Laboratory of Cardiovascular Development and Disease

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Institutions

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Keywords

Cardiovascular developmental biology, Epicardium and coronary blood vessels, Heart valves, Ventricular walls and cardiac septa, Progenitors and stem cells, Regenerative medicine, Fibrosis, Inflammation

Research Lines

✓ Cardiovascular embryonic development: the origin of congenital and acquired cardiovascular diseases
✓ Regulation of cardiovascular progenitor cell differentiation
✓ Repair and regeneration of cardiovascular tissues.
✓ Cardiovascular regenerative medicine: from the embryo to preclinical cell-based therapies

Scientific Activity

The DeCA group has a longstanding experience in the study of the cellular and molecular mechanisms that control cardiovascular embryonic development. During the last ten years, the team has worked to translate basic knowledge on the differentiation of cardiovascular cell progenitors into applied biomedical science, with the aim of improving early diagnosis of congenital and adult (acquired) cardiac diseases. Moreover, the group also performs pre-clinical research in animal models, contributing to the development of advanced therapies to treat the ischemic and non-ischemic diseased heart.

Research lines:

✓ **Cardiovascular embryonic development: the origin of congenital and acquired cardiovascular diseases**

Our group performs research on the development of the embryonic cardiovascular system and has pioneered the study of epicardium and coronary blood vessels. Moreover, we have a longstanding experience on the study role of mesenchymal tissues in heart morphogenesis. We focus our research on the molecular and cellular mechanisms that control the formation of a variety of cardiac and vascular structures, paying a special attention to tissue interactions along development; many of our studies demonstrate that non-cell autonomous mechanisms are crucial to the formation of the ventricular walls, coronary arteries and atrioventricular valves, all of which are substrates for prevalent human cardiovascular disease. It is our objective to identify new markers for the early diagnose of a variety of congenital diseases. In order to carry out this research we work with transgenic mice (using the Cre/LoxP technology for the conditional deletion of genes or the tracing of defined cell populations), perform surgery and transplantations in these animals. Phenotypes are characterized by qPCR, ISH, IHC, WB and FACS among other techniques to study protein and gene expression.

✓ **Regulation of cardiovascular progenitor cell differentiation**

The DeCA laboratory also studies the molecular interplay active during the differentiation of cell progenitors and stem cells along cardiovascular development and works to characterize the properties of cardiac stem cell niches (microenvironments). We use both in vivo (analysis of mouse embryos) and in vitro (culture of embryonic stem cells and progenitors) methods to unveil transcriptional interactions and hierarchies and the involvement of new molecules in the regulation of cell differentiation. This research also implies the identification of the lineage relationships existing between different cell populations, suggesting strategies for the guided differentiation of defined cell types from common progenitors. Our aim is to develop new protocols for the controlled differentiation of functional cells for substitutive, cell-based therapies, as well as to characterize the molecular bases of cardiovascular diseases involving anomalous cardiac cell differentiation and maturation. This latter objective, could, in turn, promote the identification of new therapeutic targets for the treatment of these diseases.

✓ **Repair and regeneration of cardiovascular tissues**

The adult amniotic heart (avians and mammals), unless that of other vertebrates (e.g. fishes and amphibians), cannot regenerate. We are currently applying our experience with a variety of vertebrate animal models to study the specific cellular and molecular responses of the amniotic heart to experimental damage from embryonic development to adulthood. We aim at identifying resident, endogenous substrates that may promote mammalian cardiac regeneration under optimal conditions.

✓ **Cardiovascular regenerative medicine: from the embryo to preclinical cell-based therapies**

The development of cell therapy clinical trials in human subjects requires detailed and careful preclinical experimentation in animals. Our laboratory has established models to study ischemic heart disease (LAD coronary ligation) and non-ischemic coronary disease (angiotensin II infusion) and combined them with transgenic bone marrow transplantations at different postnatal and adult stages. This approach allows us to study the process of ventricular remodeling that follows heart damage and to evaluate the role of inflammation in the limitation of regenerative responses including neovascularization and the promotion of pathologic fibrosis. Our goal for the next years is to translate results from these small animal models to a large animal model for cardiac diseases (i.e. pig) and to propose specific trials to ameliorate the injured heart in humans.

Collaborations

❖ **Leiden University Medical Center** (The Netherlands); Prof. Christine Mummery; Research on human pluripotent stem cell differentiation into cardiovascular cell types.

❖ **Institut de Biologie du Développement de Marseille-University Aix-Marseille** (France); Dr. Robert Kelly; Research on the morphogenesis of the ventricular walls and coronary arteries.

❖ **Centro Nacional de Investigaciones Cardiovasculares, CNIC** (Spain); Dr. José Luis de la Pompa; Research on the role of the Notch signaling pathway in cardiac development.

❖ **Centre for Life-Newcastle University** (U.K.); Prof. Deborah Henderson; Research on the origin of congenital heart disease.

❖ **University of Twente** (The Netherlands); Prof. Robert Passier; Research on the biotechnological and biomedical applications of human pluripotent stem cells.

❖ **Clínica Universitaria de Navarra-Universidad de Navarra-CIMA** (Spain); Dr. Felipe Prósper; Research on post-infarction cardiac ventricular remodelling.

❖ **Human Genetics Unit-MRC** (Edinburgh, U.K.); Prof. Nicholas D. Hastie; Research on the role of Wilms tumor suppressor gene (Wt1) in cardiac development.

❖ **Centro Nacional de Investigaciones Cardiovasculares, CNIC** (Spain); Dr. Vicente Andrés; Research on the role of lamins in cardiovascular aging: progeria models.

❖ **Academic Medical Center-University of Amsterdam** (The Netherlands); Dr. Maurice van den Hoff; Research on the role of Wnt secreted molecules in cardiac inflow tract formation.

❖ **Centro de Investigaciónes Energéticas, Medioambientales y Tecnológicas, CIEMAT** (Spain); Dr. José Carlos Segovia; Research on the role of inflammation in post-infarction ventricular remodelling.

Research Projects in the last 5 years

- Origin and diversity of cardiac interstitial cells (BFU2009-07929, Spanish Ministry of Science and Innovation). 2010-2012. PI: J.M. Pérez Pomares.
- Embryonic developmental functions of Wilms tumor supresor gene (Wt1). (BFU2011-25304, MICINN). 2012-2014. IP: R. Muñoz-Chápuli.
- Translational Training Network on the Cellular and Molecular Bases of Heart Homeostasis and Repair (EU FP7, CardioNet 28960). 2012-2015. PI: J.M. Pérez Pomares; Coordinator: M. Torres (CNIC, Madrid, Spain).
- Contribution of embryonic coelomic epitelial derivatives to development and visceral homeostasis. (CTS-7564, Consejería de Innovación, Ciencia y Empresa, Junta de Andalucía). 2012-2015. IP: R. Muñoz-Chápuli.
- Study on the development, structure and regulation of the pericoronary interstitial cardiac niche. (BFU2012-35799, MINECO). 2013-2015. PI: J.M. Pérez Pomares.
- Epicardial derivatives in cell therapy (TERCEL, RD12/0019/0022, MINECO-ISCIII). Node 23 of the Spanish Cooperative Research Network on Cell Therapy. 2013-2016. PI: J.M. Pérez Pomares.
- Wilms tumor supresor gene (Wt1). Expression regulation and roles in embryonic development, adult homeostasis and pathophysiology. (BFU2014-52299-P, MINECO). 2015-2017. IP: R. Muñoz-Chápuli.
- Study on the genetic and mechanistic interactions in familial cardiomyopathy through advance modeling of the disease (SAF2015-71863, Spanish Ministry of Economy). 2015-2018. PI: J.M. Pérez Pomares; Coordinator: J.L. de la Pompa (CNIC, Madrid, Spain).
- Cardiac pericoronary niche: cell interaction, homeostasis and pathological de-regulation. (BFU2015-65783-R, MINECO). 2016-2019. PI: J.M. Pérez Pomares.

Publications in the last 5 years

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