The splice of life – a new point of intervention for age-related disease?

On 16 November 2023 30 u3a members gathered at the RILD (Research, Innovation, Learning and Development) building – part of the University of Exeter Medical School – on the RD & E Wonford site, to hear a talk by Lorna Harries, Professor of Molecular Genetics. Those of us who had attended Lorna's lectures before Covid, on the genetics of ageing, and her research on rare forms of diabetes, were looking forward to seeing her again. Those new to her presentations would have been impressed by her ability to explain complex scientific material in an engaging and accessible way. ('I make my talks suitable for my grandmother,' Lorna explains).

There are plenty of statistics about the ever-increasing older population and the consequent toll of age-related diseases on health and social care services. Scientists cannot make us live longer but what they can try to do is improve our later years by tackling some of the diseases we are susceptible to. The most successful way to do this is probably to look at what happens to the body within its individual cells. At any stage in our lives, cells can mutate and age but not actually die. This is called senescence and it is undesirable because these cells are no longer reacting properly to their internal and external environments. They become unsupportive to surrounding tissues and can give rise to damaging inflammatory processes. Younger people have robust immune systems, which can throw out mutated cells, but as we age we have less capacity to do this. Research on mice has demonstrated that removing old cells has a positive effect, reducing fat in the liver, cognitive decline, cataracts, muscle wasting and bone loss. But what if we could bring old cells back to useful life?

Within cells our genes group together in different ways according to the functions they need to carry out. This is the 'splicing' referred to in Lorna's title. When negative events such as inflammation, damaged DNA, free radicals or disruption to metabolism occur, the messages which instruct the various genes to combine – the 'splicing factors' – become compromised, cells deteriorate, and disease can result. Researchers have been looking at new medications which seem able to block the stressors and allow correct gene splicing. Cells are thus rejuvenated, minimising the effects of disease.

Lorna and her team have been looking at the effect of one drug on IPF – idiopathic lung fibrosis, an incurable illness which causes the lung to become stiff and solid. It has a poor prognosis and is currently treated with medication taken twice a day for life, with side effects. The new drug is take only once every three months and appears to reverse the cell senescence which causes this disease by 50%, which is highly significant.

Although this drug appears to work on a range of different cell types and to be very safe, getting a new medication ready for use in the general population takes 5 – 10 years. There must be numerous safety trials and a whole package of information needs putting together to go before the regulators. Testing on animals does form part of this although is not always found to be a reliable indicator of what happens in humans.

The eventual aim however is that using technology which can actually rejuvenate cells and mend faulty DNA will provide a new and more effective generation of treatments for the diseases of ageing.

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