

Unexpected outcomes: a warning for gene editing in embryos

Researchers from the South Australian Health and Medical Research Institute (SAHMRI) and the University of Adelaide have uncovered a significant hurdle to realising the potential benefits of gene editing in embryos. North American research published in 2017 seemed to indicate that gene editing in human embryos with so-called molecular scissors, CRISPR-Cas9, was highly effective in repairing defective genes in most embryos. However, the SAHMRI team says their research provides an alternative explanation for the apparent gene corrections, suggesting that the gene editing technology was not fixing small errors, but generating much larger ones. The researchers replicated the North American study in preclinical animal models, as Australia has strict legislation restricting gene editing in human embryos. "We looked beyond the small deletions, exploring larger areas of DNA," the researchers wrote. "When we searched a wider area, we found that repair of the DNA break generated by 'molecular scissors' resulted in deletion of large stretches of DNA." CRISPR-Cas9 is used by scientists to cut specific regions of a cell's DNA. Repair of the cut can alter the target DNA sequence, resulting in a specific change or "edit", so that faulty genes can theoretically be repaired. However, as the SAHMRI researchers have shown, DNA can sometimes be lost during the repair process, resulting in large deletions that would not restore function to the faulty gene. "Understanding the fundamental mechanisms by which these tools work [is an important advancement] for research and for clinical translation to treat a host of genetic diseases." The SAHMRI research findings were published in *Nature*.

<https://www.nature.com/articles/s41586-018-0380-z>

Exercise for mental health: more may not be better

A study of 1.2 million Americans has found that people who exercise report having 1.5 fewer days of poor mental health per month than people who do not exercise. The authors of the largest observational study of its kind, published in *The Lancet Psychiatry*, found that team sports, cycling, aerobics and going to the gym were associated with the biggest reductions. More exercise was not always better, and the study found that exercising for 45 minutes three to five times a week was associated with the biggest benefits. Small reductions were still seen for people who exercised more than 90 minutes a day, but exercising for more than 3 hours a day was associated with worse mental health than not exercising at all. The authors noted that people undertaking extreme amounts of exercise may have obsessive characteristics that could place them at greater risk of poor mental health. The researchers analysed data from 1.2 million adults who completed the Behavioural Risk Factor Surveillance System surveys in 2011, 2013 and 2015, which collected demographic data and information about their physical and mental health, and health behaviour. Participants were asked to estimate how many days in the past 30 days they would rate their mental health as "not good" because of stress, depression or emotional problems. They were also asked how often they exercised in the past 30 days outside their regular job, as well as how many times a week or month they exercised and for how long. Compared with people who reported no exercise, people who exercised reported a reduction of 43.2% in the mean number of days of poor mental health (2.0 days/month *v* 3.4 days/month for people who did not exercise). The reduction in number of poor mental health days was greater for people who had previously been diagnosed with depression, for whom exercise was associated with 3.75 fewer days of poor mental health than for people who did not exercise, a 34.5% reduction (7.1 *v* 10.9 days/month). Even completing household chores was associated with an improvement of about 10%, or half a day per month.

[https://www.thelancet.com/journals/lanpsy/article/PIIS2215-0366\(18\)30227-X/fulltext](https://www.thelancet.com/journals/lanpsy/article/PIIS2215-0366(18)30227-X/fulltext)

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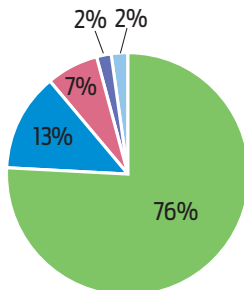
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Dr Chris Schilling is an Associate Director of KPMG Australia, and a health economist teaching at the University of Melbourne. He discusses predictors of inpatient rehabilitation after total knee replacement, to accompany his co-authored research published online on 27 August 2018.

Associate Professor Judy Kirk is the Head of the Familial Cancer Service at Westmead Hospital in Sydney. She injects a note of caution into the debate about Medicare-funded cancer genetic tests, to accompany her co-authored perspective published in this issue.

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