

Additional file 2: Expression of MGF genes in bone marrow cell populations and during normal plasma cell differentiation.

Table S-I. Myeloma MGF genes.

Table SI-A.

name	MMC n=131		WBM n=75		CD14 n=5		PMN n=5		CD3 n=5		BMSC n=5		Ocs n=7	
	Median (range)	Nb P	median	Nb P	median	Nb P	median	Nb P	median	Nb P	median	Nb P	median	Nb P
FGF7	124 (10-480)	101	57	64	29	1	42	1	84	5	29	0	75	6
NRG3	190 (2-1088)	96	47	39	13	0	6	0	13	0	4	0	4	0
WNT10A	64 (1-269)	75	21	24	32	0	28	0	30	0	11	0	17	0
FGF18	35 (2-261)	27	13	8	17	0	13	0	4	0	16	0	21	0
NRG2	53 (3-338)	46	19	7	9	0	10	0	12	0	17	0	14	0
WNT4	6 (1-1057)	20	12	16	1	0	1	0	1	0	1	0	1	0
WNT11	12 (2-233)	10	6	2	2	0	2	0	3	0	2	0	4	0
WNT16	5 (1-212)	22	5	7	4	0	2	0	3	0	4	0	1	0

Table SI-B.

name	MMC n=131	Subpopulations CD3, CD14, PMN	BMSC n=5	Ocs n=7
	Median	FC	FC	FC
FGF7	124	2.5	4.3	2.2
NRG3	190	14.6	47.5	47.5
WNT10A	64	2.1	5.8	3.8

Genes overexpressed in MMC versus CD14, PMN, CD3, BMSCs and osteoclasts (Ocs) populations are listed. Genes in the upper part of the table (FGF7, NRG3 and Wnt10A) were statistically significantly overexpressed in MMC versus other populations ($p \leq .05$, fold-change ≥ 2). Other 5 genes were not significant, but they displayed an absent call in all environment samples, and they were thus considered as “myeloma genes”. (A) Median expression and number of samples which display a “present call” (Nb P). Data from 131 MMC samples and 75 WBM samples are indicated here. Data from 44/131 MMC and 44/75 WBM samples, both from the same patients, are depicted in Figure 2. (B) Fold-change (FC) in expression in MMC versus other BM populations.

Table S-II. Myeloma niche MGF genes.

Table SII-A

name	BMSC n=5		Ocs n=7		MMC n=131		WBM n=75		CD14 n=5		PMN n=5		CD3 n=5	
	median	Nb P	median	Nb P	median	Nb P	median	Nb P	median	Nb P	median	Nb P	median	Nb P
11 BMSC GENES														
BDNF	1089	5	3	0	13	9	3	1	3	0	2	0	2	0
FGF1	155	5	3	0	2	0	1.5	0	2	0	2	0	7	0
FGF2	742	5	4	0	25	38	7	3	4	0	1	0	3	0
FGF5	42	3	13	0	20	1	8	1	7	0	7	0	12	1
GDF15	755	5	137	7	22	2	14	1	25	1	17	0	17	1
IL-6	1867	5	107	7	55	47	28	28	125	5	18	0	25	2
JAG1	1636	5	216	7	214	127	144	74	191	2	257	5	17	5
LIF	238	5	37	0	8	1	16	6	40	0	6	2	8	0
VEGFC	1685	5	11	0	67	82	23	37	17	2	27	0	23	0
Wnt3	30	1	2	0	4	1	4	1	1	0	2	0	2	0
Wnt5B	540	5	2.6	0	77	43	39	21	6	0	10	0	4	0
3 OSTEOCLAST GENES														
April	31	5	2900	7	92	77	518	75	1539	5	545	5	67	5
IGF1	12	1	1104	7	424	131	113	70	8	0	15	0	17	0
IL-10	9	0	264	7	7	2	13	15	39	4	10	5	19	5

Table SII-B

name	BMSC or OCs Median	Subpopulations CD3, CD14, PMN FC	MMC n=131 FC	Ocs or BMSC FC
11 BMSC GENES				
BDNF	1089	544.5	83.8	363
FGF1	155	51.7	77.5	51.7
FGF2	742	247.7	29.7	185.8
FGF5	42	5.3	2.1	3.2
GDF15	755	42	34.4	5.5
IL6	1867	68.1	33.4	17.2
JAG1	1636	8.7	7.6	7.6
LIF	238	15.9	29.8	6.3
VEGFC	1685	76.6	25.1	153.2
WNT3	30	15	7.5	15
WNT5B	540	90	7	180
3 OC GENES				
April	2900	5.3	31.5	93.5
IGF1	1104	78.9	2.6	92
IL-10	264	12.6	37.7	29.3

Genes overexpressed in BMSC or osteoclasts Ocs versus CD14, PMN, CD3, MMC and Ocs/BMSCs, respectively, are listed ($p \leq .05$, fold-change ≥ 2). (A) Median expression and number of samples which display a “present call” (Nb P). (B) Fold-change (FC) in expression in BMSC or Ocs versus other populations.

Table S-III. Environment MGF genes.

Table SIII-A.

name	WBM n=75		CD14 n=5		PMN n=5		CD3 n=5		MMC n=131		BMSC n=5		Ocs n=7	
	median	Nb P	median	Nb P	median	Nb P	median	Nb P	median	Nb P	median	Nb P	median	Nb P
BAFF	1841	75	2751	5	2308	5	143	5	72	106	78	5	772	7
FGF9	31	14	48	4	17	0	175	5	24	14	17	0	16	0
FGF13	518	74	27	1	815	5	35	2	92	91	15	0	44	5
HB-EGF	144	60	1328	5	38	0	18	0	60	13	272	4	139	3
IL-1 β	645	75	4289	5	512	5	67	4	93	47	138	5	765	7
IL15	107	69	444	5	21	2	122	5	158	129	129	5	73	7
OSM	484	75	662	5	1033	5	116	5	30	4	4	0	80	4
TNF- α	58	54	443	5	24	0	104	3	46	13	7	0	115	7

Table SIII-B.

name	CD14 n=5	MMC	BMSC	OCS	PMN n=5	MMC	BMSC	OCS	CD3 n=5	MMC	BMSC	OCS
	median	FC	FC	FC		FC	FC	FC		FC	FC	FC
BAFF	2751	38.2	35.3	3.6	2308	32.1	29.6	3	175	7.3	10.3	10.9
FGF9												
FGF13					815	9	54.3	18.5				
HB-EGF	1328	22.1	5.9	9.5								
IL-1 β	4289	45.6	31.1	5.6								
IL15	444	2.8	3.4	6.1								
OSM	662	22.8	165.5	8.3	1033	35.6	258.3	12.9				
TNF- α	443	9.6	55.4	3.9								

Genes overexpressed in at least in one of the population CD14, PMN, CD3 versus MMC, BMSCs and Ocs ($p \leq .05$, fold-change ≥ 2) are listed. (A) Median expression and number of samples which display a “present call” (Nb P). (B) Fold-change (FC) in expression in CD14, PMN or CD3 versus other BM populations.

Table S-IV. Genes not statistically significantly overexpressed in cell populations.

name	MMC n=131		WBM n=75		CD14 n=5		PMN n=5		CD3 n=5		BMSC n=5		Ocs n=7	
	median	Nb P	median	Nb P	median	Nb P	median	Nb P	median	Nb P	median	Nb P	median	Nb P
AREG	1201	131	610	75	1323	5	337	5	1150	5	60	5	64	5
CCL3	721	119	547	75	1880	5	162	5	608	5	6	0	2012	7
CLCF1	60	4	39	12	69	0	58	0	85	3	129	5	42	0
FGF12	59	114	19	35	33	5	36	5	37	4	27	5	38	6
HGF	218	106	89	71	99	5	102	5	7	0	194	5	36	7
JAG2*	69	39	29	29	75	5	55	1	84	5	49	3	48	5
NRG1*	42	19	6	2	39	1	19	0	27	1	27	1	26	0
PTN*	186	70	34	19	79	0	75	0	111	0	104	5	89	4
VEGF	374	131	296	75	1081	5	313	5	25	5	1654	5	35	7
VEGFB*	47	32	25	14	3	0	8	0	24	0	38	0	68	6
Wnt5A	339	103	60	53	13	2	10	1	10	0	585	5	311	7
Wnt6*	319	34	30	3	226	4	158	1	209	5	120	2	197	5

Genes that were not found to be statistically significantly overexpressed in one cell population compared to the others ($p > .05$ and/or ratio < 2) are listed. The table indicates the median expression and number of samples which display a “present call” (Nb P). * indicates genes (PTN, NRG1, JAG2, VEGFB and Wnt6) that were also expressed in MMC and environment cells, but without any change in signal between present or absent call (data not shown). This may suggest that those probe sets poorly work. It may also be that the expression level is at the limit of sensitivity and thus can hardly be detected by Affymetrix probe sets.

Table S-V. Expression of MGF during normal plasma cell differentiation and in MMC.

		Gene Name	Fold-change	median in MB	median in PPC	median in BMPC	median in MM
Comparison MB versus (PPC+BMPC)	Genes overexpressed in MB	OSM	2.7	65.5	17	41	30
		WNT6	2.9	555	153	230	319
		WNT16	3.5	33	20	4	5
		FGF9	6.4	251.5	32	70	23
	Genes overexpressed in PPC+BMPC	FGF7	3	42	114	134	124
		CCL3	5.3	53	138	736	721
		WNT5B	10.3	9.5	135	65	77
		IGF1	12.2	28.5	480	297	424
Comparison PPC versus BMPC	Genes overexpressed in PPC	IL15	2.2	129.5	303	139	158
	Genes overexpressed in BMPC	PTN	2.0	51	21	42	186
		VEGFB	2.6	63.5	25	65	47
		BAFF	3.6	104.5	30	107	72
		VEGFC	3.7	30	17	63	67
		WNT10A	3.8	38	30	115	64
		FGF2	4.3	13	6	26	25
		CCL3	5.3	53	138	736	721
		WNT5A	6.3	9.5	8	50	339
		AREG	10.5	218.5	31	326	1201
		JAG1	12.0	16.5	14	168	214
		APRIL	12.8	102	14	179	92
Comparison MMC versus BMPC	Genes overexpressed in BMPC	No gene					
	Genes genes overexpressed in MMC	AREG	3.7	218.5	31	326	1201
		NRG3	3.9	10	4	49	190
		WNT5A	6.8	9.5	8	50	339

A supervised analysis was performed in order to compare the MGF gene expression profile of memory B cells (MB) versus (PPC+BMPC), that of PPC versus BMPC and that of BMPC versus MMC. Genes differentially expressed genes between 2 populations in each comparison group are listed here ($p \leq .05$, fold-change ≥ 2). The median expression and fold-change are indicated for each gene, and genes are ranked according to the fold-change in each comparison group.

Table S-VI. Expression of MGF receptors during normal plasma cell differentiation and in MMC.

			foldchange	median in MB	median in PPC	median in BMPC	median in MM
Comparison MB versus (PPC+BMPC)	genes overexpressed in MB	IL10RA	2.8	929	294	428	212
	Genes overexpressed in PPC+BMPC	FZD3	2	24	45	52	80
		FZD1	2.7	25	48	92	75
		FZD6	3.2	30.5	60	138	229
		IL6ST	3.3	263.5	516	1220	1681
		IL15RA	3.5	58.5	179	251	142
		IL6R	6.8	64	816	564	502
		c-Met	7.1	5.5	60	19	78
		TNFRSF17	16.3	184.5	2525	3373	3794
Comparison PPC versus BMPC	Genes overexpressed in PPC	IL21R	4.2	4.5	244	58	6
		FZD1	2	25	48	96	75
	Genes overexpressed in BMPC	TNFRSF1A	2.0	48	42	85	63
		FZD6	2.3	30.5	60	138	229
		IL6ST	2.4	263.5	516	1220	1681
		NTRK2	2.4	91	45	107	84
		NOTCH4	2.4	59	29	69	40
		CCR1	3.4	76.5	74	248	136
		FZD7	3.7	30.5	35	128	102
		FZD8	3.9	67.5	12	47	34
		LIFR	12.0	5	3	36	16
		FZD2	70.7	9.5	3	212	30
Comparison MMC versus BMPC	Genes overexpressed in BMPC	FZD2	7	9.5	3	212	30
	Genes overexpressed in MMC	No gene					

A supervised analysis was performed in order to compare the MGF receptor gene expression profile of memory B cells (MB) versus (PPC+BMPC), that of PPC versus BMPC and that of BMPC versus MMC. Genes differentially expressed genes between 2 populations in each comparison group are listed here ($p \leq .05$, fold-change ≥ 2). The median expression and fold-change are indicated for each gene, and genes are ranked according to the fold-change in each comparison group.

Table S-VII. Expression of MGF and MGF receptors in BMPC and MMC samples from a public data set.

Table SVII-A.

MGF genes	Median BMPC (n=22)	Median MMC (n=345)	fold-change MMC/BMPC
NRG3*	81.5	688.0	8.4
HGF	115.5	866.0	7.5
Wnt5A*	422.5	2183.0	5.2
AREG*	257.0	686.0	2.7
IL6	79.5	193.0	2.4

MGF receptor gene	Median BMPC (n=22)	Median MMC (n=351)	fold-change MMC/BMPC
IL11R	91.5	325.0	3.6

Table SVII-B.

MGF genes	Median BMPC (n=22)	Median MMC (n=345)	fold-change BMPC/MMC
WNT2	780.5	352.0	2.2
TNFSF13B	678.5	328.0	2.1

MGF receptor gene	Median BMPC (n=22)	Median MMC (n=351)	fold-change BMPC/MMC
IL1R	179	51	3.5

We used Affymetrix data of 22 normal BMPC samples and a cohort of 345 purified MMC from the Arkansas Research Group (Little Rock). These data are publicly available in the NIH Gene Expression Omnibus (GEO) under accession numbers GSE2658 and GSE5900. A supervised analysis was performed in order to compare the MGF and MGF receptor gene expression profile of BMPC and MMC samples ($p \leq .05$, fold-change ≥ 2). (A) Genes overexpressed in MMC versus BMPC. (B) Genes overexpressed in BMPC versus MMC. The median expression and fold-change are indicated for each gene.