IBJ Plus IberoAmerican Journals

"Insulin receptor substrate 2 (IRS2) deficiency reduces inflammatory and fibrogenic responses of the liver to cholestatic injury".

Andrea Villar-Lorenzo[1], Patricia Rada[1], Carmelo García-Monzón[2], Ángela M Valverde[1], Águeda González-Rodríguez[2]

[1]Instituto de Investigaciones Biomédicas "Alberto Sols" (CSIC), CIBERdem, Madrid, Spain.
[2]Unidad de Investigación, Hospital Universitario Santa Cristina, Instituto de Investigación Sanitaria Princesa, CIBERehd, Madrid, Spain.

*Corresponding author:
Águeda González-Rodríguez, Unidad de Investigación, Hospital Universitario Santa Cristina, Instituto de Investigación Sanitaria Princesa, CIBERehd, Madrid, Spain. E-mail. aguedagr.phd@gmail.com

Introduction: Hepatocellular injury is the major triggering event of the wound healing response that leads to liver fibrosis. As insulin receptor substrate 2 (IRS2) is one of the key downstream mediators of insulin signaling pathway, which play major roles in liver disease, we investigated whether IRS2 influences the hepatocellular stress response in the liver.

Methods: For that goal, cholestatic liver injury was induced by bile duct ligation (BDL) in wild-type (WT) and IRS2-deficient (IRS2KO) mice. Histological analysis, inflammatory and fibrogenic responses were evaluated in livers from these mice 3, 7 and 28 days following BDL.

Results: Although no differences between genotypes were found at the end of the experiment (28 days), IRS2KO mice displayed less BDL-induced liver histological alterations, including hepatocyte damage and excess deposition of extracellular matrix components compared to WT mice after 3 and 7 days. Moreover, hepatic expression levels of collagen 1 alpha, transforming growth factor 1 and smooth muscle actin were all lower in IRS2KO mice than in WT animals after 3 and 7 days. In parallel, mRNA expression of pro-inflammatory cytokines such us tumor necrosis factor alpha and interleukin 6 was also reduced in livers from IRS2KO mice at these time points. Interestingly, hemeoxygenase 1 expression, used as a maker of oxidative stress, was also decreased in livers lacking IRS2.

Conclusions: Taken together, our results indicate that IRS2 contributes to the progression of cholestatic liver injury since its deficiency reduced inflammatory and fibrogenic responses induced by BDL. Modulation of this protein represents a potential therapeutic strategy for cholestatic liver diseases.

Keywords: Liver, Cholestasis, IRS2
Published May 18, 2018.

Editor: Name of the editor here.
Cite as: Andrea Villar-Lorenzo, Patricia Rada, Carmelo García-Monzón, Ángela M Valverde, Águeda González-Rodríguez. "Insulin receptor substrate 2 (IRS2) deficiency reduces inflammatory and fibrogenic responses of the liver to cholestatic injury". IBJ Plus 2018 (S2):e00047 doi: 10.24217/2531-0151.18v1s2.00047.
Funding: Funding explanation.
Competing Interests: No Competing interest.