ROLE OF PEROXISOME PROLIFERATORS ACTIVATED RECEPTORS ALPHA (PPAR-α) IN ACUTE PANCREATITIS INDUCED BY CERULEIN

1Angelina De Sarro, 1,2Emanuela Mazzon,1,2Tiziana Genovese, 1,2Rosanna Di Paola, 1Carmelo Muià, 1Giuseppe Malleo, 3†Emanuela Esposito, 1,2Achille P. Caputi and 1,2Salvatore Cuzzocrea

1Department of Clinical and Experimental Medicine and Pharmacology, School of Medicine, University of Messina, Italy; 2IRCCS Centro Neurolesi "Bonino-Pulejo", Messina, Italy; 3Dipartimento di Farmacologia Sperimentale, Università di Napoli “Federico II”, Napoli, Italy

The peroxisome proliferator-activated receptor-α (PPAR-α) is a member of the nuclear receptor superfamily of ligand-dependent transcription factors related to retinoid, steroid and thyroid hormone receptors. The aim of the present study was to examine the effects of endogenous PPAR-α ligand on the development of acute pancreatitis caused by cerulein in mice.

Intraperitoneal injection of cerulein in PPAR-α WT mice resulted in severe, acute pancreatitis characterized by edema, neutrophil infiltration and necrosis and elevated serum levels of amylase and lipase. Infiltration of pancreatic and lung tissue with neutrophils (measured as increase in myeloperoxidase activity) was associated with enhanced expression of the adhesion molecules intercellular adhesion molecule-1 (ICAM-1) and P-selectin. Immunohistochemical examination demonstrated a marked increase in the staining (immunoreactivity) for TGF-β and VEGF in the pancreas of cerulein-treated PPAR-α WT mice in comparison to sham-treated mice. Acute pancreatitis in PPAR-α WT mice was also associated with a significant mortality (20% survival at 5 days after cerulein administration). In contrast, the degree of (1) pancreatic inflammation and tissue injury (histological score), (2) upregulation/formation of ICAM-1 and P-selectin, (4) neutrophils infiltration and (5) the expression of TGF-β and vascular endothelial growth factor (VEGF) was markedly enhanced in pancreatic tissue obtained from cerulein-treated PPAR-α KO mice. Thus, endogenous PPAR-α ligands reduce the degree of pancreas injury caused by acute pancreatitis induced by cerulein administration.