



Figure S2. Ratios of chloroquine IC_{90} to IC_{50} values in *pfcr*-modified lines. Ratios are presented as means \pm SEM, which were calculated from an average of 7 independent assays (range 4–10) performed in duplicate. Analysis of the chloroquine (CQ) IC_{90}/IC_{50} ratios for the different lines revealed a very different set of responses between the three CQ-sensitive genetic backgrounds. In 3D7, both mutant *pfcr* clones revealed mean ratios of 2.0, the same as 7G8 and noticeably greater than the ratios of 1.3–1.4 observed with 3D7^C ($P < 0.01$) and 3D7. For D10, where mean CQ IC_{50} values were unchanged compared to D10^C (Table S1), the ratios were 1.8–2.3, a significant increase over the ratios of 1.3–1.4 again observed with D10^C ($P < 0.01$) and D10. Thus, in both these backgrounds the relatively modest increase in CQ IC_{50} values appeared to be compensated by a substantial increase in the ability of these parasites to withstand high CQ concentrations. For the GC03 mutants, where the baseline CQ IC_{50} values were already high, the increase in the IC_{90}/IC_{50} ratio was more modest (1.5 for both GC03^{G8-1} and GC03^{G8-2} vs. 1.2–1.3 for the control CQ-sensitive lines GC03^C ($P < 0.05$) and GC03), suggesting that the expression of mutant *pfcr* rendered GC03 parasites intrinsically more resistant to CQ than was the case for 3D7 or D10 parasites. Statistical comparisons comparing mutant *pfcr*-modified lines against recombinant control lines of the same genetic backgrounds were performed using one-way ANOVA with a Bonferroni post-hoc test.