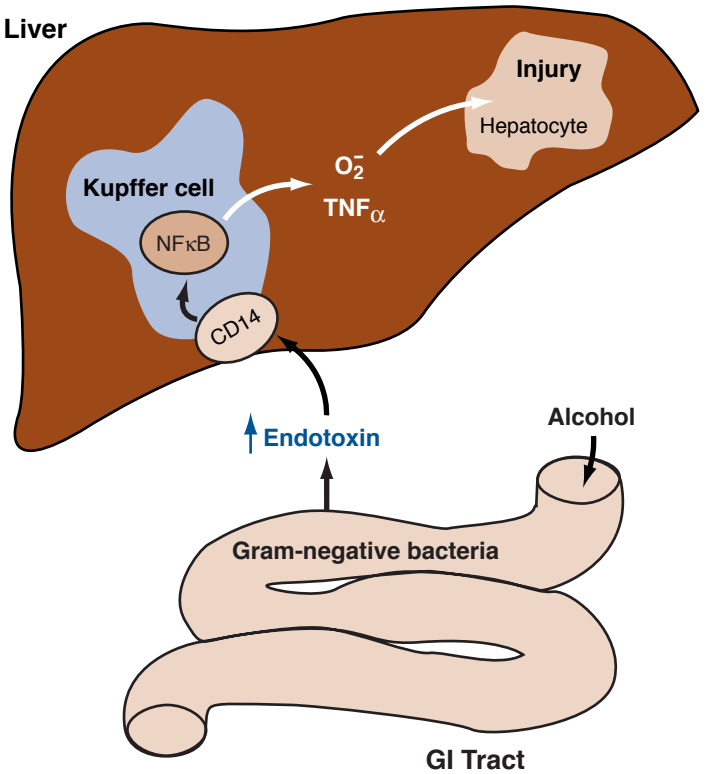
Model showing the link between endotoxin release and liver injury



Following chronic alcohol ingestion, endotoxin released from certain intestinal bacteria moves from the gut into the bloodstream and into the liver. There the endotoxin activates Kupffer cells—a type of immune cell (i.e., macrophages) residing in the liver—by interacting with a molecule called CD14 located on the surface of those cells. This interaction causes the production of the regulatory nuclear factor kappa B (NFκB), which in turn leads to the generation of significant amounts of cytotoxic factors, namely superoxide radicals (O_2^-) and various signaling molecules (i.e., cytokines), most prominently TNFα. TNFα has been shown to be an essential factor in the injury to primary liver cells (i.e., hepatocytes) associated with alcoholic liver disease.

Source: Wheeler, M.D. Endotoxin and kupffer cell activation in alcoholic liver disease. *Alcohol Research & Health* 27(4):300–306, 2003.

Prepared: February 2005