Alcohol-induced alterations in cell function, hepatic inflammation, and fibrosis are prominent features of liver disease in general and of alcoholic liver injury in particular. The link between these processes, however, remains unclear. A virtually universal characteristic of liver injury and subsequent inflammation is the induction of hepatocellular damage, and we have extensively studied the effect of ethanol administration on the hepatocyte and the process of endocytosis by these cells, using the asialoglycoprotein receptor (ASGP-R) pathway as a model. Our recent studies have shown that the hepatocellular ASGP-R is involved with uptake and clearance of several proteins known to play a role in the inflammatory process, including cellular fibronectin (CFn), apoptotic bodies, and desialylated carcinoembryonic antigen (CEA). Impaired uptake of these ligands by the ASGP-R leads to an ethanol-induced accumulation, which then contributes to enhanced activation and cytokine production by non-parenchymal cells such as Kupffer cells and liver endothelial cells. Indeed, our recent data shows that factors produced by Kupffer cells incubated with CEA, CFn or apoptotic bodies can lead to production of TNF-alpha and IL-6, and that this effect is exacerbated in the setting of alcohol administration. It appears that the interaction of these proteins with the sinusoidal cells of the liver, as well as the cooperation and regulation between the different cell types after ethanol administration is especially important. In our work we aim to acquire a better understanding of the cross-interactive associations that occur between the cell types following chronic ethanol administration, and which contribute to inflammation.