



A scheme for the resolution of telomere-telomere fusions by replications through single-stranded gaps present in telomere repeat sequences. Telomeric sequences are shown as solid lines and internal chromosomal sequences as dashed lines. The inset shows the sequence organization of the end of the *Tetrahymena* telomere. Telomere-telomere fusion creates a dicentric chromosome, but this fusion is resolved when replication forks pass through regions of telomere repeat sequences that contain single-stranded gaps. No telomerase activity is represented, and therefore some sequence information is lost at the 5' end of the newly synthesized DNA strands (*). Fusions of telomeres to non-telomeric ends are also resolved but in this case the non-telomeric end acquires a short stretch of inverted telomeric repeats.

Once the breakage-fusion-bridge cycle has begun, it perpetuates itself by continually generating new, reactive, non-telomeric DNA ends. This cycle can be broken if the new chromosomal ends become unreactive, a process referred to as healing. With the telomeric repeat sequences in hand, the molecular nature of healing events has now been investigated in the malarial parasite, *Plasmodium falciparum*¹⁹, and man⁴. In both cases healing has occurred by the acquisition of telomeric repeats at a site that previously lay deep within a chromosome.

The human healing event was discovered by Wilkie *et al.*⁴ in a person with thalassaemia who carried a chromosome on which α -globin genes were present but not expressed. Molecular analysis showed that this chromosome had acquired a new telomere just upstream of the α -globin locus. There is an abrupt transition between the sequence at the globin locus and a stretch of human telomeric repeats. The stability of this chromosome over at least two generations shows that the telomeric repeat sequence is sufficient to form a functional chromosomal telomere even in the absence of more complex telomere-associated sequences, a conclusion that had

previously been reached with yeast²⁰.

Does the sequence at which the new telomeric repeats have been added reveal anything about the nature of the healing event? Intriguingly, a G- and T-rich sequence within 10 base pairs of the site of telomere addition has a marked similarity to the human telomere repeat sequence. In yeast, telomeric repeats can be added to a non-telomeric sequence provided that telomeric repeats are within 30 base pairs of the end of the DNA molecule²¹, suggesting that telomerase may have a substrate recognition site spatially distinct from the site at which new telomeric repeats are added.

Finally, two studies in *Drosophila* suggest that not all broken chromosome ends are highly reactive^{22,23}. In both cases, terminal deletions are maintained for many generations with a slow loss of DNA from the ends of the chromosomes. These ends lack any sequences that could be recognized as telomeric repeats, showing that under certain circumstances non-telomeric ends can be relatively inert. □

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Fibrillated food

DIETARY fibre, that fashionable food component, has two virtues. First, it provides no calories, being indigestible. Second, it is a healthy tonic for the alimentary canal. Some foodstuffs high in amylose starch, like rice and spaghetti, actually increase in fibre content on being cooked. The amylose molecules aggregate into crystallites which defeat our digestive enzymes.

Daedalus is now generalizing this observation. He is devising food additives which subtly convert other components of our diet into indigestible fibre. DREADCO's chemists have set up shop in the firm's canteen and, over the protests of the cooks, are submitting selected meals to some simple chemical tricks. Traces of formaldehyde should cross-link the protein of a foodstuff into insoluble, enzyme-resistant polymers. Carbonyl chloride might couple its sugars into polycarbonates, while sulphur should usefully vulcanize its unsaturated fats. As additives, these crude and brutal reagents are unlikely to please the regulatory authorities. But in carefully controlled traces they will help Daedalus to discover how much of any given foodstuff can be converted to insoluble fibre without degrading its taste and texture too much. Since the taste of a food depends mainly on trace flavour substances, while its texture should be little affected by the microscopic polymer aggregates of new fibre, quite a lot of it may be 'fibrillated' without any detectable effect. Once the feasibility of the process has been demonstrated, subtler and more acceptable fibrifying additives can be developed for the job.

DREADCO's Fibrillated Foods should be widely welcomed by health freaks of all persuasions. Cream cakes, savoury pies, heavy puddings, all the richest and wickedest of cordon-bleu creations will soon be available in virtuous low-calorie, high-fibre versions. With sufficiently cunning chemistry, fast-acting fibrillating reagents could even be deployed as novel seasonings or condiments. Domestic cooks could outflank the family's bad eating habits by subtly fibrillating its meals, and guilty fast-food addicts could upgrade their hasty purchases to approved dietary standards.

But Daedalus senses a streak of masochism and puritanical fervour on the fringes of the health-food market. For the true vegetarian jogger, health is won by suffering. To capture this market, he is studying quite severe levels of dietary vulcanization. The DREADCO team is cross-linking the most delicate lettuce leaves into chewy tastelessness, reinforcing nuts and lentils to a sort of vegetable gravel, and devising a vegeburger which almost meets military specifications. Even the inherent wickedness of meat may be redeemed by brutal enough treatment.

David Jones