THE FIT AT ANY AGE ISSUE

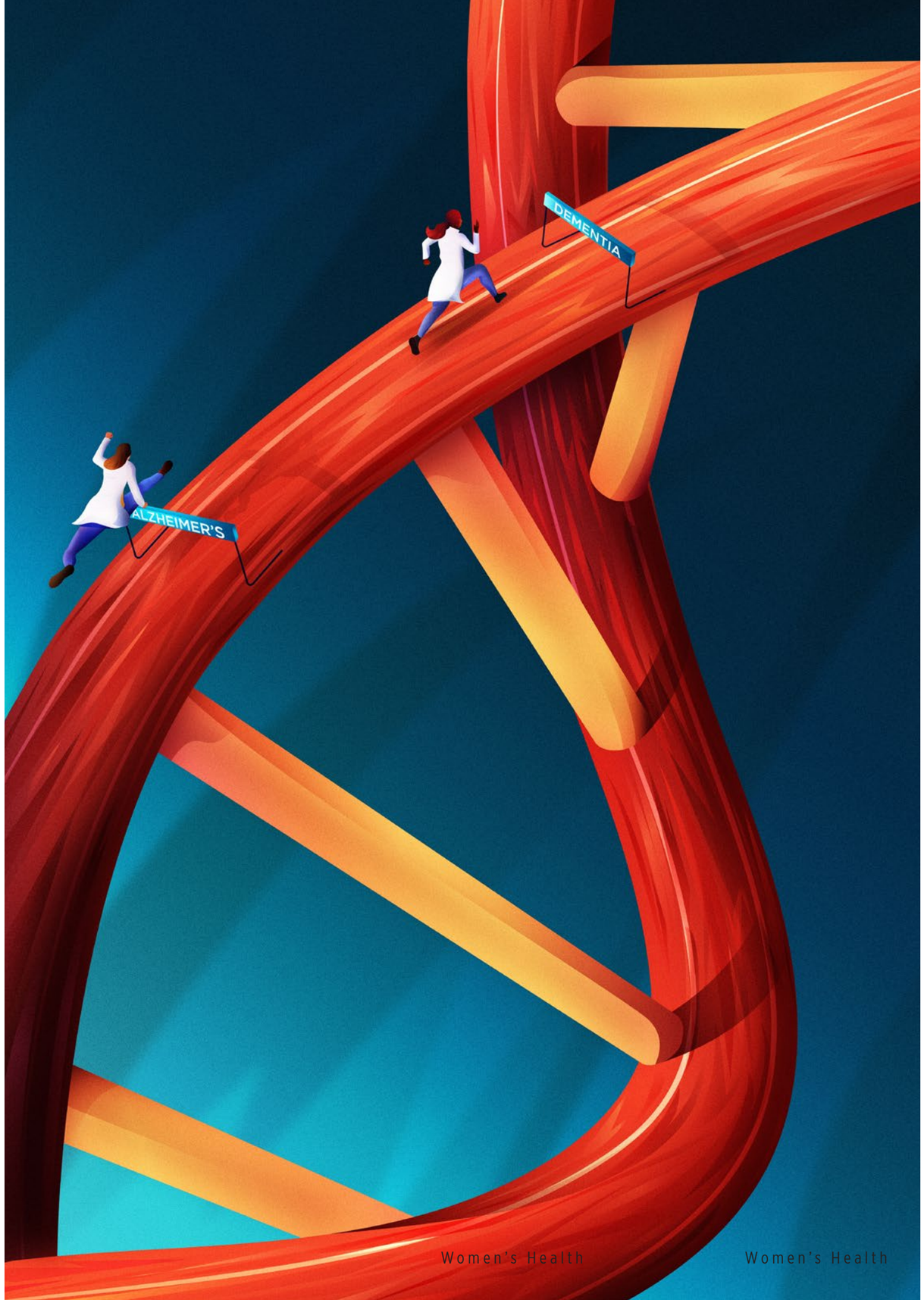
THE RACE TO LIVE FOREVER

Living longer is a million-dollar industry, with scientists and tech gurus in simultaneous pursuit of evidence-based methods of delaying death. *WH* hears from some of the front runners

WORDS GEMMA ASKHAM

Illustration | CODY MUIR

One block back from Las Vegas's famous strip, the marble floors of the hotel that was once the world's largest are eerily quiet. In normal times, prep would be underway to ready this space for the annual Revolution Against Ageing and Death, or RAADfest. Since the festival was founded in 2016, the $1,195 VIP passes have been snapped up with the kind of gusto usually reserved for Glasto tickets. Researchers, AI innovators and anyone angry about the 'unnecessary evil' of growing old have gathered to learn about the latest in stem cell therapy and at-home oxygen chambers and, failing the efficacy of those interventions, reserving a slot for cyrogenic preservation. What prevents RAADfest from finding a resting place in ridicule is that it counts among its attendees leading scientists in ageing and Google's director of engineering, along with those with pockets deep enough to fund the six-zero bank transfers needed to bring living-longer experiments to life. Of course, the irony of putting on a gathering to promote longevity at a time when gathering itself is proving deadly was not lost on the event's organisers; much like just about every other event in the 2020 calendar, this one's been cancelled. Instead, RAAD-ers will meet online, united in the belief that midway through a pandemic that disproportionately targets the elderly is certainly not the time to halt progress into understanding how humans can live longer and healthier lives.



It's a goal that both scientists who specialise in ageing– called gerontologists – and Silicon Valley entrepreneurs are racing towards, with the sector forecasted to be worth £514million by 2023. 'I'm hesitant to compare gerontology's importance in magnitude with other urgent priorities, such as pandemics, climate change and poverty, but it's up there with the biggest,' confirms Tom Kirkwood, emeritus professor in ageing at Newcastle University, and one of the pioneers of longevity research. Among those who've joined Professor Kirkwood on the starting blocks are Amazon mogul Jeff Bezos and PayPal's billionaire co-founder Peter Thiel, both of whom have ploughed millions into Unity Biotechnology, a company developing drugs to zap senescent – or 'zombie' – cells, known to contribute to Alzheimer's, among other things. Then there's Google, which has been applying its search function to the quest for longer life since 2013; parent company Alphabet has since pumped $1billion into a top-secret age-hacking research lab called the California Life Company, or Calico. Scientific brains are joined by big-data programmers, whose ambitions include regenerating fertility post-menopause via restoring the quality of egg cells to reversing damage to telomeres – the protective caps at the ends of chromosomes, the eroding of which has been linked with an increase in age-related diseases. And since measuring indicators of ageing (known as biomarkers) is cryptic-crossword complex and incredibly slow – you literally have to wait for people to age – AI computer modelling is essential to solving the hottest topic of our age: if human life is malleable, is it malleable to the point of immortality?

'Stopping the network of systems that conspire to kill us will give us extraordinary lifetimes'

OLD RUSH

Among the more surprising things about this field is that, while ancient philosophers mused about the meaning of life, Mary Shelley's *Frankenstein* revived dead body parts in the 1820s and four Keanu Reeves films bent the laws of time, there's one community that's historically had little interest in ageing: scientists. When Professor Kirkwood began researching ageing in 1974 – fascinated by why a freshwater creature called a hydra could live forever, while a mouse struggles to survive three years – his peers thought the 23-year-old was committing career suicide. 'The view was that ageing was of little scientific interest, it was just something that happened,' he tells *WH*. Ageing, it was assumed, was fixed; a person's lifespan determined by some combination of genetic lottery and their success in swerving both childhood illnesses and accidents. Undeterred, three years later, Professor Kirkwood published a paper in the journal *Nature* that argued – convincingly – that humans aren't preprogrammed to die by a fixed point, clocking off like a microwave timer; instead, ageing is a side effect of how the body allocates resources to three evolutionary processes: growing, reproducing and maintenance. Other researchers took note and, over the following decades, the gerontology elite discovered multiple mechanisms (of which telomere shortening is just one) that play a part in how humans age.

Since then, interest – and investment – in longevity research has exploded. Today, there are 500 labs globally with a clear focus in this area – 15 to 20 of which are in the UK – and 25 drugs in various stages of testing. 'That's likely five or 10 times greater than it was two decades ago, and growing fast,' says Professor Kirkwood. From studies on twins, he explains, we know that around 25% of human longevity is inherited; aside from genetics, eating well (head to page 37 for more), quitting smoking and exercising regularly are all tangible, do-today ways of tinkering with your life expectancy. His goal, like Unity Biotechnology's, is an increase in 'healthspan' – how long humans live happily and independently without age-related disease or disability – and he expects widely available longevity treatments to focus on lifestyle factors. Things like dietary supplements that boost levels of nicotinamide adenine dinucleotide (NAD) – a molecule that supports cellular function that your body produces less of as you age. 'Other possibilities are longer term and the timescale is... as yet unclear,' he explains.

FOREVER YOUNG

Academics like Professor Kirkwood are understandably guarded, having spent the best part of their professional lives turning longevity into a serious area of study. But not everyone operating in this field is prone to such caution. The headline speaker at this year's digital-only RAADfest is Dr Aubrey

Women's Health

de Grey, a California-based Brit more outspoken than a tabloid columnist clamouring to stay relevant, with a beard so biblical it would make a hipster barista weep. 'Stopping the network of systems that conspire to kill us will give us extraordinary lifetimes – thousands of years, as good as immortal,' he claims. As out-there as that sounds, this is a man with two degrees from Cambridge. He studied computer science before moving into AI research, all the while assuming longevity was quietly being solved behind the scenes. It was only in the late 1980s when he met a fruit fly geneticist – who would later become his wife – at a Cambridge graduate party and began talking to her and her colleagues about ageing, that he realised none of them had even *thought* about it. So, he pivoted. In 2000, de Grey earned a PhD in biology for a thesis on how stopping damage to mitochondrial DNA might extend lifespan, and in 2009 he co-founded the SENS Research Foundation, which funds research into medicine that can repair age-related damage – the end goal being that we will someday get old without ever becoming sick or frail.

Despite the ease with which Dr de Grey discusses immortality – a word scientists tend to swerve, presumably for its *Twilight* connotations – he's aware that reversing ageing in humans is, scientifically speaking, a big ask. 'There are many different types of damage that need to be repaired, meaning multiple rejuvenation therapies need to be developed and employed in tandem in order to restore the machinery of the human to proper working order,' he says. He's optimistic about stem cell therapies, which are being used in trials against Parkinson's disease. Eradicating senescent cells is another strategy he's pinning his hopes on. Otherwise known as 'zombie' cells, they're so-called because they stop dividing but don't disappear; instead, they linger on like a drunk party guest who refuses to go home, seeping a protein that inflames and scars tissue and contributes to osteoarthritis, Alzheimer's and glaucoma. Unity Biotechnology's senolytic drug ('senolytic' referring to strategies that remove dead senescent cells from aged tissues and organs) – UBX0101 – is undergoing phase two studies, meaning rigorous safety tests are taking place in animals. Phase three, human trials, is set for next year. It's progress like this that contributes to Dr de Grey's belief that humans have a 50:50 chance of out-pacing death entirely within 16 to 17 years, by repairing and reversing damage at a quicker rate than time passes – a concept known as reaching longevity escape velocity. 'Like an old machine with frequent parts replacements and continuous oiling, the rejuvenation will keep you ticking over and over indefinitely,' he says. He'll be 73 in 17 years' time, but he's arranged to be frozen in liquid nitrogen when he dies (prices start at £22,300, FYI) just in case rejuvenation therapies haven't kept pace.

If it feels a little crass to be talking about reserving a place in a human freezer in the midst of Covid-19, Dr de Grey believes the pandemic will only spur interest in solving later-life health issues once dismissed as mere inevitabilities, since there will be a 'much stronger and more effective case for funding research into the regeneration of elderly immune systems'. Indeed, some scientists are already integrating Covid-19 into their longevity research; scientists like Dr Alex Zhavoronkov, founder of Insilico – a start-up that uses AI for drug discovery and ageing research. So dedicated is Dr Zhavoronkov to his work that he's made his body a shrine to it. He reportedly takes 100 pills a day (90% are widely available supplements, the other 10% are untested self-experimentation), and has no interest in having a partner or kids – both of which he fears could distract him from his quest. In March this year, Dr Zhavoronkov published a paper in the journal *Ageing*, explaining that he's added Covid-19 to a list of infections that are more harmful to the elderly, which he calls 'gerolavic' – from the Greek for 'old man' and 'harmful'; he's now looking at repurposing existing drugs that could work alone or alongside a vaccine to boost its effectiveness (in older people, decline in immune function means that vaccines don't always work well). Among them is rapamycin – designed to prevent organ rejection after a transplant, which has already been shown to decrease Covid-19 infection rates in a very small sample of elderly patients; and metformin – a drug for type 2 diabetes that reduces liver sugar production and inflammation.

Some scientists are already integrating Covid-19 into their longevity research

STOP THE CLOCK

Which all means what, for you? Current life expectancy for women in the UK is 82.9 years, but a collaborative forecast by Imperial College London and the World Health Organization predicted that when a British woman turns 65 in 2030, she can expect to live for an additional 22.7 years – bringing the total to 87.7 years – based on continuing improvements in the prevention of cardiovascular diseases and cancers, safer roads and quitting smoking. But the key factor in longer living, according to the study authors, is an equitable health system 'that provides universal free access to high-quality care for prevention and treatment'. Last March, the UK All-Party Parliamentary Group for Longevity was set up to create a strategy to ensure the benefits of living longer are applied fairly to everyone in society. What the interventions being cooked up in labs will add to this remains unknown. Even if a single chronic disease was eradicated, such as atherosclerosis – the build-up of fat on artery walls that can cause heart attacks and strokes – it would actually only add two or three years on to life expectancy. But by targeting the ageing process itself, you can prevent multiple age-related disorders in one swoop – it's this that's leading some to dream of three-figure lifespans.

As with a lot in longevity science, the line between good and too-good-to-be-true is a blurry one. While any intervention that slows ageing, and your susceptibility to debilitating age-related illnesses, has to be a positive move, critics have questioned whether life-extension will ever truly be available to all, or whether it's nothing more than a hobby for millionaires. 'There's always going to be something that limits us in longevity,' says Dr Jamie Dananberg, chief medical officer at Unity Biotechnology. He explains that, 50 years ago, cardiovascular disease was the killer. Once that was under better control, cancers became more prominent. Now, socio-economic issues are the ultimate hurdle to scale in adding years to people's lives – both in making treatments available and in maintaining a population on the planet for longer. His hope is that redistributing the huge amount of money currently spent on later-life ill health will offset these other costs. For now, we wait. In 2014, the Palo Alto Longevity Prize offered $1million to anyone who could rejuvenate or extend the lifespan of a mammal by 50%. The prize money remains unclaimed. Only time will tell how much life, or how little, we really have left. WH

ADDITIONAL REPORTING: EMILY PRITCHARD. ICONS: EUCALYP/SUPALERK LAIPAWAT/FLATART AT NOUN PROJECT

DO TODAY, THRIVE TOMORROW

Gains while you wait for a miracle pill

TAKE FIVE

Half an hour of exercise a day, five times a week, meant telomeres – protective caps at the ends of chromosomes – looked nine years younger than in non or low-exercisers, found a 6,000-person study by Brigham Young University. Thank exercise's ability to suppress inflammation and oxidative stress.

PROTECT YOUR O-ZONE

Four months of omega-3 supplementation led to a 15% reduction in oxidative stress and longer telomeres in immune cells, found a report in *Brain, Behavior, And Immunity.* To get max O-ffect, lower your omega-6:omega-3 ratio – ditch sunflower oil (full of pro-inflammatory omega-6) and go big on omega-3-rich oily fish, flax and chia seeds.

STRAIN YOUR BRAIN

Do tasks that give your brain the equivalent of muscle ache, says psychologist Lisa Feldman Barrett, who studies 'super-agers' – over-65s with the memory recall of a 25-year-old. Only when challenged or stressed (say, by educating yourself about a tricky concept) do you boost the function of cerebral regions, which are thicker and better connected in super-agers.