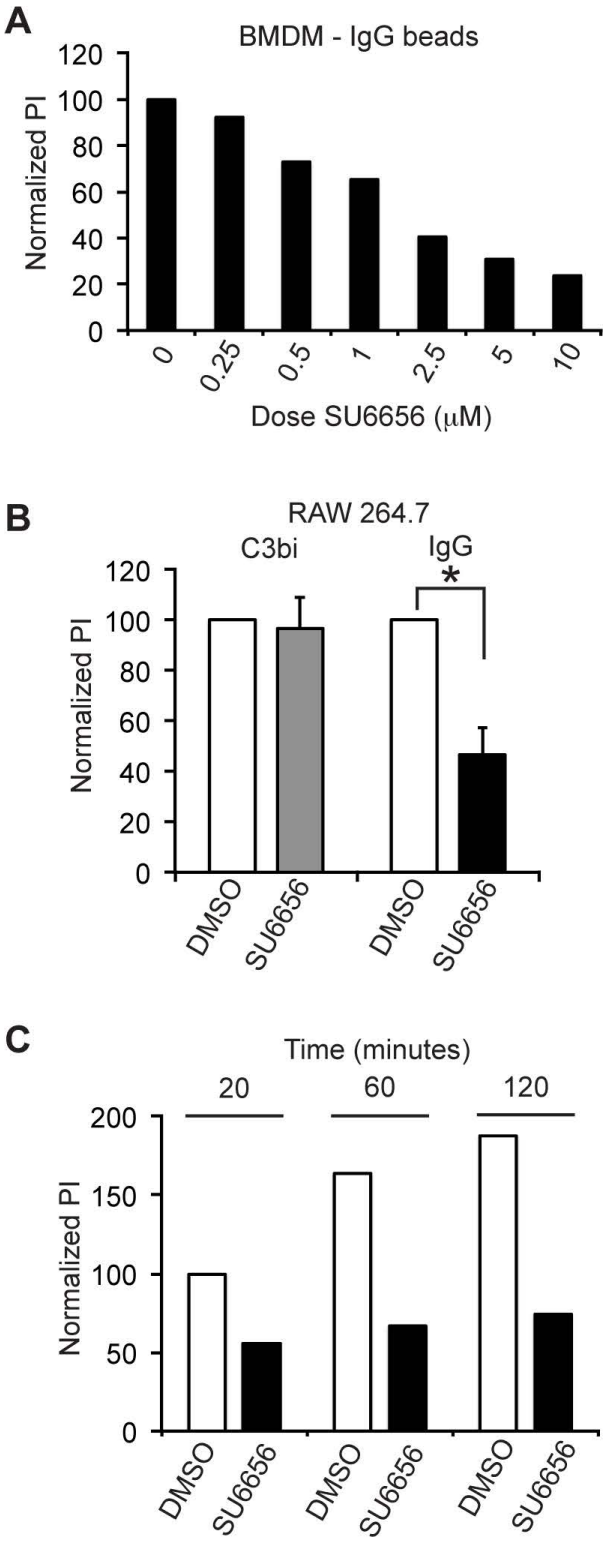

**Fig. S1. The effect of SU6656 on IgG-mediated uptake is dose-dependent but not time-dependent.** (A) Titration of SU6656's effects on IgG-coated bead uptake. After treatment with the listed doses of SU6656 or 0.1% DMSO for 2 h, BMDM were incubated with beads for 30 min. Shown is the PI for each condition normalized to DMSO (100%). A representative experiment of 2 experiments is shown. (B) SU6656 decreases IgG-coated bead uptake by RAW 264.7 cells but not C3bi-coated bead uptake. Bars show the mean PI $\pm$ standard error (PE) for RAW 264.7 cells treated with 2.5 μM SU6656 normalized to the DMSO-treated PI (100%) for each experiment. *, $p < 0.05$ by two-tailed *t*-test. (C) The relative decrease in PI in SU6656-treated BMDM does not change after 2 h of incubation. After 0.1% DMSO or 2.5 μM SU6656 treatment for 2 h, BMDM were incubated with amastigotes for the length of time shown. The PI is shown for each time point of SU6656-treated BMDM, normalized to DMSO-treated BMDM at the first time point. Shown is one representative experiment of two experiments.

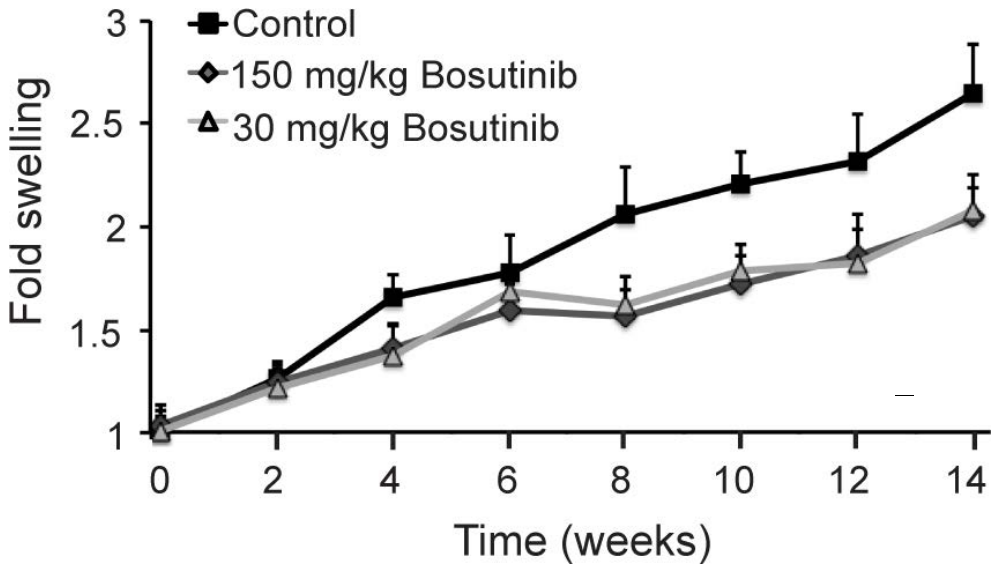


**Fig. S2. 150 mg/kg bosutinib does not improve lesion size over 30 mg/kg bosutinib.** Mice were injected with 1 X $10^6$ *L. amazonensis* promastigotes and treated with 150 mg/kg/d or 30 mg/kg/d of bosutinib (dissolved in drinking water acidified to pH 4.5) or acidified water alone, starting 4 days before infection and continuing until sacrifice. Two experiments were performed; shown is a representative experiment containing 5 mice per experimental group and 10 mice in the control. Bars represent the increase in foot size compared to the uninfected foot (normalized to 1) + standard deviations. For the last four measurements, the differences between bosutinib categories and controls are statistically significant by two-way ANOVA; however, there are no differences seen between the 150 mg/kg bosutinib and 30 mg/kg bosutinib treatment categories.

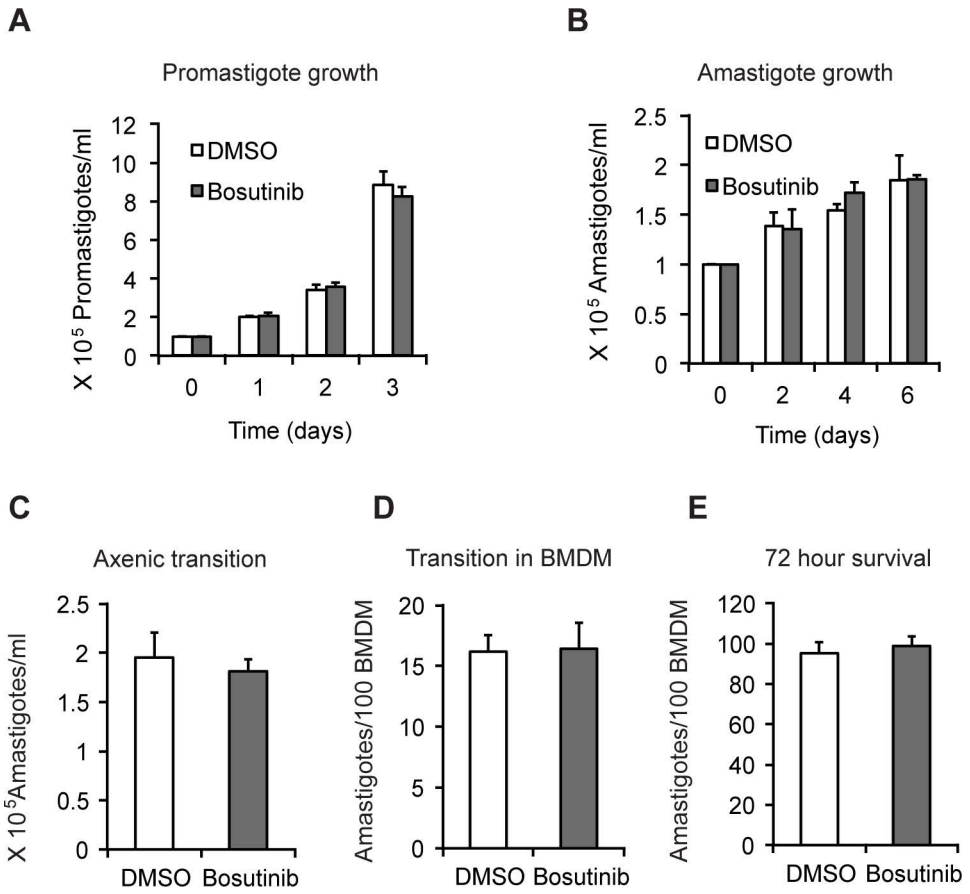


**Fig. S3. Bosutinib does not affect parasite growth, the promastigote-amastigote transition, or intracellular survival.** (A) Bosutinib has no effect on promastigote growth in culture. Shown is a representative experiment of two experiments following promastigotes per ml in triplicate in 0.1% DMSO or 10 μM bosutinib-treated media over 3 days. (B) Bosutinib has no effect on amastigote growth in culture. Shown is a representative experiment of two experiments following amastigotes per ml in triplicate in 0.1% DMSO or 10 μM bosutinib-treated media over 6 days. (C) Bosutinib has no effect on axenic promastigote to amastigote transition. In triplicate, 1 X $10^5$ promastigotes were inoculated into amastigote media containing 0.1% DMSO or 10 μM bosutinib and moved to 32°C. Amastigotes were counted after a week. Shown is a representative experiment of two experiments. (D) Bosutinib has no effect on the promastigote to amastigote transition within BMDM. In triplicate, 10 promastigotes were added per G-CSF-starved BMDM. After 4 h, the BMDM were extensively washed and 0.1% DMSO or 2 μM bosutinib was added. Shown is the average number of amastigotes per BMDM after 24 h in a representative experiment of two experiments. (E) Bosutinib has no effect on amastigote survival within BMDM. Shown is the average number of amastigotes per BMDM after 72 h in a representative experiment of two experiments performed as in (D).

**Table S1. Bosutinib treatment during *L. amazonensis* infection does not skew cytokine secretion towards a Th1 or Th2 response.** Ratios of IFNγ:IL-4, IFNγ:IL-10, IFNγ:IL-13, and IFNγ:IL-4+10+13 were calculated from the data shown in Table 1.

| **Ratio** | **DMSO – High stimulation** | **Bosutinib – High stimulation** | **DMSO – Low stimulation** | **Bosutinib – Low stimulation** |
|---|---|---|---|---|
| IFNγ:IL-4 | 12.6 | 23.0 | 4.8 | 12.6 |
| IFNγ:IL-10 | 22.4 | 12.1 | 8.4 | 14.4 |
| IFNγ:IL-13 | 22.7 | 5.5 | 7.2 | 15.1 |
| IFNγ: IL-4+10+13 | 6.0 | 2.2 | 2.1 | 4.6 |

**Table S2:** Culturing draining lymph nodes with bosutinib does not decrease cytokine secretion. Isolated draining lymph nodes from 4 infected DMSO treated mice were cultured as described as in Table 1, except that DMSO or 2 μM bosutinib was added during culture for 72 hours. Cytokine ELISAs were performed on harvested supernatants. The lone statistically significant effect of *in vitro* bosutinib treatment (via two-tailed *t*-test) is the opposite of what would be expected if bosutinib directly inhibited cytokine secretion.

| **Cytokine** | **Treatment** | **Cytokine secretion (pg)** | |
|---|---|---|---|
| | | **High stimulation** | **Low stimulation** |
| IFN-γ | DMSO | 10,274 ± 509 | 13,455 ± 3,689 |
| | Bosutinib | 14,140 ± 4,374 | 19,226 ± 5,478 |
| | p | n.s. | n.s. |
| IL-4 | DMSO | 3,300 ± 379 | 2,937 ± 344 |
| | Bosutinib | 5,467 ± 1,829 | 4,112 ± 1,188 |
| | p | n.s. | n.s. |
| IL-10 | DMSO | 1,631 ± 442 | 2,013 ± 820 |
| | Bosutinib | 2,664 ± 424 | 2,451 ± 657 |
| | p | n.s. | n.s. |
| IL-13 | DMSO | 342 ± 34.5 | 330 ± 36.6 |
| | Bosutinib | 491 ± 20.3 | 452 ± 53.2 |
| | p | 0.021 | n.s. |
| IL-17 | DMSO | 202 ± 13.5 | 205 ± 6.0 |
| | Bosutinib | 202 ± 6.0 | 210 ± 22.7 |
| | p | n.s. | n.s. |

**Table S3: Chemokine profile changes in DMSO treated, bosutinib-treated, imatinib-treated, and PP2-treated *Leishmania*-infected mice**. Shown are profiles of draining lymph nodes isolated from A) 8 DMSO versus bosutinib, B) 8 DMSO versus imatinib, and C) 8 DMSO versus PP2-treated mice as described in Table 1. Multiplex chemokine ELISAs were performed on harvested supernatants, with the exception of CXCL9, which was profiled individually. p values were determined by two-tailed *t*-tests and are listed if $p < 0.1$. IP-10 was also profiled, but all values were < 50 pg.

**A. Bosutinib**

| | | Chemokine secretion (pg) after | | |
|---|---|---|---|---|
| | Treatment | High stimulation | Low stimulation | Con A stimulation |
| MIP-1α | DMSO | 37.9 ± 21.8 | 37.0 ± 20.1 | 87.5 ± 42.1 |
| | Bosutinib | 118 ± 53.0 | 128 ± 61.4 | 137 ± 52.4 |
| | p | n.s. | n.s. | n.s. |
| MIP-1β | DMSO | 137 ± 61.0 | 105 ± 28.9 | 76.2 ± 2.62 |
| | Bosutinib | 119 ± 42.0 | 165 ± 66.2 | 106.2 ± 29.7 |
| | p | n.s. | n.s. | n.s. |
| MIP-2 | DMSO | 17.2 ± 8.98 | 16.2 ± 8.99 | 24.7 ± 14.5 |
| | Bosutinib | 26.9 ± 9.70 | 26.4 ± 9.08 | 46.9 ± 20.1 |
| | p | n.s. | n.s. | n.s. |
| RANTES | DMSO | 138 ± 55.6 | 139 ± 51.9 | 174 ± 60.5 |
| | Bosutinib | 156 ± 35.4 | 167 ± 35.2 | 181 ± 28.9 |
| | p | n.s. | n.s. | n.s. |
| CXCL9 | DMSO | 156 ± 40.0 | 237 ± 67.4 | 150 ± 48.5 |
| | Bosutinib | 104 ± 22.6 | 136 ± 27.7 | 101 ± 19.3 |
| | p | n.s. | n.s. | n.s. |

**B. Imatinib**

| | | Chemokine secretion (pg) after |
|---|---|---|

| | Treatment | High stimulation | Low stimulation | Con A stimulation |
|---|---|---|---|---|
| MIP-1α | DMSO | 143 ± 90.9 | 75.0 ± 25.8 | 287 ± 105 |
| | Imatinib | 40.8 ± 25.8 | 77.8 ± 54.5 | 63.9 ± 20.5 |
| | p | 0.089 | n.s. | 0.085 |
| MIP-1β | DMSO | 202 ± 125 | 252 ± 176 | 283 ± 97.9 |
| | Imatinib | 106 ± 29.7 | 160 ± 83.0 | 97.7 ± 14.2 |
| | p | n.s. | n.s. | 0.068 |
| MIP-2 | DMSO | 274 ± 145 | 280 ± 80.7 | 226 ± 74.6 |
| | Imatinib | 131 ± 73.6 | 143 ± 61.0 | 91.0 ± 56.9 |
| | p | n.s. | n.s. | n.s. |
| RANTES | DMSO | 453 ± 150 | 832 ± 285 | 388 ± 98.5 |
| | Imatinib | 308 ± 36.1 | 464 ± 60.7 | 314 ± 42.0 |
| | p | n.s. | n.s. | n.s. |
| CXCL9 | DMSO | 125 ± 38.5 | 127 ± 52.7 | 142 ± 51.8 |
| | Imatinib | 119 ± 25.8 | 353 ± 129 | 435 ± 214 |
| | p | n.s. | n.s. | n.s. |

**C. PP2**

| | Treatment | Chemokine secretion (pg) after | | |
|---|---|---|---|---|
| | | High stimulation | Low stimulation | Con A stimulation |
| MIP-1α | DMSO | 646 ± 140 | 670 ± 114 | 600 ± 114 |
| | PP2 | 196 ± 118 | 217 ± 131 | 297 ± 169 |
| | p | 0.037 | 0.061 | n.s. |
| MIP-1β | DMSO | 222 ± 84.0 | 353 ± 107 | 250 ± 76.9 |
| | PP2 | 165 ± 83.0 | 379 ± 167 | 228 ± 126 |
| | p | n.s. | n.s. | n.s. |
| MIP-2 | DMSO | 1295 ± 440 | 803 ± 256 | 1295 ± 437 |
| | PP2 | 56.0 ± 17.3 | 49.3 ± 14.0 | 101 ± 31.7 |
| | p | 0.026 | 0.061 | 0.027 |
| RANTES | DMSO | 392 ± 61.6 | 335 ± 57.9 | 308 ± 47.0 |
| | PP2 | 173 ± 13.4 | 190 ± 16.5 | 220 ± 34.4 |
| | p | 0.086 | 0.079 | n.s. |
| CXCL9 | DMSO | 363 ± 69.6 | 395 ± 96.7 | 313 ± 76.6 |

| | | | | |
|---|---|---|---|---|
| | PP2 | 174 ± 27.3 | 189 ± 29.6 | 154 ± 23.0 |
| | p | 0.025 | 0.061 | 0.066 |