Q & A

Tom Kirkwood

Tom Kirkwood is Professor of Medicine and Director of the Institute for Ageing and Health at Newcastle University, UK. After training in mathematics and biology at the Universities of Cambridge and Oxford he first worked on the measurement of blood clotting and fibrinolytic factors. Early in his career he began an interest in the biology of ageing which he has followed since 1975. In 1977 he put forward the 'disposable soma' theory that unites the evolutionary and mechanistic understanding of ageing within a single framework. His subsequent research has included pioneering studies on the intrinsic ageing of stem cells, on the genetic factors underpinning longevity, and on systems biology approaches to unravelling the complexity of the mechanisms of ageing. He was awarded the inaugural Henry Dale Prize of the Royal Institution for multidisciplinary research and was BBC Reith Lecturer in 2001 bringing the science of ageing to a global audience. His books include the award winning Time of Our Lives: The Science of Human Ageing *written for a general readership,* Chance, Development and Ageing *(with Caleb Finch), and* Accuracy in Molecular Processes: Its Control and Relevance to Living Systems.

What led you to a career in science? Like many kids I was always fascinated by the natural world — ants, rock pools and, in particular, reptiles. But I went to a very old-fashioned first school that filled me with Latin and Greek while barely touching on science, although a little surprisingly it did teach practical skills like woodworking. About the only science lesson I remember from then involved holding hands in a circle and being given an electric shock from a Wimshurst machine! At senior school, I developed a new passion for applied mathematics including quantum theory and relativity.

In those days it was nearly impossible in the British school system to combine serious mathematics with biology so I opted to study mathematics and went to Cambridge, where the kinds of subjects I liked were big on the curriculum. However, I found much of the teaching style dispiriting and was at a loss for what to do next until I took a non-examinable 3rd year course on statistical applications in biology taught by the late David Kendall. This was so exciting that, with Kendall's encouragement, I went to do an MSc in the Biomathematics Department at Oxford, where I learnt from inspirational biostatisticians like Maurice Bartlett and Michael Bulmer. From there I got a job at the National Institute for Biological Standards and Control (NIBSC) in London working on the bioassay of components of the blood clotting system. I even had the distinction of inventing and validating the International Normalized Ratio (INR), a clinical measure that is now used worldwide to monitor anticoagulant therapy.

Serendipity then intervened. The NIBSC was an offshoot from the National Institute for Medical Research (NIMR), with which close links continued. A chance encounter with Robin Holliday at the NIMR sparked a collaboration on the cell and molecular mechanisms of ageing. Holliday lent me a copy of John Kendrew's *The Thread of Life* and my delight in discovering, by this roundabout route, the incredible world of molecular biology gave direction to my interests that led to a PhD and to my subsequent career.

Ageing was not a widely recognised research field when you entered, was it? That's an understatement. There were very few groups working on ageing. Indeed, many leading scientists thought it was a complete waste of time to address something so complicated and which, after all, 'just happened'. Luckily, Robin Holliday saw very astutely the excitement of the subject and he was closely connected with Leslie Orgel and John Maynard Smith, who had each made some really important advances over the last decade. So although the world in general had yet to wake up to the fascination of ageing science, I was fortunate to be in a privileged corner where the research was intense and the exchange of ideas was exhilarating.

Within a couple of years, I'd published an article on the evolution

of ageing in *Nature* and one on cell senescence in *Science*. I wasn't being paid to study ageing, but my employers at the NIBSC could see how much I was enjoying it and I was doing the day job well enough that they had the generosity to indulge me. Soon I moved to a tenured scientist position at the NIMR where I was able, in time, to form and lead a new research division of Mathematical Biology. But I was still keen to focus full time on ageing and to do this I moved in 1993 to the University of Manchester as Professor of Biological Gerontology, the UK's first chair to be established in the science of ageing, and then to Newcastle University which has provided an excellent environment for the multidisciplinary research that ageing requires.

Who are your scientific heroes? John Maynard Smith, Leslie Orgel and John Cairns all stand out, as well as David Kendall. Each has inspired me in one way or another. However, I'd like best to erect a monument to the 'unknown scientist' who embodies everything that is so special about a life in science. This includes: humility in the face of the unknown; dedication to truth; resilience to keep going when the sheer difficulty seems overwhelming; and openness to new data and ideas. Some of the scientists I've most admired are individuals who are unlikely ever to achieve fame or distinction outside their own narrow research fields, but who nevertheless hold steady to the core principles that underpin scientific drive and integrity. For all its faults, including those of its practitioners who fail to live up to the core principles, science is just amazing.

What are the big questions in your field? We know in broad terms quite a lot now about why ageing occurs and the mechanisms that drive it. We know, for example, that the root cause of ageing is the gradual, lifelong accumulation of a host of unrepaired molecular and cellular damage. And we know that underlying this is the evolutionary logic that dictates that it is not worthwhile to invest sufficiently in the mechanisms of somatic maintenance and repair to have provided us with a body that lasts forever. This is the core of the 'disposable soma' theory. A lot of attention has been paid recently to the discovery that metabolic regulators like insulin signalling pathways affect longevity and, not surprisingly, they do this by adjusting the relative investments in maintenance, growth and reproduction, each of which is costly.

But for all the interest in these discoveries, they are neither fundamentally original (we should have anticipated them) nor do they sufficiently address the specific mechanisms that actually cause ageing to occur. They simply make these mechanisms run faster or slower. The big questions now are: How do we address the awesome complexity of a process that is driven by so many elements working and interacting together? How can we intervene to produce healthier old age? And, at a deeper level of biological curiosity, what are the mechanisms that sustain the 'immortality' of the germ line – the essential lineage of reproductive cells that carries life onward from generation to generation?

Much attention is focused on the social responsibilities of scientists: do you agree with this emphasis? Yes, of course. My primary motivation for doing science is curiosity, pure and simple. I am still thrilled by an unexpected discovery in almost any branch of science. But I have also come to appreciate the need for scientists to take careful account of the social world in which we operate. In my field of ageing, the imperatives are clear. Life expectancy in developed countries is still increasing at the startling rate of five or more hours every day, and in many developing countries the rate is even faster as they catch up. It is really quite amazing that this isn't better appreciated, because it's not new. In Western Europe, we've gained the same increase in life expectancy every day for 200 years.

The fact we are living longer is in many ways humanity's greatest success but there is a sting in the tail. Are all those hours which are being added daily of the quality we would like? Society as a whole is rather confused about population ageing and scientists have an important role to play. This is why I get quite angry with those who suggest that the goal of our research is merely life extension, or even the banishment of ageing altogether. Such an outcome, based on what we know now, is extremely remote. To focus on this when there are such pressing challenges arising from the growing numbers of older people in the world is frankly ageist and should not be tolerated outside the realm of fantasy.

You care strongly about issues like ageism and equality: where does that come from? I was born in South Africa just as apartheid came into being and my father, who was South African too, was deeply committed to opposing apartheid and to practical race-relations efforts. I suppose I soaked up something of his spirit. I detest unfairness with a passion.

If you were granted the opportunity to time travel into the past or future, just for five minutes, how would you use it? What a tantalising thought. There's so much I'd love to know that's unlikely to be discovered in my lifetime. But I'd feel it was cheating to travel forward and peek. So I'd love just to watch Charles Darwin and August Weismann at work – two and a half minutes with each would be much too short to satisfy but far better than nothing.

Institute for Ageing and Health, Newcastle University, Campus for Ageing and Vitality, Newcastle upon Tyne NE4 5PL, UK.
E-mail: tom.kirkwood@ncl.ac.uk

Quick guide

Orangutans

Anne Russon

What is an orangutan? Orangutans are Asia's only great apes. Close relatives of Africa's chimpanzees, bonobos and gorillas, they share basic great ape features: very large bodies and brains, high intelligence, long, slow lives, eclectic fruit-based diets, and nest-making. Uniquely, orangutans are the only red-headed great apes, the world's largest primarily arboreal mammal, and the slowest to grow and breed of all land mammals, even elephants. Perplexing idiosyncracies include their genius with tools in captivity but not in the wild, their solitary lives, and male bimaturism (see below).

Orangutans' slow biology includes lifespans of up to 55 years, exceptionally slow development and reproduction (7–10 years of dependency; first birth at 15–16 years; 6–9 years between births) and very slow activity. They meander along at 0.3 km/hr (gibbons can clock 56 km/hr) and can rest 40% of the day. Rarely do they jump or brachiate like other apes; they cautiously climb, clamber, or languidly 'pole vault' across forest gaps on slender trees. "Live to eat" could be their motto. After rising from the night's nest at dawn, they eat, travel, eat, rest, eat, and eat some more — foraging on average 50–60% of the day. They spend only about 5% of their day socializing, probably less avoiding predators (they have few, other than tigers in Sumatra and humans). Their day ends with building a new nest, typically in a different place each night, near trees that offer today's dinner and tomorrow's breakfast.

Orangutans were the neglected apes of the 20th century, ignored as boring dullards while attention focused on dramatic chimps, sexy bonobos and 'gentle giant' gorillas. We are only now appreciating many of their qualities. Into the 1990s, for instance, they were considered one species with two subspecies, one on Borneo and the other on Sumatra. Anatomical and genetic findings now indicate that Borneans