The quest to bring osteoarthritis to its knees

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Millions of people in Europe and elsewhere suffer degeneration of joint cartilage in the knee, driving EU research into better treatments.

Beyond making a tray of sushi rolls delectable, the potential uses of seaweed are growing fast amid discoveries that it may do everything

from improve diets to ease bowel disease.

Now seaweed is the focus of EU research into helping the millions of people worldwide who suffer from degeneration of cartilage in that oh-so-crucial joint: the knee.

Dance away

Called osteoarthritis of the knee, the condition typically emerges as of middle age and causes joint pain as well as stiffness. The hindrance can leave even the shyest and clumsiest dancers in their youth yearning for a renewed chance to strut their stuff on the floor.

"People with knee osteoarthritis have severe pain," said Liam Farrissey, chief executive officer of an Irish medical-device company called CrannMed. "They can't sleep, they can't move."

There are currently no ways to stop or reverse osteoarthritis of the knee and pharmaceutical treatments such as pain killers are unsuitable for long-term use.

But new insights into the condition could offer a solution: seaweed injections.

Around 360 million people globally face osteoarthritis of the knee, according to the World Health Organization. In Europe, an estimated 13% of adults have the joint condition. Most endure 10 to 15 years of increasing pain and decreasing agility before having to resort to knee-replacement surgery.

Osteoarthritis used to be thought of as just wear and tear. Bone rubbing on the knee cartilage causes it to break down, leaving bone rubbing on bone.

But it's now regarded also as an inflammatory disease. As the knee wears down, it becomes inflamed and new, tiny blood vessels known as "neovessels" form around the inflammation.

All this adds to the pressure on the knee joint, which in turn increases erosion and leads to more inflammation and additional neovessels.

"There is an inflammatory cascade that accelerates the breakdown of the cartilage in the knee," said Farrissey.

Renewed promise

He leads a research project to advance a breakthrough treatment for osteoarthritis of the knee based on seaweed.

Called EmboSure after the new method, the two-year project runs through April 2024.

The research builds on—and offers more promise than—a discovery almost a decade ago that briefly created hopes of a breakthrough.

In 2014, scientists in Japan came up with the idea of destroying the neovessels to cure the inflammation.

In a series of studies, the scientists injected tiny particles known as microspheres into the knees of people with osteoarthritis. The idea was that the spheres would block blood flow to the neovessels and kill them, a process known as "embolization."

People reported big reductions in pain and MRI scans showed improved knee function, with the effects lasting for at least four years.

But there was a catch: the researchers relied on microspheres made of

imipenem—a powerful broad-spectrum antibiotic used to treat multidrug-resistant bacterial infections.

As a result of concerns about antimicrobial resistance and the declining effectiveness of imipenem, its widespread use in a non-infectious disease was ill-advised.

"Great outcome with lots of potential, but what they used is not something that can be launched globally," said Farrissey.

Alginate spheres

His project has created microspheres composed of alginate, a carbohydrate derived from seaweed. The beads also contain an enzyme that breaks down the alginate.

The spheres themselves break down soon after they're injected, so the blocking of the neovessels lasts only some hours.

This means that there is little risk of them cutting the blood flow to other blood vessels and that the patient can go home without the need for further treatment.

"These neovessels are kind of artificial vessels created because of the inflammation, so if you block them for a couple of hours they are dead," Farrissey said.

He said the project has so far conducted laboratory and pre-clinical tests in animals and the trials have gone well.

The goal over the next year is to start clinical trials, which could lead to the treatment being available towards the end of 2025.

"What we are doing is launching a product that allows this embolization procedure to be done on a more global level," Farrissey said.

Twisted knee

As well as being a degenerative disease, osteoarthritis of the knee can develop following a traumatic injury that causes a complex meniscus tear.

Such damage can occur by twisting a knee while, say, playing a sport such as football.

The meniscus provides shock-absorbing protection to the articular cartilage as well as stability to the knee.

Nonetheless, many meniscus tears are still treated by removing the damaged tissue—a procedure known as meniscectomy. And this creates its own difficulties.

"People who have had their meniscus removed at a relatively young age develop osteoarthritic changes in the knee joint much, much earlier than the natural course of this disease," said Dr. Evelyne Hasler, a senior scientific education manager at a Swiss regenerative medicine company called Geistlich Pharma.

While nowadays surgeons try to repair torn menisci if possible or remove only a small amount of tissue, not all tears are fixable.

"If the meniscus tissue is so damaged that a suture repair would not work anymore, then you need another solution to replace the damaged tissue instead of just cutting it," said Hasler.

She is administrative coordinator of a project that came up with an

answer. Called MEFISTO, the project began in April 2019 and is due to run through May 2024.

It is led by Professor Elizaveta Kon of Humanitas University in Milan, Italy and involves 13 partners from eight European countries.

Biodegradable implant

The researchers developed two novel approaches to treat meniscus loss. One is based on a biodegradable implant to regenerate meniscus tissue in younger patients and the other is based on a non-biodegradable device to replace lost tissue in older patients.

The biodegradable scaffold is designed to interact with the native meniscal tissue. The implant is 3D printed from collagen, the human body's main structural protein. The scaffold works with biological growth factors and drug-loaded particles to stimulate meniscus regeneration.

"With this approach, we want to regrow missing meniscus tissue and ultimately stop patients needing a knee prosthesis at a young age," Hasler said.

She said that developing the implant has been challenging because, while the meniscus has a vascular outside region, there are no—or very few—blood vessels in the middle of the structure.

In the lab, the MEFISTO team has created menisci that support this vascular structure. The researchers are now gearing up to test the implant in animals.

If successful, the team intends to pursue the project and a future step includes testing the implant in a clinical study in patients.

More information:

- EmboSure
- MEFISTO

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