Introduction:
The Sepsis Induced Cardiomyopathy (SIC) is a serious condition during sepsis with a mortality rate up to 70% (1). SIC is clinically manifested with left ventricle impaired contractility (2). Melusine is a muscle-specific protein involved in sustaining cardiomyocyte survival thorough the activation of AKT signaling pathways (3). PI3K–AKT signaling pathway plays a pivotal role in regulating calcium channel activity (4). We hypothesized that Melusine overexpression could exert a protective effect on cardiac function during septic injury.

Methods:
Animals were treated with an intraperitoneal injection of lipopolysaccharide (LPS) at 12 mg/kg. SV129 strain Knockout mice (KO) for Melusine gene and FVB strain with cardiac-specific overexpression (OV) of Melusine were compared. Each group was studied together with a control group (WT). Hemocardiac parameters were studied at 0 hour and 6 hours through echocardiography. Another cohort of animals was sacrificed 6 hours after 20 mg/kg LPS treatment and cardiac tissues and blood sample were harvested for Wb analysis to quantify the expression of AKT, P-AKT and CACNA1C and Elisa analysis for Troponin levels.

Results:
SV129 WT, KO Melusine and FVB WT mice groups, fractional shortening (FS) was significantly impaired after LPS challenge and was associated with compensatory tachycardia. FVB OV mice group didn´t show decrease in FS. Consistent with the increased AKT phosphorylation observed in OV mice, the expression of CACNA1C was also significantly higher both at basal levels and after LPS treatment in OV mice compared to WT mice. Troponin levels didn´t differ between mice groups after LPS treatment

Conclusion:
Melusine has protective role in LPS induced cardiomyopathy, likely through Akt phosphorylation controlling the CACNA1C protein density.

References:
Panel A. Changes in Fractional Shortening (FS) versus time. Experimental groups are: SV129 WT, SV129 KO for Melusin expression, where n=12 for both groups. B. Changes in Heart Rate (HR) versus time. The groups were the same in A. C. M-mode echography of Left Ventricle (LV) before and after LPS challenge.

Panel B. A. Changes in Fractional Shortening (FS) versus time. Experimental groups are: FVB WT, FVB OV for Melusin expression, where n=8 for FVB WT and n=12 for FVB OV. B. Changes in Heart Rate (HR) versus time. The groups were the same in A. C. M-mode echography of Left Ventricle (LV) before and after LPS challenge.

Image 2:

A. Changes in CACNA1C expression versus LPS exposure. Experimental groups are: FVB WT sham and FVB

B. Changes in p-AKT expression versus LPS exposure.

C. Changes in AKT expression versus LPS exposure.

D. Changes in Vinculin expression versus LPS exposure.

E. Changes in Troponin I (ng/ml) versus LPS exposure. Experimental groups are: Baseline, sham 8h, LPS 8h.
OV for Melasin Expression sham, where n=2 for both groups. B. Changes in pAKT expression versus LPS exposure. Experimental groups are the same in A. C. Changes in pAKT/AKT expression versus LPS exposure. Experimental groups are the same in A. D Western Blot E Changes in plasma Troponin level before and after LPS challenge. Experimental groups are: FVB WT (in white sham and treated), FVB OV (in grey sham and treated).