Colorectal cancer is common worldwide and the second largest cancer killer in the United States. Although inherited/heritable risk has played an important role as hosts for colorectal xenografts, a simple and cost-effective xenotransplant animal cancer model is needed for more efficient drug screening. Whole-in-life xenotransplantation of human colorectal cancer Colo320 cells were microinjected into 3 dpf zebrafish (Brachydanio rerio) via microinjection and cancer cell proliferation, metastasis, and formed tumor masses in zebrafish. We then successfully developed a quantitative microplate-based whole xenotransplant zebrafish chemoluminescence ELISA using an anti-human Survivin monoclonal antibody which did not cross react with zebrafish tissues. The chemiluminescence ELISA was highly sensitive and enabled detection of signal from as few as 10 human colon cancer Colo320 cells in vitro. After xenotransplant, zebrafish were treated with 5 FDA-approved anti-colorectal cancer drugs (5-Fluorouracil, Oxaliplatin, Camptothecin, Leucovorin, and Camptothecin) or a drug combination (Leucovorin + 5-Fluorouracil), respectively, by soaking. Effects on human colorectal cancer cell proliferation in zebrafish were assessed 3 days after drug treatment using the chemiluminescence ELISA. Drug concentration-dependant drug cell inhibition was observed after treatment with 5-Fluorouracil (2% - 60% inhibition), Oxaliplatin (3% - 65% inhibition), 5-Fluorouracil (14% - 39% inhibition), and Leucovorin + 5-Fluorouracil (23% - 48% inhibition) from treatment with 1000 µM 5-Fluorouracil, 1000 µM Oxaliplatin, and 250 - 1000 µM 5-Fluorouracil, respectively. The chemiluminescence ELISA based on transplanted human colon cancer Colo320 cells xenotransplanted into zebrafish and treated with 5 FDA approved colorectal cancer drugs was a highly specific and sensitive high throughput method for drug screening.

Conclusion
Zebrafish xenotransplant model combined with our whole animal microplate-based chemoluminescence ELISA is a reproducible and predictive animal model for drug screening.