

# Young blood turns back time

Could transfusions reverse some of the ravages of ageing? **Helen Thomson** reports

IT SOUNDS like the dark plot of a vampire movie. In October, people with Alzheimer's disease will be injected with the blood of young people in the hope that it will reverse some of the damage caused by the condition.

The scientists behind the experiment have evidence on their side. Work in animals has shown that a transfusion of young mouse blood can improve cognition and the health of several organs in older mice. It could even make those animals look younger. The ramifications for the cosmetics and pharmaceutical industries could be huge if the same thing happens in people.

Disregarding vampire legends, the idea of refreshing old blood with new harks back to the 1950s, when Clive McCay of Cornell University in Ithaca, New York, stitched together the circulatory systems of an old and young mouse – a technique called heterochronic parabiosis. He found that the cartilage of the old mice soon appeared younger than would be expected.

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It wasn't until recently, however, that the mechanisms behind this experiment were more clearly understood. In 2005, Thomas Rando at Stanford University in California and his team found that young blood returned the liver and skeletal stem cells of old mice to a more youthful state during heterochronic parabiosis. The old mice were also able to repair injured muscles as well as young mice (*Nature*, doi.org/d4fkt5).

Spooky things seemed to happen in the opposite direction,

too: young mice that received old blood appeared to age prematurely. In some cases, injured muscles did not heal as fast as would be expected.

Several other experiments have shown similar effects. In 2012, Amy Wagers at Harvard University showed that young blood can reverse heart decline in old mice. Her team paired healthy young mice with old mice that had cardiac hypertrophy – a condition which swells the size of their heart – and connected their circulatory systems. After four weeks, the old mouse's heart had shrunk to the same size as its younger partner. In this experiment, the young mouse

was seemingly unaffected by the old blood, its heart not changing in size.

Once the researchers had ruled out the effect of reduced blood pressure on the older mice, they identified a protein in the blood plasma called growth differentiation factor 11 (GDF11) that appeared to fall with age. To see if it was linked to the rejuvenating effects, the team gave old mice with enlarged hearts daily injections of GDF11 for 30 days. Their hearts decreased in size almost as much as they had in the parabiosis experiments (*Cell*, doi.org/q2f).

A year later, the same team showed in mice that daily

injections of GDF11 also increases the number of blood vessels and the number of stem cells in the brain – both factors known to improve brain function. A separate team led by Tony Wyss-Coray at Stanford performed similar experiments. His team injected blood plasma from young mice into old mice and showed an improvement in the old mice's physical endurance and cognitive function (*Nature Medicine*, DOI: 10.1038/nm.3569).

In both mice and humans, GDF11 falls with age. We don't know why it declines, but we know it is involved in several mechanisms that control growth. It is also thought to mediate



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some age-related effects on the brain, in part by activation of another protein that is involved in neuronal growth and long-term memory.

So the billion-dollar question is: would a GDF11 boost have the same effect in humans? Wyss-Coray thinks it will, having taken the next step of injecting young human blood plasma into old mice. His preliminary results suggest that

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human blood has similar rejuvenating benefits for old mice as young mouse blood does.

"We saw these astounding effects," he says. "The human blood had beneficial effects on every organ we've studied so far."

Now, the final step – giving young human blood plasma to

older people with a medical condition – is about to begin. Getting approval to perform the experiment in humans has been relatively simple, says Wyss-Coray, thanks to the long safety record of blood transfusions. He warns against swapping blood at home because transfusions need to be screened for disease, matched for blood type and the plasma needs to be separated out. "Certainly you can't drink the blood," he says. "Although obviously we haven't tried that experiment."

So in early October, a team at Stanford School of Medicine will give a transfusion of blood plasma donated by people under 30 to older volunteers with mild to moderate Alzheimer's.

Following the impressive results in animal experiments, the team hopes to see immediate improvements in cognition, but Wyss-Coray cautions that it is still very experimental. "We will assess cognitive function immediately before and for several days after the transfusion, as well as tracking each person for a few months to see if any of their family or carers report any positive effects," he says. "The effects might be transient, but even if it's just for a day it is a proof of concept that is worth pursuing."

All researchers involved in the work agree that GDF11 is unlikely to be the only factor that keeps organs youthful. "It's too optimistic to think there would be just one factor," says Francesco Loffredo, who studies the effects of young blood in old animals at Harvard University. "It's much more likely to be several factors that exert these effects in combination."

Loffredo says the approach of testing the effects of young blood in people with Alzheimer's is fascinating, but reckons in the long-term it is best to continue to strive to identify the individual factors that are exerting the rejuvenating effects so that they can be translated to humans more easily. "Imagine if you had to be



Human blood plasma

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transfused with young blood all the time – it's hard to imagine as a therapy. Who is going to be donating all this blood?" he asks.

Wyss-Coray agrees. "It would be great if we could identify several factors that we could boost in older people," he says. "Then we might be able to make a drug that does the same thing. We also want to know what organ in the body produces these factors. If we knew that, maybe we could stimulate that tissue in older people."

## Chemotherapy aid

Alessandro Laviano at the Sapienza University of Rome in Italy says that the research on diseases of ageing certainly holds promise, but he is more interested in the potential use of young blood in chronic disease. People with cancer who resist muscle loss have better chances of survival, he says. "So I'd like to consider the possibility of using these youthful factors in young blood to reduce the muscle wasting that occurs during chemotherapy."

Before moving to clinical trials in people with cancer we need to learn more about the dynamics of the beneficial factors in blood, says Laviano, such as when they are at their peak. Do we reach a peak at 5 or 35 years? "We just don't know," he says. He would also like to investigate what happens when you give "too much" GDF11 – does it result in extra benefit or a negative outcome?

Laviano is currently looking at the effect of GDF11 on tumours in animals to see if it inhibits their growth, but he would also like to start an observational trial in humans. It would be very simple, he says, to find the age of the blood given to people receiving transfusions and test whether it has any effect.

"I certainly think that this therapy might be beneficial in a number of different conditions," says Wyss-Coray. "Blood might contain the fountain of youth after all. And it is within us all – that's the crazy thing. It just loses its power as we age." ■



Time to give something back