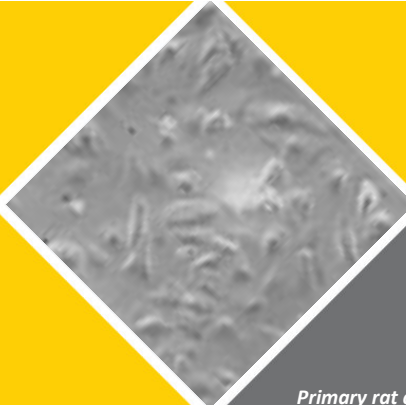




SEPTIC SHOCK



*Primary rat cardiomyocytes
challenged with LPS*

Background

Septic shock is a medical condition as a result of severe infection and sepsis, though the microbe may be systemic or localized to a particular site results in inadequate blood supply to the body's tissues, resulting in ischemia and organ dysfunction. Cardiac dysfunction in sepsis is characterized by decreased contractility, impaired ventricular response to fluid therapy, and in some patients ventricular dilatation. Current data support a complex underlying physiopathology with a host of potential pathways leading to myocardial depression. Circulating factors such as cytokines (TNF-alpha, IL-1beta), lysozyme c, endothelin-1 have direct inhibitory actions on myocyte contractility. Nitric

oxide has a complex role in sepsis-induced cardiac dysfunction

Pathology Model

Primary cardiomyocytes will be isolated from the heart of P2 Sprague Dawley rats. Cells will be cultured in vitro, either in the presence/absence of primary activated macrophages, and challenged with either MMP9, Elastase or LPS. Cells will be either cocultured in static conditions, or tested in dynamic microenvironmental conditions, flushing activated macrophages on primary cardiomyocytes.

Readouts

The following parameters will be analyzed:

- Quantitative evaluation of cell metabolism
- Quantitative evaluation of cell survival
- Quantitative evaluation of mitochondrial damage
- Expression of troponin C
- Qualitative evaluation of cell morphology
- Quantitative evaluation of selected genes of interest
- Quantitative evaluation of beating rate
- Quantitative evaluation of intracellular calcium dynamics