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Meeting abstract

New epithelial and mesenchymal cell lines from primary liver cancer to study cell interactions in hepatocarcinogenesis

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To study cell interactions in tumor development, new epithelial and mesenchymal cell lines were established from human hepatocellular carcinoma by spontaneous outgrowth in culture. We obtained several hepatocarcinoma (HCC), B-lymphoblastoid (BLC) and myofibroblastoid (MF) lines. In-depth characterization included cell kinetics, genotype, tumorigenicity, expression of cell-type specific markers and proteome patterns. Many functions of cells of origin were found to be preserved. Thus, HCC cells secrete albumin and α_1-antitrypsin, BLC cells phagocytose and release TNF-β, other cytokines and reactive oxygen species upon stimulation, while MF cells express fibulin-2, vimentin and hepatocyte growth factor (HGF). We studied the impact of the mesenchymal lines on hepatocarcinogenesis by in vitro assays. BLC and MF supernatants strongly increased DNA replication of premalignant hepatocytes. The stimulation by MF lines was mainly attributed to HGF secretion. In HCC cells, MF supernatant had only minor effects on cell growth but enhanced migration. MF lines also stimulated neoangiogenesis via vEGF release. BLC supernatant induced dramatically death of HCC cells, which could be largely abrogated by neutralizing the supernatant with TNF-β-antiserum. In conclusion, the new cell lines reveal stage-specific stimulatory and inhibitory interactions between mesenchymal and epithelial tumor cells. They offer new tools to unravel the role of the microenvironment during hepatocarcinogenesis.