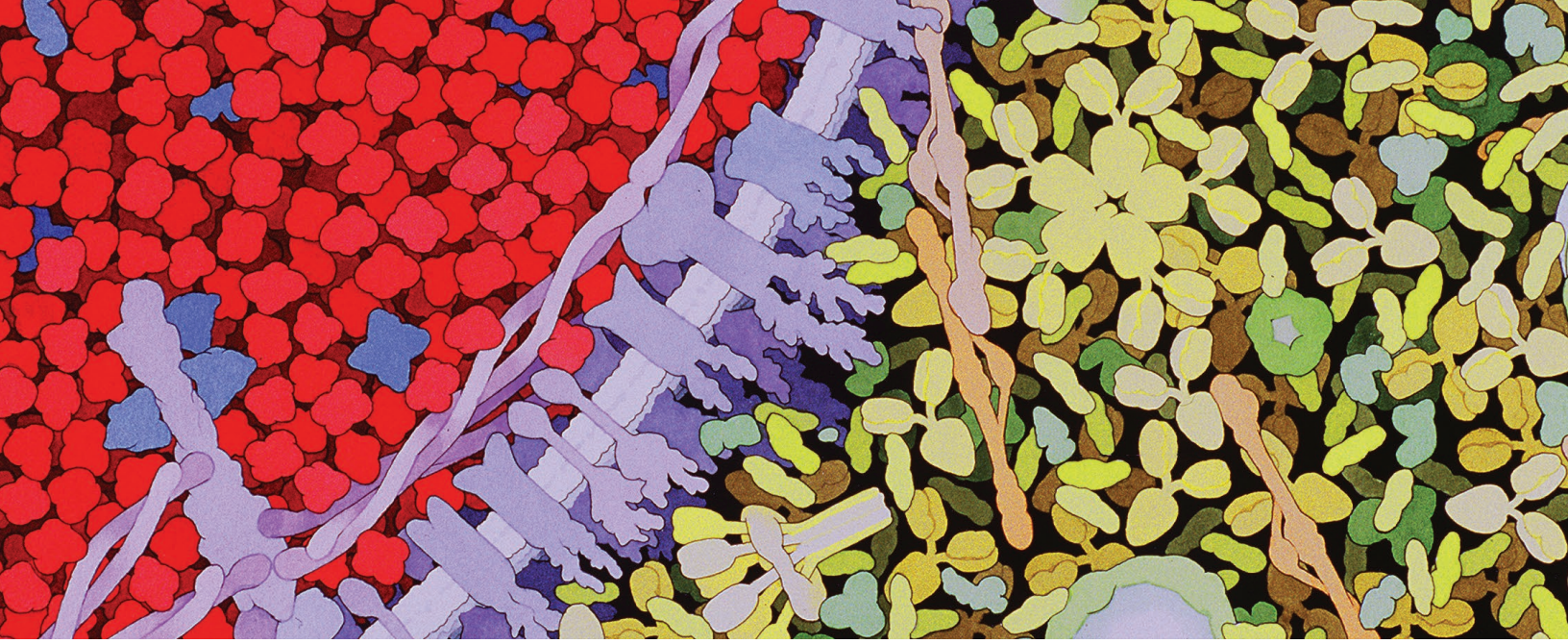

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Day 1 Abstracts

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Exploration of a novel mechanism of cardiac troponin release: in silico evidence of non-classical secretion

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Cardiac troponin is one of the most important biomarkers in cardiology. Traditionally, it has represented a biochemical sign of necrosis, a characteristic of acute myocardial infarction (AMI). However, with the arrival of high-sensitivity detection assays, cardiac troponin is now detected in healthy patients and in a number of uncommon scenarios unrelated to AMI (such as strenuous exercise, rapid atrial pacing and COVID-19). This suggests that troponin could be released as a consequence of alternative processes other than the well-stablished necrotic cell death. To try to explain this phenomenon, multiple mechanisms of troponin release have been postulated, although there is still no consensus on this matter. Furthermore, the term *myocardial injury* (a troponin determination above the upper reference limit, not necessarily associated with a specific diagnosis) was included in the Fourth Universal Definition of Myocardial Infarction. Nevertheless, the histological or pathobiological process responsible for *myocardial injury* has not been determined. Here, we studied the possibility of troponin release through non-classical secretion, a pathway specially triggered by cellular stress and inflammation. The protein sequences of the eight different isoforms of troponin (I, T and C of fast-twitch skeletal, slow-twitch skeletal and cardiac muscle) were retrieved from UniProtKB and the Protein Data Bank. *SecretomeP 2.0*, a neural networks-based program, was used to predict if any of these proteins undergoes non-classical release. *SignalP 5.0* and *TMHMM 2.0* were also applied to rule out the possibility of classical (endoplasmic reticulum/Golgi dependent) and Type IV (transmembrane) non-classical secretion. After analyzing the sequences, the cardiac T isoform was predicted to be non-classically secreted, as well as the I, T and C subunits of the fast-twitch skeletal muscle and the I subunit of the slow-twitch skeletal muscle. None of the troponin isoforms was found to be subject to classical or Type IV secretion. We believe that troponin T release through a non-classical pathway may contribute to the pathobiological definition of *myocardial injury*. There are already some experimental studies showing the release of troponin through extracellular microvesicles (a type of non-classical secretion) in various cell lines. Nonetheless, more evidence is needed to fully understand this intriguing phenomenon in cardiomyocytes.