Toward regrowing cartilage

Novartis researchers aim to improve the lives of patients with osteoarthritis.

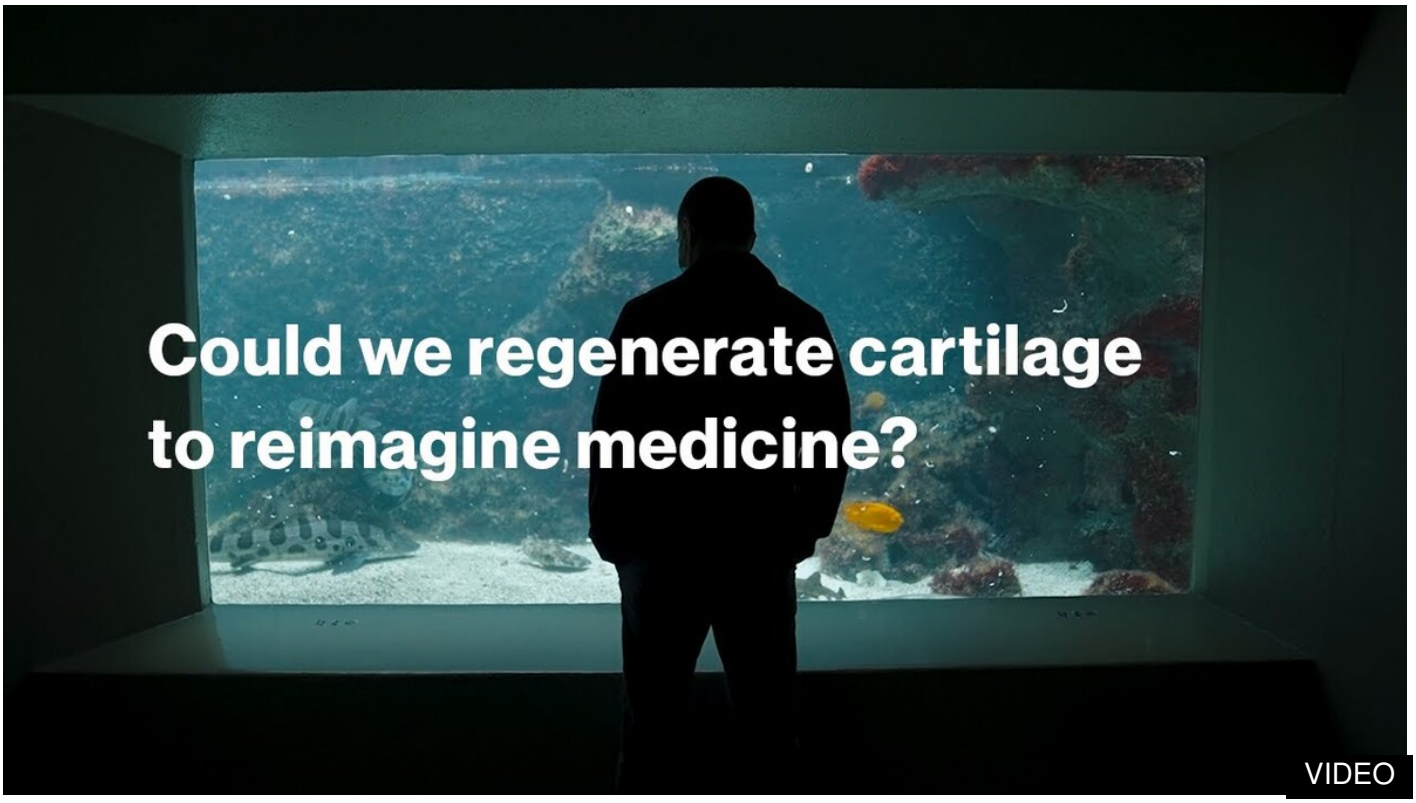
By Maryse Jandrasits | Sep 14, 2021

In a recent wildlife documentary, a shark bites off an octopus's arm. The octopus hides for days and then reappears. Its tentacle has started to grow back.

Unlike octopuses, humans can't regrow body parts. At least, not yet.

Novartis researchers are inspired by these wild survival artists. They are developing a treatment that has the potential to regrow cartilage in the knees of patients with osteoarthritis. Though not quite equivalent to the regenerative powers of wildlife, it's an ambitious attempt to regenerate tissue. The approach is part of a wider effort at Novartis to find a way to treat osteoarthritis.

The condition occurs when the smooth cushion that protects a joint has degenerated over time until there is little protection left. Advanced patients often need surgical joint replacements. If successful, this regenerative approach could reduce pain, avoid knee replacements and enable patients to regain mobility.



Osteoarthritis affects more than 300 million people worldwide.[1] It is the single most common cause of disability in older adults.[2] As the global population continues to age, and knee injuries become more common in younger people, the burden of osteoarthritis will increase.[3]

To date, there are no approved disease-altering treatment options. Existing medicines focus on relieving symptoms rather than addressing the source of the disease. People may get temporary pain relief but nothing can prevent the disease from getting worse.

“The options that are out there at the moment only mask the progression of osteoarthritis,” says Marina Milutinovic, who is leading the development of a number of potential treatments for osteoarthritis at Novartis. “There is a huge need for treatments that can stop or, ideally, even revert the disease.”

The “wear and tear” disease

Cartilage enables knee joints to move smoothly. But in some people, factors like injuries and obesity can erode cartilage and cause pieces to come loose.

In response, the knee’s cleaning service springs into action. This natural housekeeper rounds up a team of proteins that dispose of discarded bits of cartilage.

If temporary, this process helps get rid of detached tissue. In patients with osteoarthritis, however, the cleaning operation persists and can damage healthy cartilage. The protective cushion wears away. Eventually, bones rub together and cause pain, stiffness and impaired movement.

“Skin heals. Bones heal. But if you have a cartilage lesion, it only gets worse over time,” says Celeste Scotti, who leads the clinical development team working on this investigational treatment.

> There is a huge need for treatments that can stop or, ideally, even revert the disease.
>
> **Marina Milutinovic**

The disease mostly affects older people, but obesity, injuries and contact sports can accelerate the condition. More than half of patients diagnosed with symptomatic knee osteoarthritis will eventually need a knee replacement.[4]

Patients with severe pain due to osteoarthritis stop walking and moving regularly. They often suffer from accompanying illnesses such as depression and cardiovascular disease. Many must take time off or even stop work or education.

“It is really a serious disease that drastically limits people’s mobility,” says Matthias Schieker, who leads the early-phase development of several investigational medicines for osteoarthritis at Novartis.

Cartilage is a protective cushion that enables knees and other joints to move smoothly. In patients with osteoarthritis, it wears away until bones rub together and cause pain, stiffness and impaired movement.

Regeneration in action

Milutinovic and her team are working on an experimental approach to treating osteoarthritis. The hope is that their investigational therapy, which was discovered by Novartis researchers, could potentially coax cartilage in the knee to grow and fill existing pits and gaps with healthy tissue that functions like natural cartilage.

In early studies of the therapy, researchers at Novartis had to figure out how to verify that regenerated cartilage was high quality without relying on painful biopsies. Advanced magnetic resonance imaging (MRI) technologies enabled them to noninvasively inspect knee joints before and after treatment and visualize regenerated cartilage at a macromolecular level.

Novartis researchers are working on an experimental approach to treating osteoarthritis. Their hope is that their investigational therapy could potentially regrow healthy cartilage. MRI technologies enabled them to visualize how their intervention made cartilage regrow. The images show how a femoral cartilage lesion is being filled with healthy cartilage over the course of six months after the administration of the investigational medicine. Further testing in clinical studies is required to demonstrate that the experimental therapy is safe and effective.[5]

Scotti remembers the first time he saw holes in cartilage close over time. “It was an eye-opening moment,” he says. “This doesn’t happen by chance. We know that cartilage lesions only get bigger over time. So in preliminary studies we were really seeing that our intervention made the cartilage regrow.”

Further testing in clinical studies is required to demonstrate that the experimental therapy is safe and effective, and a Phase IIb study is underway at various sites around the world. If successful, the treatment could help patients experience less pain, regain mobility and avoid knee replacement surgery.

“Our ultimate goal is to improve patients’ quality of life,” Milutinovic says.

Novartis researchers are working on an experimental approach to treating #osteoarthritis.

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