CIRCULATION RESEARCH: CNIC scientists identify the crucial role of the protein neuregulin-1 in heart development

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Neuregulin-1 (Nrg1) plays an essential role in the transformation of the heart from its delicate primordial structure into the powerful beating mature organ

A team of scientists at the Centro Nacional de Investigaciones Cardiovasculares (CNIC) has identified a key element of the machinery of heart formation. In a study published in the journal Circulation Research, researchers led by Dr. José Luis de la Pompa reveal the essential role of the protein neuregulin-1 (Nrg1) in the intricate transformation of the heart from its delicate primordial structure into a powerful pumping organ.

The findings not only highlight the pathways through which the human heart forms, but also suggest important directions for future medical advances. Commenting on the study, Dr. de la Pompa, head of the Intercellular Signalling in Cardiovascular Development and Disease laboratory at the CNIC, said, “Understanding these fundamental processes takes scientists a step closer to unraveling the mysteries of the human heart and devising strategies to promote better heart health

The heart is the body’s engine and is composed of a number of specialized parts. One of these essential components is the ventricles, the heart chambers whose muscular contractions make the ‘lub’ and ‘dub’ sounds of the heartbeat and are responsible for pumping blood to the lungs and around the body throughout life.

Scientists have long been fascinated by how these chambers, initially structured in delicate protrusions called trabeculae, grow and mature into the robust structures that keep the heart beating.

Trabeculae: the heart’s blueprint

Study first author Joaquín Grego-Bessa explained that trabeculae can be likened to a scaffolding that supports the heart as it grows: “We can think of trabeculae as small, primitive projections that form the foundation of the heart.” Understanding how these structures develop into the mature ventricles is not just a fascinating biological question; it also has immense potential to advance regenerative medicine, offering new perspectives on heart conditions and their treatment.

The new study identifies a crucial actor in this process: Nrg1, a signalling protein that guides the trabeculae formation. Nevertheless, mystery still surrounded the intricate mechanisms through which Nrg1 operates and its role in the maturation of the heart wall.

To resolve this mystery, the CNIC team carried out experiments using advanced imaging techniques, genetic analysis, and biochemical studies in mice. Manipulation of the amount of Nrg1 expressed in cardiac cells revealed fascinating patterns.

“The experiments revealed that Nrg1 orchestrates a symphony of events within cardiac cells,” explained Donal MacGrogan, joint lead author on the study. Through these actions, he continued, “Nrg1 coordinates the division of cardiac cells to form trabeculae, ensuring that these structures grow in the appropriate orientation.”

The scientists view Nrg1 as the guiding hand that molds the architecture of the heart. Commenting on the results, Donal MacGrogan said that “when Nrg1 levels were altered, the cardiac cells changed their behaviour, and this resulted in structural and functional irregularities. These changes are like a stumbling block in the growth of the heart, potentially leading to cardiac problems in affected individuals in the future.”

José Luis de la Pompa emphasized that understanding how Nrg1 functions is more than an intellectual exercise and “could provide a route to revolutionary treatments in the future. Decoding

the language of heart development could unblock new strategies for the repair of cardiac injury. This research not only deepens our understanding of how the heart grows and functions, but also provides hope for those engaged in the fight against heart diseases."

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- Grego-Bessa J, Gómez-Apiñaniz P, Prados B, Gómez MJ, MacGrogan D, de la Pompa JL. Nrg1 Regulates Cardiomyocyte Migration and Cell Cycle in Ven-tricular Development. Circ Res. 2023 Oct 17. doi: 10.1161/CIRCRESAHA.123.323321. Epub ahead of print. PMID: 37846569.