must have been virtually the same as the lines of wild-type mated males are very similar in the two graphs. Therefore, we believe that Van Voorhies's conclusions concerning the significance of spermatogenesis in *C. elegans* are not yet justified. There may be other important factors involving costs before or during mating that have influenced his results (for example any unknown effects of the locus *spe-26*).

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VAN VOORHIES REPLIES — Frischknecht and Wedekind raise two major points about my paper[1]. First, if spermatogenesis is the main factor affecting *C. elegans* lifespan then male worms with mutations blocking spermatogenesis should live longer than wild-type worms. I showed a large increase in lifespan of mutant hermaphrodites, but no such increase in male lifespan. I agree that this implies that there may be other factors affecting lifespan and that the *spe-26* mutations might have pleiotropic effects in addition to blocking spermatogenesis, and I am now doing experiments to test these possibilities.

Frischknecht and Wedekind's second point, that mating *per se* could reduce lifespan, is excluded by my data: the mutant males apparently engage in all normal mating activities, yet their lifespan is slightly longer than unmated males (my Fig. 4). Additional support for the assertion that the act of mating or premating activity are not the factors reducing mated male lifespan comes from an experiment in which wild-type males were mated only for 30 hours and then isolated from hermaphrodites. Survivorship in this group of males was similar to that of males kept with hermaphrodites throughout their entire lives.

This contrasts sharply with results in *Drosophila*, where the activity of mating reduces lifespan. Male *Drosophila* mated for a short time and then removed from mates assume the survivorship pattern of flies which have been unmated their entire lives[2].

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Aluminium in Alzheimer's?

SIR — Landsberg *et al.*[1] reported the absence of evidence for aluminium in senile plaque cores of cases of Alzheimer's disease. They used particle-induced X-ray emission (PIXE) for elemental analysis of brain tissue sections immunostained for complement factor C3d, and of unstained sections. The authors concluded by questioning the potential role of aluminium in the aetiology of Alzheimer's disease. But their studies focused exclusively on senile plaques in an attempt to replicate the findings of Candy *et al.*[2] of high concentrations of aluminium and silicon in colocalization with this structure.

It is important to note that the evidence linking aluminium to Alzheimer's disease rests primarily on the association of this element with neurofibrillary tangles rather than senile plaques. Indeed, data showing aluminium accumulation in neurofibrillary tangle-bearing neurons has been obtained from Alzheimer's disease brains[3,4] and from brains with Guam ALS/parkinsonism–dementia complex using scanning electron microscopy with energy-dispersive[5] and wavelength-dispersive X-ray analysis[6], laser microprobe mass analysis (LAMMA)[7], secondary ion mass spectrometry (SIMS)[8] and histochemistry[9]. In these studies, both stained[4,5] and unstained[4–6] specimens have yielded positive results. The consistent finding of aluminium in association with the neurofibrillary tangle, using such widely differing analytical approaches, suggests that chance contamination cannot explain these results.

We agree that it is important in microanalytic studies of this type carefully to control for various sources of exogenous contamination. However, using LAMMA, where tissues are viewed and analysed in semithin plastic-embedded sections[5,10], non-biological particles can be identified and avoided. As Landsberg *et al.* noted, in 1986 we reported a failure to identify aluminium or silicon accumulation in senile plaque cores of Alzheimer's disease[11] using LAMMA with an elemental detection limit in the one p.p.m. range. Finally, analysis of unfixed, unstained cryostat sections of affected brain tissues has yielded comparably prominent aluminium-related peaks within neurons in tangle-rich areas[4–6].

Together, these data strongly suggest that the association of aluminium with the neurofibrillary tangle represents a biological characteristic of this key pathological feature of the disease rather than a postmortem artefact. The large body of positive scientific evidence of aluminium accumulation in neurofibrillary tangles has not been directly questioned by Landsberg *et al.*[1]. This evidence remains the basis by which this potentially toxic element could be linked to Alzheimer's disease.

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Maker's mark

SIR — We would like to present evidence for the existence of a controlling influence in the construction of human chromosome 4, and possibly others.

Searching the GENBANK/EMBL combined DNA sequence database (release 74) with a short piece of the cloning vector pBSIISK+ reveals a puzzling number of near-perfect matches to sequence tagged sites (STS) on human chromosome 4. For example, the first 50 bases of HUM4STS184 show perfect homology to the multiple cloning site of pBSIISK, as do sequences in HUM4STS182, HUM4STS170, HUM4STS183, HUM4STS181, HUM4STS311 and HUMXT009966. We can only interpret this to mean that man, unlike most other species, was indeed 'manufactured', presumably by some all-powerful deity. This individual must have used standard cloning techniques to piece together chromosome 4 (did he/she use different vectors for different chromosomes?). Despite leaving behind evidence of the construction, this work is clearly a *tour de force*.

The company that sells pBSIISK+ must, presumably, have a licence from God to market and sell his vector. One wonders, perhaps, if other well-known repetitive elements, for example Alu sequences, represent the fossil remains of earlier divine cloning vectors.

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