



Highly Commended

Science Writing Year 11-12

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Science Daily

Australia June 2020

THE SCIENTIFIC ELIXIR OF ETERNAL YOUTH

*Link to subject outline: human beings culture cells for
a variety of reasons*

Newly **developed** stem cell technology can now be used to reprogram elderly cells to resemble youthful cells and cure age-related diseases like arthritis. Using cell culturing, scientists can induce pluripotency; a method to prompt cells into their early embryonic state, prior to differentiation (Papapetrou, 2016). Through **collaborative** approaches microbiologists have identified ‘Yamanaka factors’ (YFs) that work like keys to induce pluripotency - rewinding many molecular hallmarks of ageing (Nature.com, 2020). The ability to synthesise YFs within cells without having to transplant tissue is a contemporary **development** made possible only by a growing understanding of the role short-lived RNA plays in artificial synthesis of these proteins. It is clear that clinical applications are vast. Whilst applying the brake to the aging process, YFs simultaneously drive governments to accelerate redirections of budget allocations towards facilities designed to accommodate the youthful outlook of future elderly patrons.

RELEVANT BIOLOGY

Arthritis and osteoporosis alongside other age-related diseases are commonly due to senescence, a process whereby cells are no longer able to divide due to a lack of essential DNA nucleotides (The Benefits Store, 2019). To resolve this issue scientists have been investigating pluripotency (Figure 1), through exposure to YFs that transform adult cells to be indistinguishable from their younger counterparts (Nature.com, 2020). Through repeated exposure to a panel of proteins vital in embryonic development, and daily introducing short-lived RNA coding for YFs, cells begin to resemble embryo-like cells (Stanford Medicine, 2020). Over time, when applied to tissue, many diseases associated with senescence may be cured.

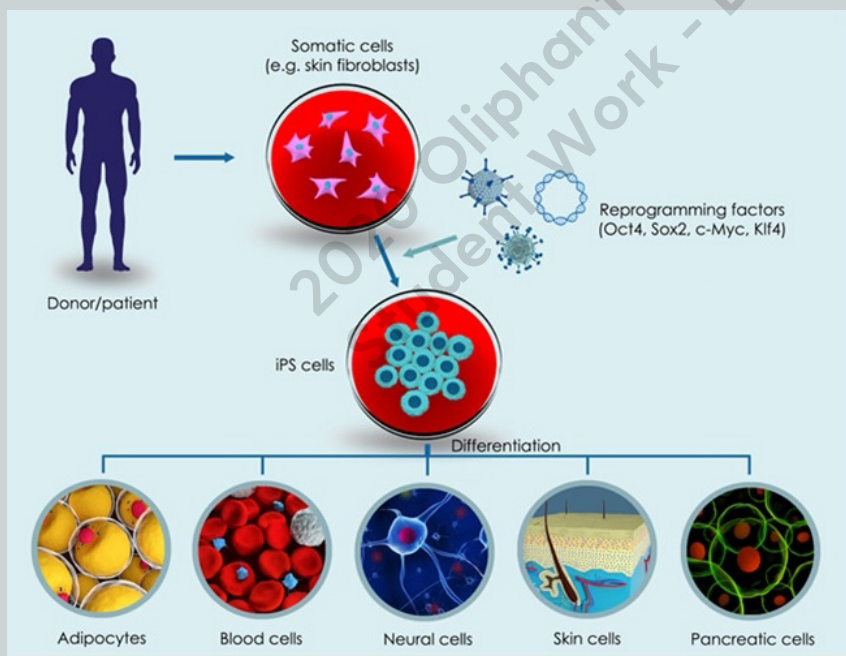


Figure 1 (Simmons, 2019): Somatic cells can be taken from elderly people and treated with reprogramming factors such as Yamanaka factors. These factors induce the cells to become induced pluripotent stem cells or iPS cells. These iPS cells are identical to early embryonic cells and thus, can differentiate into any body cell and be as effective as young cells in its role.



Advancements in methods used to induce cells to synthesise YF proteins using short-lived RNA has driven **development** of a promising new method in stem cell synthesis that may cure age-related diseases. Scientists Vittorio Sebastiano, senior author of a study conducted at Stanford University of Medicine, and Tapash Sarkar, devised a way to use messenger RNA (mRNA) to temporarily express six reprogramming factors (four YFs and two additional proteins) in skin and human blood vessel cells. Researchers were able to control the duration of exposure to mRNA signals as this molecule degrades (Stanford Medicine, 2020). Inducing pluripotency has been made significantly easier as there is no longer a need for tissue to be transplanted and thus, the procedure can be fast-tracked by alternatively injecting short-lived RNA – a cheaper approach benefitting both governments and patients thus decreasing the socio-economic divide between rejuvenated individuals and those that cannot afford this technology.

Refined review and **verification** of the link between gene expression and aging has highlighted the importance of YFs for curing age-related diseases. In a study undertaken at Stanford University, gene-expression patterns of treated cells and untreated control cells from elderly people were compared to untreated cells from younger people. This comparison revealed that after four days of exposure to reprogramming factors, elderly cells exhibited signs of aging reversal and resembled their younger counterparts. Whereas, untreated cells expressed higher levels of genes associated with known aging pathways (Stanford Medicine, 2020). These findings clearly highlight the effect of YFs on gene expression, thus significantly widening opportunities for stem cell technology beyond age-related diseases. Findings have propelled scientists to apply similar ideas to the growing field of epigenetics and simultaneously attracted funding from governments.

Preliminary research with mice and now human muscle cells has **fundamentally altered clinical approaches** to curing osteoarthritis. In an article published in support of YFs in 2020, revealed that the lifespan of mice can be extended by 20% when treated with YFs. Researches then further isolated cells from the cartilage of patients of osteoarthritis and those without age-related diseases (Stanford Medicine, 2020). They exposed diseased cells to reprogramming factors and discovered that secretion of inflammatory molecules had been decreased and the cell's ability to divide and function had significantly improved. Not only do these findings **fundamentally revolutionise clinical science and microbiology** but also open new thresholds for other diseases that can be cured using this same technique. YFs provide compelling future opportunities for cheaper treatment options, revolutionising applications and buoying the workforce through the retention of elderly employees.

The contemporary concept of utilising reprogramming factors to rejuvenate cells, to allow elderly people regain youthful strength, originated from collaboration between scientists at Stanford University. Thomas Rando, professor of neurology and director of Stanford's Glenn Centre for the Biology of Aging, has been collaborating with Howard Chang, professor of dermatology and genetics at Stanford since the early 2000's. Together (2012) they proposed using short-lived RNA, coding for reprogramming factors such as YFs, to induce cells into pluripotency to resemble an embryonic state (Stanford Medicine, 2020). In 2020, this idea was applied to mice after studying patterns of aging-associated chemical tags (methyl tags) that indicate a cell's chronological age. Scientists found treated cells were, on average, 1.5 – 3.5 years younger than elderly people with the lowest age being 7.5 years younger (Stanford Medicine, 2020). These findings form the

foundation for applications of technology that branch out from reprogramming factors. This will not only alter the future of curing age-related diseases but also the cosmetics industry which has been striving for years to uncover the key to eternal youth. Yet, such enhancing applications of this technology will parallel procedures such as Botox or plastic surgery that highlight socio-economic divides in today's society.

Worldwide, many studies concerning YFs are now published 'online' thereby increasing accessibility for review and verification. A new study published by Vittorio Sebastian from the Woods Family Faculty in Paediatric Translational Medicine in Nature Communications, revealed that elderly mice can regain their youthful strength and resemble younger mice after exposure to YFs. This article is now available globally and has prompted new studies, in particular, exposure periods

of YFs and pluripotency intensity, by Stanford Medicine (Stanford Medicine, 2020). This suite of studies uncovered that exposure for weeks caused cells to reach full-on pluripotency and erased all molecular tags, pushing them too far back along the developmental timeline. Exposure for only four days caused elderly cells to exhibit signs of rejuvenation, highlighting that long periods of exposure are unnecessary (Stanford Medicine, 2020). Publishing findings online not only fast-tracks the process of global scientific communication to propel science without having to travel internationally or have personal contact with scientists that are undertaking these studies. This global contribution to YF research means that its clinical application will quickly be available for patients and thus, governments need to act quickly to provide scientists and doctors with ethical guidelines and funding for these processes.



Contemporary studies provide evidence that the current Australian population suffers from age-related diseases that significantly reduce the time Australians are able to spend in the workforce. Approximately 24% of the population suffers from arthritis (Centres for Disease Control and Prevention, 2019), which is the second most common cause of early retirement (Ackerman, et al., 2016). Studies undertaken on YFs have revealed that arthritis, alongside many other diseases, will be able to be cured in the near future meaning people will remain in the workforce for longer. This not only means that people will be able to work for longer and earn more income, but opportunities for younger people to join the workforce will decline, potentially causing the unemployment rate in Australia to increase. Figure 2 illustrates that the 30-34 age range is the most abundantly employed in Australia and Figure 3 shows that as age increases, the prevalence of osteoarthritis increases. Thus, if these elderly individuals were cured of osteoarthritis, they will retire later, and younger individuals may not be able to work. Therefore, if this new stem cell technology was to be used throughout Australia, governments would need to contribute more funding towards supporting those that are unemployed and currently looking for jobs that are still occupied by older individuals.

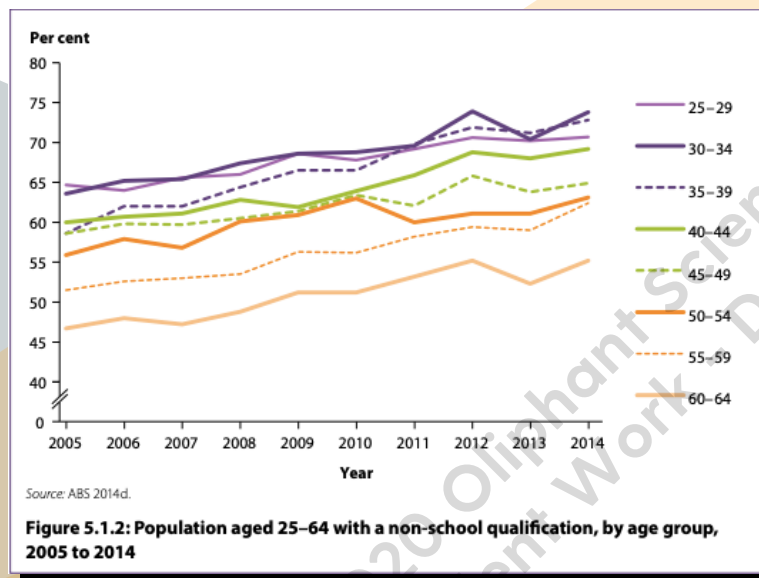
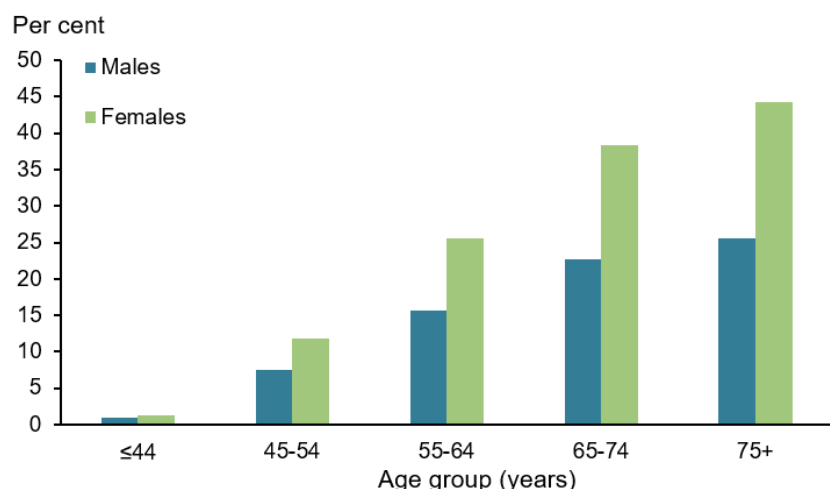


Figure 2 (Australian Government, 2015): This graph shows the profusion of different aged Australians in the workforce between 2005 and 2014. The most abundant is younger people aged between 30-34 years and the least is people aged between 60-64 years. Reprogramming factors such as Yamanaka factors may be able to allow these elderly people to become more agile and thus, remain in the workforce for longer and become a larger abundance in the workforce.

Figure 3 (Australian Institute of Health and Welfare, 2019): this graph shows the prevalence of self-reported osteoarthritis by age and sex between 2017-2018. The graph shows the trend that the number of cases of osteoarthritis increases as age increases.



LOOKING INTO THE FUTURE

The dynamic of aged-care facilities will need to be fundamentally altered to care for individuals that may no longer need physical assistance. The new YF therapy will allow elderly people to become more mobile and no longer need assistance from aged-care facilities, or, not need these facilities at all - a consideration for governments as 216,300 workers (Parliament of Australia, 2013) in a \$20 billion-a-year industry will need to be redeployed (Robertson, 2019).

Yamanaka technology can branch out to not only diseases that affect elderly people, but also gene-product related diseases and enhancement. Diabetic patients can be treated with alternate mRNA that codes for normal insulin to be synthesised. The approximate 1.7 million Australians with diabetes will no longer require treatment, thus further contributing to loss of jobs (Diabetes Australia, 2013). Not only are YFs applicable to muscle cells, they can be used on skin to make people appear younger and can become part of the cosmetic industry which amounts to \$7,417 million in 2020 (Statista, 2020). This significant industry can heavily benefit the Australian economy thus, it is vital that governments begin funding YF studies for this new pathway for the economy and society to be paved while ensuring that they support all individuals that may be affected by the widespread use of this new technology.



CONCLUSION

Stem cell rejuvenation may not be the youthful elixir many people globally are searching for, but it certainly has power to alter how we treat age related disease. The ability of YFs to rejuvenate tissue without needing transplants has allowed the application of this technology to become more cost effective and less time-consuming – making it more accessible to all Australians. For widespread application to become a reality, governments will need to consider that advancing technology will result in a more mobile population of elderly with differing needs to those currently residing in aged care facilities. Consequently, there are many social and economic factors associated with loss of jobs and late retirement that need to be considered by governments. The benefit, of course, will be a more agile elderly community that can continue to make meaningful social contributions.

Word count: 1500

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