Fatty acid amide hydrolase deficiency shows harmful effects on ischemic cardiomyopathy.

**Ischemic cardiomyopathy is associated with ischemia and reperfusion (I/R), leading to inflammation and left ventricular (LV) dysfunction. Animal studies provided evidence for cardioprotective effects of the endocannabinoid system via CB2. Otherwise, endocannabinoids can act as Peroxisome proliferator-activated receptor (PPAR)-alpha agonist, and its activation causes lipotoxicity and cardiomyocyte loss. We investigated the impact of elevated levels of endocannabinoid anandamide in fatty acid amide hydrolase (FAAH)-/-mice undergoing repetitive I/R.**

**Methods**

Daily 15 min. LAD occlusion was performed over 3 and 7 d in C57/B16 (WT) and FAAH/-/-mice (n=8). PPAR-alpha mediated effects of high anandamide levels in FAAH/-/-mice were eliminated with selective PPAR-alpha antagonist GW6471 i.v. As a proof of principle we blocked the effect of agonist Wy14,834 on PPAR-alpha downstream gene-regulation with GW6471 in WT mice. LV function (M-mode echocardiography), collagen deposition (picrosirius red), accumulation of macrophages (MAC-2) and myofibroblasts (ASMAG) were evaluated. Hypertrophy was measured via cardiomyocyte area. Molecular analyses involved Taqman® RT-qPCR.

**Results**

Fatty acid amide hydrolase deficient mice show persistent infiltration, hypertrophy and loss of function after I/R but recover after PPAR-α inhibition with GW6471.

**Conclusion**

Our study gives novel insights into the role of endocannabinoids acting via PPAR-α. We hypothesize that increase in endocannabinoids may have partially detrimental effects on cardiomyocyte survival due to PPAR-α activation.