PublisherInfo		
PublisherName	:	BioMed Central
PublisherLocation	:	London
PublisherImprintName	:	BioMed Central

Fish genes work in human cells

ArticleInfo		
ArticleID	:	5013
ArticleDOI	:	10.1186/gb-spotlight-20041027-01
ArticleCitationID	:	spotlight-20041027-01
ArticleSequenceNumber	:	76
ArticleCategory	:	Research news
ArticleFirstPage	:	1
ArticleLastPage	:	3
ArticleHistory	:	RegistrationDate : 2004–10–27 OnlineDate : 2004–10–27
ArticleCopyright	:	BioMed Central Ltd2004
ArticleGrants	:	
ArticleContext	:	130595511

Cathy Holding
Email: cathy.holding@absw.org.uk

Researchers based in the United States have discovered significant differences in the regulation of gene splicing between mammals and fish. Their findings, reported in Proceedings of the National Academy of Sciences this week, could help scientists develop transgenic techniques using pufferfish DNA sequences in mouse and human cells (*Proc Natl Acad Sci USA* 2004, **101:**15700-15705).

The genome of the pufferfish - or Fugu - contains all the alternative promoters and splice exons and introns that are present in mammalian genomes, but because the introns are so much smaller, genes are about an eighth the size, said lead author Christopher B. Burge, at Massachusetts Institute of Technology (MIT).

This makes the Fugu genome a potentially powerful tool for functional gene analysis, Burge said, but scientists have until now been frustrated in their attempts to use the resource because mammalian cells do not correctly splice the fish genes.

Burge's team developed a variant of a previously devised method for predicting splicing enhancer sequences. The new technique - dubbed RESCUE-ISE - predicts intronic splicing enhancers (ISEs), and by comparing human, mouse, zebrafish, and Fugu genomes, Burge's group discovered that this class of splicing regulatory element appears to differ substantially between mammals and fish.

Burge told *The Scientist* that "89 to 96% of all the hexamers that we predicted as ISEs in mammals fall into one of two clusters - they're either G-rich or C-rich. But when we applied the same method to Fugu introns, we just got a completely different spectrum of motifs."

Burge proposes that by applying a scoring method to individual intron sequences, Fugu genes can be tested for problem motifs and modified for transgenic experiments in mice - a method he has successfully piloted. "You have to do a bit of extra cloning or site-directed mutagenesis," he said. "But these Fugu genes would be much easier to manipulate and that much more genetically tractable."

"I think the paper's of interest in terms of understanding the potential of regulation and some of the details of the mechanisms of splicing," said James L. Manley, at Columbia University, NY. "With this kind of really rigorous genomic analysis, I think these sequences will stand up and really be important elements."

However, Manley said he thought the paper had not addressed the issue of negative splice regulators. "I think some elements they refer to as enhancer elements might turn out to be negative or silencer elements," he said.

"The difference between fish and mammals is intriguing. It seems to give us some insight into how splicing is done and what the rules are, what is allowed and what is not," said Tomaso Poggio, professor in the Department of Brain and Cognitive Sciences, also at MIT. According to Poggio, although the fish genome is much simpler, the greater diversity of regulatory sequences might point to greater complexity at another level.

"Splicing is an important part of increasing diversity, and the estimates of genes with alternative splicing keep going up," added Manley. "Splicing is becoming of more and more interest as the number of genes in the human genome seems to keep going down."

References

1. Choi C: Lots of splicing regulators *Genome Biology*, October 19, 2004., [http://genomebiology.com/researchnews/default.asp?arx_id=gb-spotlight-20041019-01]

2. *Proceedings of the National Academy of Sciences USA*, [http://www.pnas.org]

3. Schultz LB: For export and decay, splicing helps along the way *The Scientist*, January 19, 2004., [http://www.the-scientist.com/yr2004/jan/hot_040119.html]

4. Christopher B. Burge, [http://genes.mit.edu/burgelab/]

5. Predictive identification of exonic splicing enhancers in human genes

6. James L. Manley, [http://www.columbia.edu/cu/biology/faculty/manley/]

7. Tomaso Poggio, [http://cbcl.mit.edu/cbcl/web-pis/poggio/]