IN BRIEF

RNA WORLD

New snRNA gene-like transcriptional units as sources of regulatory transcripts.

Pagano, A. *et al. PLoS Genet.* 20 November 2006 (doi:10.1371/journal.pgen.0030001.eor)

To search for novel non-coding RNAs, the authors scanned the genome for the consensus sequences of promoters that RNA polymerase III transcribes from. The 31 putative transcripts that they identified had homology to protein-coding transcripts that are transcribed by RNA polymerase II, and are often located at a different locus and in an antisense orientation. They found that one such transcript, 21A, negatively regulates expression of the CENPF protein. The authors therefore propose a *trans*-acting system of antisense regulation through inhibition of mRNA maturation or translation.

GENE EXPRESSION

Transcriptional regulation by competing transcription factor modules.

Hermsen, R., Tans, S. & Wolde, P. R. *PLoS Comput. Biol.* **2**, e164 (2006)

Transcription factors bind to *cis*-regulatory regions in response to various signals. To understand the complex architecture of these *cis* regions that results from such multiple inputs, the authors created a computer model of transcriptional regulation that was allowed to evolve by mutation. The resulting *cis*-regulatory regions have tandem and often overlapping binding sites, to which transcription factors bind both cooperatively and competitively, enabling the efficient integration of signals.

TECHNOLOGY

P[acman]: a BAC transgenic platform for targeted insertion of large DNA fragments in *Drosophila melanogaster*.

Venken, K. J., He, Y., Hoskins, R. A, & Bellen, H. J. *Science* 30 November 2006 (doi:10.1126/science.1134426)

The integration of large DNA fragments into the *Drosophila melanogaster* genome is technically challenging, but this study describes a method that overcomes this by combining three technologies. Recombineering allows the retrieval of DNA fragments that are larger than 100 kb and their subsequent site-directed mutagenesis in conditionally amplifiable BACs. Insertion of these large BAC-carried transgenes can then be driven by the bacteriophage ϕC31 integrase, which guarantees integration at specific sites in the genome.

CANCER GENOMICS

Novel patterns of genome rearrangement and their association with survival in breast cancer.

Hicks, J. *et al. Genome Res.* **16**,1465–1479 (2006)

The authors screened diploid breast tumours with a representational oligonucleotide microarray analysis (ROMA), which can detect genomic amplifications and deletions at high resolution. This technique uses a representation that is much less complex than the whole human genome, but still allows the identification of several patterns of variation in genomic copy number. Among these, the 'firestorm' signature, which is characterized by multiple amplifications that are limited to single chromosome arms, was predictive of aggressive disease and poor survival.

DNA REPAIR

Dedicated protection for the female germ line

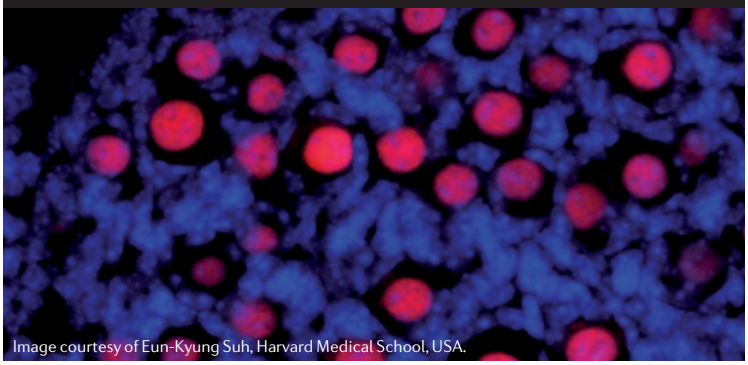

Image courtesy of Eun-Kyung Suh, Harvard Medical School, USA.

In mammals, meiosis in the female germ line has a well-documented but peculiar feature — oocytes enter meiosis during fetal development, but arrest in meiosis I until ovulation. In humans, this arrest can last decades! New work by Frank McKeon and colleagues shows that an isoform of p63 is highly expressed in these arrested oocytes, and that it functions exclusively in the female germ line to eliminate oocytes with DNA damage.

Since the discovery of p63 and p73, two genes that are related to the p53 tumour suppressor, researchers have been interested in how the functions of these three related genes might fit together. To investigate this problem, the authors made antibodies to a specific, so far unstudied isoform of p63 — TAp63. They found TAp63 protein was expressed specifically in mouse oocytes during the meiotic arrest. TAp63 is not required for oogenesis *per se*, which proceeds normally in p63 null mice. But the authors show that radiation-induced DNA damage brings about TAp63 phosphorylation and its binding to p53 DNA sites. By showing that the response of p53-deficient mice to radiation — the extent of oocyte loss — is similar to that of the wild type, the authors resolved previous controversy regarding the involvement of p53 in the germ line.

To show that TAp63 is specifically required for DNA-damage-induced oocyte death, the authors generated mice that lacked TA-isoform-specific exons in the p63 open reading frame. When irradiated, these mice are resistant to doses that kill almost all oocytes in wild type and p53-null mice.

Next, McKeon and colleagues used a range of radiation doses and antibodies against a phospho-epitope on histone H2AX to mark the sites of double-strand break repair. This showed that, as is the case for p53 in somatic cells, the threshold of cell-death response by p63 in oocytes might be determined by one or a few DNA breaks. They also saw a relationship between the amount of TAp63 phosphorylation and the amount of oocyte death in response to DNA damage. Moreover, the higher the radiation dose, the faster the TAp63 phosphorylation and oocyte death, indicating "…a temporal link between the onset of DNA-damage-dependent TAp63 phosphorylation and the death of oocytes."

As well as providing important information about how DNA is protected from damage in the mammalian female germ line, the authors offer interesting thoughts on the phylogenetic relationship between p53, p63 and p73. Their phylogenetic analysis suggests that, of the three vertebrate genes, p63 is the most closely related to the p53 homologue from the fly and worm, and that TAp63 is the primordial member of the p53 family — p53 might only have arisen during vertebrate evolution of tumour suppression.

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ORIGINAL RESEARCH PAPER Suh, E.-K., Yang, A., Kettenbach, A. *et al.* p63 protects the female germline during meiotic arrest. *Nature* 22 November 2006 (doi:10.1038/nature05337)