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癌基因成瘾——肿瘤分子靶向药物研发的一种新思路 点此下载全文

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摘要:

摘 要 肿瘤作为一种多基因突变的慢性累积病,某些肿瘤的生成和发展存在着依赖于某个癌基因的现象,即癌基因成瘾或癌基因依赖现象。癌基因成瘾理论由Weinstein在2002年首先提出,癌基因成瘾的机制目前有"怪诞"网络模型、致癌性休克模型和选择淘汰模型三种假设。肿瘤发生、发展的复杂性和显著的个体差异性,使得确认所谓的依赖性癌基因变得较为困难,除了基因组分析、高通量的蛋白功能分析、基因敲除等方法外,通过RNA干扰技术来寻找依赖性癌基因日益受到关注。癌基因依赖理论能够很好地解释某些分子靶向药物良好疗效的机制,为分子靶向药物的研发增添了理论依据,具有较好的临床应用价值,但该理论同时也面临着巨大的挑战,有待于进一步深入研究并加以完善。

关键词:肿瘤 癌基因成瘾 靶向药物

Oncogene addiction: a new approach for tumor-targeted drugs

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Abstract:

Abstract Tumor is a chronic disease caused by accumulation of gene mutation, but the development and progression of certain tumors is dependent on one or a few genes, which is called oncogene addiction or oncogene dependent phenomenon. Weinstein first described this phenomenon as 'oncogene addiction' early in 2002, and to date there have been 3 models to explain this phenomenon, namely, the 'bizarre circuitry model', 'oncogenic shock model', and 'oncogenic selection model'. The complexity of cancers and heterogeneity of cancer patients set great barriers for identifying the 'additive oncogene'. Here we introduce the high-throughput screening methods for identifying the state of oncogene addiction, including genomics, high-throughput proteomics, gene knockout system, and the emerging RNA interference. The 'oncogene addiction' theory can well explain the mechanism of target therapy and enforce the evidence for development of molecular target agents. 'Oncogene addiction' theory has been viewed as of great potential for cancer target therapy, although it faces some challenges and needs further research.

Keywords: neoplasms oncogene addiction target drug

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