

Table S1. Identity among several tissue- and venom-type VEGFs in amino acid and nucleotide levels

Identities are calculated from nucleotide and amino acid sequences in VHD. Identities in nucleotide and amino acid levels are listed above and below the diagonal line, respectively. Comparisons among tissue- and venom-type VEGFs are colored in blue and pink, respectively.

		Tissue-type VEGF (VEGF-A)					Venom-type VEGF (VEGF-F)									
		<i>Vaa</i> A ₁₆₆	<i>App</i> A ₁₆₆	<i>Tf</i> A ₁₆₆	<i>Bg</i> A ₁₆₅	<i>Hs</i> A ₁₆₅	barietin	apiscin	cratrin	<i>Tf</i> -svVEGF	Pm-VEGF	<i>Bi</i> -svVEGF**	vammin	VR-1	HF	ICPP
Tissue-type VEGF (VEGF-A)	<i>Vaa</i> A ₁₆₆		95.3	95.3	97.5	74.3	58.9	58.8	59.1	59.1	58.6	58.4	62.1	59.9	N.D.*	N.D.
	<i>App</i> A ₁₆₆	91.5		98.6	94.6	74.3	60.5	57.2	57.2	57.6	57.0	57.6	59.9	58.6	N.D.	N.D.
	<i>Tf</i> A ₁₆₆	90.4	98.9		94.6	74.6	58.4	57.6	57.6	57.9	57.3	57.9	59.0	59.0	N.D.	N.D.
	<i>Bg</i> A ₁₆₅	93.6	89.4	88.3		73.6	60.9	58.4	58.8	58.8	58.9	58.8	61.8	59.5	N.D.	N.D.
	<i>Hs</i> A ₁₆₅	74.5	74.5	73.4	72.3		63.8	63.7	64.0	64.0	63.8	64.4	65.5	65.5	N.D.	N.D.
Venom-type VEGF (VEGF-F)	barietin	49.5	50.5	49.5	50.5	52.6		79.1	77.3	80.2	80.3	80.6	87.4	84.2	N.D.	N.D.
	apiscin	47.4	46.3	45.3	45.3	49.5	68.4		92.1	92.8	92.4	92.5	82.4	81.7	N.D.	N.D.
	cratrin	48.4	47.4	46.3	45.3	47.4	64.2	84.2		90.0	91.7	91.4	81.0	80.3	N.D.	N.D.
	<i>Tf</i> -svVEGF	50.5	49.5	48.4	48.4	52.6	66.3	85.3	82.1		96.4	92.5	83.5	81.7	N.D.	N.D.
	Pm-VEGF	49.5	48.4	47.4	49.5	51.6	68.4	84.2	83.3	92.6		91.7	82.7	80.9	N.D.	N.D.
	<i>Bi</i> -svVEGF	47.4	48.4	47.4	46.3	50.5	66.3	85.3	84.4	83.2	80.0		82.8	81.4	N.D.	N.D.
	vammin	52.6	49.5	48.4	50.5	50.5	73.7	66.3	66.3	71.6	65.3	68.4		93.5	N.D.	N.D.
	VR-1	49.5	46.3	45.3	47.4	49.5	69.5	65.3	63.5	67.4	61.1	67.4	88.4		N.D.	N.D.
	HF	52.6	49.5	48.4	50.5	50.5	74.7	67.4	67.7	70.5	64.2	69.5	98.9	89.5		N.D.
	ICPP	52.6	50.5	49.5	50.5	54.7	74.7	67.4	66.7	70.5	64.2	69.5	93.7	89.5	94.7	

*When cDNA cloning of HF and ICPP was not performed, sections are labeled as N.D. (not determined).

***Bi*-svVEGF from the venom of *Bothrops insralis*.

Table SIIA. Nucleotide length of exons and introns of the genes encoding *Tf* VEGF-A (tissue-type) and *Tf*-svVEGF (venom-type).

Exons									(bp)
Exon	1 (ORF*)	2	3	4	5	6 (ORF)	7	8 (ORF)	total
<i>Tf</i> VEGF-A	190 (66)	52	197	77	33	72	132	573 (19)	1,326
<i>Tf</i> -svVEGF	242 (45)	31	197	80	42	618 (43)			1,210

* Exon-1, exon-6 encoding VEGF-F, and exon-8 encoding VEGF-A are composed of UTR and ORF.

Nucleotide numbers of ORF in exon-1, exon-6 and exon-8 are in parentheses.

Introns									(bp)
Intron	1	2	3	4	5	6	7	total	
<i>Tf</i> VEGF-A	6,071	6,626	1,860	1,295	2,956	1,130	1,941	21,879	
<i>Tf</i> -svVEGF	735	413	138	471	170			1,927	

Table SII B. Identities between *Tf* VEGF-A (tissue-type) and *Tf*-svVEGF (venom-type).

Exons (ORF)						
Exon	1	2	3	4	5	6
Nucleotide (%)	48.6	45.2	58.4	58.4	48.3	47.5
ratio (bp)	17/35	15/31	115/197	45/77	14/29	19/40
Amino acid (%)	22.2	20.0	53.0	33.3	0	0
ratio (AA)	2/9	2/10	35/66	9/27	–	–

–, non-homologous sequences

Introns					
Intron	1	2	3	4	5
Nucleotide (%)	43.5	45.8	43.3	45.5	44.1
ratio (bp)	327/751	192/419	61/141	70/154	78/177

Table SIII A. Heparin-binding ability of VEGFs

	NaCl (M) (n=4)
<i>Hs</i> VEGF-A ₁₆₅	0.72 ± 0.007
barietin	0.60 ± 0.002
vammin	0.38 ± 0.002

Table SIII B. Kinetic parameters for binding of barietin to immobilized VEGF receptors

	k_{ass} $s^{-1} (\times 10^4)$	k_{diss} $M^{-1} s^{-1} (\times 10^6)$	K_d $M (\times 10^{-9})$
Flt-1 (R1)			
<i>Hs</i> VEGF-A ₁₆₅	4.29	0.46	0.011
barietin	2.51	0.83	3.31
vammin	–	–	–
KDR (R2)			
<i>Hs</i> VEGF-A ₁₆₅	4.24	11.0	0.26
barietin	6.58	0.26	0.40
vammin	1.12	4.60	0.41
Flt-4 (R3)			
<i>Hs</i> VEGF-C	0.000017	1220.0	7.23
barietin	–	–	–
vammin	–	–	–
NP-1			
<i>Hs</i> VEGF-A ₁₆₅	0.66	95.6	14.4
barietin	–	–	–
vammin	–	–	–

–, no specific binding ability

Table SIV. K_A/K_S values for pairs of tissue- and venom-type VEGFs

The K_A and K_S values for the C-terminal tail-coding region of venom-type VEGFs (exons V and VI) were not calculated due to the number of framing errors.

Pair of VEGF cDNAs			Signal peptide coding region			VHD coding region		
			K_A	K_S	K_A/K_S	K_A	K_S	K_A/K_S
<i>Tissue-type</i>	<i>Vaa</i> VEGF-A	<i>App</i> VEGF-A	0.0167	0	0	0.037	0.091	0.404
	<i>Vaa</i> VEGF-A	<i>Tf</i> VEGF-A	0.0167	0	0	0.041	0.072	0.577
	<i>App</i> VEGF-A	<i>Tf</i> VEGF-A	0	0	0	0.005	0.053	0.085
<i>Venom-type</i>	vammin	apiscin	0	0.0531	0	0.184	0.234	0.788
	vammin	<i>Tfsv</i> VEGF	0	0	0	0.163	0.250	0.653
	apiscin	<i>Tfsv</i> VEGF	0	0.0531	0	0.066	0.099	0.672