• Salvesen, G.S. and Duckett, C.S. (2002) IAP proteins: blocking the road to death's door. *Nat. Rev. Mol. Cell Biol.* 3, 401–410
• Shi, Y. (2002) Mechanisms of caspase activation and inhibition during apoptosis. *Mol. Cell* 9, 459–470
• Srinivasula, S.M. *et al.* (2001) A conserved XIAP-interaction motif in caspase-9 and Smac/DIABLO regulates caspase activity and apoptosis. *Nature* 410, 112–116
• Suzuki, Y. *et al.* (2001) Ubiquitin-protein ligase activity of X-linked inhibitor of apoptosis protein promotes proteasomal degradation of caspase-3 and enhances its anti-apoptotic effect in Fas-induced cell death. *Proc. Natl. Acad. Sci. U. S. A.* 10, 10

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Book Review

The end of the beginning

A Means to an End: The Biological Basis of Aging and Death by William R. Clark
Oxford University Press, 2002. £13.50 pbk (234 pages) ISBN 0 19 515375 8

Genetics and molecular biology have revolutionized aging research in the past two decades, just as they had developmental biology previously. This historical precedent has had a significant impact on the thinking of many researchers entering the aging field, by fueling their search for a biological aging 'program' analogous to the developmental program. The difficulty is that programs have a 'purpose'. Evolutionary biologists, who constitute another segment of the aging research community, have cogently addressed the lack of purpose in aging, a phenotype that has escaped the force of natural selection through its appearance in post-reproductive individuals. The dilemma then is to acknowledge this, while searching for the proximal causes of aging and the principles that govern its course in various species.

In *A Means to an End*, Clark takes a narrow view of the evolutionists' position and dismisses it by pointing out the existence of single-gene mutants that have large effects on lifespan and by confidently asserting that there are relatively few genes that govern aging. The word 'program', in turn, is usually in quotes in his book, indicating its guarded use. However, clear guidance to its meaning in the context of aging is lacking. The source of this inadequacy could reside in one of the strengths of this book, which treats the cell as the basic aging unit. Replicative senescence and programmed cell death are the terminal phenotypes of the aging cell. The translation of replicative senescence into the aging of the organism is not easy, but Clark does an excellent job in spanning this gap. However, his insistence that programmed cell death causes the demise of the organism is difficult to sell.

Aging plays out in individual cells; however, multicellular organisms do not die because all their cells die. The new era opening up before aging research by virtue of the completion of the Human Genome Project, to which Clark often refers, will allow us to bridge the gap between the cell and the organism. This, however, is where the book ends. Cells need not die or even lose most of their function for the organism to senesce. The realization that the organism is a complex system in the nonlinear dynamic sense provides a means for understanding this apparent discrepancy.

What is the nature of the genetic determinants of longevity? Three types of gene that influence aging are enumerated by the author: senescence effector, senescence repressor and senescence regulator genes. The first two categories are postulated to be common to all aging species. Clark astutely searches for this commonality in the distant phylogenetic past among the protists. Here, he makes the oft-asserted connection between sex, reproduction and aging, which provides the resolution of the evolutionary dilemma surrounding the origins of aging. This is also where the difficulty with programmed cell death arises. The senescence regulator genes, in contrast to the other two classes of senescence genes, make their appearance throughout phylogeny and determine the characteristic differences between species' maximum potential lifespans. Statements are made indicating that there is good evidence for these types of genes in different species, including human. This categorization of senescence genes is neat, but there is little, if any, evidence presented to support it.

Clark devotes relatively little space to the genetics of aging in invertebrate models. This is surprising given the generic focus on genes. The details of the involvement of the *daf-2–age1* pathway in nematode aging were already known when the book was written. (Inexplicably, Clark states that the identity of the *age-1* gene is not known.) The omission of the genetics of aging in model systems is a pity, because it would have enhanced the author's otherwise excellent discussion of the role of metabolism and oxidative stress in aging, which includes a nice encapsulation of the life extension and senescence retardation by caloric restriction. This rendition is highlighted by the conclusion that caloric restriction might actually allow the realization of the maximum potential lifespan of the species, rather than altering the maximum lifespan, which would require genetic change if maximum lifespan is a heritable characteristic of a species.

A Means to an End is targeted to a lay audience. The citations that would render it more satisfying to the scientist are missing. These citations would have prevented certain inaccuracies and facile statements. There are, however, interesting perspectives and generalizations made by the author that can benefit anyone interested in aging research, once the reader gets past some of the implausible ones.

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The tail that wags the dog

The Monkey in the Mirror: Essays on the Science of What Makes us Human by Ian Tattersall Oxford University Press, 2002. $25.00 hbk (xiv+203 pages) ISBN 0 19 851569 3

Ian Tattersall, a curator of Anthropology at the American Museum of Natural History, presents eight short essays on his view of

science, evolution and anthropology. These are essays with neither bibliographies nor an index, but there is most certainly a theme.

They start well, with one of the finest descriptions of science aimed at students and the public that I have ever found. This first essay deals with the structure of science, the nature of discovery and its relationship with changes in science, science as a collective enterprise, why paleoanthropology is science (especially close to my heart), and very clear statements of how science differs from religion and creationism. I consider this the best piece of writing by Tattersall that I have encountered.

The remaining essays are a rather different matter. The downward spiral begins, appropriately, with Tattersall's treatment of the New Synthesis – the theory integrating Mendel's theory of heredity with Darwin's theory of evolution and natural selection. Tattersall has an unusual interpretation of this, viewing the New Synthesis as a disaster from which evolutionary theory is only now recovering. For the most part this is because he equates the New Synthesis with gradualism, meaning an explanation of evolution in which all change is slow and cumulative; that is, macroevolution is microevolution continuing for a very long time, and all speciation is anagenic, with gradual transformation of one species into another without any split or boundary between them. In fact, he specifically equates it with linear progressionism, asserting, 'thanks to the overwhelming triumph of the Evolutionary Synthesis…human evolution, like that of other organisms, came to be seen as a gradual, linear process that, come hell or high water, continued doggedly along a path of inexorable betterment.'

But this is all wrong. It ignores the fundamental contribution of the New Synthesis – population-scale evolutionary thinking. It also disregards the attempts of Rensch and Mayr, key authors of the New Synthesis, to connect the evolutionary mechanisms elaborated by population geneticists with the observations of paleontologists who focused on the origins of higher taxa, and Mayr's attempts to explain the origin of evolutionary novelties. It was Mayr [1], and not Eldredge and Gould, who first proposed a model of genetic reorganization permitting the rapid emergence of evolutionary novelties at the time of speciation. That the 'punctuated-equilibrium' theory is not credited to Mayr is because of the equilibrium part, not the punctuation, as it never occurred to him (or the other synthesists) that branching speciation could be the only way that evolution worked [2]. Mayr never characterized human evolution the way Tattersall does, as 'the long history of the hominid family [with] vast periods of monotony'.

In fact, these essays are packed with unusual ideas about how evolution works. For the most part, they reflect an imperfect understanding of how mathematical population genetics has contributed to the theory of evolution. For example:

- 'Most features will linger in a population as long as they simply don't get in the way.' (p. 33)
- 'Evolution is best described as opportunistic, simply exploiting or rejecting possibilities as they arise…there is nothing inherently directional…about this process.' (p. 139)
- 'For true innovations to arise and become permanently incorporated into some component of the human population, it will be necessary for that population to become fragmented.' (p. 189)

Or, my own personal favorites:

- 'There is no mechanism by which particular characteristics – still less, genes – can be singled out for favored or disfavored treatment.' (p. 187)
- 'Either the whole creature (or species) succeeds reproductively, warts and all, or it fails.' (179)

One wonders how precepts like these could possibly lead to a coherent picture of human evolution. The short answer is that they don't!

One of the key examples of this is in how brain size and intelligence evolved. Although the overwhelming body of fossil evidence shows a gradual increase in human brain size across the Pleistocene, Tattersall cannot accept this because it does not fit his idea of how evolution works. He writes, 'Two million years of evolution have seen significant increase in the average human brain size…yet, if we look more closely, the trend evaporates' (p. 186), and 'We cannot attribute the advent of modern cognitive capacities simply to the culmination of a slow trend in brain improvement over time' (p. 149). His solution is to unlink the brain from what it does, and argue that its intellectual properties appeared suddenly and inexplicably. '[Our] unprecedented symbolic cognitive capacities [are] the result of a chance coincidence of acquisitions in the brain,' he states (p. 181).

Evolutionary psychology takes a big hit in these essays, as it must because it supports the argument of how different parts of the brain could have evolved gradually for different adaptive purposes, whereas Tattersall believes the main functions of the brain were acquired together, suddenly and by chance. But it is the Neanderthals who are singled out for really special treatment, as a curiously demented human-like species. The Neanderthals are described as 'hominids'; the humans are 'people'. The products of Neanderthal and human technologies are 'as far as can be told, functionally identical' (p. 145). Identical technologies, however, cannot convince Tattersall that Neanderthal cultures were the same as human ones because if they were interbreeding between Neanderthals and humans would be possible. Culture is the significant mediating frame for human mate choice, but, he says, it cannot have been so for the Neanderthals, who were not human, and interbreeding did not occur simply because they were too physically different from humans (p. 132). Besides, in spite of the technological similarities with humans, could it even be said that Neanderthals had culture? Probably not, because Tattersall believes they were mentally challenged, or just plain couldn't think, and writes, 'It seems fair to regard the Neanderthals as exponents of the most complex…lifestyle that it has ever proved possible to achieve with intuitive processes alone.' (p.155). If this is not actually fair, it is at least consistent with Tattersall's view that in spite of their modern brain size, Neanderthals could not communicate with a 'human-like' language.

What a weird picture of evolution emerges, from Neanderthal hunters huddled over a stream eating raw fish on the spot where they were caught, so they didn't have to be nice and share with their friends and relatives, to an evolutionary process producing them that involved selection but had no direction. Looking through these essays to grasp how Tattersall tries to explain human evolution without the insights of population genetics is like looking at a tail trying to wag a dog.

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References

1 Mayr, E. (1954) Changes of genetic environment and evolution. In *Evolution as a Process* (Huxley, J.S. *et al.*, eds), pp. 188–213, Allen and Unwin.
2 Futuyma, D.J. (2002) Stephen Jay Gould à la recherche du temps perdu. *Science* 296, 661–663