IFN & 63 PEG), including 6 mitochondrialopathies. SVR was achieved in 20% of IFN pts vs 27% of PEG pts (p = 0.047). In those who did not discontinue treatment, virological response rates were at W4 (12 vs 20%), W12 (34 vs 41%), W24 (41 vs 54%), W48 (34 vs 52%) and W72 (6 vs 35%), respectively. Virologic response at W12 predicted SVR with 87% Positive Predictive Value and its absence had a 99% Negative Predictive Value. SVR varied with genotypes 1 or 4 (11%) vs 3 or others (43%), but not with the Metavir score or the adjusted ribavirin dose. Response-associated pretreatment characteristics included genotypes other than 1 or 4 (OR = 5.9), no protease-inhibitor therapy (OR = 2.0), age=40 years (OR = 1.9) and elevated ALT (OR = 1.8). Necro-inflammation significantly decreased in the PEG pts (-0.20 vs 0.02, p = 0.0008). Fibrosis stabilized in virological responders and worsened in non responders. Steatosis improved significantly in patients infected by genotype 3 who had a SVR (p = 0.017).

Conclusions: Hepatocytes exposed to the reagent turned out to secrete activin in response to activated IFNα2b and ribavirin dose. Response with activin was not altered by follistatin treatment. Exogeneous follistatin resulted in a marked activation of the transcription factor NF-κB, indicating that calcium translocation enters into the intracellular calcium chelator BAPTA-AM. BAPTA-AM completely blocked resistin-induced activation of NF-κB, as indicated by phosphorylation of the inhibitory protein IκBα, and electrophoretic mobility shift. Resistin also induces a rapid and transient increase in intracellular calcium concentration. To establish a possible link between calcium influx and NF-κB, we assessed the effects of the intracellular calcium chelator BAPTA-AM. BAPTA-AM completely blocked resistin-induced activation of NF-κB, indicating that calcium transients are necessary for this pro-inflammatory pathway. Moreover, calcium chelation inhibited MCP-1 secretion in response to resistin. Exposure of HSC to resistin did not affect mRNA levels of TGF-β or procollagen type I. Interestingly, resistin mRNA was markedly up-regulated in liver tissue obtained from patients with end-stage liver disease. Resistin overexpression in HSCs did not affect mRNA levels of TGF-β or procollagen type I. Interestingly, resistin was markedly up-regulated in liver tissue obtained from patients with end-stage liver disease. Resistin overexpression was confirmed by immunohistochemistry that revealed specific signal in sinusoidal cells and in biliary epithelial cells.

Conclusions: Resistin exerts pro-inflammatory actions in human HSCs, by activation of a pathway requiring calcium influx and NF-κB. In addition, resistin expression is up-regulated at the mRNA and protein levels in the liver of patients with severe fibrosis. These findings may be relevant for the pathophysiology of liver fibrosis especially in the context of non-alcoholic steatohepatitis.