IN THE NEWS

Gene doping: a new threat for the Olympics?

Forget the next generation of steroids or growth hormones and imagine the following headline from the Beijing 2008 Olympics: "Top Molvanian athlete misses a gene doping test." (See Cilauro, S. *et al*. *Molvania: A Land Untouched by Modern Dentistry* (Jetlag Travel Guide S., 2004).)

The story that this might be possible broke following the announcement from the University of Pennsylvania that inserting *IGF-1* into rat muscles improved their muscle performance. Even if possible in humans, who would want to receive such a genetic boost? According to Lee Sweeney, who has been inundated with calls ever since he published this work, there might be many: "…anyone who doubts that athletes would alter their genes to win gold need only speak with him" (*PRWeb*).

And there are other hints of how muscles could be strengthened. For example, the *New England Journal of Medicine* reported on the mutation that explains the extraordinary strength of a child: "…by the time he was 4, he could lift almost seven pounds with each hand" (*The Globe and Mail*).

The World Anti-Doping Agency (WADA) is worried, especially that gene doping will be difficult to detect. "WADA is researching and developing new genetic approaches, such as imaging and molecular methods, to detect evidence of genetic enhancement, but even these might not be enough" (*PRWeb*).

Whereas some think that gene doping raises important ethical issues (see *Nature Reviews Genetics'* ethics watch in July 2003 by Thomas Murray from The Hastings Center), others such as Julian Savulescu from Oxford University think otherwise: "Genetic enhancement is not against the spirit of sport, it is the spirit of sport" (*Australian Broadcasting Corporation*).

Magdalena Skipper

EPIGENETICS

Silent transmission

In mammals, DNA and histone methylation together provide an effective, long-term mechanism for silencing gene expression, but how specific methylation patterns are 'remembered' during cell division is unclear. In a recent paper, Sarraf and Stancheva showed that this depends on the coupling of the two types of methylation during DNA replication.

At sites of constitutive heterochromatin and transcriptionally silenced promoters, silencing is mediated by methylation of DNA at CpG dinucleotides and of histone H3 at lysine 9 (H3-K9). During DNA replication, the methyltransferase DNMT1 interacts with the replication machinery to ensure that DNA methylation patterns are faithfully copied. By contrast, little is known about how histone methylation is reproduced. One model proposes that this is somehow coordinated with DNA methylation, but evidence has so far been lacking.

By co-immunoprecipitation, Sarraf and Stancheva showed that MBD1 — a protein that specifically binds methyl-CpG groups — associates with a complex that contains an H3-K9-specific methyltransferase activity, providing a possible link between DNA and histone methylation. The other components of the complex were identified as the H3-K9-specific methyltransferase SETDB1 and CAF1, a protein involved in chromatin assembly. So, MBD1 bound to methylated DNA could recruit SETDB1 and, through its interaction with CAF1, promote H3-K9 methylation at specific sites during chromatin assembly.

Consistent with this, the three proteins were shown to form a complex *in vivo* specifically during DNA replication. The authors also showed how DNA replication is coupled to the activation of the CAF1–MBD1–SETB1 complex. CAF1 is only transiently associated with MBD1 and SETDB1 during S-phase and this depends on MBD1 being displaced from DNA. Specific inhibition of replication elongation showed that this displacement depends on the progression of the replication complex. This seems to knock MDB1 off the DNA strand, allowing it to bind CAF1 and promote

RNA SILENCING

Small RNAs take the tube

A new study published in *Plant Cell* reveals that, rather than being limited to the cells that produce them, small RNAs in plants can hitch a ride in the phloem to exert their effects on gene expression over long distances.

In plants, mRNAs are transported between tissues in the network of phloem tubes that carry sap. In addition, the antiviral effects of RNA interference (RNAi) can spread over long distances from the site of infection, indicating that the small interfering RNAs (siRNAs) that block viral gene expression might be transported in a similar way.

To find out whether small RNAs are carried in the phloem, Lucas and colleagues analysed sap from several plant species and identified a population of small RNAs of 18–25 nucleotides, corresponding to the sizes of known small regulatory RNAs. Comparing the sequences of these RNAs with plant databases revealed a range of potential targets, indicating that both siRNAs and microRNAs (miRNAs) that are involved in regulating plant gene expression are carried in the phloem.

To prove that small RNAs can move from their site of expression into the phloem — and are not just expressed in phloem cells — Lucas and colleagues expressed a viral coat protein transgene (*CP*) in the leaves of a species of squash. A corresponding siRNA was detected in the phloem sap from these plants, but not from a silencing-defective strain that expressed the same transgene. To confirm that small RNAs in phloem are genuine sap components, and not contaminants from surrounding tissues, the authors carried out heterografting experiments. They expressed the *CP* transgene in one plant (the stock) and grafted on part of another plant that did not express the transgene (the scion). Identifying *CP* siRNA in the sap of the scion confirmed that this molecule must have been transported in the phloem from the stock plant.

The authors also confirmed that RNAi signalling triggered by viral infection, rather than artificial expression of a viral transgene, can be transmitted in the phloem sap.

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