

We examined whether mast cells and macrophages could play a pivotal role MMP-1, MMP-3, MMP-9, TIMP-1 and TIMP-2 in carbon tetrachloride-induced fibrosis/cirrhosis in a rat's liver. Furthermore, we sought to determine what type of cells or what type of MMPs play an important role in liver fibrolysis.

The fibrosis of the liver of rat was induced by carbon tetrachloride for 14 weeks. The MMPs and TIMPs in the livers were examined by histopathology, immunohistochemistry and immunoblotting.

At week 0, the MMP-1 expression was detected only in the mast cells. They increased in proportion to the development of fibrosis and reached a maximal number for liver cirrhosis at week 14. In the first four weeks, the MMP-3 expression was mainly observed in many hepatocytes. At week 8, the macrophages in the fibrous septa expressed MMP3 as well as hepatocytes. Between weeks 12 and 14, only a few macrophages expressed MMP3. MMP-9 was detected in the Kupffer cells and macrophages from week 4, peaked at week 8, and then decreased at cirrhosis. TIMP-1 and -2 progressively increased throughout the experimental periods. The MMP-1 expression in the mast cells, however, did not decrease the degree of liver cirrhosis. At the recovery stage, only the MMP-3 expression of the macrophages increased strongly in the unresolved fibrous septa and MMP-9 sustained the same levels. These immunohistochemical data were in perfect agreement with the results of immunoblotting on the MMP/TIMP expression pattern in liver fibrosis/cirrhosis in recovery.

We showed that MMP-1 and TIMP-1, as well as the TIMP-2 expression increased, while MMP-3 and MMP-9 significantly decreased during the late stages of fibrosis and cirrhosis. During recovery, however, the MMP-3 expression of macrophages increased highly in the unresolved fibrous septa. In addition, we demonstrated that the mast cells might participate in fibrolysis by producing MMP-1 throughout the experiment. Therefore, MMP-1 and MMP-3 in mast cells and macrophages might contribute to the reversal of fibrosis during liver fibrosis and recovery, respectively.

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P#43

Up Regulation of Metabotropic Glutamate Receptor 3 (mGluR3) in Rat Fibrosis and Cirrhosis Model of Persistent Hypoxia Condition

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Glutamate is the major excitatory neurotransmitter in the central nervous system (CNS) but evidence for peripheral glutamatergic fibers in mammals is still lacking. However, glutamate receptors have been identified in peripheral organs, including taste buds, the myenteric plexus, and pancreatic islet cell. Protection against anoxic damage could be explained by mechanisms mediated by postsynaptic metabotropic glutamate receptor 2 (mGluR2) or mGluR3 such as the inhibition of membrane excitability resulting from reduction of cAMP formation by a G-protein-dependent modulation of ion channels. Thus, mGluR2/3 behaves potentially as a major defensive mechanism anoxia-tolerant species. There are a few reports for the regional pattern of hypoxic damage which was inversely related to the expression of mGluR2/3. The aim of this study was to characterize expression of mGluR3 in the hypoxic liver in experimental model of rat liver cirrhosis. Proteomic analysis of protein extracts from CCl₄ induced cirrhotic rat livers revealed the presence of the mGluR3. The presence of mGluR3 in the macrophages was confirmed by immunohistochemical analysis in the fibrous septa. These results demonstrate that mGluR3 is involved in the liver in response to persistent hypoxic status such as fibrotic and cirrhotic conditions, and suggest that the expression of mGluR3 may be a key role liver functional metabolism and viability by interacting with the glutamate receptors in vivo.

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Paget's Disease of the Breast in a Canine

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Paget's Disease of the breast is a rare lesion that accounts for 2% of mammary gland tumors in humans, presenting clinically as an erythematous or eczematous rash of the nipple. The features may be clinically indistinguishable from eczema or other chronic forms of dermatitis. A 9-year-old Maltese female presented with pain in the right breast. The skin around the nipple was chronic ulcerated and the skin was inverted and hemorrhagical discharge flowed from the lesion. The epidermis contains an infiltrate of small groups of large pleomorphic cells that usually have abundant vacuolated clear-staining cytoplasm. Some larger groups of cells may form acinar structures. The tumor cell population showed positive staining for