行政院國家科學委員會專題研究計畫成果報告

與肝再生有關之生長因子受體在肝細胞癌之表現

Expression of receptors of growth factors related to liver regeneration in hepatocellular carcinoma

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一、中文摘要

高再發率以及低長期存活率一直是肝細胞癌臨床上面臨的問題。肝局部切除後，肝細胞生長因子、介白質 6、轉形生長因子、表皮生長因子促成肝的再生。我們檢驗了 40 例手術切除之肝細胞癌的標本，測定上述生長因子的受體是否在肝細胞癌有表現以及它們的表現是否與肝細胞癌的再發有關。我們發現大部分的肝細胞癌都有表現上述生長因子的受體。受體的量與癌大小無關。肝細胞的再發與受體的量，肝硬化的有無，病人年齡、性別， HBsAg 及 Anti-HCV 無關。在 71%病人，介白質 6 受體在正常肝細胞與肝細胞癌大小不同。總結為肝細胞癌有表現與肝再生有生長關因子之受體。肝細胞癌再發與受體之表現無關。肝細胞癌生長之主要控制機轉可能與肝再生控制機轉不同。

關鍵詞：肝細胞癌、肝細胞生長因子、介白質 6、表皮生長因子、
受體

Abstract

high recurrence rate and poor long term survival of patients with hepatocellular carcinoma (HCC) receiving operation remains a serious clinical problem. After partial hepatectomy, hepatocyte growth factor, interlukin-6, transforming growth factor and epidermal growth factor contribute to the regeneration of liver. We examined 40 surgical resected HCC samples to determin whether the receptors of above growth factors were expressed in HCC and how they correlated with tumor recurrence. We found that most of the HCC did express receptors for growth factors. The amount of receptors did not correlate with the tumor size. The recurrence of HCC did not correlate with the amount of receptors in tumor tissue, age, sex, HBsAg, Anti-HCV and presence of liver cirrhosis. There is size difference of interleukin 6 receptor between nontumor and tumor tissue in 71% cases. In conclusion, HCC expresses receptors for growth factors related to liver regeneration. The recurrence of HCC did not related to expression of growth factor receptors. The growth of HCC is probably mainly controlled by different mechanisms from liver regeneration.

Keywords: hepatocellular carcinoma, hepatocyte growth factor, interleukin 6, transforming growth factor, epidermal growth factor, receptor

二、緣由與目的

After surgical resection for hepatocellular carcinoma, the high recurrence rate and poor long term survival of patients remains a serious clinical problem. This poor outcome is partly due to remaining, clinically undetectable, microscopic tumor in the liver remnant.

After partial hepatectomy, HGF, IL-6, TNF-a, EGF and TGF-a are key factors responsible for liver regeneration. If there were cancer cells remained in the remnant liver, these same factors may also stimulate the growth of tumor. To examine this possibility, we determined the receptors of above-mentioned growth factors in surgical resected HCC and correlate them with tumor recurrence.

三、結果與討論

We have collected 40 surgical resected HCC samples. Proteins and RNA were extract from the non- tumorous (NT) and tumorous (T) part. Western blots were done to detect c-met (HGF receptor), TNF-R1 (TNF-a receptor), IL6R (IL-6 receptor) and EFG receptor. We are unable to detect any signals of receptors in both NT and T part in 9 cases. This probably represents poor samples preservation resulting in protein degradation. All the receptors can be detected in the remaining 32 cases. There are 3 cases with undetectable c-met in tumor part, and one case without IL6R in tumor part . We compute the quantities of receptors by scanning densitometry. No correlation of amount of growth factor receptor was found between non-tumor and tumor tissue. The amount of receptors in HCC did not relate to tumor size. The recurrence of HCC did not correlate with the amount of receptors in tumor tissue, age, sex, HBsAg, Anti-HCV and presence of liver cirrhosis. However, we found size difference of IL6R between NT and T in 71% cases.

In summary, we find expression of growth factor receptors responsible for liver regeneration in hepatocellular carcinoma. No correlation was found between recurrence and abundance of receptors in tumor. This probably implied that growth of tumor is manly regulated by mechanisms different from that of normal tissue. Another possibility is that recurrent tumors contain different amount of receptors from original tumors. Another factor complicated the interpretation is that recurrence could arise from original dormant tumor not removed by surgery or from newly growing tumor. However the presence of above-mentioned receptors in HCC implied that during liver regeneration, HCC are exposed to the same growth factors as normal hepatocyte, and potentially could be stimulated to grow.

四、計畫成果自評

We found expression of receptors of growth factors related liver regeneration in HCC. Although we did not find correlation between these receptors and recurrence of HCC, there is possibility that growth of HCC could be stimulated by liver regeneration following hepatectomy. We also found

size difference of IL6R between nontumor and tumor tissue. This may imply different response to IL6 signal. Our findings deserve further investigation.

五、參考文獻

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