Scientists led by Dr. Andrés Hidalgo at the CNIC have discovered that circulating neutrophils acquire different behavior patterns during inflammatory processes. The study, published in *Nature*, identifies a harmful neutrophil behavior associated with cardiovascular disease.


Scientists at the CNIC and Columbia University, New York have published a review article in *Nature Cardiovascular Research* examining the role of acquired mutations linked to clonal hematopoiesis in cardiovascular disease.


Organ growth and regeneration require the entry into the cell nucleus of proteins that activate essential genes for these processes. This process is the subject of a new study by CNIC scientists, led by Dr. Miguel Ángel del Pozo, who heads the Mechnoadaptation and Caveolae Biology group, and group member Dr. Asier Echarri. The scientists have identified the mechanism that controls the nuclear import of these proteins in response to mechanical stimuli, such as the hemodynamic forces generated by arterial blood flow, tumor rigidity, or locomotory movements during routine activities like walking or sports.

CIRCULATION
A CNIC STUDY HIGHLIGHTS THE RISKS OF MITOCHONDRIAL THERAPEUTIC INTERVENTIONS

Research carried out at the CNIC has demonstrated that mixing mitochondrial DNAs (mtDNAs) of different origins can have damaging effects over the medium and long term. mtDNA is a component of the genetic material that is transmitted exclusively from mothers to their children.


JOURNAL OF THE AMERICAN COLLEGE OF CARDIOLOGY: CARDIOVASCULAR IMAGING
3D MATRIX ULTRASOUND ACCURATELY IDENTIFIES CARDIOVASCULAR INJURY IN HEALTHY INDIVIDUALS

A new imaging technique for real 3D vascular ultrasound could become a key tool in strategies aimed at preventing cardiovascular disease in apparently healthy persons, complementing traditional risk parameters such as cholesterol and high blood pressure. The new results, published in JACC: Cardiovascular Imaging, show that real 3D vascular ultrasound is reliable, accurate, and faster than previous methods for the assessment of plaque volume in the carotid and femoral arteries.


EUROPEAN HEART JOURNAL
BONE MARROW CONTRIBUTES TO THE DEVELOPMENT OF ATHEROSCLEROSIS

The activation of the bone marrow appears to play a key role in the origin and development of atherosclerosis, the pathological process underlying cardiovascular conditions such as myocardial infarction and stroke. A study carried out by scientists at the CNIC and led by cardiologists Drs. Valentín Fuster and Borja Ibáñez suggests that the bone marrow is activated in response to known cardiovascular risk factors. In the study, published in the European Heart Journal, the researchers show that these risk factors lead to an increase in the number of circulating inflammatory cells, which go on to trigger the initiation and subsequent progression of atherosclerotic disease.

eBIOMEDICINE: SCIENTISTS DISCOVER A NEW METHOD FOR THE EARLY DETECTION OF SUBCLINICAL ATHEROSCLEROSIS

A study published in the journal eBioMedicine identifies new biomarkers that predict the presence of subclinical atherosclerosis. The study was carried out by scientists from the Spanish Cardiovascular Research Network (CIBERCV) working at the CNIC and the Instituto de Investigación Sanitaria-Fundación Jiménez Díaz-Universidad Autónoma de Madrid (IIS-FJD-UAM), in partnership with other institutions.


REDOX BIOLOGY
CNIC SCIENTISTS DISCOVER A NEW MECHANISM INVOLVED IN THE MODULATION OF HEART MUSCLE ELASTICITY

Scientists at the 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.


NATURE CARDIOVASCULAR RESEARCH
A CNIC TEAM CREATES A DYNAMIC 3D ATLAS OF THE FORMATION OF THE EMBRYONIC HEART

Scientists at the CNIC have used a collection of mouse tissue samples to create a 3D atlas of the formation of the heart during embryonic and fetal development. The 3D atlas has allowed the scientists to identify the first appearance of left-right asymmetry in the heart. The study, published today in Nature Cardiovascular Research, provides important information on the development of congenital heart malformations.

**ELIFE**

**STUDY REVEALS HOW DUCHENNED MUSCULAR DYSTROPHY CAUSES HEART RHYTHM PROBLEMS**

Abnormalities in the proteins responsible for transmitting electrical signals in the heart likely cause abnormal heart rhythms in patients with Duchenne muscular dystrophy (DMD), shows a study published in eLife.


**HEPATOLOGY**

**IMMUNE CELLS IN THE LIVER REGULATE BODY TEMPERATURE**

A study published in Hepatology demonstrates that the activation of thermogenesis in the livers of obese mice contributes to weight loss and improves diabetes symptoms.


**EUROPEAN JOURNAL OF HEART FAILURE**

**SPANISH SCIENTISTS COMBINE GENETIC AND IMAGING DATA TO IMPROVE THE TREATMENT OF DILATED CARDIOMYOPATHY**

Combining a person’s genetic profile with imaging data obtained by cardiac magnetic resonance accurately predicts the prognosis of patients with dilated cardiomyopathy, the most frequent cause of heart failure.

Many cardiovascular disorders can be prevented by taking action to reduce risk factors. Making even small behavioral changes and sticking with them over the long term can help to preserve cardiovascular health. This is the conclusion of a study conducted at the CNIC and published in the European Heart Journal. The study also demonstrates that the workplace is an ideal setting for programs promoting the adoption of heart-healthy habits and producing major health benefits.

A study carried out by scientists at the Centro Nacional de Investigaciones Cardiovasculares (CNIC) and led by Dr. Guadalupe Sabio has identified a key role for the MKK3/6–p38γ/δ signaling pathway in the development of cardiac hypertrophy. The results, published in the journal eLife, suggest that inhibition of p38γ/δ could be a useful therapeutic strategy for diseases such as hypertrophic cardiomyopathy; however, this avenue remains unexplored because of the lack of specific inhibitors for these kinase enzymes. The study also shows the opposite effect upon inhibition of another member of this protein family, p38α, indicating that long-term clinical use of p38α inhibitors to treat chronic disease risks damage to the heart.

Researchers at the Centro Nacional de Investigaciones Cardiovasculares (CNIC), Universidad Pompeu Fabra, ICREA, Centro de Investigación Biomédica de Enfermedades Neurodegenerativas (CIBERNED) and Centro de Investigación Biomédica en Red Fra-

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THE NEW ENGLAND JOURNAL OF MEDICINE
THE POLYPILL REDUCES CARDIOVASCULAR MORTALITY BY 33% IN PATIENTS TREATED AFTER MYOCARDIAL INFARCTION

The polypill developed by the Centro Nacional de Investigaciones Cardiovasculares (CNIC) and Ferrer, which includes three drugs (aspirin, an angiotensin-converting enzyme (ACE) inhibitor, and a statin), is effective at preventing secondary adverse cardiovascular events in people who have previously had a heart attack. The polypill reduces mortality from cardiovascular causes in this population by 33%.

JOURNAL OF THE AMERICAN COLLEGE OF CARDIOLOGY
SCIENTISTS AT THE CNIC AND HOSPITAL PUERTA DE HIERRO DEVELOP A TOOL TO DETERMINE IF DILATED CARDIOMYOPATHY HAS A GENETIC ORIGIN

Scientists at the CNIC and Hospital Universitario Puerta de Hierro Majadahonda have developed a software application that predicts the likelihood that a case of dilated cardiomyopathy is caused by a genetic mutation. The research was carried out in collaboration with hospitals in Spain, Italy, and the Netherlands. The findings, published in the Journal of the American College of Cardiology (JACC), will allow physicians to adjust the treatment of dilated cardiomyopathy patients appropriately and to identify family members who have also inherited the disease. The software application is available online at www.madridmcmscore.com.

CELLULAR AND MOLECULAR LIFE SCIENCES
NEW MECHANISM LINKING INflammATION AND PATHOLOGIC CARDIOVASCULAR REMODELING

The immune-inflammatory response contributes to the pathological remodeling of arteries in various cardiovascular diseases. Research published in CMLS has shed new light on one of the mechanisms linking the immune-inflammatory response to vascular disease by describing the key role played by the early lymphocyte activation antigen CD69.
BRITISH JOURNAL OF PHARMACOLOGY

CNIC SCIENTISTS IDENTIFY A NEUROPROTECTIVE ACTION OF METOPROLOL AFTER A STROKE

A drug costing just €2 a shot can protect the brain during a stroke and greatly reduce long-term incapacity. Metoprolol, a beta-blocker in routine use in cardiology for more than 40 years, has now been shown to have a specific neuroprotective effect.


JOURNAL OF CLINICAL INVESTIGATION

CNIC SCIENTISTS IDENTIFY A FACTOR THAT PROTECTS THE HEART AGAINST DAMAGE AFTER A HEART ATTACK

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, was published 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.


NATURE CARDIOVASCULAR RESEARCH

CNIC SCIENTISTS IDENTIFY THE CAUSE OF ARRHYTHMIAS AND SUDDEN DEATH IN ANDERSEN-TAWIL SYNDROME TYPE 1

The Centro Nacional de Investigaciones Cardiovasculares (CNIC) has discovered the cause of arrhythmias and sudden death in the rare disease Andersen-Tawil syndrome type 1 (ATS1), which is caused by mutations affecting potassium channels that regulate electrical activity and the intracellular calcium cycle in cardiac and skeletal muscle.

CIRCULATION
SPECIFIC MODIFIER GENES DETERMINE THE EFFECT OF MUTATIONS THAT CAUSE NON-COMPACTON CARDIOMYOPATHY

Non-compaction cardiomyopathy is a heart condition caused by defects that arise during fetal development and can have diverse health impacts in affected individuals, including sudden cardiac death. The Intercellular Signaling in Cardiovascular Development and Disease group at the Centro Nacional de Investigaciones Cardiovasculares (CNIC) previously reported that this disease can be caused by two distinct mutations in the Mindbomb1 gene (Mib1).

BASIC RESEARCH IN CARDIOLOGY
A NEW THERAPEUTIC TARGET FOR THE PREVENTION OF HEART FAILURE DUE TO AORTIC STENOSIS

Scientists at the Centro Nacional de Investigaciones Cardiovasculares (CNIC) have identified a new therapeutic target for the prevention of heart failure linked to aortic stenosis. The study was led by Dr. Borja Ibáñez, Clinical Research Director at the CNIC, cardiologist at Hospital Universitario Fundación Jiménez Díaz, and member of the Spanish cardiovascular research network (CIBERCV). The study shows that overexpression in cardiac muscle cells of beta-3 adrenergic receptor, a member of the beta adrenergic system, can prevent or even reverse heart failure in a mouse model of aortic stenosis, a condition that currently has few therapeutic options.

EUROPEAN JOURNAL OF HEART FAILURE
A PROMISING DRUG TREATMENT FOR PATIENTS WITH PULMONARY HYPERTENSION ASSOCIATED WITH HEART DISEASE

There is currently no specific treatment for pulmonary hypertension associated with heart disease, a highly prevalent condition with a poor prognosis. Now, a study from the Centro Nacional de Investigaciones Cardiovasculares (CNIC) and Hospital Clinic de Barcelona/IDIBAPS has shown that mirabegron, a drug that acts on the beta-3 adrenergic receptor, may have a beneficial effect on right ventricular function.
ELIFE

CNIC SCIENTISTS IDENTIFY THE ESSENTIAL ROLE OF CELL-SURFACE “NANOFOLDS” AND “GLUE” IN THE MECHANICAL RESPONSE OF CELLS

A study at the Centro Nacional de Investigaciones Cardiovasculares (CNIC) has revealed that subcellular structures called caveolae play an essential role in cell mechanics. The results suggest that impaired caveolar function could be involved in a variety of processes, including platelet aggregation, cardiovascular disease, fibrosis, and tumor formation.


BLOOD

RXR, THE CELL PROTEIN THAT KEEPS BLOOD STEM CELLS YOUNG AND FIT

The cell protein retinoid X receptor (RXR) is a key factor in the maintenance of hematopoietic stem cells, the immature stem cells that give rise to all the blood cell lineages. RXR ensures that these cells remain youthful and fit, thereby reducing the risk of developing myeloproliferative syndromes as the body ages.


NATURE

RESEARCHERS CHARACTERIZE RARE, DAMAGED CELLS THAT BLOCK THE FUNCTIONS OF THEIR NEIGHBOUR HEALTHY CELLS AND IDENTIFY WAYS TO NEUTRALIZE THEM AND IMPROVE TISSUE REGENERATION

Researchers at the Universitat Pompeu Fabra (UPF), ICREA, CIBERNED, CNIC and Altos Labs, among other national and international collaborators, have characterized how damaged cells (senescent cells) that inevitably arise after injury negatively impact tissue regeneration, and how this mechanism operates actively in old age, but surprisingly also in young age. This negative action can be overcome genetically and pharmacologically, hence restoring stem cell regenerative functions.


NATURE CELL BIOLOGY

A CNIC STUDY SHOWS THAT CELLS POSSESS 2 MECHANISMS TO ALLOW THEM TO RESPOND TO DIFFERENT FORCE RANGES

A study carried out at the Centro Nacional de Investigaciones Cardiovasculares (CNIC) heralds a paradigm change in the field of mechanobiology. The study reveals that cells respond to forces of differing strength using two distinct mechanisms, one mediated by minute, cup-like invaginations on the cell surface called caveolae and the other by newly discovered large membrane depressions the study authors call dolines.