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RNA异常与肿瘤调控研究进展 点此下载全文

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摘要:

肿瘤的发生是一个多因素、多步骤的过程,其根本原因是细胞稳态的失衡。近年研究发现,在肿瘤的发生、发展中除了蛋白质功能紊乱、DNA突变之外,还存在着大量RNA的异常,包括异常的microRNA(miRNA)、长链非编码RNA(long non-coding RNA,lncRNA)、循环RNA等;此外,肿瘤细胞中还存在RNA转录、加工及调控功能的异常,如RNA选择性剪接、RNA编辑、竞争性内源RNA调控等。这些非编码RNA可以在转录后水平及表观遗传学水平调控癌基因和抑癌基因的功能,影响肿瘤的发生和发展,是肿瘤诊断、治疗及预后判断的潜在靶标。竞争性内源RNA使得lncRNA与mRNA通过miRNA相互调控,以"miRNA结合位点"为媒介,形成 RNA调控网络。RNA选择性剪接使得癌基因或抑癌基因产生功能异常的转录本,进而影响其生物学功能。肿瘤中究竟哪些机制导致这些RNA表达及功能的异常,RNA表达及功能的异常又如何影响肿瘤的发生和发展,有哪些表达或功能异常的RNA可以作为肿瘤诊断及预后判断的标志物,又有哪些RNA可以作为肿瘤靶向治疗的靶标?等等问题亟待深入探讨,RNA异常与肿瘤调控已成为肿瘤研究的前沿热点领域。

关键词: 肿瘤 microRNA 长链非编码RNA RNA选择性剪接 RNA编辑 生物标志物 靶向治疗

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Abstract:

The development of cancer is a complex multistage process, which is primarily due to the unbalance of cellular homeostasis. In addition to the well-characterized protein coding dysfunction and DNA mutation, dysregulation of non-coding RNAs including microRNA (miRNA), long non-coding RNA (lncRNA) and circulating miRNA was found in the initiation and progression of cancer. Moreover, aberrant RNA transcription, processing and regulation, such as RNA alternative splicing, RNA editing and competing endogenous RNA regulation, have emerged as important regulatory molecules or mechanisms in cancer cells. These non-coding RNAs may play vital roles in tumorigenesis by regulating oncogene and tumor suppressor gene at either post-transcriptional level or epigenetic level, and act as potential targets for tumor diagnosis, prognosis and cancer therapy. Through competing endogenous RNA, the lncRNA cross-talk with mRNA in a miRNA-dependent manner, and thus form a regulatory network. Via RNA alternative splicing, oncogene and tumor-suppressor gene could generate tumor-specific alternative-splicing transcripts, and therefore affect their biological functions. However, several questions remain to be elucidated: What are the underlying mechanisms of abnormal expression pattern and dysregulation of RNA in cancer? How do the aberrant expression and function of RNAs affect tumorigenesis and progression? Which abnormal RNA can be used as a biomarker for tumor diagnosis, prognosis, as well as the therapeutic target for cancers? Taken together, RNA dysregulation in cancer has become a new research frontier in cancer research.

Keywords: neoplasms microRNA long non-coding RNA RNA alternative splicing RNA editing biomarker targeted therapy

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