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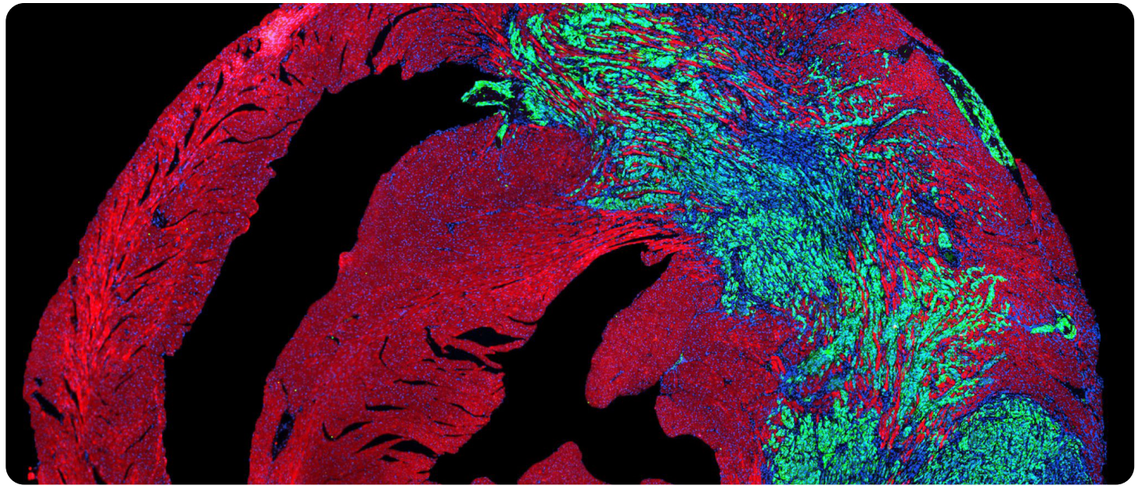

Image of lung cancer cells (in green) growing in a heart, in which cardiomyocytes are stained in red. Nuclei are stained in blue.

ACADEMIA IN ACTION

Mechanomedicine, a new therapeutic language for cancer?

The heart almost never develops cancer. Prof. Serena Zacchigna's team at the International Centre for Genetic Engineering and Biotechnology (ICGEB) and at the University of Trieste, Italy have worked out why, and stumbled on a new idea for fighting the disease: not with a drug, but with force. Their finding, that the muscle's mechanical motion switches off the genes cancer cells need to divide, opens a field she calls mechanomedicine, another therapeutic language to set beside chemistry.

Prof. Serena Zacchigna
Cardiovascular Biology Laboratory, International Centre for Genetic Engineering and Biotechnology . University of Trieste . Italy

For years, Prof. Serena Zacchigna has worked to make hearts heal, not to cure cancer. Her team in Trieste had been working at the question as to why the muscle cells of an adult heart stop dividing, so the organ cannot repair itself after a heart attack. That question led somewhere no one expected.

"For years, we had been studying cardiac regeneration and asking why adult cardiomyocytes stop proliferating," she told nexxahealth. "This led us to look at the mechanical load (the physical force, stress, or pressure applied to a biological mechanical system), as we, and others, observed that unloading the heart can reactivate cell proliferation. At some point we asked a very simple question: if mechanical load inhibits proliferation during regeneration, could it also inhibit proliferation in cancer? This connection between regeneration and cancer was probably the conceptual step that allowed us to see something that had been in front of us all along."

The hunch was a fit for a fact that every pathologist knows, yet few can explain. The heart, one of the busiest organs in the body, almost never develops a tumour, and the cancer that spreads there from elsewhere tends to grow far more slowly than it does in the lungs, the liver or the bones. In April 2026, in the journal Science, Prof. Zacchigna's team and a European network of collaborators reported why: the heart's constant motion is itself a form of protection.

Turning the force up and down

To test the idea, the team controlled the heart's mechanics directly. Working with mice, they mechanically 'unloaded' the heart, and under the reduced strain, were able to confirm that tumour cells within it proliferated markedly more. In the laboratory they grew engineered heart tissues, small pieces of beating muscle whose load they could dial precisely, and seeded them with cancer cells. The pattern held everywhere: while the tissue beat and bore load, tumour growth slowed; reduce the load, and the cancer cells resumed dividing.

"Mechanobiology itself is not new," Prof. Zacchigna says. "We have known for a long time that cells respond to mechanical signals, and cancer researchers have extensively studied variables such as extracellular matrix stiffness. What was less explored was the possibility that the dynamic movement of an organ itself could regulate tumour growth. The heart gave us a unique way of seeing this because it experiences an extraordinarily strong, rhythmic mechanical stimulus throughout life."

I would not describe mechanomedicine as an alternative to pharmacology. I see it as another therapeutic language.

PROF. SERENA ZACCHIGNA, CARDIOVASCULAR BIOLOGY LABORATORY, ICGEB, AND UNIVERSITY OF TRIESTE, ITALY

When force reaches the genes

The striking part is where the force ends up. Mechanical load does not simply press on a cancer cell from the outside; it reaches inside and changes how the cell reads its DNA. A protein called Nesprin-2 acts as the mechanosensor, converting a physical force into a biochemical signal, and under load the cell's chromatin, the way its DNA is packaged, is remodelled so the genes that drive division are harder to switch on.

The human tissue pointed the same way. "We compared cardiac metastases with primary tumours and metastases from the same patients in other organs," Prof. Zacchigna says. "We observed that cancer cells growing in the heart showed a distinct molecular adaptation. In particular, histone demethylases emerged as the most strongly upregulated genes in cardiac metastases, and we subsequently observed this phenomenon across different cancer types."

"Histone methylation is a mechanism by which cells quickly adapt and shape their gene expression profile in response to environmental stimuli," she explains, "and our subsequent experiments suggested that this was paralleled by extensive remodelling of the chromatin, switching on genes that control cancer cell proliferation."

From a dish to a patient

That human check is what lifts the work from a peculiarity in mouse to a claim about real disease, and it did not arrive as a single flash of insight.

"I would not describe it as one cinematic eureka moment. Science rarely works that way," Prof. Zacchigna says. "It was more the accumulation of independent observations suddenly beginning to tell the same story. That is probably the most exciting moment in research: when results from very different experiments start converging on one biological explanation."

It took an unusually broad team to get there, drawing together cardiologists, oncologists, bioengineers and computational modellers across a European network that included the University of Trieste and ICGEB, the Monzino Cardiology Centre in Milan, the European Institute of Oncology, and groups in Innsbruck, Hamburg, Oslo and London.

What mechanomedicine could treat

"I think the most realistic starting point is superficial solid tumours, such as melanoma or other skin tumours, where mechanical stimulation can be applied locally, precisely and non-invasively," Prof. Zacchigna says. "This is one reason why we are developing wearable devices that reproduce heartbeat-like mechanical stimulation to be applied on the skin."

The broader question interests her more. "Are there other organs whose mechanical environment naturally suppresses tumour growth? Skeletal muscle, the lung and other continuously or intermittently moving tissues are obvious candidates, although their mechanical environments are very different from that of the heart." Prevention is on her mind too. "Metastasis requires cancer cells to adapt to very different physical environments as they move from one organ to another. Our findings suggest that mechanical compatibility between a cancer cell and the tissue it enters may be one determinant of whether a metastasis successfully grows."

A drug, not just a device, may follow. "There may also be a pharmacological route," she adds. "If we identify the molecular and epigenetic changes induced by mechanical stimulation, we may eventually be able to mimic some of its effects with drugs rather than devices." But she is emphatic about the distance still to travel. "We have discovered a biological principle, not yet a therapy. We need to optimise the devices, establish dose and safety, validate efficacy in additional preclinical models and then move into first-in-human studies... it may be perhaps five to ten years before we know whether this can benefit patients. The important point is that we now have a mechanism that can be tested and translated."

She is just as clear about what mechanomedicine is not. The strongest objection, she says, is that "cancer is highly heterogeneous, while mechanical stimulation sounds like a very simple intervention. Why should something as complex as cancer respond to something as simple as rhythmic force?" Her answer reframes the claim. "We are not proposing that mechanical stimulation will replace molecularly targeted therapies, immunotherapy or chemotherapy. We are asking whether mechanics represents another layer of tumour biology that we have largely ignored therapeutically."

"Cancer cells do not live in isolation. They constantly sense stiffness, pressure, tension and deformation," she says. "We have shown that rhythmic mechanical forces can reach the nucleus, reorganise chromatin and alter cell proliferation. The challenge now is to determine which tumours are mechanically sensitive, what stimulation is required and whether the effect is strong enough to have therapeutic value. That remains an open question."

The paper puts it in one line. The results, the authors write, "shed light on the role of mechanical forces in protecting the heart from cancer and may pave the way to cancer therapies based on mechanical stimulation." Physical forces, in other words, are not just a backdrop to disease. They could be a brake on it.

The gap Europe must close

Carrying the idea further will test Europe's appetite for risk, because this is pure academic science with no company behind it. "The first requirement is strong preclinical validation," Prof. Zacchigna says. "Before thinking about a company, we need to understand dose, frequency, duration, safety, tumour specificity and the molecular response to treatment." Then, she says, "we need engineering... because translating a biological principle into a reproducible medical intervention requires precise control of the forces delivered to the tissue."

Beyond that lies work no single laboratory can do. The next stage, she says, needs "expertise that an academic laboratory cannot provide alone, including medical-device development, manufacturing, regulatory science, intellectual property and clinical trial design. In Europe, this means bringing together academic funding, translational programmes, hospitals and eventually industrial partners."

She has crossed that boundary before. "My career has actually moved repeatedly across this boundary, from angiogenesis and cardiovascular gene therapy to RNA therapeutics, engineered tissues and now mechanobiology," she says. Even so, she is candid about the obstacles. "There is still a difficult funding gap between an exciting academic proof of concept and something sufficiently mature to attract serious industrial investment. That is the gap we will have to close."

European money built the ground this stands on. "European and national funding mechanisms have been essential for building the multidisciplinary environment in which discoveries like this become possible," she says. But the system struggles with exactly the kind of idea that produced it. "Genuinely high-risk ideas remain difficult to fund. Funding systems often ask for feasibility, preliminary evidence and a clear translational pathway. The paradox is that the most disruptive ideas often emerge before all this exists." Her own project is a case in point. "We did not start with the idea of developing a mechanical cancer therapy. We started by asking a fundamental question about cardiac regeneration. Curiosity-driven research took us somewhere we did not expect."

The European Union has made cancer a strategic priority through Europe's Beating Cancer Plan, launched in February 2021, and its research Mission on Cancer. Whether that machinery can back genuinely unpredictable science is the open question. "Europe is very good at creating collaborative scientific ecosystems," Prof. Zacchigna says, "but we still need mechanisms that are comfortable funding questions with final application cannot be predicted at the outset."

Prof. Zacchigna trained as a physician before she turned to the bench, and this affects how she reads the finding. "Medicine naturally tends to think in terms of molecules: identify a molecular abnormality and find a drug that blocks it. That approach has transformed cancer treatment and will remain fundamental," she says. "But biology does not rely only on chemistry. Cells also live in a physical world. They are stretched, compressed, moved and exposed to forces, and they continuously translate those forces into biological information."

"What this work has changed for me is the concept that we may be able to treat disease not only by changing the molecules surrounding a cell, but also by changing the physical information that the cell receives," she says. "We have learned how to play with biochemical signalling. Perhaps now we can also learn how to intervene in mechanical signalling." The heart has been making that argument every second of every life. Someone finally worked out what it was saying. ■

5 to 10 years

Prof. Zacchigna's honest estimate of how far a mechanical therapy is from reaching patients.

ABOUT PROF. SERENA ZACCHIGNA

- Physician turned scientist. Trained as a medical doctor at the University of Trieste (MD, 2000), then a PhD in Trieste (2005).
- Where she works. Heads the Cardiovascular Biology Laboratory at ICGEB in Trieste, and is Professor at the Department of Medicine, Surgery and Health Sciences, University of Trieste.
- A career crossing the bench-to-clinic boundary. From angiogenesis and cardiovascular gene therapy to RNA therapeutics, engineered tissues and now mechanobiology.
- Lead author. Led the Science study (April 2026) showing that mechanical load restrains tumour growth in the heart; first author, Dr Giulio Ciucci.