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### Better cloning for zebrafish

Zebrafish are popular models for studies of genetics, development and diseases such as cancer and cardiovascular disorders. To increase their utility in biomedical research, scientists have worked to develop methods of gene manipulation in zebrafish. Previous attempts have had limited success, but Jose Cibelli and colleagues (Michigan State University, East Lansing) have now refined a technique based on somatic cell nuclear transfer.

In the basic technique, DNA is removed from a zebrafish egg and replaced with DNA from a donor. The modified egg is then induced to divide in hopes that it will produce an adult that is genetically identical to the donor.

Cibelli's group introduced several important refinements that allowed the researchers to successfully produce adult fish that expressed the donor DNA and passed it on to their offspring (*Nat. Methods* published online 30 August 2009; doi:10.1038/nmeth1369). First, they used mature eggs and maintained them in an inactive state in Chinook salmon ovarian fluid. Second, they used a laser to ablate the recipient DNA, leaving the cytoplasm intact, and delivered the donor DNA through the micropyle, the same route of entry used by fish sperm. The researchers believe that this procedure could make zebrafish a more useful model for developmental and disease studies.

### Prion prediction fulfilled

For the first time, scientists have experimentally shown that a disease-associated prion protein mutation can generate a unique infectious agent that can transmit this disease to a normal animal (*Neuron* **63**, 438–450; 2009). These results support a central aspect of the prion hypothesis—that prion protein mutations can spontaneously generate infectivity.

Prion diseases are a diverse group of infective neurodegenerative diseases that affect animals and humans (e.g., Creutzfeldt-Jakob disease), progressively destroy brain tissue and ultimately kill those infected. Prions, which are thought to cause these diseases, primarily consist of misfolded prion proteins that are coded by the infected animal or person.

In this study, Susan Lindquist of the Whitehead Institute for Biomedical Research (Cambridge, MA) and her team replaced the endogenous prion protein gene in healthy mice with a gene that carries the mouse equivalent of a human mutation associated with fatal familial insomnia (FFI), an inherited prion disease.

Mice with the FFI mutation showed abnormalities that were very similar to those of people with FFI. And when the researchers injected brain tissue from the FFI mice into normal mice that expressed physiological amounts of prion proteins, the normal mice showed the unique FFI pathology. The researchers hope these mice will help to uncover the mechanism of action of FFI.

### Preventing unnecessary animal testing

On 10 August, in an effort to prevent unnecessary animal testing, the European Chemicals Agency (ECHA) made its first public call for data on the reproductive toxicity of a new chemical substance that has been registered, as required by Europe's REACH legislation.

REACH (Registration, Evaluation and Authorisation of Chemicals) requires that by 2018, companies register and submit toxicity data on all chemicals sold in quantities greater than one ton in the European Union. If there is not enough toxicity data available on a particular substance, then the manufacturer or importer of the substance must submit a testing proposal to ECHA, the agency responsible for administering the REACH system.

REACH also requires that vertebrate animal testing of the toxicity of new substances be carried out only as a last resort when ECHA officials cannot sufficiently assess the potential harmful effects of a substance on humans. The company that registered this particular compound had proposed two animal experiments on the reproductive toxicity of this substance. When determining whether proposed tests must be carried out, ECHA will take any reproductive toxicity data submitted about this chemical into account. The agency plans to make many more such public calls on new substances in the coming years.