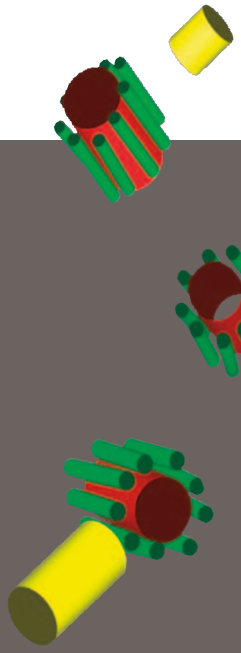

in diameter during PNM, and single microtubules started to assemble around the central tube at hook-like appendages during PNR.

So, which centriole proteins are required for which step in the assembly process? No daughter centriole structures were detected in *sas-5* and *sas-6* (RNA interference) embryos, but formation and elongation of the central centriole tube still occurred in *sas-4* (RNAi) embryos, although no single microtubules were observed. This implies that SAS-4 is needed to assemble or maintain single microtubules on the central tube, which is consistent with the previously reported ring-like distribution of SAS-4 around the central tube. By contrast, SAS-5 and SAS-6 are required for tube formation and elongation, and SPD-2 and ZYG-1 function further upstream as possible triggers for duplication or direct drivers of the assembly process, as the recruitment of the SAS proteins was blocked in their absence.

As several of the known *C. elegans* centriole proteins have mammalian homologues, aspects of the centriole-assembly process are likely to be conserved.

Arianne Heinrichs

ORIGINAL RESEARCH PAPER Pelletier, L. *et al.* Centriole assembly in *Caenorhabditis elegans*. *Nature* **444**, 619–623 (2006)

mouse oocytes during the meiotic arrest. TAp63 is not required for oogenesis *per se*, which proceeds normally in *p63*-null mice. But the authors showed 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 germline.

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 observed 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 germline, the authors offer interesting thoughts on the phylogenetic relationship between p53, p63 and p73. Their phylogenetic analysis indicates 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.

Magdalena Skipper, Chief Editor,
Nature Reviews Genetics

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

CANCER

A rapid-response stress switch

The protein p53 exerts a pivotal role in controlling the cell cycle, apoptosis and DNA repair in response to various forms of genotoxic stress. The rapid activation of p53 following genotoxic stress is ensured through complex regulation that occurs mainly at the post-translational level. Huang and colleagues now add an extra factor to the regulation of p53 by showing that the lysine methyltransferase SMYD2 methylates p53.

The authors first showed that SMYD2 monomethylates p53 at residue K370 *in vitro* and *in vivo*. But what is the significance of this modification for p53 function? SMYD2 negatively regulates the expression of p53-responsive genes (such as *p21* and *Mdm2*) in a p53-dependent manner, and it does so by downregulating the transcriptional activity of p53. Increased amounts of SMYD2 resulted in reduced p53 binding to the *p21* promoter, and decreased levels of promoter-associated p53 correlated with decreasing amounts of *p21* mRNA and protein. This indicated that SMYD2-mediated K370 modification reduces the DNA-binding efficiency of p53.

Huang and co-workers also investigated a possible crosstalk between the previously identified SET9-mediated p53-activating K372 modification and the p53-repressing K370 modification. Intriguingly, K372 methylation inhibits K370 methylation *in vitro* and *in vivo*. On the basis of these data, the authors proposed that "there is an equilibrium between promoter-bound and free p53." SMYD2-mediated K370 methylation results in the dissociation of p53 from DNA, whereas SET9-mediated K372 methylation promotes the association of p53 with promoters by blocking SMYD2-mediated methylation.

What does all of this have to do with the p53 response to genotoxic stresses? The authors propose that this mechanism could provide a rapid response to DNA damage. In physiological conditions, SMYD2-mediated methylation of K370 holds p53 in an inactive state. However, following DNA damage the SET9-mediated K372 modification inhibits SMYD2-mediated methylation and promotes binding of p53 to promoters of genes that control cell-cycle arrest and apoptosis. Whether SMYD2 might function as an oncoprotein that methylates p53 and represses its tumour-suppressive function remains to be seen.

Ekat Kritikou

ORIGINAL RESEARCH PAPER Huang, J. *et al.* Repression of p53 activity by Smyd2-mediated methylation. *Nature* **444**, 629–632 (2006)

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