MICROBIOLOGY

Showering with bacteria

Singing in the shower may never feel the same again, if one dwells on the results of a study by Norman Pace and colleagues (L. M. Feazel *et al. Proc. Natl Acad. Sci. USA* doi:10.1073/pnas.0908446106; 2009). While you trill to an aria from your favourite operetta, an audience of "microbes of potential public health concern" may well have prime seats in your shower head.

Shower heads are known to harbour microorganisms, mainly because they provide a warm, moist environment prone to the formation of biofilms — aggregates of microbes that adhere to surfaces. Previous studies have sought to identify the organisms that reside in shower heads by culturing them. But as most bacteria can't easily be grown in the laboratory, shower-head biofilm assemblages have remained largely uncharacterized.

In their study, Pace and colleagues use molecular techniques to analyse the microbes found in 45 shower heads obtained from nine cities in the United States. The authors sequenced bacterial genes isolated from each shower-head biofilm and identified the resident microbes by comparing their results with the genes of known bacteria. Such non-culture — or metagenomic — techniques have revolutionized our ability to characterize the microbial communities that live among us.

Pace and co-workers found that the shower heads contained many types of bacteria commonly found in water and soil. The striking result, however, was the abundance of non-tuberculous mycobacteria, in particular *Mycobacterium avium* — the amounts in the biofilm were 100-fold higher than those found in the associated water supply. About 20% of shower-head swabs harboured *M. avium* DNA sequences, and this figure rose to a staggering 78% when the authors used molecular techniques that specifically detect this organism.

Why are non-tuberculous mycobacteria so common in shower-head environments? These organisms are known to be chlorine-resistant, and they may actually be enriched by the treatments used to disinfect municipal water supplies. In fact, when the researchers attempted to clean one shower head harbouring a *Mycobacterium gordonae* species with bleach, they managed only to increase its relative abundance.

Non-tuberculous mycobacteria are opportunistic pathogens

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that can cause severe disease in immunocompromised people, and they can also infect healthy people. The rates of infection with these mycobacteria are increasing in resource-rich countries. Pace and colleagues' work lends support to the possibility that our predilection to soap in the shower, rather than soak in the bath, may be a contributory factor.

Shannon Amoils

expressed from the maternal or the paternal chromosome is controlled by methylation of stretches of regulatory DNA, the imprinting control regions[3]. Most methylation imprinting marks are inherited from the mother and are put onto the genome in oocytes by the DNA-methyltransferase enzyme DNMT3A[4].

It has been a challenge to unravel how, in germ cells, DNMT3A restricts its DNA-methylation activity to imprinting control regions[4]. A breakthrough was the discovery that DNMT3L, a similar but enzymatically inactive protein, forms complexes with DNMT3A. Like DNMT3A, DNMT3L is essential for imprinting[5]. It recognizes and binds to the tail of histone H3 and can thereby recruit DNMT3A to chromatin and to its target DNA sequences. However, when H3 is methylated on its amino-acid residue lysine 4 (designated H3K4), DNMT3L cannot bind, suggesting that methylated H3K4 might prevent DNA methylation[6].

It has long been known that there are enzymes that methylate lysine residues; some of these enzymes control DNA methylation in fungi and plants[2]. More recently, proteins with the opposite action have been discovered. These lysine demethylases include KDM1 (lysine demethylase-1, also called LSD1 or AOF2), an enzyme that specifically demethylates H3K4. KDM1 is expressed in many tissues and is essential for mammalian development, but it is probably not involved in imprinting[7]. Ciccone and colleagues[1] now describe KDM1B (AOF1), an H3K4 demethylase that, in adult mice, is almost exclusively expressed in oocytes. Significantly, if this demethylase is disrupted, there is an overall increase in H3K4 methylation in oocytes, which subsequently fail to acquire DNA-methylation marks at imprinting control regions. These exciting findings raise the possibility that H3K4 methylation needs to be removed (by KDM1B) to allow DNA methylation (Fig. 1). Not surprisingly, embryos that are derived from KDM1B-deficient oocytes show aberrant expression of imprinted genes and so die halfway through gestation[1].

An intriguing theory is that KDM1B may have evolved in mammals specifically to control imprinting in female germ cells. However, KDM1B deficiency does not affect all of the maternal imprints[1], indicating that, at some imprinting control regions, other mechanisms guide the acquisition of DNA methylation by DNMT3A. Another unresolved problem is how KDM1B and the DNMT3L–DNMT3A complex are recruited to their targets. Does the DNA-methylation machinery recognize all nucleosomes that lack H3K4 methylation, or are there additional requirements for its recruitment?

One hypothesis is that specific histone modifications need to be present to instruct the DNA-methylation machinery (Fig. 1). Besides modifications on other amino acids of histone H3 (ref. 2), one candidate for such an instructive histone code could be methylation at amino-acid arginine 3 on histone H4 (H4R3). A recent study[8] of developing blood cells suggests that H4R3 methylation is recognized by DNMT3A and facilitates DNA methylation. Furthermore, although KDM1B does not control the establishment of the few imprints that originate from sperm, changes in H3K4 methylation could nevertheless guide their acquisition[9]. It also seems plausible that similar mechanisms could aid the acquisition of new DNA methylation, unrelated to genomic imprinting, in the developing embryo.

Even with Ciccone and colleagues' inspiring work[1], we are still far from understanding the intricacies of genomic imprinting. Those who thought this was going to be a simple story will be disappointed. Besides DNA methylation, histone methylation is clearly part of the imprinting business. Specific DNA-binding proteins may be involved in imprint establishment as well, possibly by inducing local histone modifications that could facilitate DNA methylation[2,10]. To make matters even more complicated, gene expression also seems to play a part: in oocytes, transcription is detected across several maternal imprinting control regions and was shown, in one case[11], to be essential for imprint acquisition. Despite the complexity of imprinting, however, future research promises to unravel the closely interdependent mechanisms that regulate this intriguing process. ■

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