

## **Anatomists studying Saturn**

The planets suite, by Gustav Holst, was probably the first long piece of classical music I got to know well. It was a natural choice for music teachers in several of my schools, I think because it is accessible, with seven relatively short movements, and because Holst was strongly associated with nearby Cheltenham. My favourite of the movements was then, and is now, Saturn, the bringer of old age. I think I was in a minority of one, most of my classmates liking the musical violence of Mars, the bringer of war, or the majesty of Jupiter and especially the part of it that was later used as the hymn 'I vow to thee, my country'. They could not understand my love for the elegiac, slowly but irresistibly developing theme of Saturn; they said it was devoid of excitement.

I have just attended a conference in which the business of Saturn generated a great deal of excitement.

One of the features of belonging to a scientific society is that most members try to attend its annual conference, even if its theme does not seem terribly relevant to their own research. This may seem like a waste of time, and I admit I do often feel that way when leaving my own busy tasks to take time away for the conference, but in reality it can be like having a long masterclass in what turns out to be a really interesting field. That is my experience of this year's Anatomical Society summer meeting. That society's journal, *Journal of Anatomy*, has for two decades had a sister journal, *The Ageing Cell*. To celebrate the anniversary, the Anatomical Society devoted its meeting to ageing.

Unsurprisingly, given the title of the journal, the focus was on the cellular level rather than on gross features of ageing. Different speakers came at the problem from different angles but, by the end, it was clear that a mad Venn diagram could be drawn, with a few things sitting in the intersection of almost all talks. One was mitochondria; slow changes in mitochondrial function, possibly because of accumulated damage, alter mitochondrial metabolism and this makes subtle changes to a vast number of cell processes, ultimately driving cells into senescence (see my earlier blog, *Second Childhood*, for more on cellular senescence). Another was a creeping methylation of DNA (at CpG sites). Several presenters showed graphs that depicted a clear relationship between the level of CpG methylation and age, for humans and for other animals, shorter-lived animals showing a faster rise and long-lived animals showing a much slower rise. There were even graphs showing how the rate of rise could predict individual lifespan, an ethically scary prospect; would you, now, want to find

out your predicted lifespan? Would it help you plan your retirement, or crush hope? And would it make you feel extra-cheated if something unpredictable happened to shorten that life even more? We do have agency and can make choices, but it was interesting to see the graphs reflect those choices too: the rise of CpG methylation is steeper in those who smoke, and settles back to its normal rate when they stop.

One particularly fascinating talk (to me) was about Axolotls, which essentially do not age. By their size and relationship to other amphibians, one would expect them to be short-lived but they are not; they live for a very long time indeed. They do not show the CpG methylation seen in most vertebrates, and they do not show the mitochondrial dysfunction. Famously, they have huge powers of regeneration, and they regenerate most of their tissues not as we do, from stem cells, but by dedifferentiation of differentiated cells, which maintain active telomerase to keep the ends of their chromosomes intact. Having ‘ageless’ animals cropping up in the middle of a clade that is run-of-the-mill is striking. Did it arise because of the paedomorphism of axolotls? (they become sexually mature in what is late-larval life, rather than completing metamorphosis – they ‘never grow up’).

There was a great deal more in the conference, about neural ageing and immune ageing and the slow takeover of tissues by single clones. There was not much about how ageing is ‘reset’ in the germ line, so that a new embryo is created afresh; that would be an interesting topic for next time perhaps. But it was a great conference that stretched that ageing research has, well, ‘come of age’ and is attracting a great deal of attention. Strikingly, it is at last attracting attention from the young (classically, scientists switch to ageing research when they start to feel the process in themselves: the amount of grey hair in conferences n ageing has always been a subject of geeky humour).

Happy Birthday, *Ageing Cell*; may you stay active and fresh for many decades to come.

Jamie Davies, Edinburgh, July 2024