Letter of intent

File number 175.2021.036
Grant 2021/2022

Applicant

Title
MYO-PHENO
A national platform for state-of-the-art (cardio)myocyte phenotyping

Abstract
NWO domain: Netherlands Organisation for Health Research and Development (ZonMw)
Research fields: Life Sciences; 21.70.00 Physiology; 21.40.00 Genetics; 21.90.00 Life sciences, other

Research into cardiac and skeletal muscle (patho)physiology is highly dependent on standardized, high-quality, in-depth phenotyping of (cardio)myocytes. MYO-PHENO will for the first time bring together wide-scale expertise and novel technology to provide a national platform for state-of-the-art phenotyping of (cardio)myocytes, combining electrophysiology, contractile function, and metabolism through:
(1) Manual and automated patch clamp (Patchliner) and multi-electrode array (MEA) for large-scale assessment of electrical disturbances, action potential characteristics, ion channel (dys)function, and arrhythmia susceptibility.
(2) The CytoCypher MultiCell system for large-scale simultaneous measurements of calcium and contractility.
(3) The C-Trap™G2 system, a turn-key system that combines high-resolution optical tweezers, super-resolution microscopy and advanced microfluidics to assess the mechanical properties of muscle filaments and how these properties are affected by mutated proteins.
(4) Assessment of key metabolic characteristics (including timsTOF mass spectrometry), and assessment of mitochondrial (dys)function (Oroboros technology for high-resolution respirometry, and bioenergetic and OXPHOS analysis).

These highly precise functional assays will facilitate both in-depth phenotyping of disease models ranging from myofilament and ion channels to intact heart and muscle preparations, as well as large-scale phenotyping with simultaneous measurements in multiple cells. MYO-PHENO will not only enable nation-wide standardized phenotyping and drug testing, but will also provide an (inter)national research and training facility. Such a facility covering broad expertise to study cardiac muscle and skeletal cell characteristics ranging from ion current, calcium handling, myofibril contractility and relaxation, and metabolomics will represent a unique research setting in the Netherlands, and will bring our world-leading position in muscle physiology to the next level of precision medicine. MYO-PHENO will furthermore play a crucial role in conserving and expanding essential physiological and metabolic knowledge and expertise, ensuring its future continuation by training and educating the next generation of leading scientists in muscle physiology and metabolism within the Netherlands.

MYO-PHENO will align with the LSRI Roadmap Medical Sciences (GWI plan: Advanced Personalized Therapies & Human Model Systems; AT&MS) in the domain: Life and Medical Sciences, linked to the LSRI application “hDMT INFRA StemCells”.

Researchers involved in MYO-PHENO will include: Dr. Carol Ann Remme (AMC, Department of Experimental Cardiology; expertise: cardiac electrophysiology), Prof. dr. Jolanda van der Velden (VUmc, Department of Physiology; expertise: cardiac muscle physiology, cardiomyopathy), Prof. dr. Coen Ottenheijm (VUmc, Department of Physiology; expertise: skeletal muscle physiology), Prof. dr. Riekelt Houtkooper (AMC, Laboratory Genetic Metabolic Diseases, Amsterdam Gastroenterology and Metabolism; expertise: metabolism, inborn errors of metabolism), Prof. dr. Yigal Pinto (AMC, Department of Clinical Cardiology; expertise: clinical cardiology), Dr. Diederik Kuster (VUmc, Department of Physiology; expertise: cardiac muscle physiology, cardiomyopathy), Dr. Michiel Helmes (VUmc; expertise: large-scale contractility phenotyping), Dr. Arie Verkerk (AMC, Department of Experimental Cardiology; expertise: cellular electrophysiology), Prof. dr. Robert Passier (UTwente; expertise: stem cell technology).

Organisation responsible for the application

Confirm letter of intent
With submitting this form via ISAAC I declare to have filled in this form completely and truthfully.

Applicant