

COUPLED VISUALIZATION AND ABLATION OF SPECIFIC CELLS AND TISSUES IN ZEBRAFISH

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Background: Zebrafish is a standard model system in the field developmental biology and is particularly useful due to its extensive regenerative capabilities. The system has been used to study development by removal of cells by physical surgery and laser-mediated ablation; however these are labor intensive, time consuming, and not as reproducible as a genetic approach. Therefore these methods are limited during genetic or pharmacological screens when analysis of a large number of samples is required. Previous attempts at genetic ablation systems were unsuccessful to do ‘leaky’ promoters causing aberrant toxin production, as well as weak expression in the absence of an inducer, driving the need for an effective targeted conditional cell ablation technique.

Technology Description: Researchers at Washington University have developed a targeted conditional cell ablation system by combining the expression of bacterial Nitroreductase (NTR) enzyme in a tissue specific manner, with treatment with the prodrug Metronidazole (Mtz), which is converted to a cytotoxic DNA crosslinking agent by the enzymatic activity of NTR. The combination of the tissue specific promoter driving NTR expression, as well as Mtz treatment, allows for high specificity and temporally and spatially controlled cell ablation. The researchers have shown that Mtz can be efficiently washed out of the system, with the affected tissue able to quickly recover and regenerate. The NTR/Mtz system described is therefore spatially controllable and strictly confined to the target cell population, temporally inducible, germline transmissible, and reversible.