Redox Biology: CNIC scientists discover a new mechanism involved in the modulation of heart muscle elasticity

27/04/2022

The results, published in Redox Biology*, show the role of conserved cysteine residues in the elastic protein titin in the modulation of the mechanical properties of the myocardium*

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 human body and it is a key protein for the function of skeletal muscle and the heart. “Simplifying a lot, we can describe titin as a molecular spring that allows muscle cells 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 amino acids are a target for oxidation in basal physiological conditions both in the mouse and the human heart”, said Dr. Elías Herrero Galán.

This mechanism provides a possible explanation for alterations affecting the heart's oxidative state, such as myocardial infarction

Doctoral Student Inés Martínez Martín described how they identified the effects of these oxidations by running computer simulations 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.

The study was supported by funding from the Spanish Ministerio de Ciencia e Innovación, Madrid Regional Government, and Fundación “la Caixa”. The study also received funding from the European Research Area Network on Cardiovascular Diseases through the MINOTAUR project.

- H Herrero-Galán, E., Martínez-Martín, I., Sánchez-González, C., Vicente, N., Bonzón-Kulichenko, E., Calvo, E., Suay-Corredera, C., Pricolo, M. R., Fernández-Trasancos, Á., Velázquez-Carreras, D., Careaga, C. B., Abdellatif, M., Sedej, S., Rainer, P. P., Giganti, D., Pérez-Jiménez, R., Vázquez, J., & Alegre-Cebollada, J. (2022). Basal oxidation of conserved cysteines modulates cardiac titin stiffness and dynamics. Redox Biology, 52, 102306. https://doi.org/10.1016/j.redox.2022.102306

Source URL:https://www.cnic.es/en/noticias/redox-biology-cnic-scientists-discover-new-mechanism-involved-modulation-heart-muscle