



UNIVERSITÀ  
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DI PADOVA

HORIZON EUROPE  
PROJECTS FUNDED AT THE UNIVERSITY OF PADOVA

### **Edit-hCOs - Precise Genome Editing to Correct Cardiomyopathies in Human Cardiac Organoids**

Inherited cardiomyopathies are a major cause of sudden cardiac death and are caused by mutations in genes encoding sarcomeric proteins. With an incidence of 3 per 1,000 adults within the European population, inherited cardiomyopathies present a substantial burden to the healthcare services of all European nations. Although a few medications can slow the progression of the disease, today there is no cure for cardiomyopathies. The CRISPR-Cas9 precision genome editing technologies, base and prime editing, can permanently edit point mutations of genes, making them ideal tools to treat cardiomyopathies. To demonstrate the efficacies and therapeutic benefits of these editors in correcting cardiomyopathy-causing mutations, it is necessary to develop robust in vitro models of mature human cardiomyocytes that recapitulate the cellular complexity of the human heart. In the Edit-hCOs project, I will generate and characterize human cardiac organoids (hCOs) harboring clinically relevant cardiomyopathy-causing mutations in the FLNC gene, which encodes for the sarcomeric protein filamin C. hCOs will be generated as three-dimensional scaffold-free cardiac microtissues using tri-cellular combinations of human induced pluripotent stem cell -derived cardiomyocytes, cardiac fibroblasts, and cardiac endothelial cells. Then, I will deploy base and prime editors to fix common FLNC gene mutations in the hCOs, and I will characterize their molecular and functional improvements following correction. In addition, I will generate humanized mouse models harboring the same mutations as patients for future studies on delivery, therapeutic safety, and efficacy of the genome editing components in vivo. Completion of the Edit-hCOs project will allow me to establish a completely innovative and ambitious research line focused on the permanent treatment of cardiomyopathies. This will establish a crucial and important pre-clinical step towards therapeutic genome editing of cardiovascular diseases.

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**Find out more:** <https://cordis.europa.eu/projects/en>