JCI: CNIC scientists identify a factor that protects the heart against damage after a heart attack

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A new study defines a mechanism that regulates inflammation after a myocardial infarction, opening a path to the use of the receptor

A study carried out at the Centro Nacional de Investigaciones Cardiovasculares (CNIC) has identified a key factor that protects the heart after a heart attack. The study, led by Dr. Pilar Martín, who heads the Regulatory Molecules of Inflammatory Processes group at the CNIC, is published today in the *Journal of Clinical Investigation*. The study shows that the expression of the receptor CD69 on regulatory T lymphocytes confers protection after a myocardial infarction by acting as a checkpoint for the exacerbated inflammation that causes medium-term cardiac injury.

The study involved the participation of researchers in the Spanish Biomedical Research Networking Center on Cardiovascular Diseases (CIBERCV), the group led by Dr. Francisco Sánchez-Madrid at the CNIC and Hospital Universitario de La Princesa, and the group led by Dr. José Martínez-González at the Instituto de Investigaciones Biomédicas de Barcelona (IIBB-CSIC) and the IIB-Sant Pau. The results show that the level of CD69 expression in peripheral blood can predict the development and progression of heart failure, which has severe consequences for heart function.

Study first author Dr. Rafael Blanco-Domínguez explained that regulatory T lymphocytes “control other elements of the immune system to prevent uncontrolled inflammatory responses from causing injury.”

By analyzing blood immunological markers from 283 patients with myocardial infarction—an ischemic emergency and the leading cause of death in the world—the authors discovered that the expression of CD69 on regulatory T lymphocytes increases in the first hours after the ischemic event. Through experiments with mouse models, the research team showed that the absence of CD69 leads to increases in inflammation, cardiac dysfunction, and the death rate after infarction

This happens, explained Dr Martín, “be**cause CD69-expressing regulatory** T cells are normally recruited to the site of infarction and are required to inhibit pro-inflammatory interleukin-17-secreting gamma-delta T cells. The presence of CD69 makes regulatory T cells more efficient at inducing the death of target cells and inhibiting interleukin-17 secretion through a novel mechanism independent of specific antigens.”

In one of the key experiments of the study, the scientists injected CD69-expressing regulatory T cells into CD69-deficient mice after an infarction, finding that this treatment was able to make up for the deficiency of this molecule and thus decrease cardiac inflammation and improve survival.

The study also produced promising clinical findings through a follow-up analysis of myocardial infarction patients from two independent cohorts, conducted through collaboration with the Cardiology Services at Hospital Universitario de La Princesa in Madrid and Hospital de la Santa Creu i Sant Pau in Barcelona.
This analysis revealed that the level of CD69 expression on peripheral blood cells predicts the development and progression of heart failure towards severe consequences for heart function.
“**Patients with low CD69 levels in the first hours after infarction had an increased risk of developing heart failure during the first two and a half years after hospital admission,**” said Dr. Blanco-Domínguez.

The authors conclude that the study reveals a new mechanism for the regulation of inflammation after myocardial infarction and opens the way to the development of CD69 as a prognostic marker and therapeutic target for this global cardiac condition.

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- *Blanco-Domínguez ... José Martínez-González, Pilar Martín. CD69 expression on regulatory T cells protects from immune damage after myocardial infarction. J Clin Invest. 2022. https://doi.org/10.1172/JCI152418.*