of macroscopic phenotype for each distribution pattern of cell proliferation were the followings: Decreasing pattern: 10.6 mm, 887 μm, protruding: 33.3%, sessile: 22.2%, LST: 11.2%. Wave pattern: 10.3 mm, 1110 μm, protruding: 63.6%, sessile: 9.1%. Convex pattern: 9.5 mm, 731 μm, protruding: 33.3%, sessile: 66.7%.
(Discussion) Immunohistochemical cell kinetics of colorectal serrated adenoma correlated with its macroscopic phenotypes as follows:
(1) Wave pattern was correlated with the protruding type.
(2) Convex pattern was correlated with the sessile type which have ducts with short length.
(Conclusion)
(1) Colorectal serrated adenoma showing Decreasing and Wave pattern may originate from hyperplastic polyp. And changes of cell proliferation pattern, Decreasing to the Wave pattern, could occur in the histogenesis of colorectal serrated adenoma.
(2) Serrated adenomas showing Convex pattern may originate de novo.

P4-14

Apoptotic imbalance of infiltrating lymphocytes between tumor and non-tumor tissue in the development of colorectal cancer

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Immunological cells play an important role in neoplastic development. Among immunological cells, lymphocytes exert a diversity of mechanisms against tumor growth. In solid tumors, the presence of tumor infiltrating lymphocytes, natural killer cells and macrophages, provides an effective antitumor response. The number of tumor infiltrating lymphocytes in resected tumor specimens negatively correlates with the size of tumor but positively with survival. The mechanism leading to the dysfunction of infiltrating lymphocytes in the tumor remains unclear. The aim of the study was to investigate whether apoptosis contributed to the loss of infiltrating lymphocytes and the inactivation of their antitumor functions in colorectal cancer. We first demonstrated a significant increase in apoptosis in infiltrating lymphocytes of colorectal cancer tissues, compared to those in non-cancerous tissues from the same patient. Furthermore, our result suggested that disturbance of apoptosis resulted from an imbalance of decreased antiapoptotic molecules and increased proapoptotic ones, reflected by reduction of Bcl-2 level and elevation of Bax level. The shift of balance of Bcl-2 and Bax in favor of the latter accelerated the activity of caspase-3, as Bcl-2 expression led to functional inhibition of caspase-3 while Bax promoted caspase-3 activity. Therefore, caspase-3 could be considered as an executer of apoptosis in Bcl-2 and Bax pathways. In line with the role of caspase-3 in apoptosis caused by a decrease in Bcl-2 and an increase in Bax, the expression of caspase-3 was found to be significantly elevated in infiltrating mononuclear cells of colorectal cancer but not those in non-cancerous tissues. The apoptosis or the activity of caspase-3 may also be associated with inducible nitric oxide synthase (iNOS), whose level increased in the present study. The inhibition of nitric oxide production may revoke immunosuppression and benefit progressively growing malignant tumors. Therefore, increase in iNOS expression in infiltrating mononuclear cells is thought to down-regulate the immune response against colorectal cancer cells and thus may contribute to the loss of lymphocyte functions in the tumor. In conclusion, this study reveals that apoptotic imbalance occurs in infiltrating lymphocytes between tumor and non-tumor tissues. This imbalance may attenuate the function of infiltrating lymphocytes in the tumor tissue and thus contribute to the development of colorectal cancer.

P4-15

Shift from high H6PDH to high G6PDH activity during carcinogenesis induced by environmental pollutants in flatfish liver

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During the past 10 years, we found frequencies of liver cancers up to 34% in flatfish (Platichthys flesus) living in highly polluted areas due to industrial and agricultural effluents. Unfortunately, the class of cancer-initiating and -promoting compounds cannot be identified because over 100 000 different chemicals are released into the sea. The pollution-induced liver lesions and progression from early eosinophilic foci to persistent basophilic foci (FAH) and hepatocellular carcinoma (HCC) show similarities with lesions in chemically-induced liver cancer in mammals. High levels of glucose-6-phosphate dehydrogenase (G6PDH) activity are the most sensitive marker at present for the detection of early preneoplastic foci of altered hepatocytes that are larger than 20 cells (Köhler and Van Noorden (1998). Aquat Toxicol 40: 233–252). G6PDH as the key enzyme of the pentose phosphate pathway is the main source of NADPH in cells and produces riboses for biosynthesis. However, we found recently that the NADPH-producing hexose-6-phosphate dehydrogenase (H6PDH) activity is upregulated in single hepatocytes and microfoci (approx. 1–5 cells). H6PDH activity was elevated in 82% of single altered hepatocytes or microfoci whereas G6PDH activity was not yet altered as compared with extrafocal liver tissue. During cell proliferation and growth of foci, G6PDH activity increased and 67% of (pre)neoplastic lesions, 15.5% adenomas and 18.2% carcinomas showed increased G6PDH activity. H6PDH activity appeared to decrease during cancer progression and was detectable only in 13% of foci, 3.6% adenomas and 1% carcinomas. H6PDH is closely linked to the polycyclic hydrocarbon metabolising system in the smooth endoplasmic reticulum and is inducible by phenobarbital. We hypothesize that environmental chemicals which initiate single hepatocytes to proliferate belong to the phenobarbital type of inducers (PCB congeners 153, 180, 194, HCB, OCS, HCH-isomers; Safe (1994). CRC Crit. Rev. Toxicol. 24: 87–149) which are also found in highest concentrations in flatfish liver.

P4-16

A Case of Clear Cell Hepatocellular Carcinoma

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A case of clear cell hepatocellular carcinoma, a rare malignancy in the liver, in a 53 years old male is documented with immunohistochemical study. The tumor was measured in 8.5×7.0×6.5 cm in the left lobe of the liver with two small daughter lesions. Microscopically, these lesions consisted of uniform large tumor cells with clear cytoplasm containing abundant glycogen. The histological features had a striking resemblance to clear cell tumors that originated in other organs, especially in kidney. The diagnosis was confirmed by focal presence of non-clear tumor cells usually seen in the hepatocellular carcinoma, occasional Mallory bodies and no tumorous lesion in other organs. A brief review of the literature about the prognosis was also done.