CELL BIOLOGY

Telomeres sans frontières

Elizabeth H. Blackburn

THE ciliated protozoa have sometimes been suspected of indulging in strange practices unique to themselves. A paper in *Cell* by Gregg Morin[1] shows that, when it comes to telomere synthesis, this suspicion is unfounded. Morin reports the identification of telomere terminal transferase (telomerase) activity in crude HeLa cell extracts. Telomerase is a ribonucleoprotein enzyme that synthesizes telomeric DNA[2-6]. The finding of activity in human cells similar to the telomerases hitherto known only in ciliates highlights the extraordinary conservation of telomere structure and function among eukaryotes.

Telomeres, the specialized DNA–protein complexes at the ends of the eukaryotic chromosome, are required for chromosome stability. Evidence has been accumulating that the molecular features of telomeres are universal. Telomeric DNA structure was first studied in the 'lower' eukaryotes but now it is known to be conserved between widely divergent lower and higher eukaryotes[7,8], including humans[9]. Telomeric DNA consists of simple, tandemly repeated sequences, usually G+C-rich, characterized by clusters of G residues and an overall strand-composition asymmetry resulting in G-rich and C-rich strands, with the G-rich strand always being orientated 5′ to 3′ towards the chromosome end and protruding as a 3′ overhang. The sequence AGGGTT has emerged as the most popular eukaryotic telomeric repeat, cropping up in corners as far flung as trypanosomes, acellular slime moulds, filamentous fungi and humans.

Ciliated protozoa are a rich source of telomeres and have been particularly useful for studies of telomere structure and metabolism. Telomerase, first discovered in the ciliate *Tetrahymena*[2-4], is a ribonucleoprotein enzyme with essential RNA and protein components[3,4]. The *Tetrahymena* enzyme adds tandem repeats of the telomeric sequence of this species, TTGGGG, onto the 3′ end of a telomeric oligonucleotide primer[2-4]. Such addition occurs independently of any added nucleic acid template[2]. Similar results subsequently emerged from study of the telomerases of the ciliates *Oxytricha*[5] and *Euplotes*[6], which synthesize analogous species-specific telomeric repeats. Now, Morin has extended these observations to include telomerase activity in human cell extracts, which synthesizes AGGGTT repeats. The human activity is also sensitive to ribonuclease, suggesting that, like the ciliate telomerases, it too is a ribonucleoprotein. Its primer recognition properties are also similar to those of the ciliate telomerases. The telomerase RNA moieties of *Tetrahymena* and *Euplotes* each contain a telomere-complementary sequence that acts as the template for addition of species-specific repeats (ref. 4 and our unpublished results). Given the evolutionary conservation of telomerase activity shown by Morin's work, we can expect that the RNA activity of the human enzyme will have an analogous role.

Human cells have also been the source of other interesting findings about telomeres. De Lange *et al.*[10] report that, in chromosome-specific sequences next to the terminal AGGGTT repeats, DNA modification occurs in a developmentally controlled manner, with telomeric-region DNA from sperm being undermodified compared with these regions in somatic cells. Modification of some trypanosome telomeric regions has also been observed to be developmental–stage–specific, as well as gene-expression-specific, although the relationship between the modifications in these two systems is not clear. The work of De Lange *et al.* also indicates that Morin's choice of cells may have been a fortunate one: telomeres in one HeLa cell line are exceptionally long[10], which may suggest that, in this HeLa cell line at least, telomerase activity is relatively high.

Telomeres can freely cross the borders of eukaryotic phyla and be used, *in vivo*, in very distantly related species. This behaviour contrasts dramatically with the species specificity of other chromosomal elements such as centromeres and replication origins. It was shown last year that human telomeres function in yeast (see ref. 1), again supporting the notion that shared properties are not restricted to the telomeres of lower eukaryotes. This passportless behaviour of telomeres *in vivo* may have as its basis the common primer recognition properties of telomerases, because all the telomerases studied can recognize as a primer every G-rich strand telomeric sequence that has been tested[1,3,5,6]. Morin's work further reminds us that, in the world of telomeric DNA, there are no Berlin walls between species. □

Elizabeth H. Blackburn is in the Department of Molecular and Cell Biology, University of California, Berkeley, California 94720, USA.

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DAEDALUS

Bubbling down

AIR-bubbles in water are usually rather deformed spheres. Daedalus reckons that toroidal bubbles should also be possible. He sees them as a form of two-phase vortex-ring — a toroidal air-bubble stabilized by the centrifugal force of the toroidally spinning liquid around it. Toroidal bubbles should persist and propagate like liquid vortices, except that the gas inside them would make them buoyant. Armed with these predictions, DREADCO's physicists are injecting air into variously spinning liquids, hoping to make toroidal bubbles and study their hydrodynamics.

Daedalus's interest is far from academic. He recalls that you can keep a hamster under water, in an air-filled silicone-rubber tent. The rubber is so permeable to oxygen and carbon dioxide that the hamster can breathe dissolved oxygen evolved from the water, and dispose of its expired carbon dioxide by the same route. A free water surface would, of course, be an even better gas-exchange membrane. Accordingly, says Daedalus, people could live and work under water in a big bubble, if it could be stabilized somehow. A spin-stabilized toroidal vortex-bubble should be ideal.

So Daedalus is planning a toroidal bubble-submarine, or 'Bubsub'. It is basically a ring-shaped raft, launched by an ingenious hydrodynamic wind machine which pushes it down into the water while blowing a toroidal bubble around it and stirring up a suitable spin. As their craft is forced powerfully downwards, the crew will see themselves magically enclosed in a sort of air-filled doughnut surrounded by spinning water. Once well submerged, the Bubsub will be stabilized by its own motor, whose drive shaft extends through the inner wall of water and through a right-angled gear drive to an upthrusting central propeller. The propeller's powerful upflow maintains the toroidal vortex, and also pushes the Bubsub down against its inherent buoyancy. Both crew and motor breathe normally, through the huge extended surface of the bubble, and will have a wonderful view of the marine world around them.

The Bubsub will be ideal for underwater exploration of all kinds. Biologists with butterfly nets will reach down through its walls to trawl plants from the sea bottom, or out to capture fish swimming past it (indeed, some may swim straight through its walls and fall astonished on the deck). Tourists will navigate scenic marine grottos and oceanographers search for sunken wrecks. The Bubsub must never be allowed actually to touch the bottom or any other solid surface, or the vortex would be fatally interrupted. But at the end of a voyage it can be allowed to float to the surface. The bubble will burst in a cloud of spray, leaving the crew safely afloat on the raft to await their mother-ship. David Jones