Aquarium fish and smart implants show the way to better bone health

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People who suffer from back pain may get relief from research showing that electrical fields and fish genes provide novel building blocks for a healthy skeleton.

Back pain can be excruciating and is increasingly common with ageing populations. Spinal surgery is on the rise in many countries, including costly—and often risky—spinal fusion surgery. As many as 18% of spinal surgeries fail, leading to devastating complications for patients.

Spinal fusion surgery fuses two vertebrae together to stabilise the area and reduce pain. Much depends, however, on the ability of the vertebrae to grow new bone matter and fuse properly following the operation.

Bind the gap

'In a lot of cases, this doesn't happen because patients are unable to bridge that gap in the bone,' said John Zellmer, coordinator of the EU-funded SmartFuse project and co-founder of Swedish medical-device company Intelligent Implants.

The inspiration for SmartFuse came from a meeting between Zellmer's brother, Swedish medical doctor Dr. Erik Zellmer, and an Irish biomedical engineer named Dr. Rory Murphy.

Both were struck by how many spinal surgeries fail due to lack of bone growth. Yet it has been known for some time that bone remodels naturally using electric signals generated by the body itself.

This led the two doctors to set up a company to develop a first-of-its-kind medical grade implant able to use carefully targeted electrical signals to accelerate, control and monitor bone growth.

'We're kind of hijacking the body's own signalling by creating an electric field right at the spot where we want the bone to grow, around the implant,' said John Zellmer.

The tiny and easy-to-use orthopaedic implant is made from PEEK plastic and titanium with a tightly sealed array of electrodes inside.

Sheep trials

The project began in April 2022 and runs through November 2024, with the EU financial support coming through the European Innovation Council.

Initial clinical trials conducted in sheep are very promising. In just six weeks, sheep using the device had three times as much bone as in those without it, according to Zellmer.

It can be a long road to recovery for patients after back surgery, taking nine to 12 months for them to grow the bone required for fusion to be completed. Often, failure goes undiagnosed for a year or more after surgery and it is difficult for doctors to gauge how well the healing process is progressing.

With SmartFuse, the implant receives signals wirelessly and is connected to a cloud-based portal providing doctors with unprecedented insight into how the bones are fusing.

As bone grows around the implant, the electric signals are increasingly smothered. Detectors can then "sense" the declining signal and estimate how much bone is present.

This ability to see how a patient is progressing would be a valuable asset for both doctor and patient. While still early days, the company hopes to obtain regulatory approval in Europe and the US by 2028.

Ancient scaffolding

Meanwhile, two common species of aquarium fish—the zebrafish and medaka—provided inspiration to a team of young researchers who trawled for clues on how to treat common skeletal problems in humans.

The skeleton has served as a scaffold for vertebrate animals—those with backbones—for about 400 million years. Since evolution works on the old adage "if it ain't broke, don't fix it," fish, reptiles, birds and mammals still often use the same genes and proteins to make their skeletal framework.

So, while fish and people are obviously quite different, similarities allow scientists studying fish skeletons to make interesting medical discoveries.

'Many genes that cause skeletal problems in humans have now been shown to generate similar problems in fish,' said Dr. Marc Muller, who led the EU-funded BioMedaqu project and is a biologist at the University of Liège in Belgium.

BioMedaqu, which ended last month after four-and-a-half years, brought together experts in fish and human skeletons. Muller and his colleagues came up with the idea of a project for training young researchers while chatting over a beer at a conference in the Algarve, Portugal.

'We thought: "why not bring together people from aquaculture, fish biology and biomedical research to share ideas, maybe even technologies, to study skeletal biology?"' said Muller.

Fifteen early stage researchers were involved in BioMedaqu, which resulted in a stream of discoveries.

One studied a bone disease in people—*osteogenesis imperfecta*—that she replicated by mutating the equivalent gene in zebrafish. The importance of phosphorous for fish bone health was investigated by another scientist. At a Parisian hospital, research revealed the importance of several genes for the development of osteoporosis in children.

Meanwhile, the Liège laboratory studied the role of genes involved in human osteoarthritis. The lab also investigated extracts from marine animals for their potential to benefit skeletal development—in both fish and people.

Skeletal matters

The overall aim of the work was to obtain deeper insights into the fundamental mechanisms that can cause skeletal malformations in humans—and in farmed fish.

The network combined stakeholders from seven European universities, a US research hospital and the French National Institute for Health and Medical Research (INSERM). Commercial interests in the aquaculture and fish food sector were also represented.

The structure of the project encouraged the flow of information and people between the biomedical and aquaculture sectors, and between academic and applied sectors. And research also revealed information of interest to the fish farmers in search of more sustainable feed options.

For example, several projects looked at the influence of trace elements such as zinc, selenium, vitamins, fatty acids and probiotics on the development of fish skeletons and how feed might be improved by adding them to the mix.

The research advanced knowledge among the scientists in a way that will ultimately benefit aquaculture, understanding of skeletal biology and, ultimately, human patients, according to Muller. More findings from the researchers are on the way.

More information: BioMedaqu
SmartFuse
EU-funded health research and innovation

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