

Supplement To:

Where is VEGF in the body? A meta-analysis of VEGF distribution in cancer

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* BC-Breast Cancer, PC-Prostate Cancer, CRC-Colorectal Cancer, RCC-Renal Cell Carcinoma, OC-Ovarian Cancer, GC- Gastric Cancer, GIC - Gastrointestinal Cancer, A - Anal Carcinoma, LC - Lung Cancer, Lym. - Lymphoma, BT - Brain Tumor, HCC – Hepatocellular carcinoma, MT - Malignant Tumor, MTC - Malignant Tumor in Children, M - melanoma

† NA-Not Applicable

‡ ELISA-Enzyme-Linked Immunosorbent Assay, QSEIT – Quantitative Sandwich Enzyme Immunoassay Technique, EIA – Enzyme Immuno Assay, ICMA – Chemiluminescence Immunosorbent Assay, IQK – Human VEGF Immunoassay Quantigo Kit, IFA – Immunofluorometric Assay

§ ben.-Benign, CIS-Carcinoma In Situ, prim.-Primary Cancer, met.-Metastatic Cancer, pre-treat.-Pre-Treatment, all pat.-All Patients, G.(1-3)-Histological Grading, S. (I-IV)-UICC Stage, pre-op.-Pre-operation, rec.-Recurrence, loc.-Localized, dis.-Disseminated, PC – Prostate Cancer, ear.-early, adv.-advanced, HE-Hormone Escaped, BPH-Benign Prostatic Hyperplasia, PSAs – PSA Stable, PSAr – PSA rising, LPF-Localized Prostatic Fluid, pol. – Polyp, DS – Duke’s Stage(A-C), CS-Clinical Stage, rem.-Remission, GIC- Gastrointestinal Cancer, OC-Ovarian Cancer, LC – Lung Cancer, ben. ex. – benign exudative effusion, ben. trans. – benign transductive effusion, indiv. – individual (values reported for each individual patient)

|| Me-Mean, Md-Median, MQ-Median And Interquartile Range, MR-Median and Range, MCI-Median and 95% Confidence Interval, MSE-Mean and Standard Error, R-Range, SD-Standard Deviation, DPP-Data Per Patient

** ^c-Estimate based on reported subgroup data

†† PLT-Platelets, PBMNC-Peripheral Blood Mononuclear Cell

‡‡ number of cancer patients (number of healthy controls)

*** PRP – platelet rich plasma, PPP – platelet poor plasma, PBMNC – peripheral blood mononuclear cell suspension, EPF – expressed prostatic fluid, SVF – seminal vesicular fluid

Table S1. Main Characteristics of the 19 studies involving Breast Cancer

Ref ¹	Year ¹	Cancer [*]	n ^{††}	VEGF source	VEGF Isoform [†]	VEGF Measurement [‡]	VEGF Diagnosis [§]	Statistics	healthy VEGF (mean/median)	healthy SD	Cancer VEGF ^{**} (mean/median)	Cancer SD	unit ^{††}
(Adams <i>et al</i> , 2000)	2000	BC	138 (63)	plasma	NA	ELISA	ben., loc., rem., met.	MR	27		37 ^e		pg/ml
(Caine <i>et al</i> , 2003)	2003	BC	30 (12)	plasma	165	ELISA	all pat.	MQ	30		310		pg/ml
(Yamamoto <i>et al</i> , 1996)	1996	BC	175	serum	121	EIA	S. (I, II,III, rec)	MSE			92 ^e		pg/ml
(Verheul <i>et al</i> , 1997)	1997	BC	27 (30)	serum	NA	QSEIT	pre-treat.	MSE, Me	287		330	206	pg/ml
(Salven <i>et al</i> , 1997)	1997	BC	33 (113)	serum	165	QSEIT	loc., dis.	MR	17		200 ^e		pg/ml
(Salven <i>et al</i> , 1999b)	1999	BC	105	serum	NA	QSEIT	ben., CIS, prim, met.	MR			112 ^e		pg/ml
(Adams <i>et al</i> , 2000)	2000	BC	138 (63)	serum	NA	ELISA	ben., loc., rem., met.	MR	186		262 ^e		pg/ml
(Heer <i>et al</i> , 2001)	2001	BC	173 (88)	serum	165	QSEIT	S. (I,II,III,IV)	MQ	168		302 ^e		pg/ml
(Colleoni <i>et al</i> , 2002)	2002	BC	48	serum	165	ELISA	pre-treat.	MCI			340		pg/ml
(Granato <i>et al</i> , 2004)	2003	BC	51	serum	NA	QSEIT	G. (1-2, 3)	MR			175 ^e		pg/ml
I(Zhao <i>et al</i> , 2004)	2004	BC	59 (59)	serum	NA	ELISA	pre-op.	MR	89		365		pg/ml
(Sancak <i>et al</i> , 2004)	2004	BC	44 (18)	serum	NA	ELISA	all pat.	MSE	105	49	136	58	pg/ml
(O'Riain <i>et al</i> , 2005)	2005	BC	30	serum	NA	EIA	pre-op.	MSE			390 ^e		pg/ml
(Obermair <i>et al</i> , 1997)	1997	BC	89	tumor cytosol	165	EIA	G. (1,2,3)	MQ			140 ^e		pg/ml prote
(Eppenberger <i>et al</i> , 1998)	1998	BC	305	tumor cytosol	121, 165	ICMA	all pat.	MR			450		pg/ml prote
(Foekens <i>et al</i> , 2001)	2001	BC	845	tumor cytosol	121, 165	ELISA	all pat.	MQ			220		pg/ml prote
(Toi <i>et al</i> , 2002)	2002	BC	110	tumor cytosol	NA	ELISA	all pat.	MSE			630	100	pg/ml prote
(Manders <i>et al</i> , 2003)	2003	BC	53	tumor cytosol	121, 165	ELISA	G. (1,2,3)	Md			693 ^e		pg/ml prote
(Desruisseau <i>et al</i> , 2004)	2004	BC	193	tumor cytosol	121, 165	ELISA	all pat.	MQ, R			218		pg/ml prote
(Bando <i>et al</i> , 2005)	2005	BC	202	tumor cytosol	NA	ELISA	all pat.	MCI			532		pg/ml prote

Table S2. Main Characteristics of the 13 studies involving Prostate Cancer

Ref ¹	Year ¹	Cancer [*]	n ^{††1}	VEGF source ^{***}	VEGF Isoform [†]	VEGF Measurement [‡]	VEGF Diagnosis [§]	Statistics	healthy VEGF (mean/ median)	healthy SD	Cancer VEGF ^{**} (mean/ median)	Cancer SD	unit ^{††}
(Duque <i>et al</i> , 1999)	1999	PC 80	(26)	plasma	121,165	QSEIT	loc., met.	MQ, Me	13		32 ^e		pg/ml
(Caine <i>et al</i> , 2003)	2003	PC 30	(12)	plasma	165	ELISA	all pat.	MQ	27		120		pg/ml
(George <i>et al</i> , 2004)	2004	PC 86		plasma	NA	ELISA	pre-op.	MR, MQ			50		pg/ml
(Li <i>et al</i> , 2005)	2005	PC 504	(502)	plasma	NA	ELISA	all pat.	MQ	49		48		pg/ml
(Kohli <i>et al</i> , 2003)	2003	PC 41		Plasma (PPP)	121,165	ELISA	PSAs, PSAr	MR, MQ			730 ^e		pg/ml
(Kaushal <i>et al</i> , 2005)	2005	PC 30		Plasma (P PP)	VEGF-A	ELISA	ear., adv.	MQ			90 ^e		pg/ml
(Salven <i>et al</i> , 1997)	1997	PC 8	(113)	serum	165	QSEIT	loc., dis.	MR, MSE	17		129 ^e		pg/ml
(Bauer <i>et al</i> , 1999)	1999	PC 10		serum	NA	IQK	pre-treat.	MR			191		pg/ml
(Jones <i>et al</i> , 2000)	2000	PC 78	(21)	serum	NA	ELISA	loc., met., HE, BPH	MSE	171	105	323 ^e		pg/ml
(Figg <i>et al</i> , 2001)	2001	PC 8		serum	NA	ELISA	pre-treat.	MSE, Me			136	123	pg/ml
(Caine <i>et al</i> , 2004)	2004	PC 30	(30)	PRP	NA	IQK	all pat.	MQ	600		690		pg/10 ⁶
(Bok <i>et al</i> , 2001)	2001	PC 100		urine	NA	ELISA	pre-treat.	MR, MSE			46, 28	58	pg/ml
(Joseph <i>et al</i> , 1997)	1997	PC 48		EPF	NA	ELISA	PC	MSE			1.1x 10 ^{6e}		pg/ml
(Joseph <i>et al</i> , 1997)	1997	PC 16		SVF	NA	ELISA	LPF	MSE			2.6x 10 ⁴	7x 10 ⁴	pg/ml

Table S3. Main Characteristics of the 13 studies involving Colorectal Cancer

Ref ¹	Year ¹	Cancer [*]	n ^{‡‡}	VEGF source ^{***1}	VEGF Isoform [†]	VEGF Measurement [‡]	V EGF Diagnosis [§]	Statistics	healthy VEGF (mean/median)	healthy SD	Cancer VEGF ^{**} (mean/median)	Cancer SD	unit ^{††}
(Hyodo <i>et al</i> , 1998)	1998	CRC 39	(20)	plasma	165	ELISA	pol., S. (II-III, IV)	MSE, Md	26	8.2	82 ^e		pg/ml
(George <i>et al</i> , 2000)	2000	CRC 116	(84)	plasma	NA	ELISA	all pat.	MQ	9		19		pg/ml
(Davies <i>et al</i> , 2000)	2000	CRC 29	(19)	plasma	121,165	ELISA	all pat.	MQ	126		180		pg/ml
(Werther <i>et al</i> , 2002b)	2002	CRC 51	(24)	plasma	165	ELISA	all pat.	MSE		57	69	83	pg/ml
(Werther <i>et al</i> , 2003)	2003	CRC 318		plasma	NA	ELISA	pre-op.	MR			36		pg/ml
(Dirix <i>et al</i> , 1996)	1996	CRC 44		serum	NA	ELISA	all pat.	MSE,MR			462, 351	338	pg/ml
(Hyodo <i>et al</i> , 1998)	1998	CRC	(20)	serum	165	ELISA	pol., S. (II-III, IV)	MSE, Md	238	125			pg/ml
(Kumar <i>et al</i> , 1998)	1998	CRC 108	(136)	serum	121,165	ELISA	S. (I, II, III, IV)	MQ	174		563 ^e		pg/ml
(Chin <i>et al</i> , 2000)	2000	CRC 81		serum	121,165	ELISA	S. (I, II-III)	MQ			377 ^e		pg/ml
(George <i>et al</i> , 2000)	2000	CRC 116	(84)	serum	NA	ELISA	all pat.	MQ	152		327		pg/ml
(Broll <i>et al</i> , 2001)	2001	CRC 122	(65)	serum	165	ELISA	all pat.	MSE, R	203	124	438	396	pg/ml
(Werther <i>et al</i> , 2002a)	2002	CRC 24		serum	NA	ELISA	pre-op.	MSE			375	246	pg/ml
(Werther <i>et al</i> , 2002b)	2002	CRC 51	(24)	serum	165	ELISA	all pat.	MSE	391	175	388	249	pg/ml
(Karayiannakis <i>et al</i> , 2002)	2002	CRC 67	(61)	serum	165	ELISA	all pat.	MQ	186		492		pg/ml
(Werther <i>et al</i> , 2003)	2003	CRC 318		serum	NA	ELISA	pre-op.	MR			231		pg/ml
(George <i>et al</i> , 2000)	200	CRC 116	(84)	PCPP	NA	ELISA	pre-op.	MQ	0.62		0.97		pg/10 ⁶ PLT
(Werther <i>et al</i> , 2002b)	2002	CRC 51	(24)	lysed NE	165	ELISA	all pat.	MSE	298	82	382	152	pg/ml
(Werther <i>et al</i> , 2002a)	2002	CRC 24		whole blood	NA	ELISA	pre-op.	MSE			700	256	pg/ml
(Werther <i>et al</i> , 2002b)	2002	CRC 51	(24)	whole blood	165	ELISA	all pat.	MSE	506	141	597	229	pg/ml
(Baker <i>et al</i> , 2000)	2000	CRC 50	(50)	tumor cytosol	NA	ELISA	all pat.	MR	27		189		pg/mg protein
(Karayiannakis <i>et al</i> , 2002)	2001	CRC 38	(65)	tumor cytosol	165	ELISA	all pat.	MSE, R	89	57	984		pg/mg protein
(Haraguchi <i>et al</i> , 2002)	2002	CRC 31		tumor cytosol	NA	ELISA	DS (A,B,C)	MSE			840 ^e		pg/mg protein

Table S4. Main Characteristics of the 19 studies involving Other Cancer

Ref ¹	Year ¹	Cancer [*]	n ^{††1}	VEGF source ^{***1}	VEGF Isoform [†]	VEGF Measurement [‡]	VEGF Diagnosis [§]	Statistics	healthy VEGF ^{**} (mean/ median)	healthy SD	Cancer VEGF ^{**} (mean/ median)	Cancer SD	unit ^{††}
(Hyodo <i>et al</i> , 1998)	1998	GC	29 (20)	plasma	165	ELISA	S. (I, II-III, IV)	MSE,Md	26	8.2	137 ^e		pg/ml
(Yoshikawa <i>et al</i> , 2000)	2000	GC	54	plasma	NA	ELISA	S. (I-II, III-IV)	MSE			93 ^e		pg/ml
(Kusumanto <i>et al</i> , 2003)	2003	BC, AC	4 (13)	plasma(PPP)	165	ELISA	all pat.	MR	9		23		pg/ml
(Dosquet <i>et al</i> , 1997)	1997	RCC	76	serum	165	ELISA	loc., met.	MR			398 ^e		pg/ml
(Hyodo <i>et al</i> , 1998)	1998	GC	(20)	serum	165	ELISA	S. (I, II-III, IV)	MSE,Md	238	125			pg/ml
(Tempfer <i>et al</i> , 1998)	1998	OC	60	serum	165	ELISA	all pat.	MR			466		pg/ml
(Viac <i>et al</i> , 1998)	1998	MT	96 (23)	serum	165	ELISA	prim., met.	MR, SD	97	89	217 ^e		pg/ml
(Salgado <i>et al</i> , 1999)	1999	LC	80	serum	NA	ELISA	all pat.	MSE, MR			453, 314	381	pg/ml
(Sato <i>et al</i> , 1999)	1999	RCC	40 (40)	serum	NA	QSEIT	all pat.	MSE	72	9	207	33	pg/ml
(Kraft <i>et al</i> , 1999)	1999	OC,GIC	83 (145)	serum	165	ELISA	OC, GIC	MR	294		681 ^e		pg/ml
(Eisen <i>et al</i> , 2000)	2000	OC, BC, HCC, M	41 (2)	serum	NA	ELISA	pre-treat.	Me, R	51		568		pg/ml
(Matsuyama <i>et al</i> , 2000)	2000	LC	49	serum	121,165	ELISA	S.(I,IIA,B, IIIA,B, IV)	MSE			407 ^e		pg/ml
(Stockhammer <i>et al</i> , 2000)	2000	BT	14	serum	165	ELISA	all pat.	MR			283		pg/ml
(Poon <i>et al</i> , 2001)	2001	HCC	100 (20)	Serum	NA	ELISA	all pat.	MR	180		269		pg/ml
(Tabone <i>et al</i> , 2001)	2001	MTC	40 (40)	serum	165	ELISA	all pat.	MR	318		400		pg/ml
(Jacobsen <i>et al</i> , 2002)	2002	RCC	161	serum	165	ELISA	all pat.	MR			344		pg/ml
(Ljungberg <i>et al</i> , 2003)	2003	RCC	61	serum	165	ELISA	S. (I-II, III, IV)	MR, Me			561 ^e		pg/ml
(Salven <i>et al</i> , 1999a)	1999	Lym.	52 (56)	PRP	NA	QSEIT	all pat.	MR	5		10.6		pg/10 ⁶ PLT
(Kusumanto <i>et al</i> , 2003)	2003	BC, AC	4 (13)	PRP	165	ELISA	all pat.	MR	0.48		0.7		pg/10 ⁶ PLT
(Salven <i>et al</i> , 1999a)	1999	Lym.	52 (56)	PBMNC	NA	QSEIT	all pat.	MR	0.9		10.6		pg/10 ⁶ PBMNC
(Kusumanto <i>et al</i> , 2003)	2003	BC, AC	4 (13)	Granulocytes	165	ELISA	all pat.	MR	72		152.5		pg/10 ⁶ cells
(Salven <i>et al</i> , 1999a)	1999	Lym.	52 (56)	Whole Blood	NA	QSEIT	all pat.	MR	298		464		pg/ml
(Kusumanto <i>et al</i> , 2003)	2003	BC, AC	4 (13)	Whole Blood	165	ELISA	all pat.	MR	301		1435		pg/ml
(Stockhammer <i>et al</i> , 2000)	2000	BT	14	cyst fluid	165	ELISA	all pat.	MR, Me			31600		pg/ml

(Eisen <i>et al</i> , 2000)	2000	OC, BC, HCC, M	41 (2)	urine	NA	ELISA	pre-treat.	Me, R	83		106		pg/ml
(Kraft <i>et al</i> , 1999)	1999	OC	35	pleural effusion	165	ELISA	all pat.	MR			5528		pg/ml
(Kraft <i>et al</i> , 1999)	1999	GIC	48	pleural effusion	165	ELISA	all pat.	MR			813		pg/ml
(Thickett <i>et al</i> , 1999)	1999	MT	40 (40)	pleural effusion	NA	ELISA	all pat.	Md	305		2500		pg/ml
(Yanagawa <i>et al</i> , 1999)	1999	LC	111	pleural effusion	165	EIA	LC, ben. ex., ben. trans	MSE	1567 ^e	897	2920	820	pg/ml
(Matsuyama <i>et al</i> , 2000)	2000	LC	6	pleural effusion	121, 165	ELISA	all pat.	MSE			532	285	pg/ml
(Kishiro <i>et al</i> , 2002)	2002	LC	5 (2)	pleural effusion	121, 165, 189	ELISA	all pat.	MSE	666	259	17526	22398	pg/ml
(Yeo <i>et al</i> , 1993)	1993	MC	7	peritoneal effusion	NA`	IFA	all pat.	DPP	21		30		pmol/L
(Matsuyama <i>et al</i> , 2000)	2000	LC	3	pericardial effusion	121, 165	ELISA	all pat.	MSE			3072	81	pg/ml

Table S5. Main Characteristics of the 6 studies involving Platelet and Leukocyte Count

Ref ¹	Year ¹	Cancer [*]	n ^{‡‡1}	Diagnosis [§]	Statistics	Healthy Platelet # (mean/ median)	Healthy PLT SD	Cancer Platelet # (mean /median)	Cancer PLT SD	Healthy Leukocyte # (mean/ median)	Healthy LK SD	Cancer Leukocyte # mean/ median	Cancer LK SD	unit ^{††}
(George <i>et al</i> , 2000)	2000	CRC	116 (84)	all pat.	Me	230								10 ⁶ /ml
(Colleoni <i>et al</i> , 2002)	2002	BC	48	pre-treat.	MCI			230.5						10 ⁶ /ml
(Werther <i>et al</i> , 2002a)	2002	CRC	24	pre-treat.	MSE			345	111			8		10 ⁶ /ml
(Werther <i>et al</i> , 2002b)	2002	CRC	51 (24)	all pat.	MSE	276	83	351	121	5.8	1.5	7.8	1.9	10 ⁶ /ml
(Jacobsen <i>et al</i> , 2002)	2002	RCC	161	all pat.	MR			306				7.4		10 ⁶ /ml
(Caine <i>et al</i> , 2004)	2004	PC	30 (30)	all pat.	MSE	254,000	36,000	261,000	60,000					10 ⁶ /ml

Table S6. Reason for Exclusion of 12 Studies.

Author	Reason of Exclusion
(Bhujwalla <i>et al</i> , 2001)	in vitro study
(Huss <i>et al</i> , 2001)	no quantitative data available
(Singh <i>et al</i> , 2004)	in vitro study
(Mabjeesh <i>et al</i> , 2003)	in vitro study
(Kelavkar <i>et al</i> , 2001)	in vitro study
(Liu <i>et al</i> , 1999)	in vitro study
(George <i>et al</i> , 2001)	does not provide mean/median values
(Calvo <i>et al</i> , 2002)	in vitro study
(Santini <i>et al</i> , 2002)	aberrant data
(May <i>et al</i> , 2005)	in vitro study
(Feldman <i>et al</i> , 2001)	aberrant data
(Cianchi <i>et al</i> , 2004)	in vitro study
(Haggstrom <i>et al</i> , 2000)	in vitro study