MyoBiomark: a novel circulating microRNA for the detection of acute myocarditis

CNIC

Dr. Pilar Martín

PROFILE

The ***Centro Nacional de Investigaciones Cardiovasculares*** **(CNIC)** is a leading international research center dedicated to understanding the basis of cardiovascular health and disease and to translating this knowledge into improved patient care. Martín´s laboratory work lines focuses on: i. Study of the molecular mechanisms of pathophysiology in myocarditis; ii. Search and validation of new Biomarkers for myocarditis and ischemic cardiomyopathies; and iii. study of new Biomarkers as predictive for the development of immune-related adverse events and fatal myocarditis during Immune Checkpoint Inhibitors cancer therapy

SPEAKER

Dr. Pilar Martín is the head of the Regulatory Molecules of Inflammatory Processes Group at the CNIC. A recognized immunologist, she has acquired wide experience in translational research involving micro-RNAs in cardiovascular diseases, including atherosclerosis, acute myocardial infarction and myocarditis. Her recent works have been published in Circulation, Nature Immunology or the New England Journal of Medicine, among others.

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PRODUCT

MyoBiomark: a novel circulating microRNA for the detection of acute myocarditis

MECHANISM OF ACTION

MyoBiomark is a novel circulating microRNA with a high diagnostic value (area under the curve `AUC´ of 0.927, 95% CI, 0.879-0.975; p<0.0001) for discriminating acute myocarditis from myocardial infarction patients.

We identified miR-721 in preclinical models as an exclusive marker of myocarditis, which was translated to its homologue novel miRNA in human plasma. The diagnostic ability to discriminate myocarditis was confirmed in plasma from four different patient cohorts (n= 151) with different comparators including myocardial infarction (n= 150), MINOCA (n= 20), autoimmune diseases (n= 152) and healthy volunteers (n= 80).

TARGET INDICATIONS

MyoBiomark provide a non-invasive unique tool for the clinically challenging diagnosis of myocarditis in plasma samples.

Due to the absence of discriminating tools at the Emergency Room, all patients presenting symptoms of myocardial infarction (MI) undergo triage for urgent coronary arteriography and antithrombotic therapy.

However, about 10-20% of all patients with MI criteria are misdiagnosed as they present myocardial infarction with non-occlusive coronary artery (MINOCA) disease, most of them

finally diagnosed as myocarditis with weeks of delay, leading to inappropriate clinical management and prognostic implications.

CURRENT STATUS

- After experimental autoimmune myocarditis, Th17 cells boost myocardial inflammation and progression to dilated cardiomyopathy. We have identified mmu-miR-721, by smallRNA-microarrays and qPCR, as specific for Th17 cells that is secreted to the plasma of mice with acute autoimmune and viral myocarditis, but not with acute myocardial infarction.
- We have cloned, sequenced and validated the human homologue in the chromosome 8 as hsa-miRNA-Chr8:96 (MyoBiomark) in four independent cohorts of myocarditis patients. The microRNA retained its diagnostic value when adjusted by age, gender, ejection fraction and troponins.
- The results of the discovery and development of **Myobiomark** are about to be published in the New England Journal of Medicine. Moreover, the CNIC leads a Prospective Registry for the validation of the new diagnostic marker in patients with clinical suspicion of myocarditis, from the clinical trials coordination unit (UCEC, CNIC).
- The Prospective Registry (Instituto de Salud Carlos III CEI authorization code: CEI PI 23_2020-v3) is being carried out in Hospital Virgen de la Arrixaca (Murcia), Hospital de la Princesa, HM Hospitales and Hospital Clínico San Carlos (Madrid), Hospital Clínico de Salamanca and Hospital General de Valencia.

INNOVATIVE ASPECTS

- Differential diagnosis of myocarditis is usually established after ruling-out coronary artery disease by coronary angiography (or CT scan) and confirming the presence of Lake-Louise criteria in cardiac magnetic resonance (CMR) imaging. Although CMR has improved the diagnosis of acute myocarditis, it also has limitations as the lack of accessibility in many hospitals and the ambulatory setting, pregnant women, and the sensitivity to detect oedema and vascular permeability decreases over time.
- Endomyocardial biopsy remains the gold standard diagnosis for myocarditis, and would be indicated in patients with clinical suspicion, but it is not routinely performed due to its risk as an invasive method and its limited sensitivity. **Myobiomark** has been validated in plasma from a biopsy-proven myocarditis cohort (AUC 0.999, 95% CI, 0.977-1.000; p= 0.0182).

IPR

The technology was originally protected under European Patent application EP15382596.3 entitled "Method for diagnosing cardiomyopathies" on December 12th, 2015. Currently, the USA application (US15/780,888) is still pending while the European Patent (EP3384043B1) was granted on January 23rd, 2020. The CNIC is the only applicant in the patent family.

PARTNERING OPPORTUNITIES

The CNIC is looking for an industrial partner interested in licensing the patent family and completing the necessary steps for the diagnostic kit to reach the market. If the company needs it, the CNIC is open to collaborate through a Research and Development Contract.