Project Title:
The structural and functional role of the protein minispryn in striated muscle

Minispryn is a striated muscle-specific protein, homologous to the C-terminal region of the myospryn protein. Both proteins are localized in and around the nucleus as well as in the sarcoplasmic reticulum in cardiomyocytes, where they form a complex with the ryanodine receptor Ca^{2+} channel. Myosprin, through its C-terminal region interacts with PKA. Given the homology of minispryn with myospryn, we hypothesize that minispryn shares interaction partners with myospryn and that the two proteins have overlapping roles and/or collaborate in the regulation of Ca^{2+} handling and in the PKA signalling, also contributing to the genesis of diseases; in fact, in mice the lack of expression of myospryn causes dilation of the left ventricle, systolic dysfunction and serious structural alterations. The objective of the project is to investigate the role of minispryn in cardiac and skeletal muscle based on the analysis of minispryn knockout mice.

Research program:
The present project aims to determine the structural and functional role of minispryn in striated muscle. This objective will be pursued by evaluating the effect of the absence of minispryn on the structure and function of cardiac and skeletal muscle. Functional studies will be conducted by applying sarcomere level mechanical techniques on skeletal and cardiac muscle tissue preparations isolated from minispryn KO (MIKO) and WT mice. In particular, the effect of minispryn on cardiac contractility will be estimated by determining the relationship between peak contraction force and sarcomere length (SL) in intact trabeculae and/or papillary muscles isolated from MIKO and WT mice. The shortening capacity and power developed for a given load will be estimated by determining the force-velocity (T-V) relationship in intact trabeculae and in both fast (EDL) and slow (Soleus) skeletal muscle.
In collaboration with the University of Chieti, the fraction of area occupied by the contractile elements in the EDL and Soleus muscles will be determined using TEM on the muscle in cross section. Furthermore, X-ray diffraction experiments will be performed at the European Synchrotron (ESRF, Grenoble) to measure the distance between thick and thin filaments. By knowing the fraction of the area occupied by the contractile elements and the interfilamentary distance, the force developed by the elementary unit of the muscle, the thick hemifilament, will be determined. Furthermore, to evaluate whether the conformation of resting myosin motors is altered in MIKO mice, the intensity profile and fine structure of myosin-based meridional reflections will be compared between MIKO mice and WT mice.