

SUPPLEMENTARY INFORMATION

MATERIALS AND METHODS

Colony-formation assay

Soft agar assay for colony formation was performed following the standard protocol (Invitrogen). ARP-1 cells (1,250 cells per well) or MΦs (1,250 cells per well) or their combinations were seeded in 24-well plates for the assay.

Cell proliferation assay

Cell proliferation was measured by MTS assay following the manufacturer's protocol (Promega).

SUPPLEMENTARY FIGURE LEGENDS

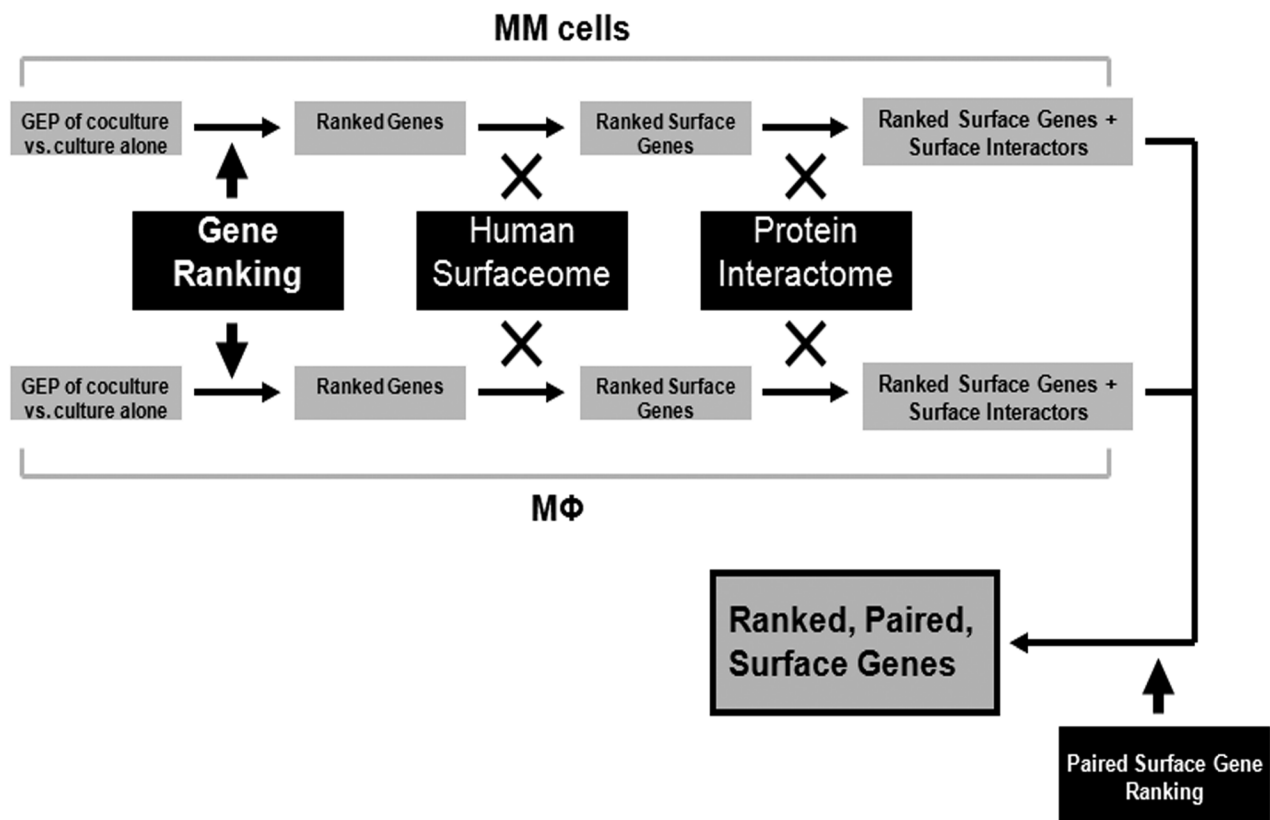
Supplementary Figure 1. Identification of differentially regulated and paired membrane protein genes. Graphic workflow of identification of differentially regulated and paired membrane protein genes from cultured MM cells and MΦs.

Supplementary Figure 2. Selectins and PSGL-1 in MΦ-mediated MM drug resistance. (A) RT-PCR for E- and P-selectin expression in monocyte-derived MΦs from three different blood donors. (B) Flow cytometry analysis and (C) western blotting showing PSGL-1 expression on and in wild-type (control), control transduced, or PSGL-1 shRNA-transduced MM cells (ARP-1 or ARK).

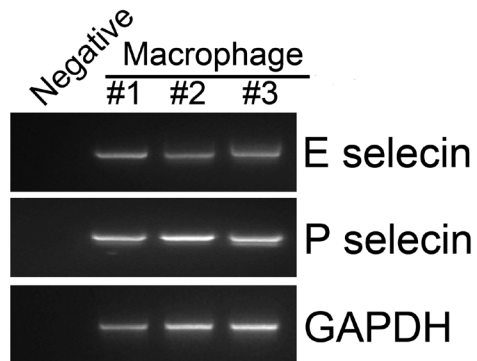
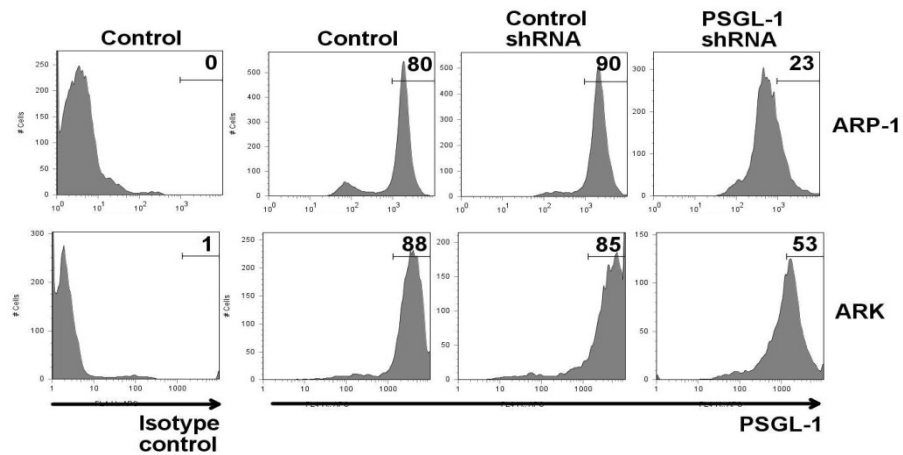
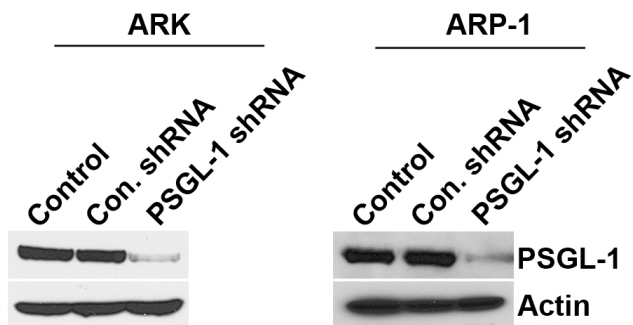
Supplementary Figure 3. Roles of CD18 and ICAM-1 in MΦ-mediated MM drug resistance. (A) Flow cytometry analysis and (B) western blotting showing ICAM-1 expression on ICAM-1 shRNA-transduced MM cells (CAG or U266). Controls include wild-type (control) and control shRNA-transduced (control shRNA) MM cells (CAG or U266).

Supplementary Figure 4. Activation of signaling pathways in MM cells under coculture conditions. Western blotting analyses showing (A) the expression of PSGL-1, c-myc, pSrc(Y416), Src, pErk1/2, and Erk1/2 in MM.1S and CAG cells; (B) expression or (C) semi-quantifies amounts (the band intensity was analyzed by ImageJ and normalized to β -actin) of the expression of PSGL-1, c-myc, pErk1/2(T202/204), Erk1/2 and actin in PSGL-1-knocked down ARK cells (PSGL-1 KD) alone or after coculture with M Φ s for 24 hours. Wild-type (con) and control shRNA-transfected (con KD) ARK were used as controls; (D) PSGL-1 expression in ARP-1 cells in cultures of MM cells alone (Al) or in coculture with M Φ s in transwell (Tr) or in direct contact (Co) for 24 hours in the presence or absence of IFN- α -blocking antibody (10 μ g/ml) or control IgG. (E) Percentage of melphalan-induced apoptotic ARP-1 cells in culture alone or in direct coculture with M Φ s in the presence or absence (control) of 10 μ g/ml of IFN- α -blocking antibody or control IgG. Summarized results from three independent experiments are shown. * $P < 0.05$.

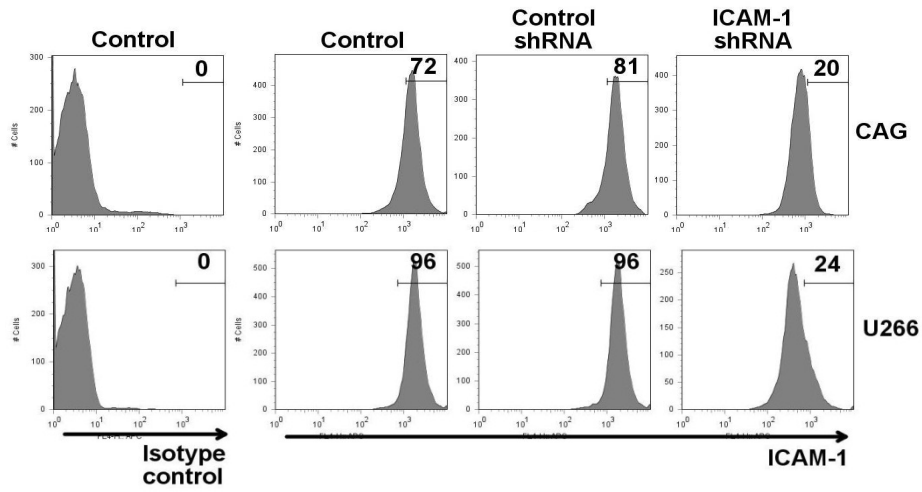
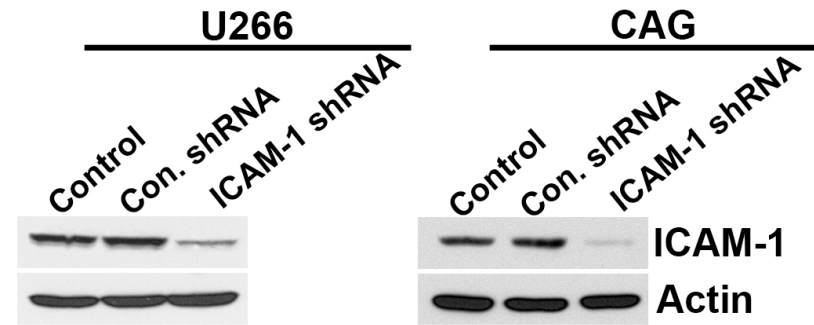
Supplementary Figure 5. In vivo and in vitro effects of M Φ s on MM cell growth/proliferation and tumorigenicity. (A) Tumor volume in SCID mice inoculated with ARP-1 alone or ARP-1 together with human monocytes without treatments. * $P < 0.05$, ** $P < 0.01$. (B) In vitro ARP-1 cell proliferation measured by MTS assay, (C) colony formation in culture of ARP-1 alone or in direct coculture with M Φ s. Representative results from three independent experiments. * $P < 0.05$, ** $P < 0.01$.

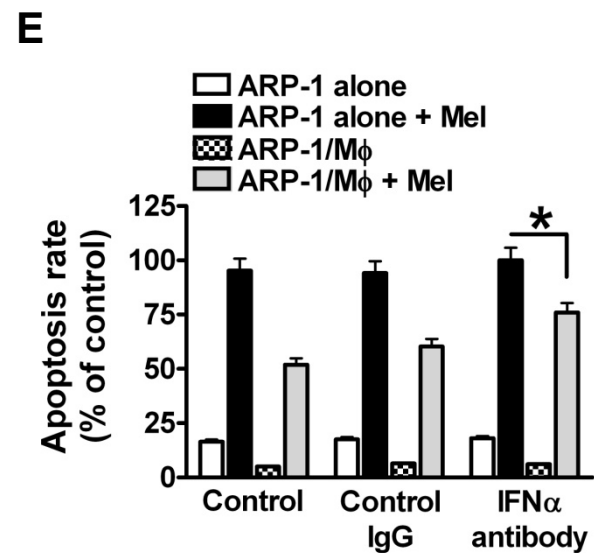
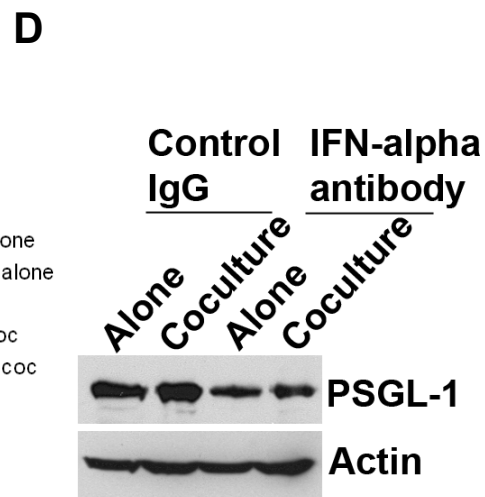
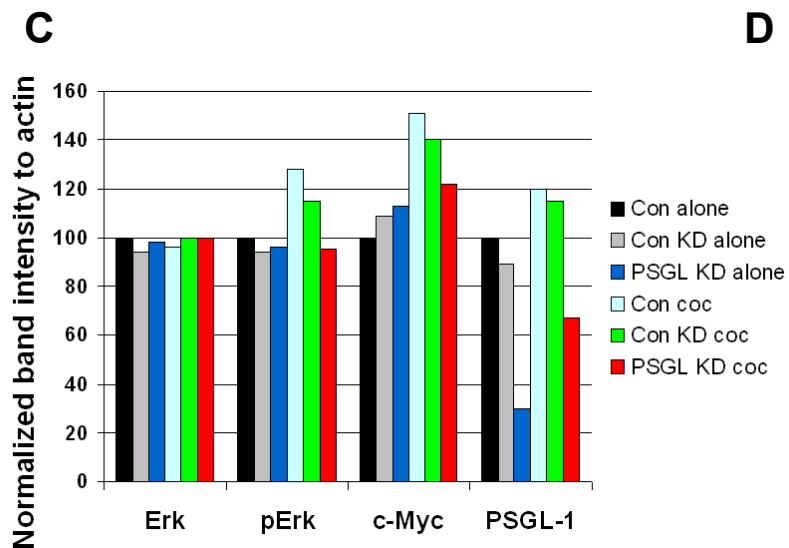
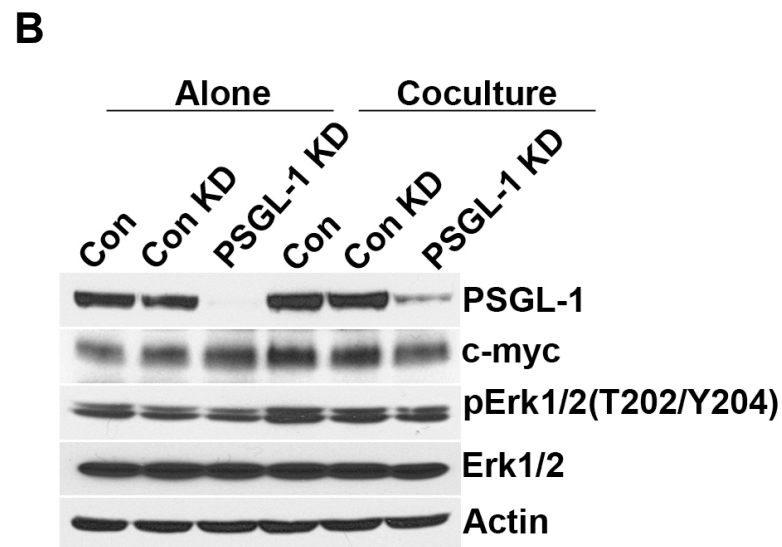
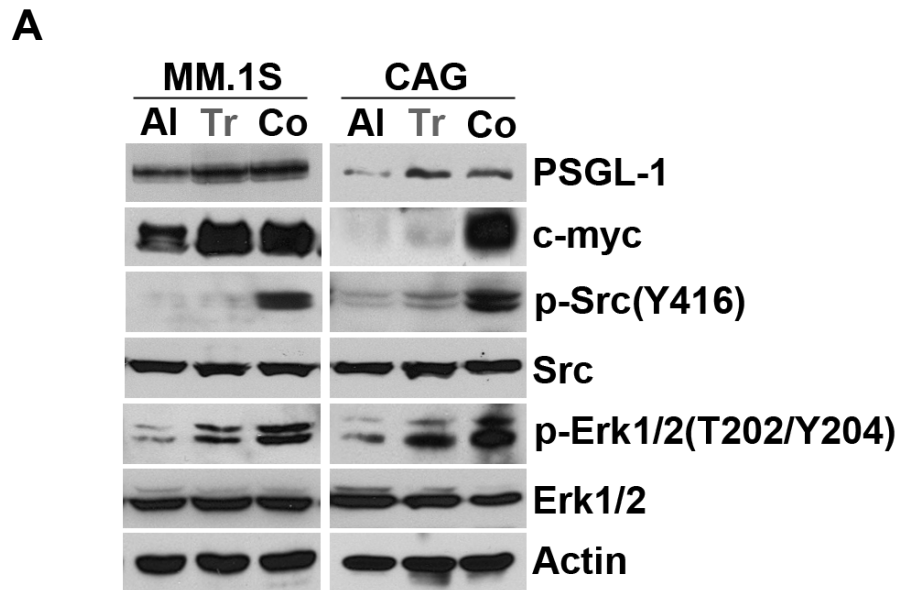


Supplementary Figure 1

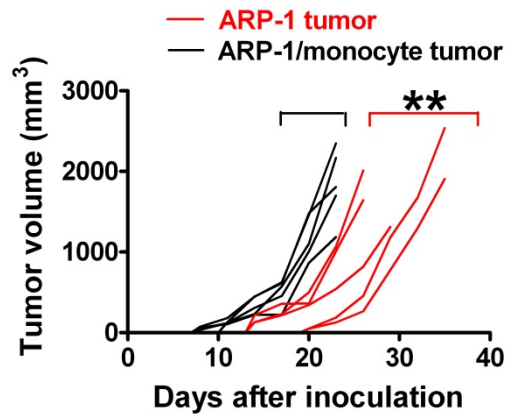
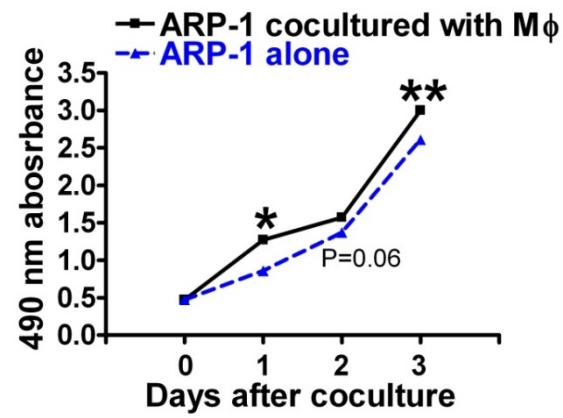
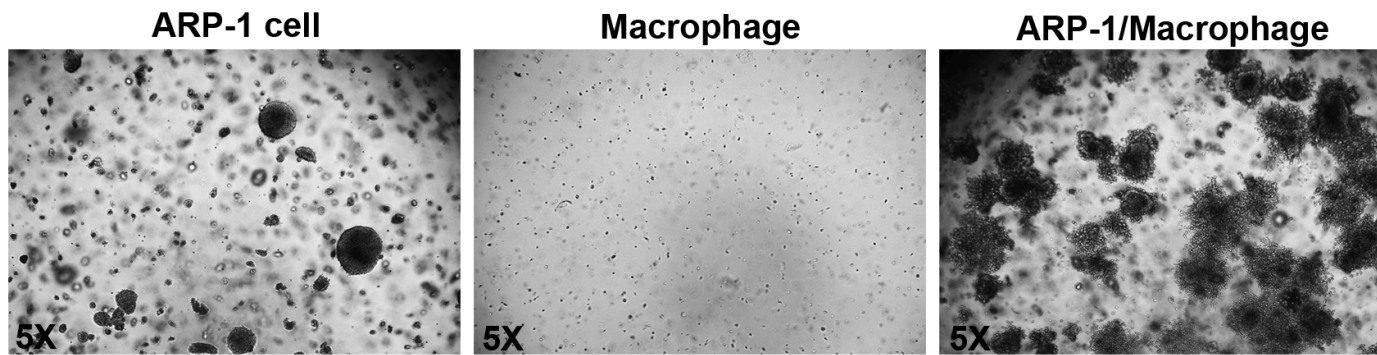
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Supplementary Figure 2

A**B****Supplementary Figure 3**



Supplementary Figure 4

A**B****C**

Supplementary Figure 5

SUPPLEMENTARY TABLE LEGEND

Supplementary Table 1. A representative subset of top 250 paired surface protein genes.

Same genes on myeloma cells are combined and alphabetically sorted. Self-interacting gene pairs are removed.

Myeloma surface protein	Macrophage surface protein
CAV1	PTPRF
	S1PR1
	INSR
	CAV2
	KDR
	GJA1
	HTR1F
	EDNRB
	PRNP
	MMP14
	APP
	CD40
	CD200
CD74	HLA-DPB1
	CD1D
	HLA-DQA1
	HLA-DQB1
	HLA-DPA1
	HLA-DRA
	HLA-DMB
	HLA-DMA
FGFR1	FLRT3
	NCAM1
	EPHA4
ICAM3	CLEC4M
ICAM4	ITGB1
NCAM1	PRNP
NOTCH2	PSEN1
	DLL1
	JAG2
PECAM1	EFNB2
	ITGB3
SELPLG	SELE
VCAM1	ITGB1
	ITGB7