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THE CELLULAR FUNCTION OF HEPATOMA-DERIVED GROWTH FACTOR (HDGF) IN HEPATOCELLULAR CARCINOMA (HCC)

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BACKGROUND/AIMS: Hepatoma-derived growth factor (HDGF) was originally isolated from the cultured media of human hepatoma cell line, HuH-7 cells. In our previous study, we found that patients with high nuclear HDGF LI had poor survival and increased recurrence ($p<0.001$). To further explore the roles of HDGF in angiogenesis and tumorigenesis, we set forth the following study.

Methods: Recombinant HDGF was generated to investigate the functions of HDGF in distinct angiogenic processes in animals. Furthermore, nonmalignant 3T3 fibroblasts stably transfected with HDGF was generated to study the effect of HDGF overexpression on proliferative properties as well as tumorigenicity of 3T3 cells.

RESULTS: Recombinant HDGF was generated and shown to stimulate the proliferation and migration of human umbilical vein endothelial cells (HUVEC) in a dose-dependent manner. Treatment of HUVEC with HDGF increased the secretion of matrix metalloproteinase-9 (MMP-9) by up to ten-fold. Implantation of hydron pellets containing HDGF induced dose-dependent neovascularization in rat corneas. Further, non-malignant NIH3T3 cells were transfected with HDGF expression vector and selected for HDGF-overexpressing stable clones. HDGF transfectants proliferated at a higher rate than that of NIH3T3 cells in serum-containing or -deprived media. Moreover, HDGF transfectants were capable of forming colonies in soft agar and inducing tumor formation when injected into nude mice.

DISCUSSION/CONCLUSIONS: The present study provided *in vitro* and *in vivo* evidences supporting that upregulation of HDGF participates in liver carcinogenesis. This is important for future treatment of HCC.

Keyword: hepatoma-derived growth factor (HDGF), hepatocellular carcinoma, cellular function