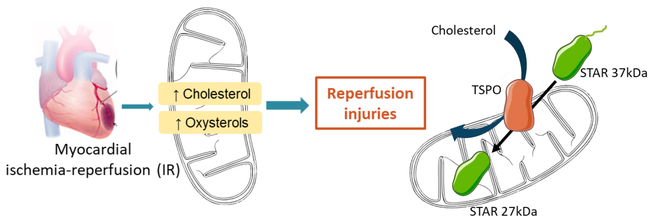
Myocardial ischemia-reperfusion induces STAR translocation into mitochondria independently from TSPO

S Leick, J Bréhat, J Musman, B Ghaleh, Didier Morin, S Pons

Myocardial ischemia-reperfusion induces STAR translocation, sterol accumulation and dysfunction in cardiac mitochondria, processes modulated by TSPO.

Shirin Leick, Juliette Bréhat, Julien Musman, Bijan Ghaleh, Didier Morin, Sandrine Pons
IMRB U955 Equipe Ghaleh, Inserm, Créteil, France

Introduction

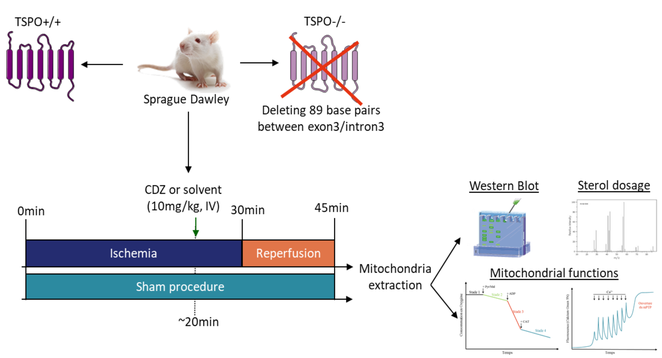


During myocardial ischemia-reperfusion, mitochondrial accumulation of sterols is deleterious for cardiomyocytes. In steroidogenic organs, cholesterol is transferred into mitochondria, via TSPO (translocator protein) and STAR (steroidogenic acute regulatory protein). However little is known regarding of the effects of these proteins in the heart.

Objective

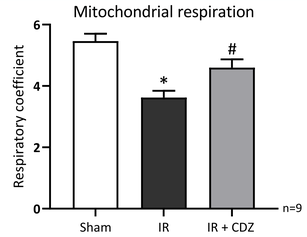
This study aims to investigate the TSPO and STAR dependent mechanisms involved in cholesterol transfer in cardiac mitochondria after IR in order to develop cardioprotective strategies.

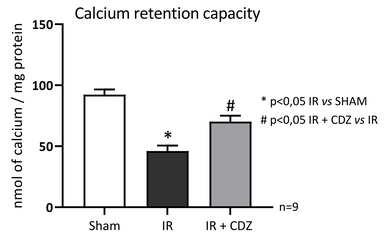
Methods



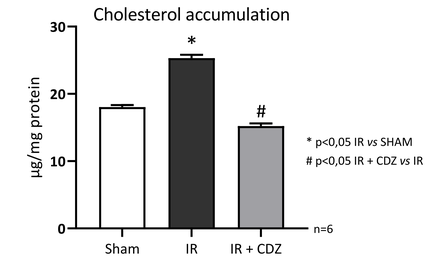
4'-chlorodiazepam (CDZ): inhibitor of TSPO

Result 1: In TSPO+/+ rats, ischemia-reperfusion (IR) alters mitochondrial function which is restored by 4'-chlorodiazepam (CDZ)

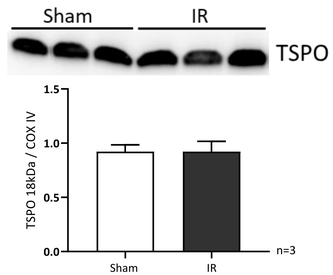




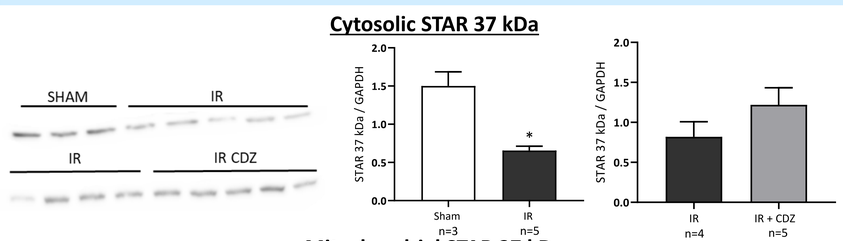
Result 2: CDZ limits cholesterol accumulation after IR

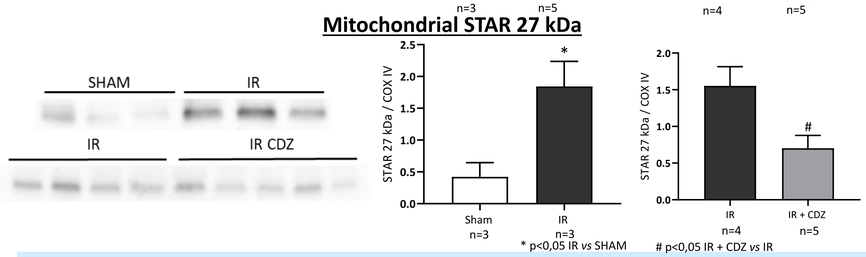


Results 3: TSPO expression remains unchanged after IR

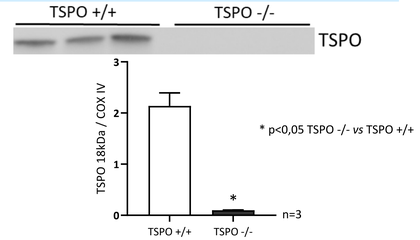


Result 4: CDZ inhibits STAR translocation in cardiac mitochondria after IR, without effet on cytosolic STAR

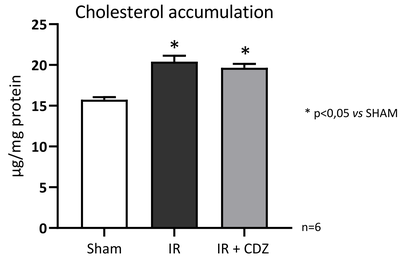




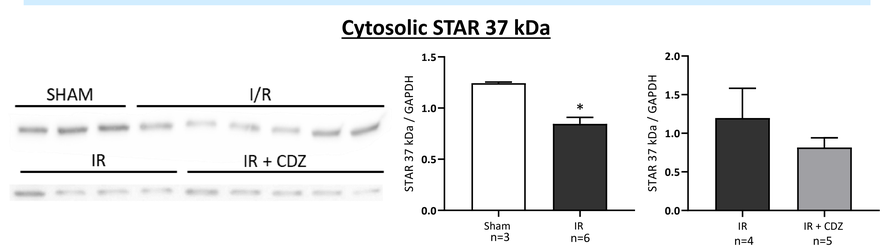
Result 5: TSPO deletion in TSPO-/- rats

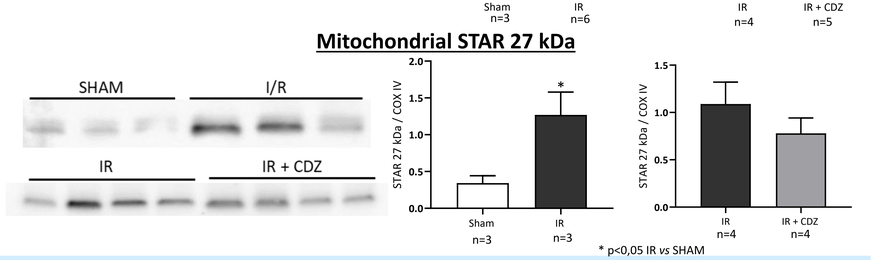


Result 7: Loss of effect of CDZ on cholesterol accumulation

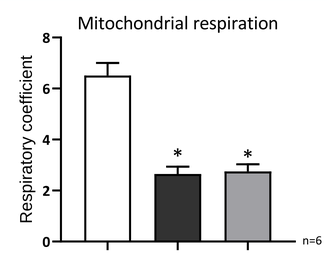


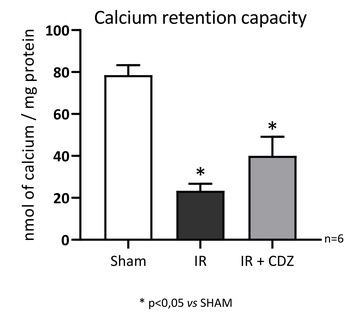
Result 8: TSPO deletion inhibits the effect of CDZ on STAR translocation





Result 6: IR alters mitochondrial function without effect of CDZ, in TSPO -/- rats





Conclusion

IR increases STAR translocation into cardiac mitochondria, sterol accumulation and mitochondrial dysfunction. This process is modulated by TSPO, as demonstrated by results obtained on TSPO-/- rats. So, targeting TSPO-STAR seems to be promising for the development of future cardioprotective strategies.