

中国肿瘤生物治疗杂志

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肝细胞癌的诱导分化治疗 点此下载全文

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摘要:

肝细胞癌是最常见的恶性肿瘤之一,虽然其诊断和治疗有不少进展,但其预后仍较差,病死率较高。诱导分化治疗这一概念的提出为肝细胞癌的治疗指明了新的方向。诱导分化治疗在血液系统肿瘤治疗方面获得了成功,其经典范例是全反式维甲酸临床治疗急性早幼粒白血病;但是其在恶性实体肿瘤领域的进展远不如血液系统肿瘤。目前特异性的肝细胞癌诱导分化剂较少,相关的临床应用更是有限。靶向性地针对肿瘤干细胞分化相关的信号转导通路或转录因子进行干预可能起到诱导肝细胞癌分化的效果,例如通过上调与肝细胞分化密切相关的转录因子肝细胞核因子4α(hepatocyte nuclear factor 4α, HNF4α)来诱导肝癌细胞,特别是诱导肝癌干细胞向成熟阶段分化,已初见成效。肿瘤发生发展过程中存在诸多表观遗传学异常改变,如甲基化、乙酰化水平异常或microRNA表达异常,有些改变与肿瘤分化密切相关,干预这些异常改变的药物如组蛋白去乙酰化酶抑制剂对肿瘤起到一定的诱导分化作用。因此,肿瘤干细胞学说的出现及表现遗传学的发展给肝细胞癌诱导分化治疗研究提供了具体的途径。

关键词: 肝细胞癌 诱导分化治疗 肿瘤干细胞 表观遗传学 microRNA

Differentiation therapy for hepatocellular carcinoma Download Fulltext

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Abstract:

Hepatocellular carcinoma (HCC) is one of the most common cancers worldwide. Despite great advances made in diagnosis and treatment of HCC, its prognosis is poor and the mortality rate remains high. Differentiation therapy introduces an attractive concept that may shed new light on HCC treatment. Differentiation therapy has been successfully used in clinical treatment of hematological tumors; and classic example is all-trans retinoic acid in the treatment of acute promyelocytic leukemia, but the clinical use of differentiation therapy in the treatment of malignant solid tumor has been limited. Up to now there have been few HCC-specific differentiation-inducing agents, and their clinical application is limited. Agents that targeting signal transduction pathway molecules or transcriptional factors associated with the differentiation of cancer stem cells may induce the differentiation of HCC. Overexpression of hepatocyte nuclear factor 4a, which is a transcriptional factor closely related to the differentiation of hepatocytes, can effectively induce the differentiation of hepatoma cells, especially liver cancer stem cells. There are lots of aberrant epigenetic changes in the development and progression of tumors, such as altered methylation and acetylation as well as dysregulated expression of microRNA, and some are correlated to the differentiation of tumors. Agents targeting these epigenetic alterations such as inhibitor of histone deacetylase can induce the differentiation of tumors in vitro and in vivo. In all, the cancer stem cell theory and the development of epigenetic may cast new lights on differentiation therapy of HCC.

Keywords: hepatocellular carcinoma differentiation therapy cancer stem cell epigenetics microRNA

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