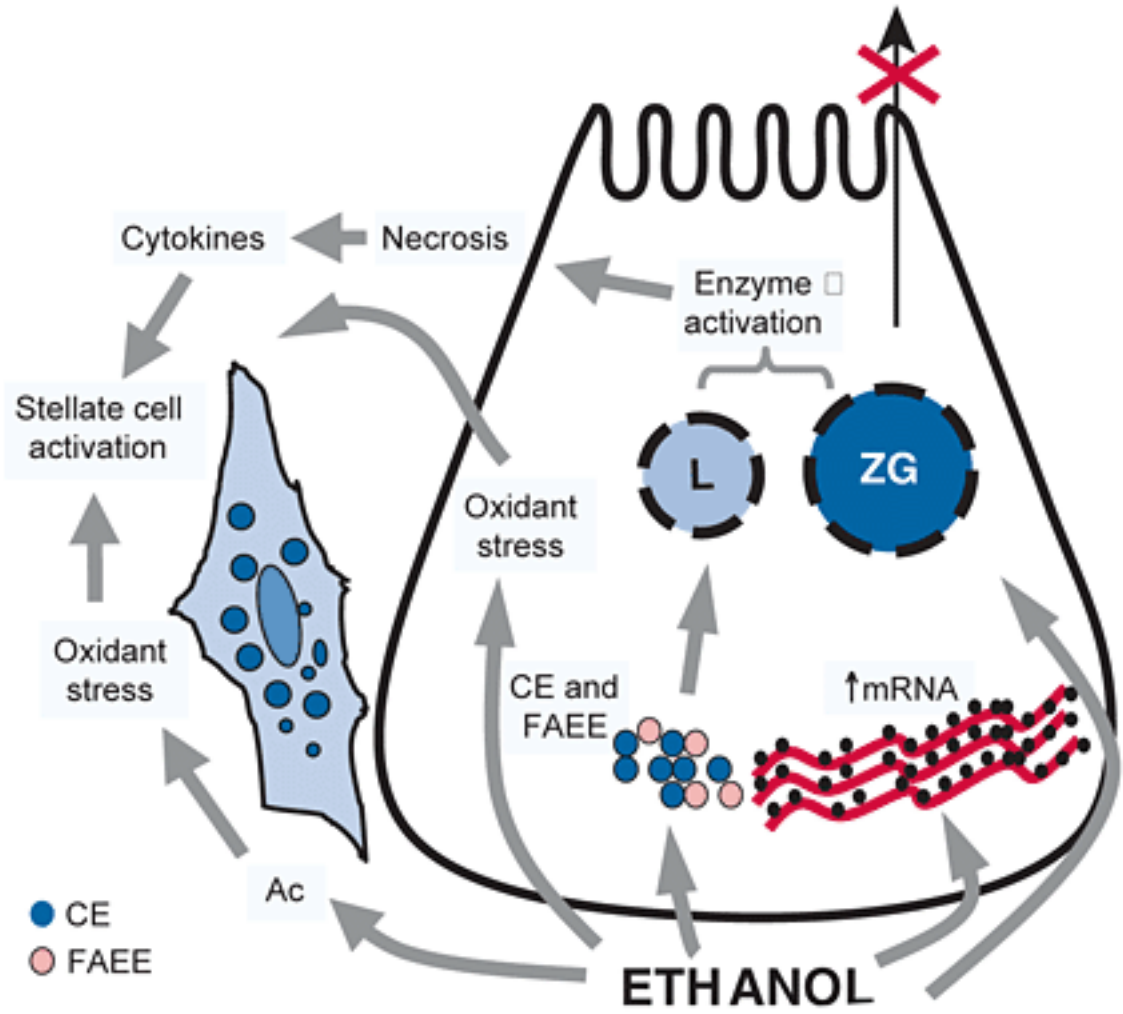
# The Figure depicts an overall hypothesis for the pathogenesis of alcoholic pancreatitis




It is postulated that ethanol, its metabolites, and oxidant stress exert a number of toxic effects on pancreatic acinar cells, which predispose the gland to autodigestive injury. These include the following:

1. Destabilization of lysosomes (L) and zymogen granules (ZG). This destabilization is mediated by oxidant stress; cholesteryl esters (CEs), which are known to accumulate in the pancreas during ethanol consumption; and fatty acid ethyl esters (FAEEs), which are nonoxidative metabolites of alcohol.

2. Increased digestive and lysosomal enzyme content attributed to increased synthesis (increased mRNA) and impaired secretion.

These changes sensitize the cell such that in the presence of an appropriate trigger/co-factor overt injury is initiated (alcoholic acute pancreatitis). Cytokines released during alcohol-induced necroinflammation activate pancreatic stellate cells (PSCs). In addition, PSCs are activated directly by ethanol, most likely via its metabolism to acetaldehyde (Ac) and the subsequent generation of oxidant stress. Activated PSCs then synthesize excess amounts of extracellular matrix proteins leading to pancreatic fibrosis.

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