



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

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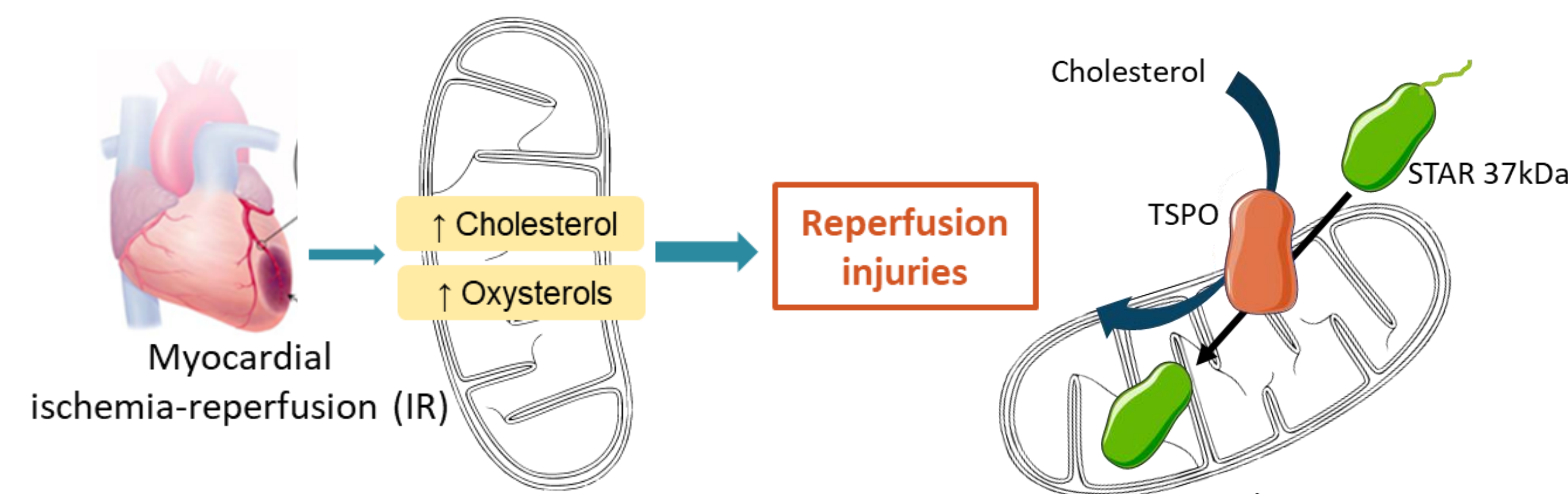
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Myocardial ischemia-reperfusion induces STAR translocation, sterol accumulation and dysfunction in cardiac mitochondria, processes modulated by TSPO.

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Introduction

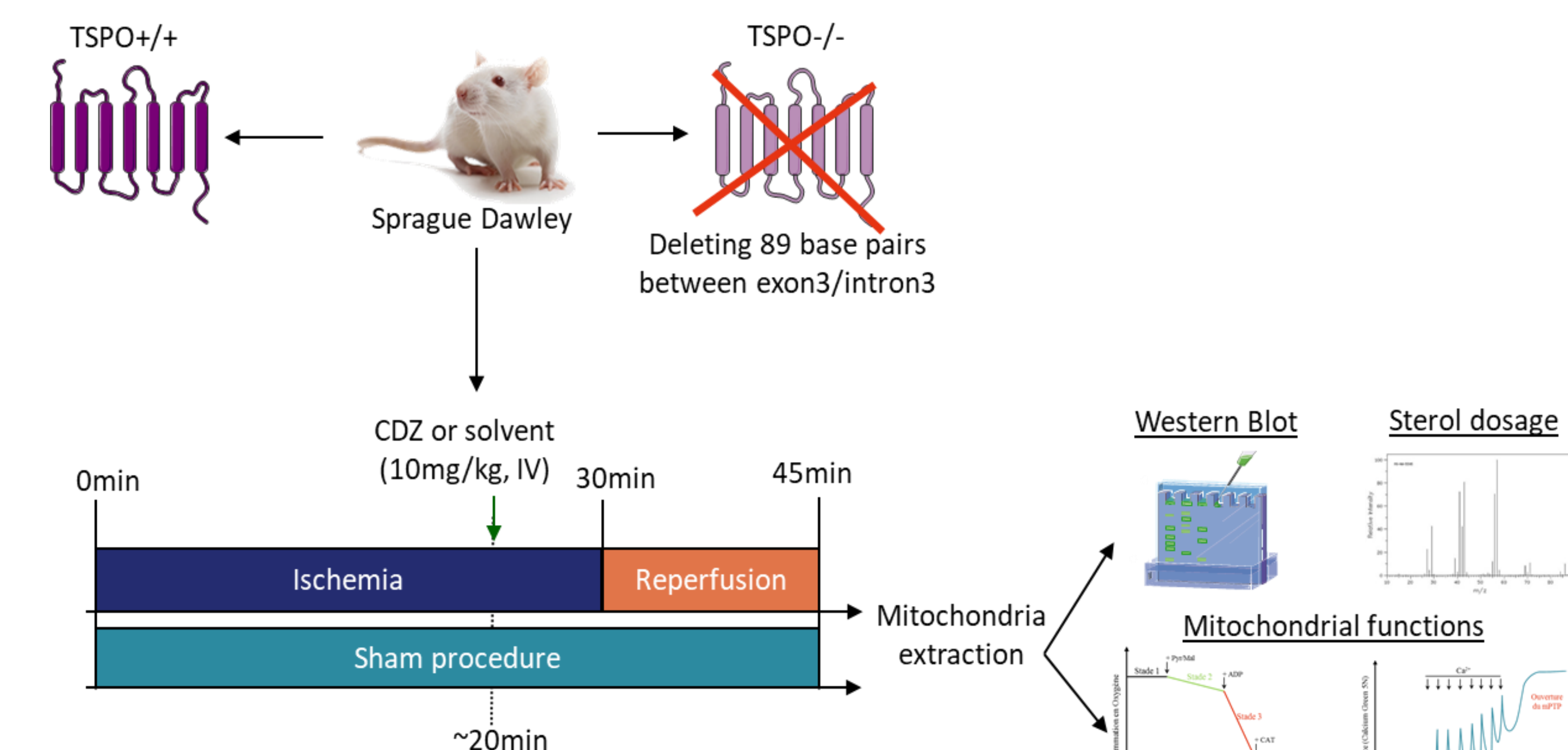


During myocardial ischemia-reperfusion, mitochondrial accumulation of sterols is deleterious for cardiomyocytes. In steroidogenic organs, cholesterol is transferred into mitochondria, via TSPO (translocator protein) and STAR (steroidogenic acute regulatory protein). However little is known regarding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

Objective

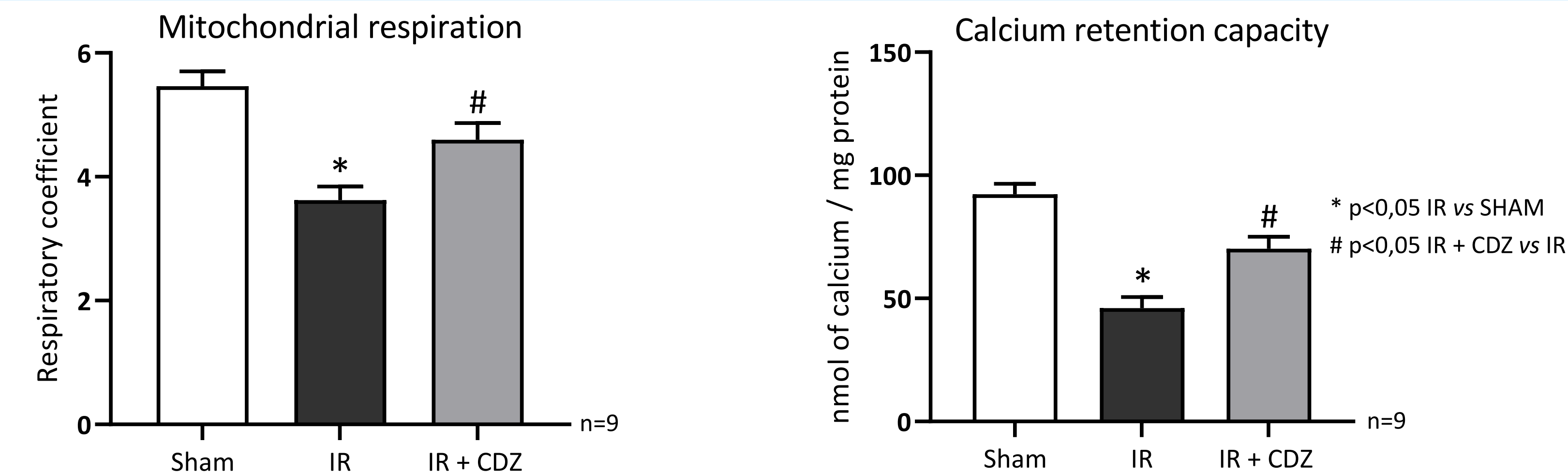
This study aims to investigate the TSPO and STAR dependent mechanisms involved in cholesterol transfer in cardiac mitochondria after IR in order to develop cardioprotective strategies.

Methods

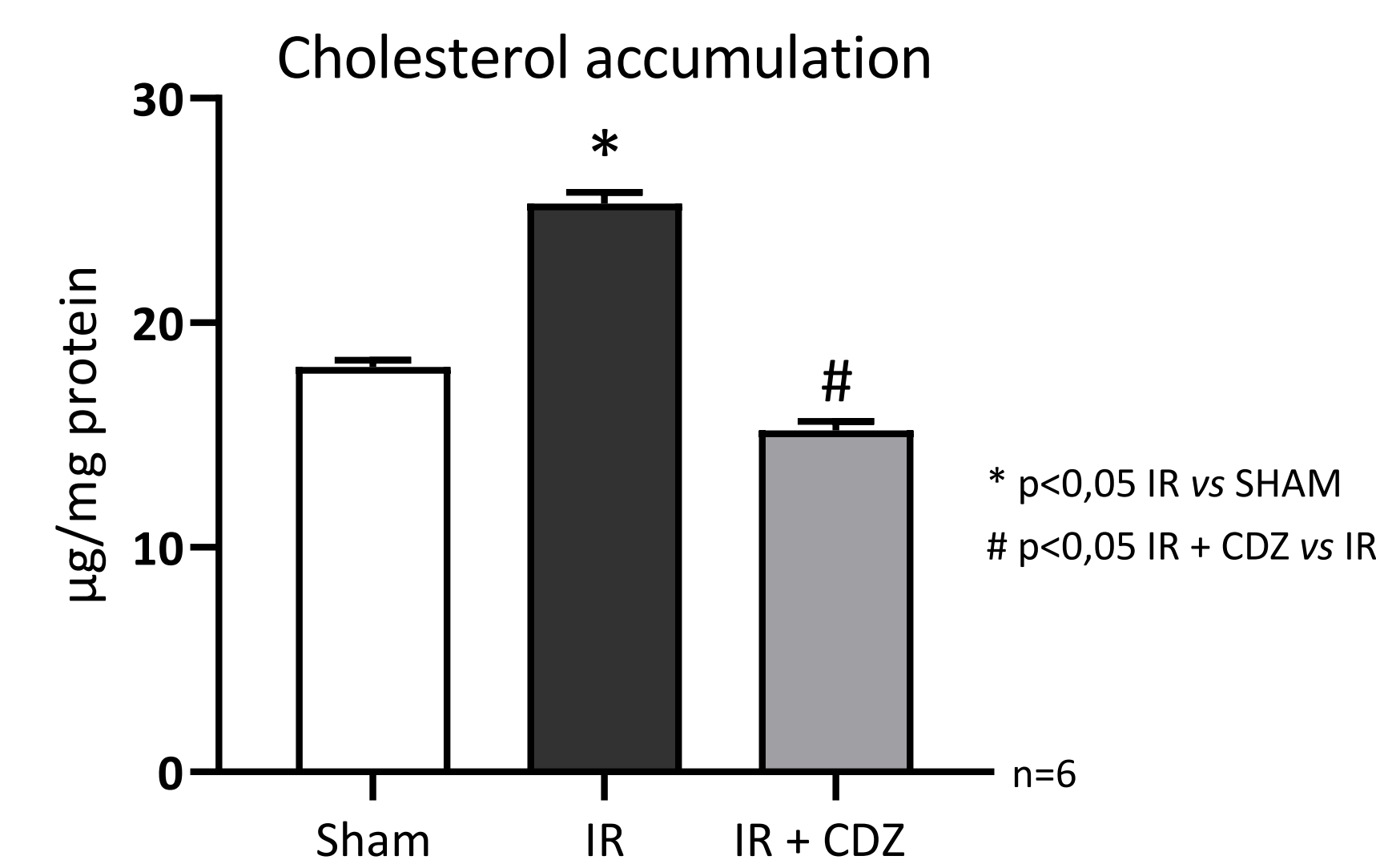


4'-chlorodiazepam (CDZ): inhibitor of TSPO

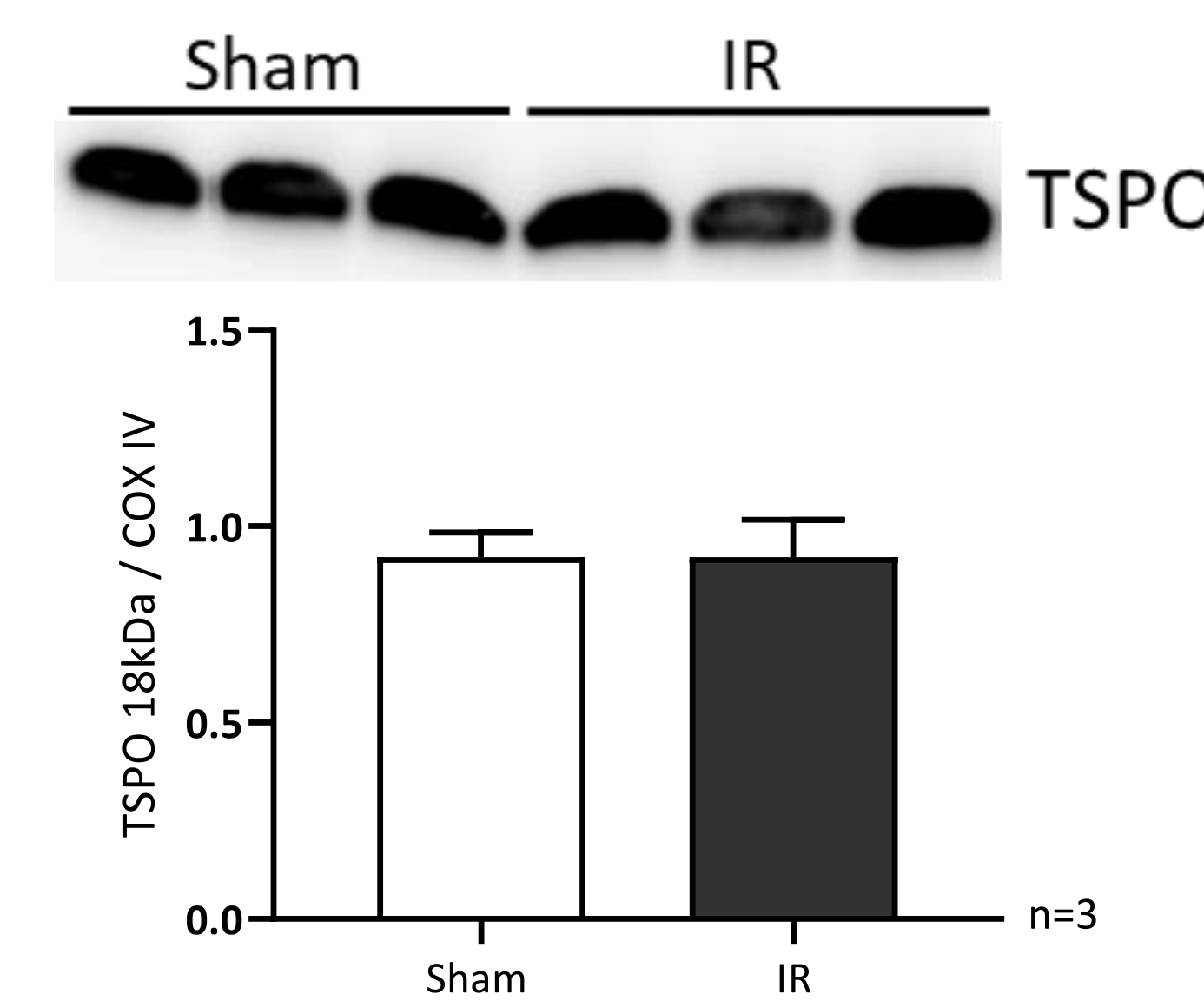
Result 1: In TSPO+/+ rats, ischemia-reperfusion (IR) alters mitochondrial function which is restored by 4'-chlorodiazepam (CDZ)



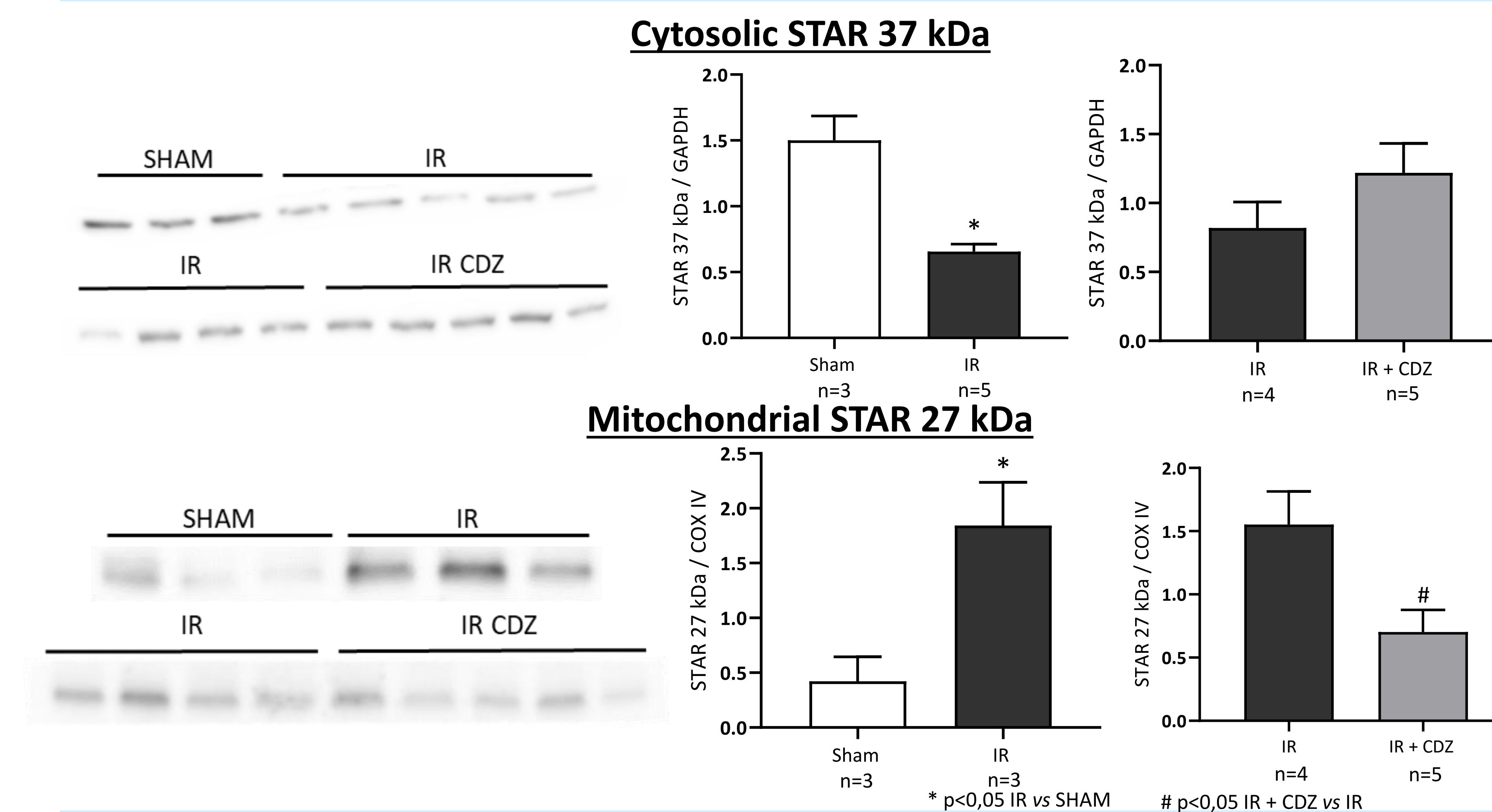
Result 2: CDZ limits cholesterol accumulation after IR



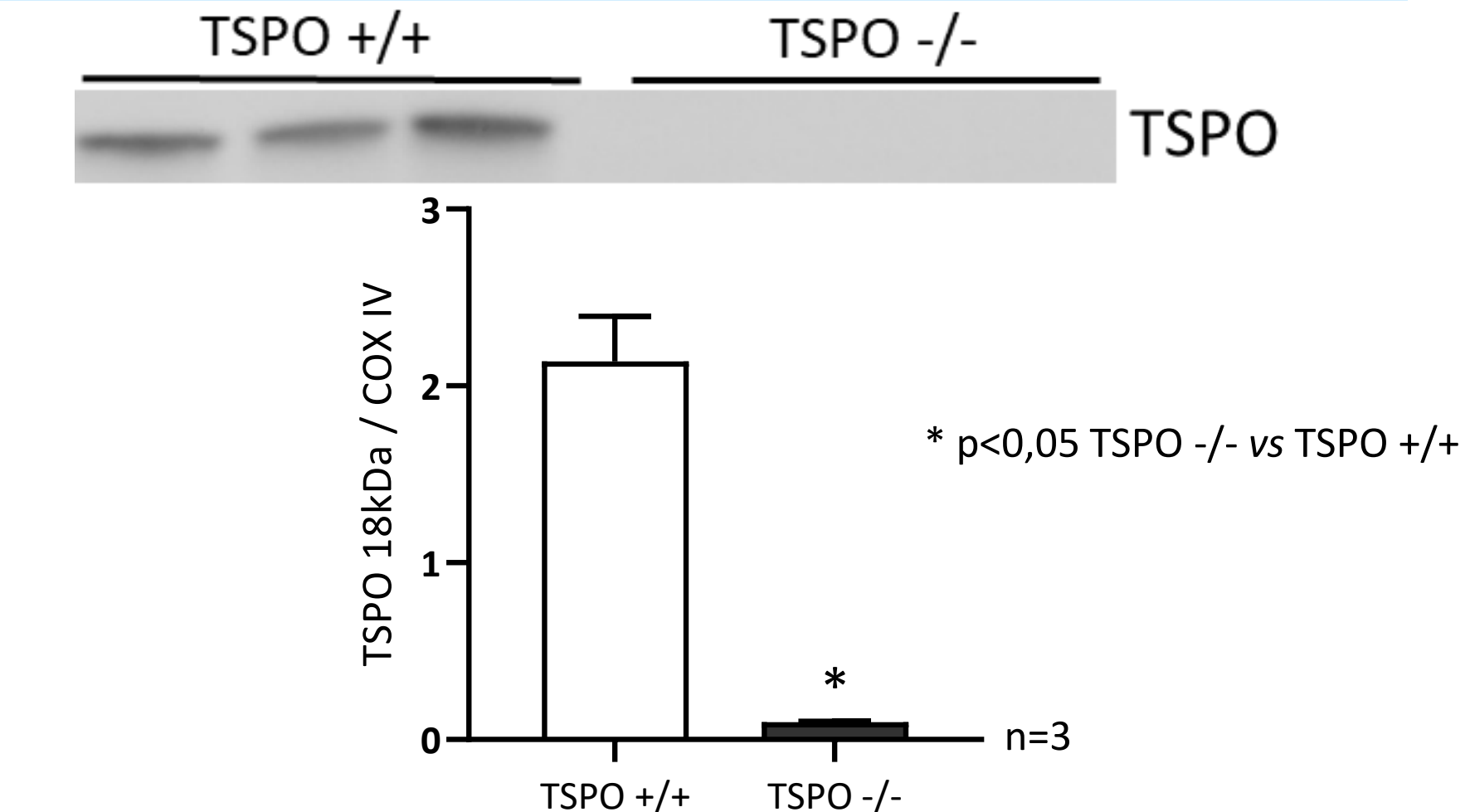
Results 3: TSPO expression remains unchanged after IR



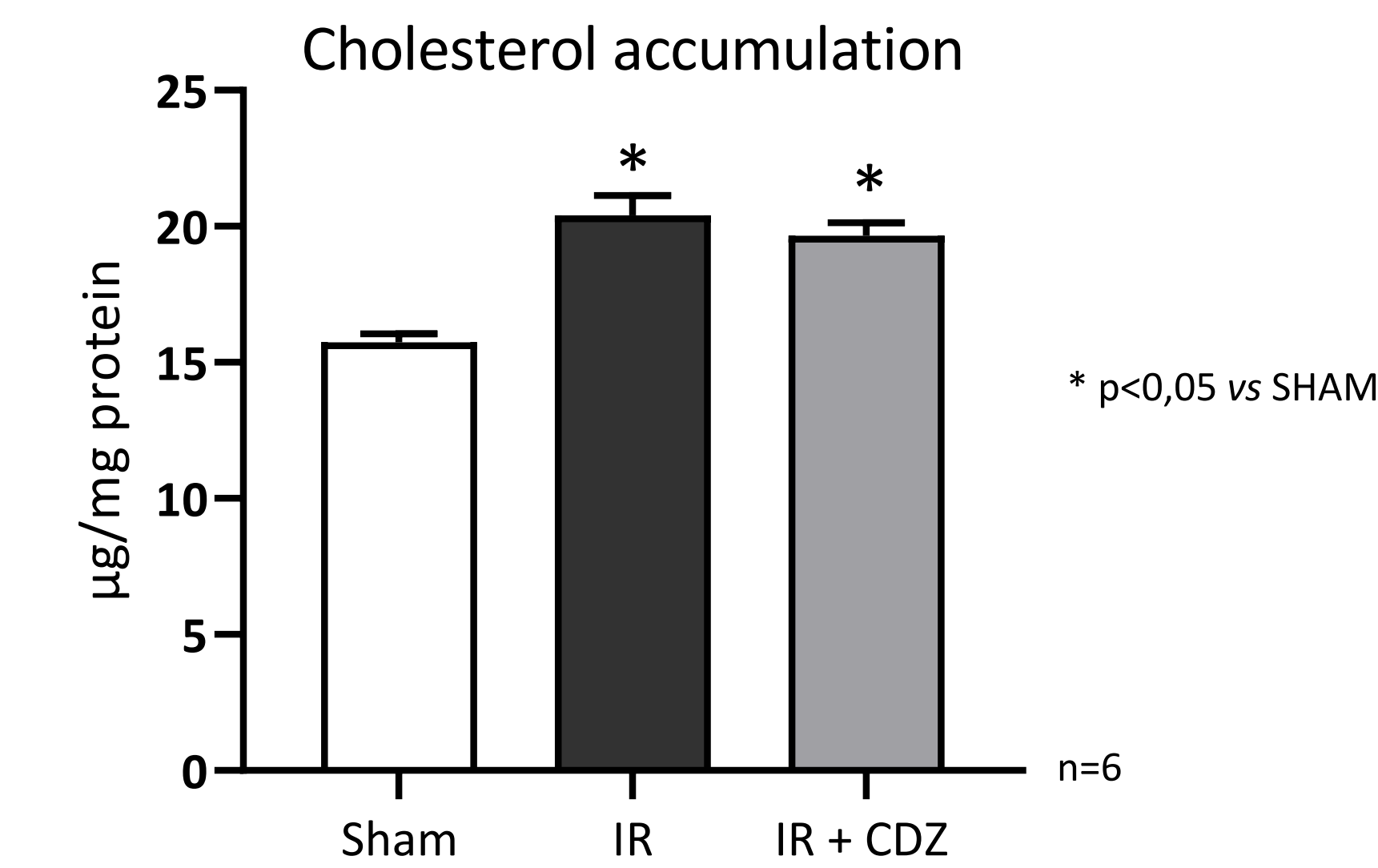
Result 4: CDZ inhibits STAR translocation in cardiac mitochondria after IR, without effect on cytosolic STAR



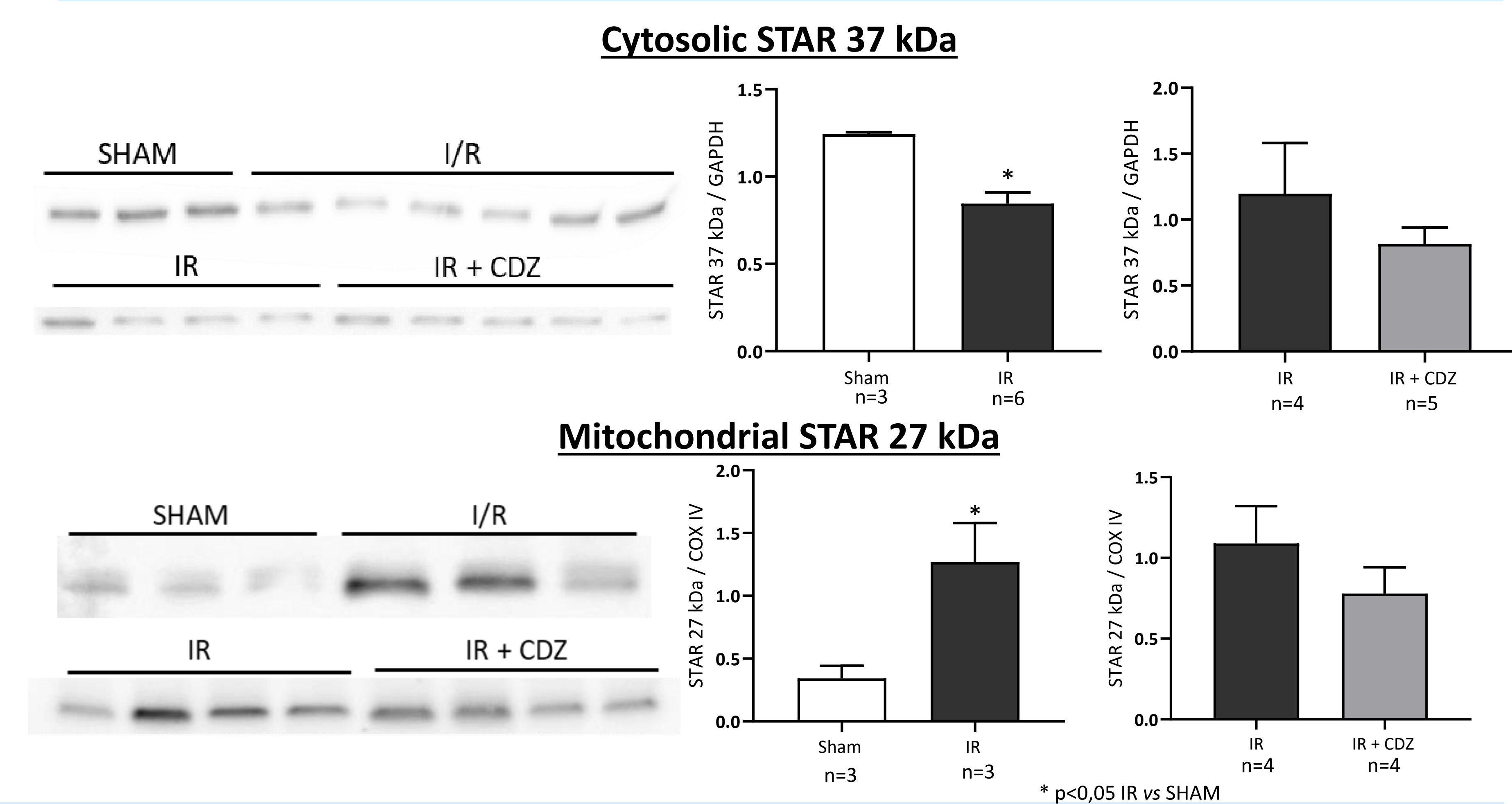
Result 5: TSPO deletion in TSPO-/- rats



Result 7: Loss of effect of CDZ on cholesterol accumulation



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



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.