An oral-gavage dosing method for zebrafish

When reviewers label a grant as a 'fishing expedition', it typically spells doom for a promising project; but a new school of researchers is turning the tables on this phrase and reimagining what it means to search for promising disease treatments.

Dr. Leonard Zon at Boston Children's Hospital is one such researcher, and a walk through his vivarium reveals not cages with mice and rats, but rows and rows of tanks filled with the small cyprinid *Danio rerio*, commonly known as zebrafish. His lab is interested in hematopoiesis, or the development of blood cells, and how these cells become cancerous in disease states like leukemia and lymphoma. His group has turned to zebrafish as a model organism, taking advantage of several technical benefits this species has to offer.

Their small size, rapid development times, and amenability to genetic manipulation make them an attractive model for large-scale *in vivo* studies. Likewise,

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zebrafish embryos, which grow outside their mother in the water, are transparent, allowing the research group to use advanced microscopy to image red blood cell development and differentiation in the intact organism.

Like all model organisms, zebrafish do have their limitations. The Zon laboratory also studies melanoma—a disease that typically befalls adults—and his group screens small-molecules for their potential anti-tumor activity. Applying these agents to adult zebrafish is difficult; dissolving them in water or mixing them in fish food does not provide a practical and rigorous approach to dosing. To overcome the hurdles of drug testing in adult zebrafish, the Zon lab developed a unique anesthesia regime and an oral-gavage technique for repeated dosing and longitudinal studies on melanoma progression (*Dis. Model Mech.* **9**, 811–820; 2016).

As a proof of principle, the group tested multi-day dosing of Vemurafenib, an FDA-approved $BRAF^{V600E}$ inhibitor, in adult zebrafish with $BRAF^{V600E}$ melanoma tumors. The fish tolerated multiple bouts of anesthesia and gavage well, and tumors declined significantly in treated groups. Based on these results, the technique is an effective drug delivery system; just as important, the method can be adopted by most labs, potentially increasing the popularity and use of adult zebrafish for drug screening and toxicity studies. Basic technical developments like these, when combined with the inherent advantages of zebrafish, ensure that research with this model will continue to go swimmingly.

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DYNAMIC GRAPHS FOR CLEAR REPORTING

Scientific publishing has undergone dramatic changes in recent decades; from print to online, and pay-walls to open access. Despite these changes, one aspect of the scientific article has yet to budge; the static graph.

Graphs and figures are the backbone of every research paper, and often provide a sanity check for discussion sections, where authors might wish to indulge in 'over interpretation' of their findings. "I think the figures are the most important part of the paper, because the abstract and body of the paper can be manipulated and shaped to tell a compelling story," says Jeremy Borniger in a recent *Science Magazine* editorial (http://www.sciencemag.org/careers/2016/03/how-seriously-read-scientific-paper).

But graphs and figures can also be misleading and unclear. More often than not, summary statistics, rather than raw data, are presented in graphs, with the details left to the whims of authors and editors. Summarizing data with means (as opposed to medians) and representing variability with standard errors (rather than confidence intervals) can influence how readers perceive the results and validity of a study. Clarity of a figure can also affect its impact. Experiments are rarely straightforward, often involving multiple groups and conditions over several sampling points, and capturing all of the important aspects of the data in one graph can be difficult for even the most seasoned of scientists.

Breaking free from the traditional static figure, a group led by Tracey L. Weissgerber at Mayo Clinic (Rochester, MN) developed an online graphical tool that allows authors to build interactive graphs for readers to explore their data (*PLoS Biol.* **14**, e1002484; 2016). Using the group's free web-based tool, authors can upload their data sets and create dynamic graphs that can be used in publications and changed (by the readers) to present different summary statistics and selectively display subsets of the data.

Although the tool developed by Weissgerber *et al.* has its potential uses, it might be too early to say it signals a shift from static to interactive scientific publishing. There are several limitations to the tool (only small data sets can be used), and it's possible that interactive graphs could simply add more confusion to a paper. Particularly in the biological sciences, towards which this tool is aimed, data is often messy and researchers can spend a good amount of time sorting, analyzing and displaying their data in order to rescue the signal from the noise. Will interactive graphs add value, or more chaos?

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