

Table S1: CAF levels in serum and bone marrow plasma of MM patients.

Total Patients									
Sera									
	ANG-2 (pg/ml)	FGF (pg/ml)	HGF (pg/ml)	IL8 (pg/ml)	PDGF (pg/ml)	TIMP-1 (pg/ml)	TIMP-2 (pg/ml)	TNFalfa (pg/ml)	VEGF (pg/ml)
Number	124	124	124	124	124	124	124	124	124
Mean±SD	264939±20833	15699±2857	66817±4080	818085±80798	110129±4071	769222±14283	415173±6061	42728±7779	619446±30566
(range)	(13405-1072635)	(2259-344121)	(9824-374475)	(6805-2177235)	(2112-229504)	(11792-817657)	(17925-442738)	(6404-671451)	(15699-1815946)
BM plasmas									
	ANG-2 (pg/ml)	FGF (pg/ml)	HGF (pg/ml)	IL8 (pg/ml)	PDGF (pg/ml)	TIMP-1 (pg/ml)	TIMP-2 (pg/ml)	TNFalfa (pg/ml)	VEGF (pg/ml)
Number	124	124	124	124	124	124	124	124	124
Mean±SD	256710±21301	67013±15318	150319±12424	567520±63861	111452±4567	791141±10579	346229±9790	41955±3068	540654±25225
(range)	(13405-1072261)	(8593-1041861)	(9824-493076)	(17303-2177104)	(7489-211233)	(30323-817657)	(17925-442738)	(7792-192997)	(33458-1510377)
V-MP									
Sera									
	ANG-2 (pg/ml)	FGF (pg/ml)	HGF (pg/ml)	IL8 (pg/ml)	PDGF (pg/ml)	TIMP-1 (pg/ml)	TIMP-2 (pg/ml)	TNFalfa (pg/ml)	VEGF (pg/ml)
Number	53	53	53	53	53	53	53	53	53
Mean±SD	255827±26922	12108±8489	71901±7824	878205±130492	106373±5863	790400±15528	424626±5966	47243±12964	679089±43561
(range)	(32604-971297)	(2673-31663)	(17809-374475)	(6805-2177235)	(2112-202310)	(11792-817657)	(159984-442738)	(8423-658833)	(15699-1815946)
BM plasmas									
	ANG-2 (pg/ml)	FGF (pg/ml)	HGF (pg/ml)	IL8 (pg/ml)	PDGF (pg/ml)	TIMP-1 (pg/ml)	TIMP-2 (pg/ml)	TNFalfa (pg/ml)	VEGF (pg/ml)
Number	53	53	53	53	53	53	53	53	53
Mean±SD	264260±37738	91784±32738	155366±19330	547656±100662	116460±7474	785809±17588	345475±15051	39519±3474	567349±43133
(range)	(13405-1072261)	(8608-1041861)	(9824-493076)	(17303-2177104)	(11100-211233)	(82385-817657)	(17925-442738)	(14827-132839)	(33458-1309659)
V-MPT									
Sera									
	ANG-2 (pg/ml)	FGF (pg/ml)	HGF (pg/ml)	IL8 (pg/ml)	PDGF (pg/ml)	TIMP-1 (pg/ml)	TIMP-2 (pg/ml)	TNFalfa (pg/ml)	VEGF (pg/ml)
Number	71	71	71	71	71	71	71	71	71
Mean±SD	271741±30471	18378±4941	63022±4083	773206±102589	112932±5616	753413±22001	408116±9558	39357±9597	574925±41817
(range)	(13405-1272561)	(2259-344121)	(9824-159319)	(9064-2475784)	(4061-229504)	(24447-817657)	(17925-442738)	(6404-671451)	(33458-1254471)
BM plasmas									
	ANG-2 (pg/ml)	FGF (pg/ml)	HGF (pg/ml)	IL8 (pg/ml)	PDGF (pg/ml)	TIMP-1 (pg/ml)	TIMP-2 (pg/ml)	TNFalfa (pg/ml)	VEGF (pg/ml)
Number	71	71	71	71	71	71	71	71	71
Mean±SD	251074±24528	48475±10696	146551±16310	582348±83001	107714±5705	795121±13091	346791±12980	43773±4700	520727±30129
(range)	(19810-1125635)	(8593-495306)	(11880-493076)	(18034-2365982)	(7489-181369)	(30323-817657)	(26279-442738)	(7792-192997)	(97211-1639584)

Table S2: Cut-off for serum levels of cytokines and angiogenic factors (CAFs)

CAFs	Cut-off (pg/ml)	AUC	St. Error	95% CI	Sensitivity%	95% CI	Specificity%	95% CI	Likelihood ratio	P value
Ang-2	5000	0,8028	0,03477	0.7346 to 0.8710	66,15	53.35% to 77.43%	65,88	54.80% to 75.82%	1,94	<0.0001
FGF-2	950	0,9814	0,008262	0.9652 to 0.9976	93,85	84.99% to 98.30%	94,12	86.80% to 98.06%	15,95	<0.0001
HGF	2000	0,8260	0,03350	0.7603 to 0.8916	76,92	64.81% to 86.47%	77,65	67.31% to 85.97%	3,44	<0.0001
IL-8	35000	0,8338	0,03313	0.7688 to 0.8987	76,92	64.81% to 86.47%	75,29	64.75% to 84.01%	3,11	<0.0001
PDGF	3800	0,7449	0,04002	0.6664 to 0.8233	67,69	54.95% to 78.77%	68,24	57.24% to 77.92%	2,13	<0.0001
TNF-alpha	1200	0,7962	0,03656	0.7245 to 0.8679	73,85	61.46% to 83.97%	74,12	63.48% to 83.01%	2,85	<0.001
VEGF	19000	0,8450	0,03108	0.7841 to 0.9059	75,38	63.13% to 85.23%	75,29	64.75% to 84.01%	3,05	<0.0001

Table S3. PFS and OS correlation with CAF levels

Cytokine	ANG-2 <5000	ANG-2 >5000	p	FGF-2 <950	FGF-2 >950	p	HGF <2000	HGF >2000	p	IL-8 <35000	IL-8 >35000	p	PDGF-BB <3800	PDGF-BB >3800	p	TNF- α <1200	TNF- α >1200	p	VEGF <19000	VEGF <19000	p
All pts																					
Mean PFS months	32	24.5	.5	36.5	15	.0001	32	18.5	.01	29	20.5	.01	27	24	.8	33	19.5	.03	29	21	.001
Mean OS months	61	50.5	.1	67	38	.0006	63	49	.1	63	49	.3	63	49	.1	62	44	.3	65	45	.004
VMP																					
Mean PFS months	29	22	.1	35	16	.0001	31	18	.0001	27	20	.3	25	20	.9	32.5	18	.003	25	20.5	.04
Mean OS months	62	46	.7	66	38	.006	64	44	.09	63	44	.06	63	46	.06	65	38	.07	63	45	.04
VMPT-VT																					
Mean PFS months	32	29	.6	40	15	.004	32	22	.8	32	21	.5	32	29	.7	35	22	.6	32	23	.02
Mean OS months	61	62	.3	67	40	.04	60	62	.8	61	62	.5	65	60	.8	60	62	.9	65	49	.03