

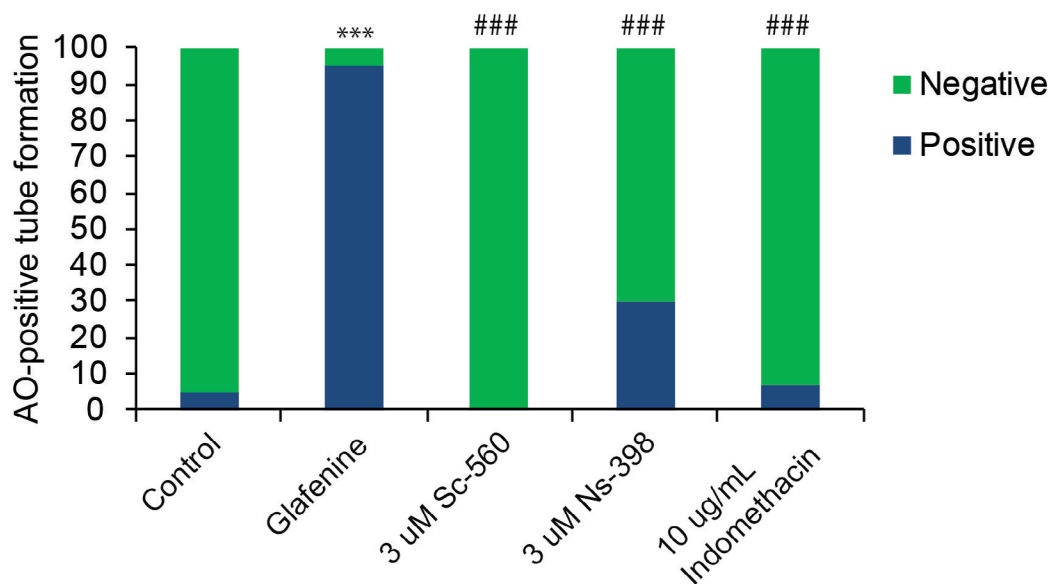
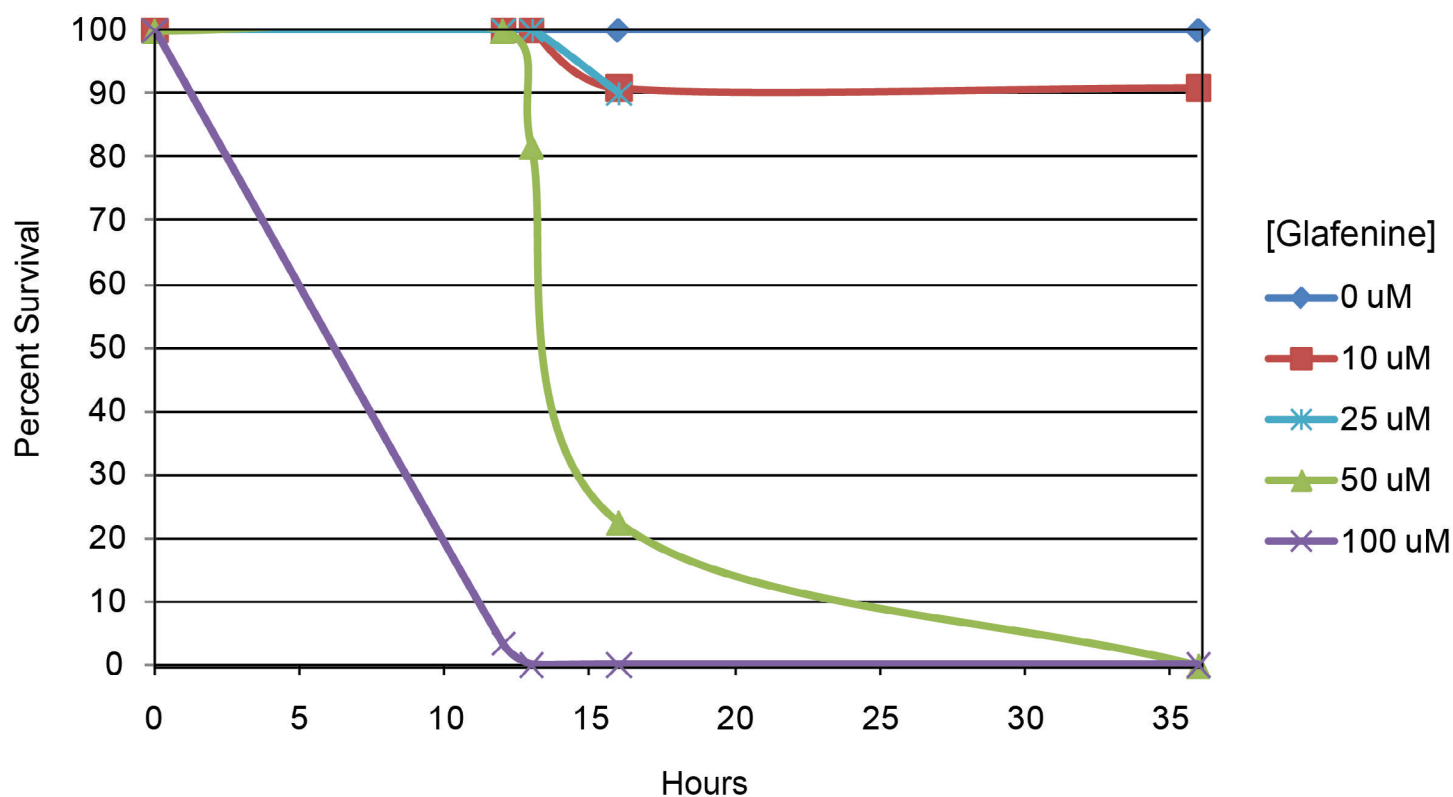
A**B**

Fig. S1. Only the NSAID glafenine induces apoptotic tubes at non-lethal dosages. (A) Studies with COX inhibitors demonstrate that the effects of glafenine are specific to the drug. *** $P < .001$ relative to control, ### $P < .001$ relative to glafenine. $n \geq 10$ per condition. (B) Dose-dependent survival studies with glafenine. Pooled results of three or more independent experiments, $n \geq 20$ for time points through 12 hours; $n \geq 10$ for longer time points.

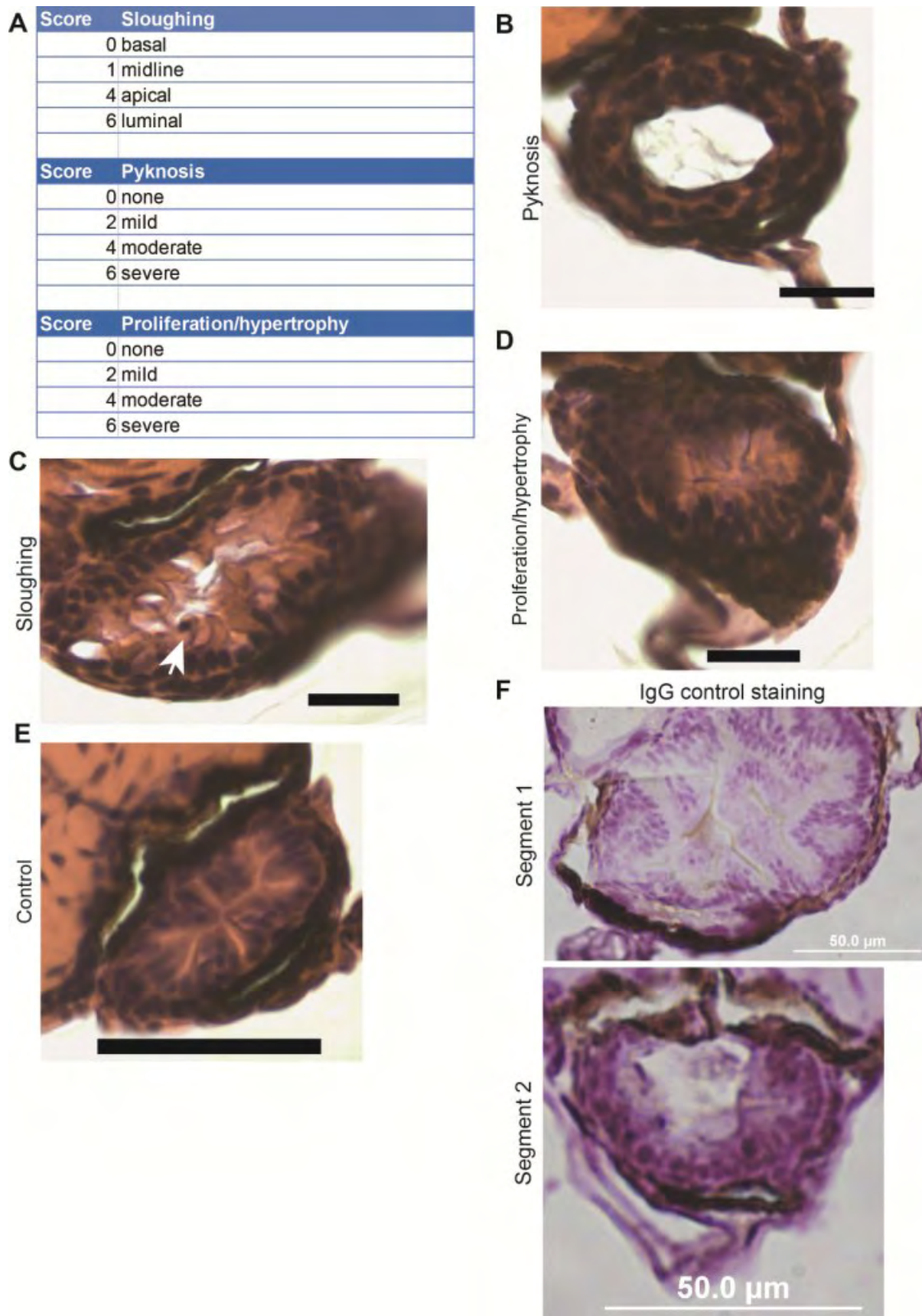


Fig. S2. Details of the segment 2 histological scoring system. (A) Histological criteria used in the intestinal damage assessment. (B-F) Scale bars: 50 μ m. (B) Example of pyknotic nuclei. Pyknosis score of 6, total score of 10. (C) Example of sloughing, arrow points to an apical nucleus. Sloughing score of 4, total score of 10. (D) Example of proliferation/hypertrophy. Proliferation score of 4, total score of 12. (E) Control fish, total score of 1. (F) IgG (rabbit) control IHC for Caspase-3 studies, which show that the Caspase-3 staining observed is enterocyte and luminal debris-specific.

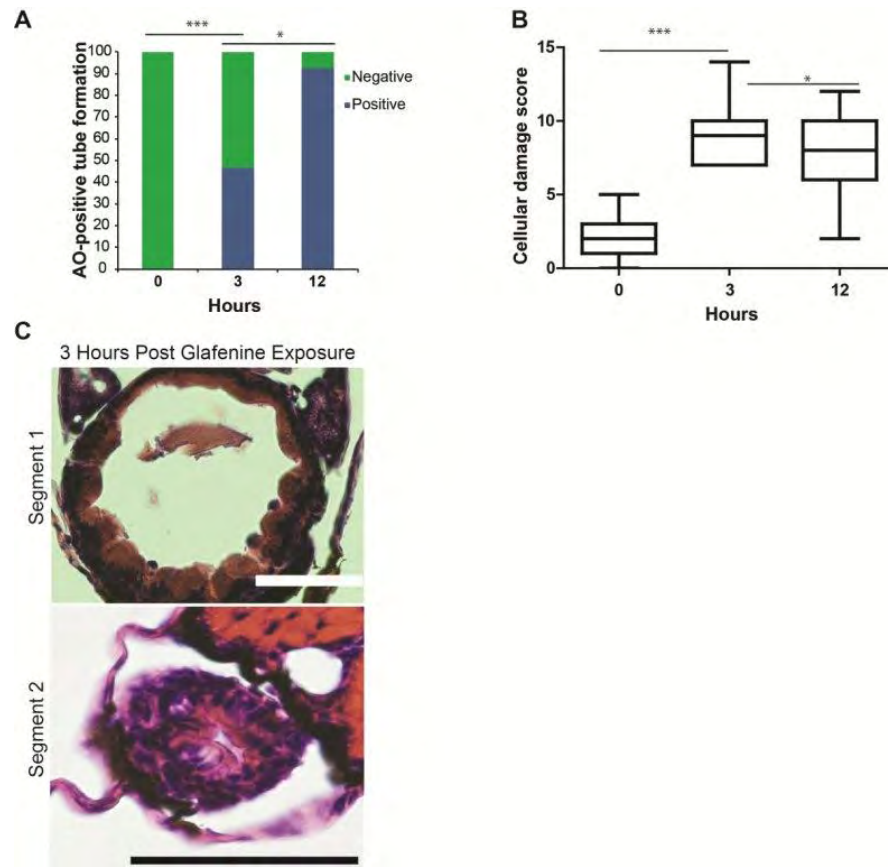


Fig. S3. Glafenine-treatment does not result in gross intestinal bleeding. Double-reporter *Tg(gata1:dsRed)^{sd2};(kdr1:EGFP)^{s843}* zebrafish track both blood cells (red channel) and vasculature (green channel). Images representative of 5 individual fish, taken after 12 hours glafenine exposure. Scale bars: 1mm. (A) The zebrafish show no gross bleeding into the intestinal lumen. (B) The zebrafish show no gross vascular defects.

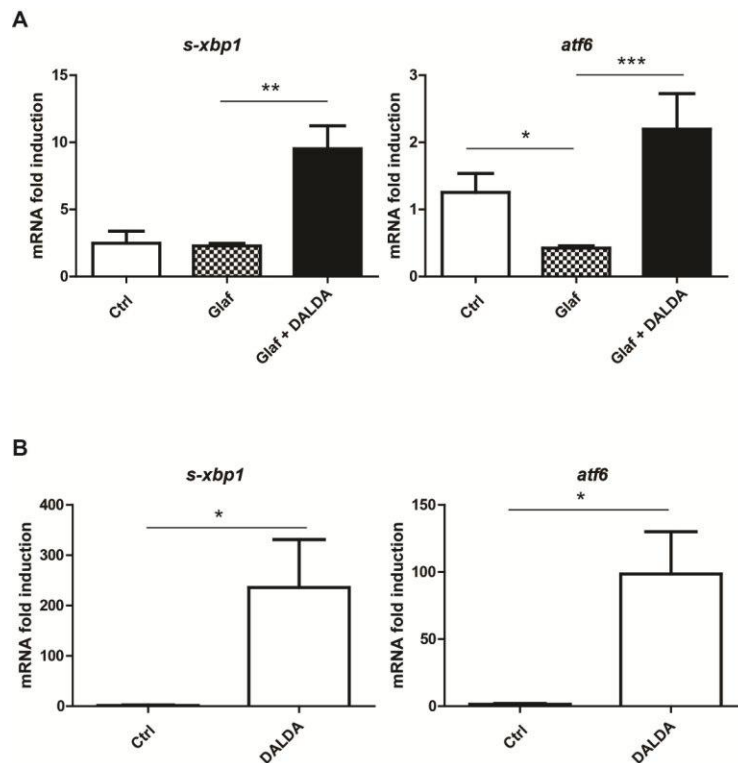


Fig. S4. UPR response genes spliced *xbp1* (*s-xbp1*), and *atf6* expression following glafenine and/or DALDA exposure. Fish were treated as indicated and RNA extracted from whole animals after 12 hours glafenine exposure. *s-xbp1* and *atf6* expression was determined using ABI Prism HT7700. Samples are from whole tissue lysates of 10 fish per sample, $n \geq 2$ per group.

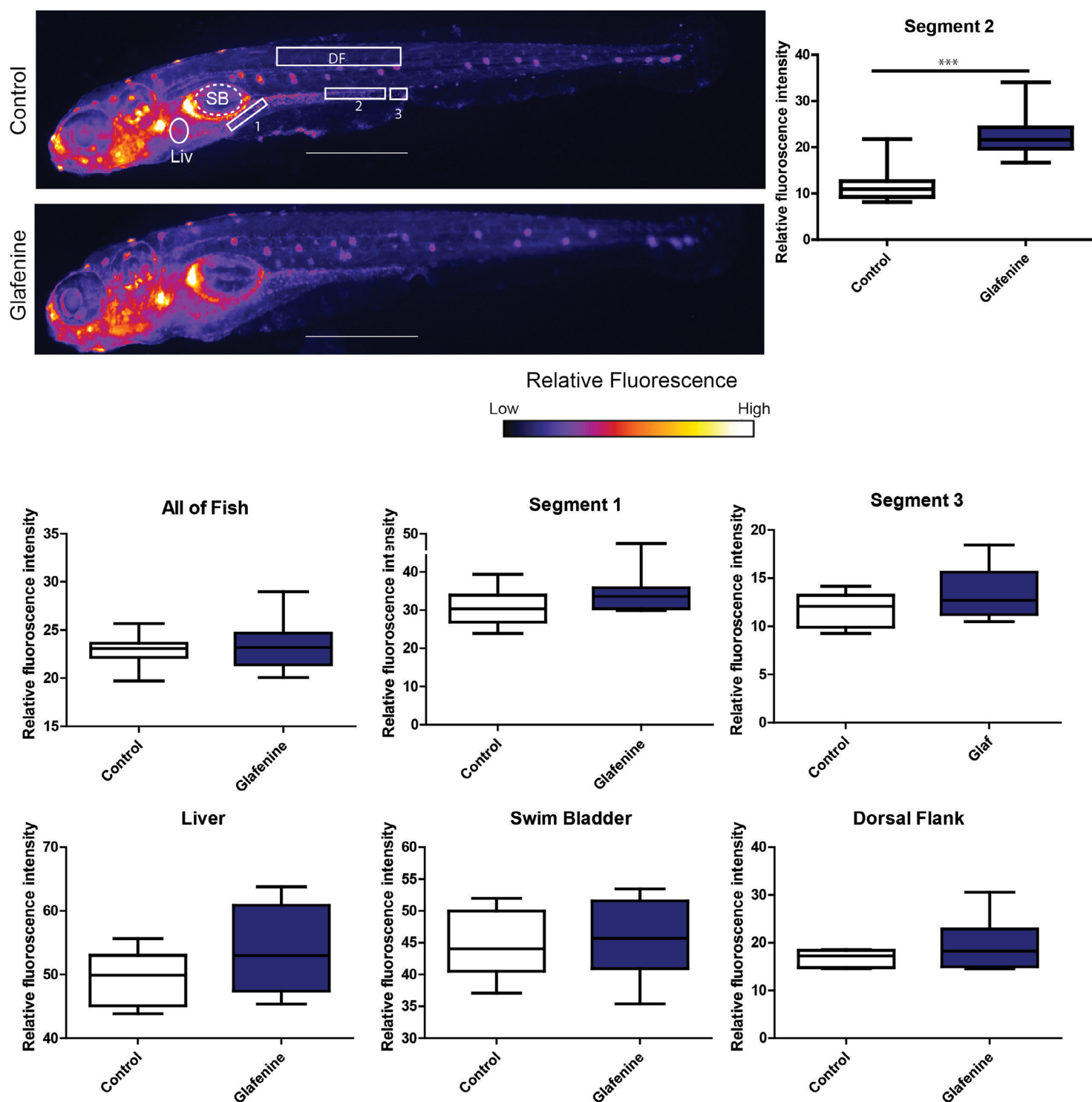


Fig. S5. *Tg(NfκB:EGFP)* fish show increased segment 2 NF-κB activation in zebrafish after injury with glafenine. *Tg(NfκB:EGFP)^{nc1}* reporter zebrafish were used to assess NF-κB activation after 12 hours of glafenine exposure. Representative of three independent experiments, *n* as portrayed. Scale bar: 1 mm. The same regions as in Fig. 7 were used, as marked on the fish. SB, swim bladder; Liv, liver; DF, dorsal fin.