Abstract: Diabetes and obesity are metabolic diseases with a prevalence of more than 13% and 30% in Spain respectively. They both share insulin resistance and are directly related with chronic liver damage and hepatocarcinoma (HCC), the third leading cause of cancer death worldwide. In our laboratory, we have developed an in vitro cellular model showing that insulin is necessary for normal hepatocyte differentiation and that insulin resistance inhibits this process. Thus, an in vivo chronic liver damage model has been used to study insulin resistance in liver wound healing and regeneration. Phenotypic analyses revealed significant differences between wt and Irs2-/- ko mouse livers after DDC treatment, measuring serum transaminases and fibrosis markers, although no differences were observed in periportal staining with the Ki67 proliferation marker or the ductular indicator Ck19. Gene expression analysis of wt and ko livers after DDC treatment, revealed significant differences in the expression of secreted and inflammatory marker Opn, and for the epithelial marker Epcam. Insulin resistance also affected the expression of paracrine FGF signaling and fibrosis markers, thus indicating a putative role of Irs2 in liver remodeling, wound healing and regeneration.