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miR-154 suppresses colorectal cancer cell growth and motility by targeting TLR2

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Abstract MicroRNAs play critical roles in the development and progression of colorectal cancer (CRC). miR-154 acts as a tumor suppressor in several tumors; however, its role in CRC is poorly understood. Herein, we found that miR-154 was decreased in CRC tissues and cell lines. Ectopic expression of miR-154 remarkably suppressed cell proliferation and colony formation, migration and invasion in CRC cells. The toll-like receptor 2 (TLR2) was found to be a direct target of miR-154 in CRC cells. Inhibition of TLR2 performed similar effects with miR-154 overexpression on CRC cells, and overexpression of TLR2 could significantly reverse the tumor suppressive effects of miR-154 on CRC cells. This study suggests an essential role for miR-154 in CRC.

Keywords miR-154 · Colorectal cancer · The toll-like receptor 2 · Growth · Motility

Introduction

Colorectal cancer (CRC) is the third leading cause of cancer deaths among all human malignancies, and still has a very poor prognosis due to its high potential for migration and invasion [1]. In the past few decades, great improvements have been achieved in surgery and chemotherapy treatments for CRC, however, the overall survival has not been significantly improved [2]. The progression of CRC involves multi-step genetic events, and the molecular underlying mechanisms still cannot be documented [3]. A newly discovered class of small non-coding RNAs, named microRNAs (miRNAs), has attracted enormous interest in CRC research [4].

Recently, increasing evidence has supported cancer-related roles for miRNAs, which negatively regulate the expression of a variety of target genes. Primary miRNAs (pri-miRNAs) are transcribed by RNA polymerase II, producing smaller precursor hairpin structures (pre-miRNAs) and exported to the cytoplasm by Exportin 5. Pre-miRNAs are further processed by RNase III enzyme Dicer to mature functional miRNAs which contain approximately 22 nucleotides [5]. Mature miRNAs inhibit translation or induce mRNA degradation by binding to specific complementary sites within the 3′-untranslated regions (3′-UTR) of their target mRNAs [6]. A variety of studies have reported that miRNAs can regulate the expression of numerous genes, including those essential for tumor proliferation, migration, invasion, and metastasis [7]. The function of miRNAs in the treatment of cancers including CRC has been demonstrated [8, 9]. miRNAs that act as tumor suppressors (e.g., miR-129, miR-124, and miR-143) [10–12] or oncogenes (e.g., miR-31, miR-32, and miR-155) [13–15] have been identified in CRC.

In this study, we investigated the expression and function of miR-154 in CRC cells. Gain-/loss-of function studies found that miR-154 suppressed CRC cells growth, migration, and invasion. Forced expression of miR-154 resulted in down-regulation of the toll-like receptor 2 (TLR2) at a post-transcriptional level. Overexpression of

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