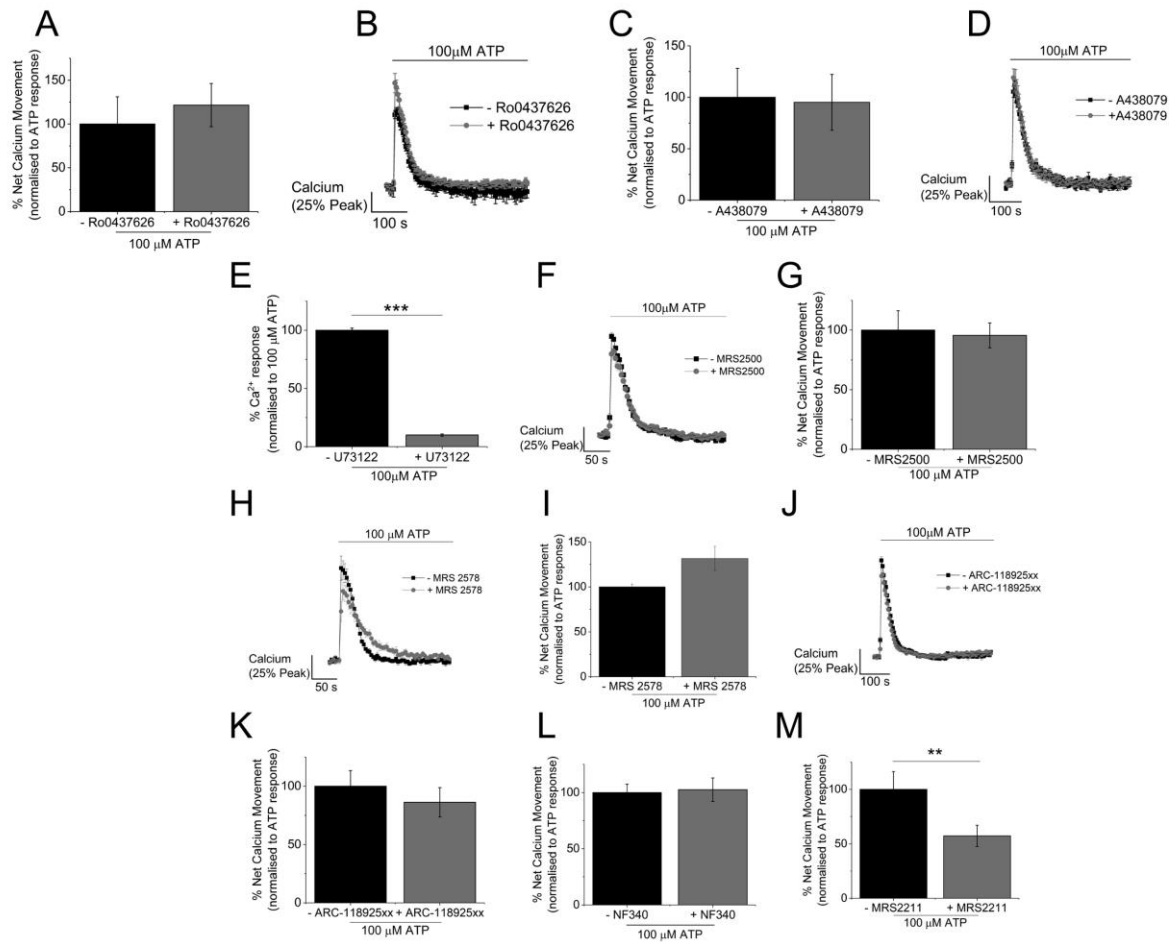
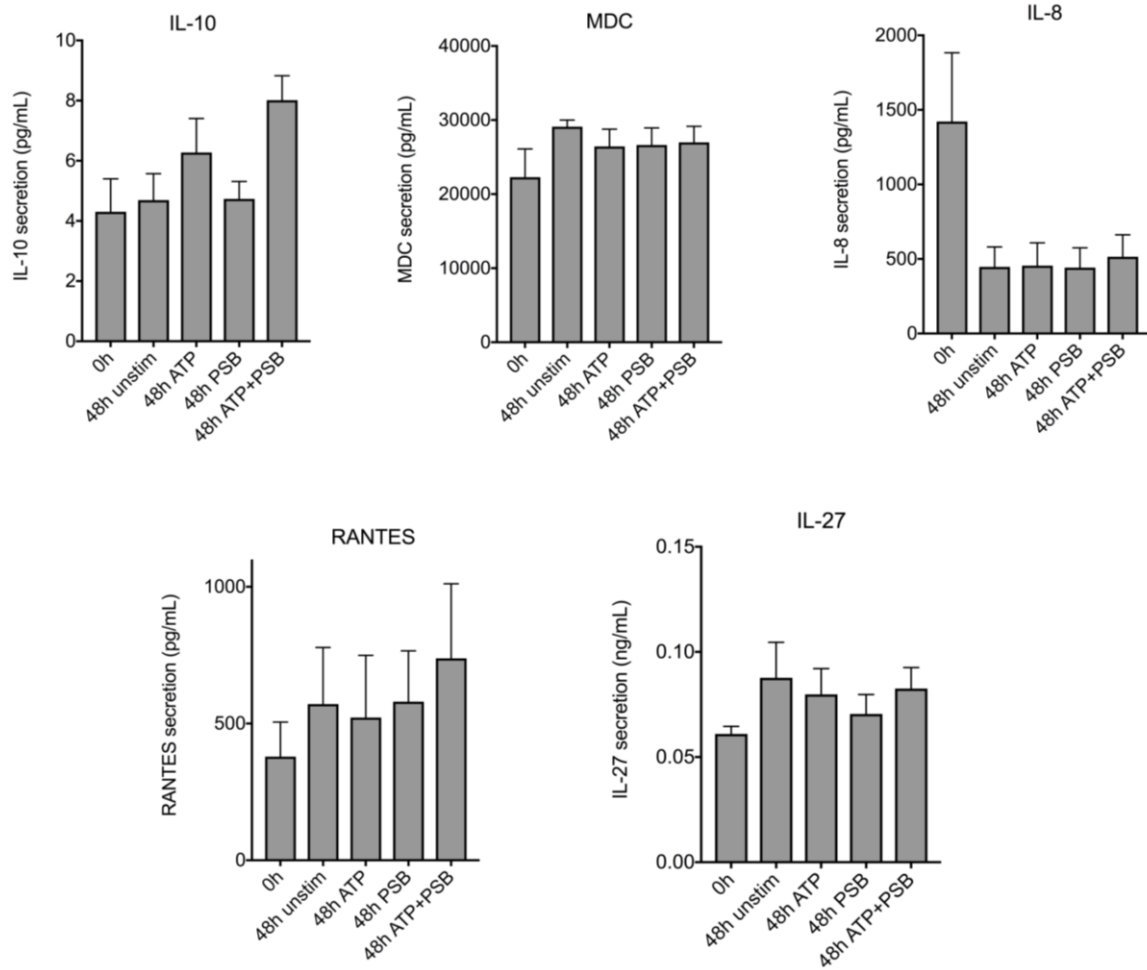


Supplementary Figure 1. Concentration-inhibition curves for PSB-12062 and BX-430 using human P2X₄ stable cells, and agonist responses in human P2X₇ stable cells. A) ATP concentration response (0.01 μ M – 300 μ M) of P2X₄ over-expressing 1321N1 astrocytoma cells ($EC_{50} = 0.12 \pm 0.0031 \mu$ M; N=3). Inhibition curve of P2X₄ antagonist: B) PSB-12062 (0.03 μ M – 30 μ M; $IC_{50} = 3.31 \pm 0.34 \mu$ M; N=3) and C) BX-430 (0.01 μ M – 30 μ M; $IC_{50} = 1.56 \pm 0.085 \mu$ M; N=3) on P2X₄ over-expressing 1321N1 astrocytoma cells. D) BzATP concentration response (1 μ M – 1 mM) of P2X₇ over-expressing 1321N1 astrocytoma cells ($EC_{50} = 43.4 \pm 7.23 \mu$ M; N=3). E) ATP concentration response (3 μ M – 3 mM) of P2X₇ over-expressing 1321N1 astrocytoma cells (no response observed below 3 mM ATP; N=3).



Supplementary Figure 2. Effect of P2X and P2Y receptor antagonists on net Ca^{2+} movement in response to 100 μM ATP in human MDMs. Effect of: A and B) selective P2X₁ receptor antagonist (30 μM Ro0437626; N=4 donors) and C and D) selective P2X₇ receptor antagonist (5 μM A438079; N=4 donors) on net calcium movement and time-response curves of Ca^{2+} response. E) Effect of PLC inhibitor (10 μM U-73122; N=3 donors) on peak magnitude of ATP-evoked Ca^{2+} response. Effect of P2Y selective antagonists on ATP-evoked Ca^{2+} response: F and G) P2Y₁ (1 μM MRS2500, N=3 donors), H and I) P2Y₆ (10 μM MRS2578; N=3 donors), J and K) P2Y₂ (10 μM ARC-118925xx; N=3 donors), L) P2Y₁₁ (NF340; N=3 donors) and M) P2Y₁₃ (MRS2211; N=3 donors), on net calcium movement. Data is represented as normalized area under the curve to ATP response. Statistical significance is represented as * $p < 0.05$, ** $p < 0.01$ and *** $p < 0.001$.



Supplementary Figure 3. Multiplex analysis of IL-10 (N=7 donors), MDC (N=7 donors), IL-8 (N=7 donors), RANTES (N=7 donors) and IL-27 (N=7 donors) under various conditions in human monocyte-derived macrophages.

Calcium response normalized to 100% ATP				
Antagonist	Peak magnitude	Area under the curve	Decay kinetics (τ)	Statistical significance
P2X1 (30 μ M Ro0437626)	131.29 \pm 10.26% (N=4)	131.27 \pm 23.41% (N=4)		Peak: $P < 0.01$ AUC: $P > 0.05$
P2X4 (5 μ M BX430)	96.21 \pm 4.61% (N=5)	42.28 \pm 12.65% (N=5)	Vehicle: 21.56 \pm 10.88 s BX430: 16.605 \pm 10.55 s	Peak: $P > 0.05$ AUC: $P < 0.05$
P2X4 (10 μ M PSB-12062)	92.34 \pm 2.71% (N=12)	61.03 \pm 7.49% (N=12)	Vehicle: 36.52 \pm 3.17 s PSB-12062: 28.06 \pm 1.47 s	Peak: $P < 0.05$ AUC: $P < 0.01$
P2X7 (10 μ M A438079)	112.77 \pm 1.10% (N=4)	101.17 \pm 22.20% (N=4)		Peak: $P > 0.05$ AUC: $P > 0.05$
P2Y1 (1 μ M MRS2500)	85.28 \pm 7.66% (N=3)	100.55 \pm 5.32% (N=3)		Peak: $P > 0.05$ AUC: $P > 0.05$
P2Y2 (10 μ M ARC-118925xx)	86.45 \pm 6.16% (N=3)	93.97 \pm 7.77% (N=3)		Peak: $P > 0.05$ AUC: $P > 0.05$
P2Y6 (10 μ M MRS2578)	73.85 \pm 7.11% (N=3)	132.69 \pm 17.73% (N=3)		Peak: $P > 0.05$ AUC: $P > 0.05$
P2Y11 (10 μ M NF340)	79.48 \pm 3.20% (N=3)	106.14 \pm 13.74% (N=3)	Vehicle: 22.03 \pm 3.17 s NF340: 22.64 \pm 7.70 s	Peak: $P > 0.05$ AUC: $P > 0.05$
P2Y13 (10 μ M MRS2211)	69.59 \pm 4.56% (N=3)	58.26 \pm 4.20% (N=3)	Vehicle: 22.03 \pm 3.17 s MRS2211: 35.17 \pm 3.92 s	Peak: $P > 0.05$ AUC: $P < 0.01$
P2Y11 (NF340) + P2Y13 (MRS2211)	54.12 \pm 4.29% (N=3)	77.47 \pm 16.62% (N=3)		Peak: $P > 0.05$ AUC: $P > 0.01$
P2X4 (BX430) + P2Y11 (NF340) + P2Y13 (MRS2211)	48.27 \pm 2.85% (N=4)	68.2 \pm 12.63% (N=4)		Peak: $P < 0.05$ (against NF340 + MRS2211) AUC: $P < 0.05$
P2X4 (PSB-12062) + P2Y11 (NF340) + P2Y13 (MRS2211)	53.52 \pm 2.95% (N=4)	78.3 \pm 16.56% (N=4)		Peak: $P > 0.05$ (against NF340 + MRS2211) AUC: $P > 0.05$

Supplementary Table 1. Effect of P2 receptor antagonists on the magnitude, shape (area under the curve), and decay kinetics (τ) of 100 μ M ATP-evoked Ca^{2+} responses in human MDMs. Data is represented as normalized values to either 100% peak magnitude or 100% area under the curve of 100 μ M ATP- Ca^{2+} response. Contribution of receptor activation towards shape of ATP-evoked Ca^{2+} response is assessed through measurements of decay kinetics as obtained through τ value. Decay kinetic values are represented in seconds (s) Statistical significance is represented for each measurement with $P > 0.05$ indicating non-significant change to vehicle data.