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URLs
Stemple laboratory web site:
http://www.sanger.ac.uk/Teams/Team31
The art and design of genetic screens:
http://www.nature.com/nrg/series/screens/index.html
Zimmerman laboratory web site:
http://www.nimr.mrc.ac.uk/devbiol/zimmerman

MODEL ORGANISMS

Xenopus tropicalis goes genetic

Its well-characterized embryology, fate map and the ability to use gain-of-function methods have contributed to establishing *Xenopus laevis* as a classic model for developmental biologists. To their frustration, however, the ability to 'do genetics' in this species has been conspicuous by its absence. A recent report from the laboratories of Derek Stemple and Lyle Zimmerman has now demonstrated the feasibility of both forward and reverse genetic screens for chemically induced mutations in *Xenopus tropicalis,* a diploid cousin of *X. laevis*. The report not only establishes the frog as a genetic system but also shows that it can be used to uncover novel gene functions.

Although many early classic embryology studies were done using *X. laevis*, it was deemed unsuitable for genetic analysis because of its unwieldy genome structure and long generation time. Free from these problems, *X. tropicalis* was slated to become the genetic amphibian model.

In preparation for forward genetic screens, the authors chemically mutagenized mature frog sperm *in vitro*, which was then used to create the F1 generation. The authors used gynogenesis — a technique that can be used in lower vertebrates to create diploid progeny derived entirely from the maternal genome — to create an F2 generation that they could screen for visible recessive phenotypes. The authors recovered 77 candidate mutations, which were grouped into 10 classes on the basis of their phenotypes. Whereas many represented familiar embryonic phenotypes some, such as *cid vicious*, which has defects in neural crest migration and eye formation, are likely to reveal new gene functions.

Next, the authors tested a reverse genetic approach — TILLING. In this approach, selected genomic fragments are amplified and, in this screen, directly sequenced to identify mutation carriers from a pool of mutagenized animals. As well as being able to confirm several nonsense mutations, the authors were able to estimate that the mutation rate for a 10 mM ENU-treated *X. tropicalis* population is about double that observed in comparable rat and zebrafish screens.

The identified mutants await further phenotypic and molecular characterization. The undisputed value of this study is the demonstration that forward and reverse genetic screens can be successfully performed in *X. tropicalis*, which given its established embryological, molecular and genomic tools is set to become an important genetic model.

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FURTHER READING Stemple, D. L. TILLING — a high-throughput harvest for functional genomics. *Nature Rev. Genet.* **5**, 145–150 (2004)
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Image courtesy of Richard Gibbons, The Sanger Institute.