C	A	A	G	C			0.022
10	C	D	T	A	A	G	G			0.022
			Bsap (-) CFI-USP (+) Coup-TF (-) ESR2 (+) Hand1:Tcf2a (+) NFE2L1:MafG (-) Pax2 (+) Pax5 (-) Pax6 (-) TFAP2A (-) Hand1 (+)							
11	C	D	T	A	C	G	G			0.018
12	C	D	T	G	C	G	G	0.017	0.019	0.065
13	C	D	C	A	A	G	G	0.013	0.02	0.027
14	A	I	C	A	A	A	C	0.012		
15	A	I	T	G	C	G	G	0.01	0.014	
16	A	I	T	A	C	A	G		0.022	0.014
17	A	I	C	G	A	G	G		0.014	0.012
18	C	D	C	A	C	G	C		0.018	

19	C	D	C	G	A	A	G	0.015		
20	C	D	C	A	A	A	G	0.014		
21	C	D	T	G	C	G	C	0.013		
22	A	I	T	A	C	A	C	0.012		
Total number							10	16	11	10

TFBS information:

TF discription

AP-1	Activator protein 1	Transcription factor which is a heterodimeric protein composed of proteins belonging to the c-Fos, c-Jun, ATF and JDP families.
Bsap	B-cell activator protein	B-cell-specific transcription factor, regulation of the CD19 gene.
CFI-USP	complement component I ubiquitin specific peptidase	Essential for regulating the complement cascade. Hydrolase that deubiquitinates polyubiquitinated target proteins
Coup (NR2F1)	chicken ovalbumin upstream promoter-transcription factor	Binds to the ovalbumin promoter and, in conjunction with another protein (S300-II) stimulates initiation of transcription. Binds to both direct repeats and palindromes of the 5'-AGGTCA-3' motif.
CREB1	cAMP responsive element binding protein	Transcription factor that is a member of the leucine zipper family of DNA binding proteins and binds as a homodimer to the cAMP-responsive element, an octameric palindrome.
En1	Homeobox protein engrailed-1	Homeobox-containing genes are thought to have a role in controlling development.
ESR2	Estrogen receptor beta	Estrogen receptor β is a member of the family of estrogen receptors and the superfamily of nuclear receptor transcription factors and is expressed by many tissues including blood monocytes and tissue macrophages, colonic and pulmonary epithelial cells.
ETS1	Protein C-ets-1	The protein encoded by this gene belongs to the ETS family of transcription factors and has been shown to interact with TTRAP, UBE2I and Death associated protein.
GABPA	GA-binding protein alpha chain	One of three GA-binding protein transcription factor subunits which functions as a DNA-binding subunit which shares identity with a subunit encoding the nuclear respiratory factor 2 gene and is likely involved in activation of cytochrome oxidase expression and nuclear control of

		mitochondrial function.
GATA2	GATA binding protein 2	A member of the GATA family of zinc-finger transcription factors that are named for the consensus nucleotide sequence they bind in the promoter regions of target genes and play an essential role in regulating transcription of genes involved in the development and proliferation of hematopoietic and endocrine cell lineages.
GATA3	GATA binding protein 3	Plays an important role in endothelial cell biology.
Hand1:Tcf2a	Heart- and neural crest derivatives-expressed protein 1: transcription factor E2A	Hand1 belongs to the basic helix-loop-helix family of transcription factors. The Tcf2a gene encodes the transcription factor E2A, a member of the "class I" a family of basic helix-loop-helix (bHLH) transcription factors (also known simply as "E-proteins"). The transcription factor E2A controls the initiation of B lymphopoiesis.
HIF1A:ARNT	Hypoxia-inducible factor 1:Aryl hydrocarbon receptor nuclear translocator	HIF1 is a homodimeric basic helix-loop-helix structure composed of HIF1a, the alpha subunit, and the aryl hydrocarbon receptor nuclear translocator (Arnt), the beta subunit. The protein encoded by HIF1 is a Per-Arnt-Sim (PAS) transcription factor found in mammalian cells growing at low oxygen concentrations. It plays an essential role in cellular and systemic responses to hypoxia.
IRF1,2	Interferon regulatory factor	Members of the interferon regulatory transcription factor (IRF) family that contain a conserved N-terminal region of about 120 amino acids, which folds into a structure that binds specifically to the interferon consensus sequence (ICS).
Klf4	Krueppel-like factor 4	Transcription factor that can act both as activator and as repressor. Regulates the expression of key transcription factors during embryonic development.
MIZF	Histone H4 transcription factor	MIZF interacts with methyl-CpG-binding protein-2 and plays a role in DNA methylation and transcription repression.
MZF1_1-5-13	Myeloid zinc finger 1	Binds to target promoter DNA and functions as transcription regulator. May be one regulator of transcriptional events during hemopoietic development. Isoforms of this protein have been shown to exist at protein level.
NFATC2	Nuclear factor of activated T-cells, cytoplasmic 2	This protein is present in the cytosol and only translocates to the nucleus upon T cell receptor (TCR) stimulation, where it becomes a member of the nuclear factors of activated T cells transcription complex.
NFIC	Nuclear factor 1 C-type	Recognizes and binds the palindromic sequence 5'-TTGGCNNNNNGCCAA-3' present in viral and cellular promoters and in the origin of replication of adenovirus type 2. These proteins are individually capable

of activating transcription and replication.

NFE2L1:MafG	Nuclear factor erythroid 2-related factor 1 Transcription factor MafG	Nuclear factor erythroid 2-related factor (Nrf2) coordinates the up-regulation of cytoprotective genes via the antioxidant response element (ARE). MafG is a ubiquitously expressed small maf protein that is involved in cell differentiation of erythrocytes. It dimerizes with P45 NF-E2 protein and activates expression of a and b-globin.
Nkx3-2	Natural killer 3 homeobox 2	This gene encodes a member of the NK family of homeobox-containing proteins. Transcriptional repressor that acts as a negative regulator of chondrocyte maturation.
NR4A2	Nuclear receptor subfamily 4, group A, member 2	Transcriptional regulator which is important for the differentiation and maintenance of meso-diencephalic dopaminergic (mdDA) neurons during development.
Pax	Paired box gene	The central feature of this transcription factor gene family is the conserved DNA-binding paired box domain. Alternative splicing of this gene results in multiple transcript variants.
RUNX1	Runt-related transcription factor 1	Heterodimeric transcription factor that binds to the core element of many enhancers and promoters. The protein encoded by this gene represents the alpha subunit of CBF and is thought to be involved in the development.
SP1	Specificity Protein 1	Can activate or repress transcription in response to physiological and pathological stimuli. Regulates the expression of a large number of genes involved in a variety of processes such as cell growth, apoptosis, differentiation and immune responses.
SPIB	Transcription factor Spi-B	SPI1 and SPIB are members of a subfamily of ETS transcription factors. ETS proteins share a conserved ETS domain that mediates specific DNA binding. SPIB and SPI1 bind to a purine-rich sequence, the PU box (5-prime-GAGGAA-3-).
SPL1	Squamosa promoter-binding-like protein 1	A member of SPL gene family, encodes DNA binding proteins and putative transcription factors.
TAL1:TCF3	T-cell acute lymphocytic leukemia 1: Transcription factor 3	Implicated in the genesis of hemopoietic malignancies. It may play an important role in hemopoietic differentiation. Serves as a positive regulator of erythroid differentiation. TCF3 has been shown to directly enhance Hes1 (a well-known target of Notch signaling) expression.
Tcfcp2l1	Transcription factor CP2-like 1	Transcriptional suppressor. May suppress UBP1-mediated transcriptional activation. Modulates the placental expression of CYP11A1.
TFAP2a	Activator protein 2	The AP2a protein acts as a sequence specific DNA-binding transcription factor recognizing and binding to the specific DNA sequence and recruiting transcription machinery.

ZFX	Zinc finger X-chromosomal protein	A member of the krueppel C2H2-type zinc-finger protein family and probable transcriptional activator.
ZNF354C	Zinc finger protein 354C	May function as a transcription repressor.