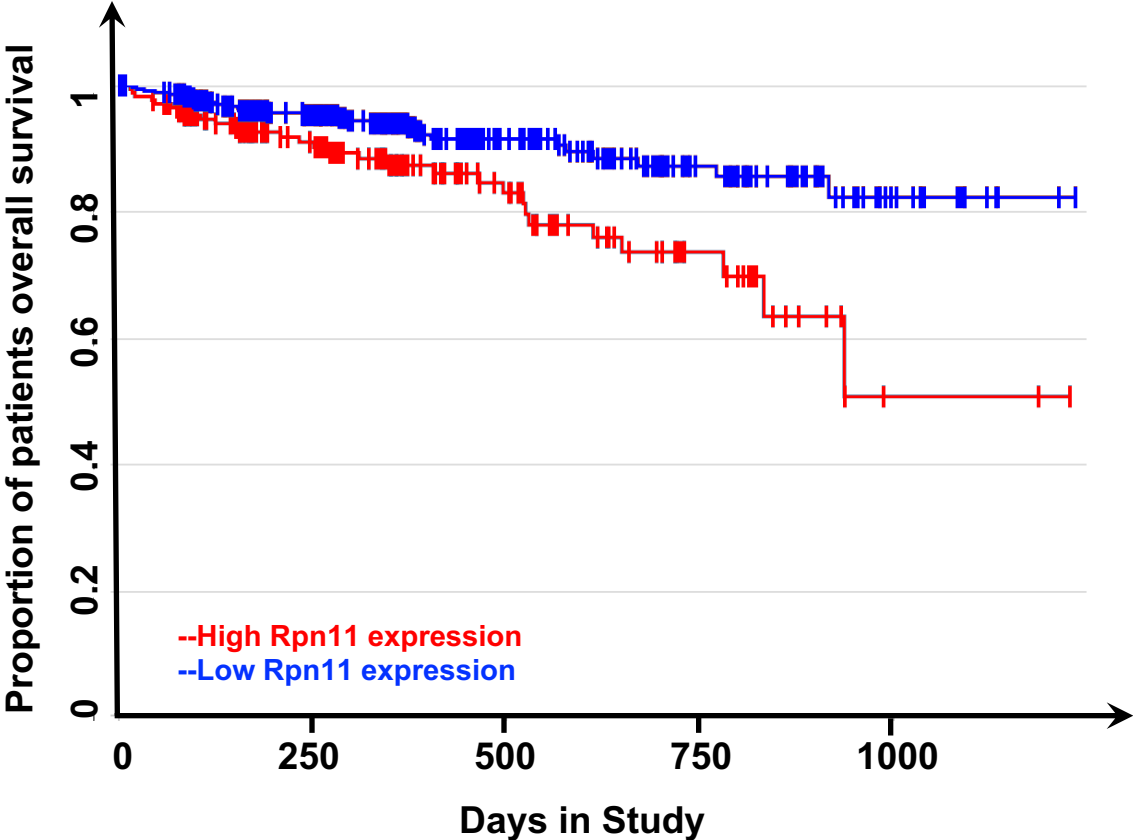


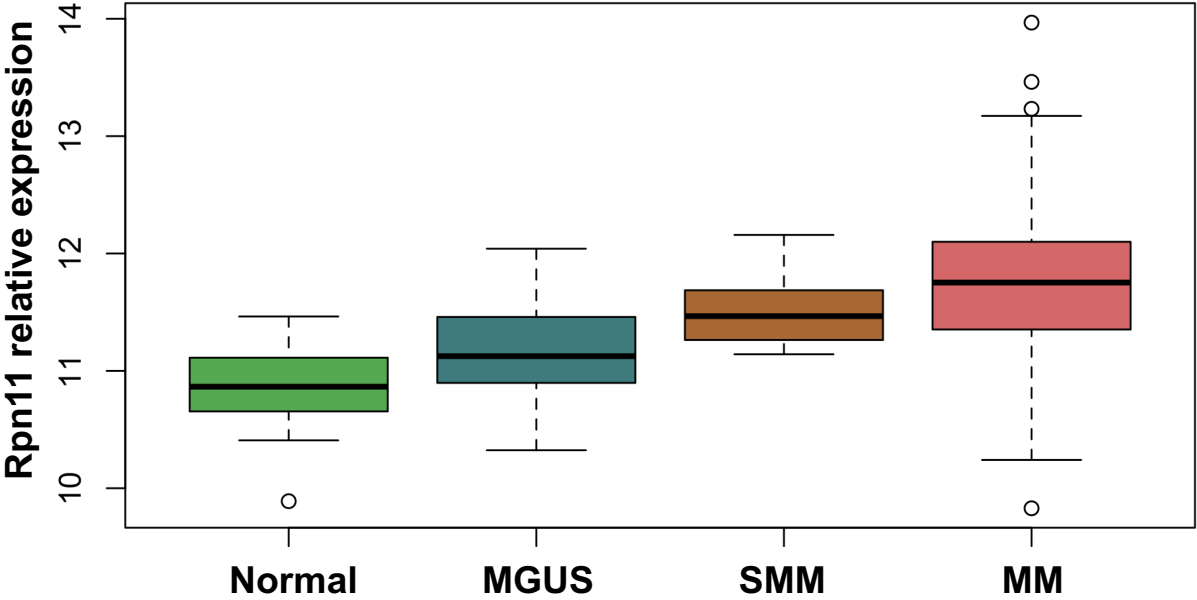
- **Supplementary Figure Legends**

- **Supplementary Figure 1, related to Figure 1** Kaplan-Meier plots of *Rpn11* expression versus overall survival of newly diagnosed, MM patients (n=550, $p < 0.001$). Red line points to the patient group with elevated *Rpn11* expression and shorter survival, whereas blue line represents patient cohort with lower *Rpn11* and longer survival.
- **Supplementary Figure 2, related to Figure 1** Relative *Rpn11* expression in normal individuals, patients with MGUS, or MSS, or MM ($p < 0.00001$).
- **Supplementary Figure 3, related to Figure 1** *Rpn11* expression in plasma cells from normal healthy donors (n= 5) and CD138+ tumor cells from MM patients (n=12).
- **Supplementary Figure 4, related to Figure 1** Comparative analysis of *Rpn11* expression in the BM biopsies from normal donors and MM patients. Red arrowheads points to the *Rpn11*+ brown cells. (Scale bar, 5 μ m).
- **Supplementary Figure 5, related to Figure 3** MM.1S and BMSCs/pDCs were cultured either alone or together in the presence or absence of OPA for 48h, and DNA synthesis was measured by 5-bromo-2'-deoxyuridine (BrdU) uptake (mean \pm SD; n=3; $p < 0.0001$).
- **Supplementary Figure 6, related to Figure 4** MM.1S cells were cultured in the presence of pan-caspase inhibitor (1h); cells were the treated with OPA (10 μ M; 24h), and analyzed for cell viability (mean \pm SD; $p < 0.0001$).
- **Supplementary Figure 7, related to Figure 4** ANBL6.BR cells were treated with OPA or bortezomib, and cell extracts were then analyzed for indicated molecules using immunoblotting.
- **Supplementary Figure 8, related to Figure 6A** OPA adds to the anti-MM activity of immunomodulatory agents Lenalidomide
- **Supplementary Figure 9, related to Figure 6B** OPA adds to the anti-MM activity of immunomodulatory agents Pomalidomide
- **Supplementary Figure 10, related to Figure 6C** OPA adds to the anti-MM activity of Dex

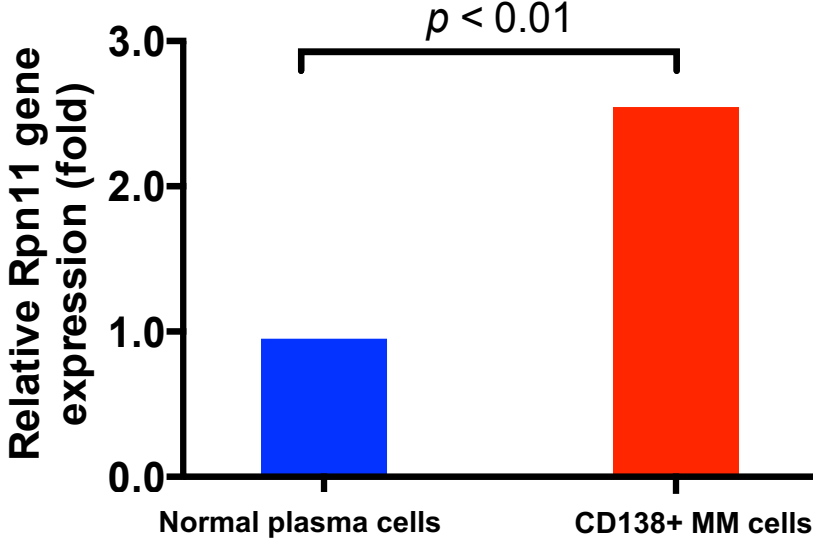
Supplementary Figure 1, related to Figure 1



Supplementary Figure 2, related to Figure 1

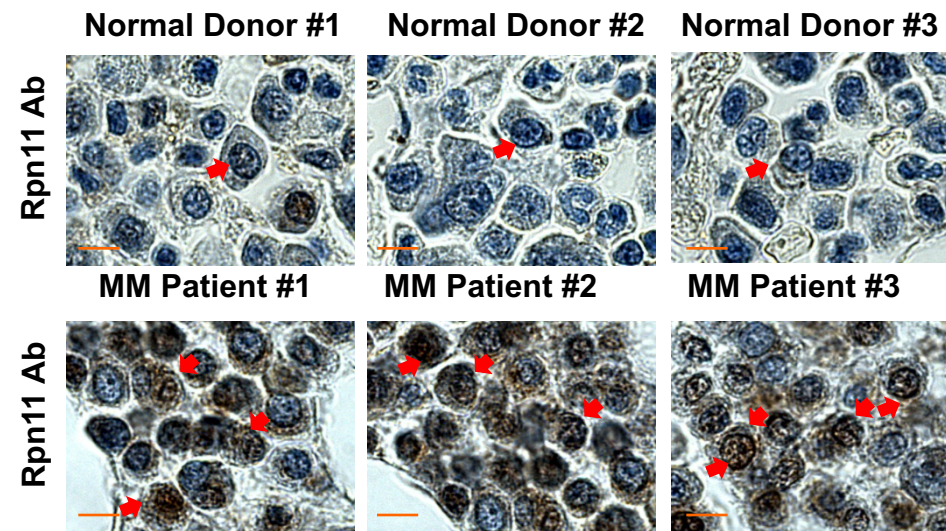


Supplementary Figure 3, related to Figure 1

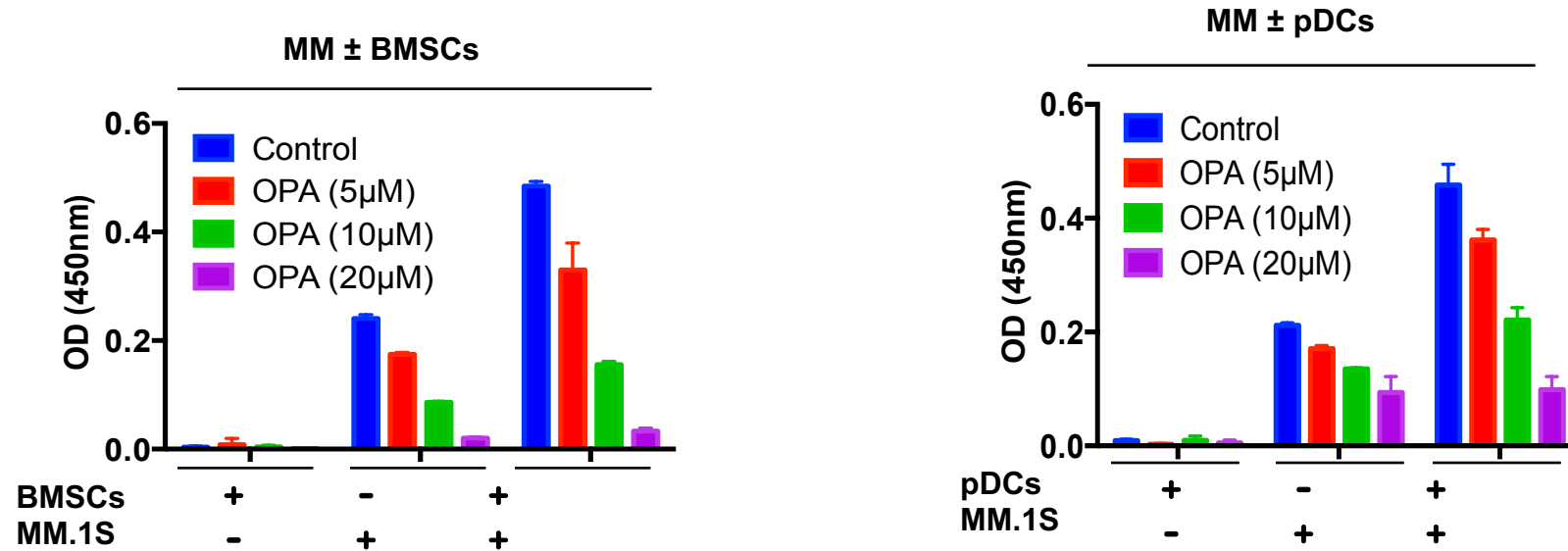


Supplementary Figure 4, related to Figure 1

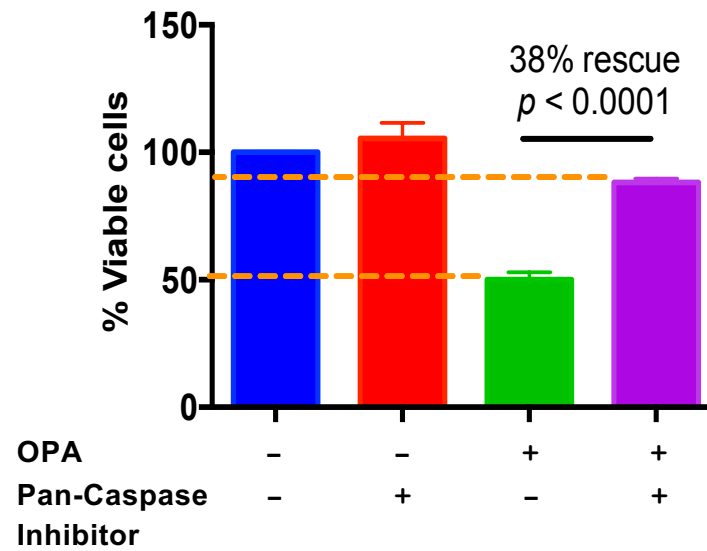
Immunohistochemistry on Bone Marrow Biopsies



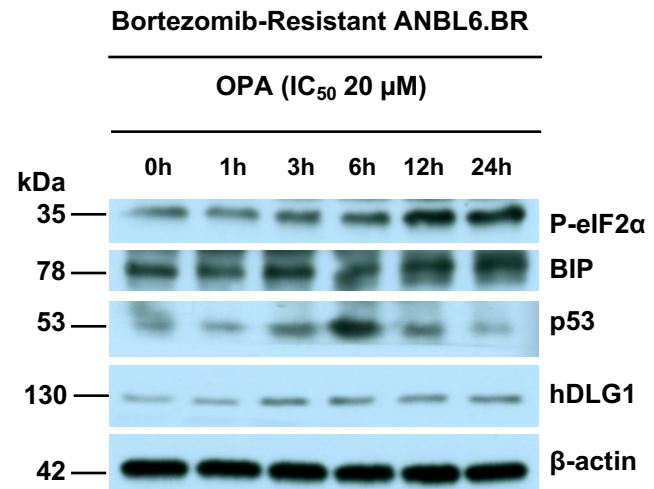
Supplementary Figure 5, related to Figure 3



Supplementary Figure 6, related to Figure 4



Supplementary Figure 7, related to Figure 4



Supplementary Figure 8, related to Figure 6A

	OPA (μM)	OPA Fa	Lenalidomide (μM)	Lenalidomide Fa	Fa	CI
1	4	0.93	1	0.91	0.66	0.487
2	4	0.93	3	0.9	0.65	0.482
3	4	0.93	5	0.87	0.63	0.471
4	8	0.63	1	0.91	0.32	0.646
5	8	0.63	3	0.9	0.31	0.638
6	8	0.63	5	0.87	0.29	0.621
7	16	0.33	1	0.91	0.16	0.996
8	16	0.33	3	0.9	0.15	0.974
9	16	0.33	5	0.87	0.13	0.928

Supplementary Figure 9, related to Figure 6B

	OPA (μM)	OPA Fa	Pomalidomide (μM)	Pomalidomide Fa	Fa	CI
1	4	0.93	1	0.63	0.57	0.429
2	4	0.93	3	0.62	0.53	0.384
3	4	0.93	5	0.6	0.45	0.328
4	8	0.63	1	0.63	0.56	0.805
5	8	0.63	3	0.62	0.41	0.612
6	8	0.63	5	0.6	0.38	0.58
7	16	0.33	1	0.63	0.29	0.979
8	16	0.33	3	0.62	0.28	0.959
9	16	0.33	5	0.6	0.26	0.918

Supplementary Figure 10, related to Figure 6C

	OPA (μM)	OPA Fa	Dex (nM)	Dex Fa	Fa	CI
1	4	0.93	10	0.63	0.56	0.968
2	4	0.93	20	0.56	0.45	0.859
3	4	0.93	30	0.47	0.41	0.906
4	8	0.63	10	0.63	0.44	0.838
5	8	0.63	20	0.56	0.38	0.902
6	8	0.63	30	0.47	0.35	0.935
7	16	0.33	10	0.63	0.22	0.879
8	16	0.33	20	0.56	0.19	0.835
9	16	0.33	30	0.47	0.1	0.591