

## Scientists discover a new mechanism involved in the modulation of heart muscle elasticity

April 27 2022



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Scientists at the Centro Nacional de Investigaciones Cardiovasculares (CNIC), in collaboration with an international scientific team, have described a new mechanism of modulation of the mechanical properties of the heart, based on the oxidation of the protein titin, which is the main protein responsible for the passive elasticity of the heart muscle.



Titin is the largest protein in the <u>human body</u> and it is a key protein for the function of skeletal muscle and the heart. "Simplifying a lot, we can describe <u>titin</u> as a molecular spring that allows <u>muscle cells</u> to stretch and contract," explained Dr. Jorge Alegre Cebollada, who leads the Molecular Mechanics of the Cardiovascular System laboratory at the CNIC.

The study, published in *Redox Biology*, builds on earlier observations showing that oxidation of the amino acid cysteine modulates the mechanical properties of titin in vitro. "We wondered whether these oxidations might be present in vivo and help to explain how the heart adapts mechanically to different situations and how it responds to disorders that alter the oxidative balance," explained Dr. Alegre Cebollada.

"We first found that titin contains a set of cysteines that are highly evolutionary conserved, suggesting that they play an important role in the function of the protein," commented Dr. Elías Herrero Galán, codirector of the study. This set of conserved cysteines are the ones observed to modulate the mechanical properties of titin in vitro. "Our experiments also showed that these <u>amino acids</u> are a target for oxidation in basal physiological conditions both in the mouse and the <u>human heart</u>," said Dr. Elías Herrero Galán.

Doctoral Student Inés Martínez Martín described how they identified the effects of these oxidations by running <u>computer simulations</u> based on mathematical models: "Depending on the type of oxidation, titin becomes more or less stiff, affecting the mechanics of the myocardium."

"In general," she added, "these oxidations make titin more dynamic and malleable, allowing the heart to adapt to different metabolic and oxidative demands."



The authors propose that this mechanism might also explain the alterations that occur in the heart during pathological processes that affect its oxidative state, such as myocardial infarction.

**More information:** Elías Herrero-Galán et al, Basal oxidation of conserved cysteines modulates cardiac titin stiffness and dynamics, *Redox Biology* (2022). DOI: 10.1016/j.redox.2022.102306

Provided by Centro Nacional de Investigaciones Cardiovasculares Carlos III (F.S.P.)

Citation: Scientists discover a new mechanism involved in the modulation of heart muscle elasticity (2022, April 27) retrieved 25 April 2024 from <a href="https://medicalxpress.com/news/2022-04-scientists-mechanism-involved-modulation-heart.html">https://medicalxpress.com/news/2022-04-scientists-mechanism-involved-modulation-heart.html</a>

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