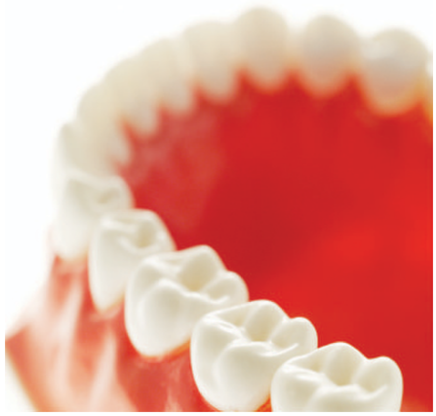
Laser therapy to regenerate teeth

Current clinical dentistry is predominantly focused on restorative approaches involving the replacement of teeth with inert materials, but tissue regeneration is an attractive alternative because artificial materials eventually fail and do not provide the same functionality as tissue. David Mooney and his colleagues at Harvard School of Engineering and Applied Sciences (Cambridge, MA) and the Wyss Institute for Biologically Inspired Engineering (Boston, MA) collaborated with biomedical researchers to demonstrate how low-power light can be used to trigger stem cells inside teeth to regenerate dentin, the hard tissue that is similar to bone and makes up the bulk of the teeth. Because lasers are already used in dentistry, it is possible that such light-based treatment could be used in dental regeneration in people. "Our treatment modality does not introduce anything new to the body, and lasers are routinely used in medicine and dentistry, so the barriers to clinical translation are low," explained Mooney.

Anecdotal evidence suggests laser therapy can reduce pain and inflammation and promote regeneration in cardiac, skin, lung and nerve tissues, effects that are collectively termed 'photobiomodulation.' But a direct link between laser treatment and stem cell biology has not yet been clearly demonstrated.

Mooney and his team drilled holes in the molars of rats. They treated the tooth pulp inside the molars, which contains abundant endogenous adult dental stem cell populations, with non-ionizing, low-power laser exposure and applied temporary caps to the molars. After 12 weeks, x-ray imaging and microscopy confirmed that the laser treatment triggered dentin formation in the molars (*Sci. Transl. Med.* **6**, 238ra69; 2014). The dentin was similar in composition to normal dentin, although with slightly different morphology.

Next, they carried out cell culture–based experiments to unveil the molecular mechanism responsible for the regenerative effects of the laser treatment. The laser induced reactive oxygen species, which activated the latent transforming growth factor beta-1 (TGF-beta1) complex. TGF-beta1 in turn triggered the dental stem cells to differentiate into odontoblasts, the bone cells that form dentin. This finding is consistent with recent studies highlighting



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the role of TGF-beta1 as a master regulator of stem cell differentiation. Mice lacking TGF-beta1 or treated with a TGF-beta inhibitor did not form dentin in response to the laser therapy.

The study lays the foundation for other clinical applications in restorative dentistry and regenerative medicine. "We are also excited about expanding these observations to other regenerative applications with other types of stem cells," said the study's first author Praveen Arany.

Kara Rosania

WHEEL RUNNING NOT JUST FOR LAB MICE

The benefits of exercise for health are becoming increasingly clear. Wheel running is often used in the laboratory to study the effects of enhanced activity levels in rodents. The biological significance of wheel running remains elusive, however, making the behavior difficult to interpret. Some have argued that wheel running is not a natural behavior but an artifact of captivity and that it may be a sign of neurosis or stereotypy.

Johanna Meijer and Yuri Robbers (Leiden University Medical Centre, the Netherlands) sought to address these concerns by studying whether wheel-running behavior is exhibited voluntarily by animals in the wild. The team placed a running wheel with automatic movement detection, a passive infrared motion sensor, a camera equipped with night vision and a food tray to attract animals inside a cage-like structure that could be entered by any animal up to the size of a rat. Cages were placed in two locations where feral mice live: a green urban area and a dune area not accessible to the public.

Meijer and Robbers collected video at these sites for more than 3 years and analyzed more than 12,000 video fragments in which wheel movement was detected by the motion sensor. The wheel was moved in both locations not only by mice but also by shrews, rats, snails, slugs and frogs (*Proc. Royal Soc. B* **281**, 20140210; 2014). Mice and some shrews, rats and frogs that manipulated the wheel were seen to leave the wheel and then enter it again within minutes, indicating that wheel running was intentional for these animals.

Wild mice ran in the wheels for lengths of time similar to those reported in captive mice. The median running speed of wild mice was lower than that of their captive counterparts, but wild mice reached higher maximum speeds. When food was no longer provided at the urban site, the number of visits to the recording site decreased, but the fraction of visits that included wheel running increased, suggesting that the animals found the activity inherently rewarding.

Research into the health effects of exercise depends on the use of running wheels, and for such research, it would be potentially problematic if wheel-running behavior was stereotypic rather than elective. But this study suggests that wheel running is in fact a voluntary behavior. The authors wrote, "Our findings may help alleviate the main concern regarding the use of running wheels in research on exercise."

Kara Rosania