Biochimica et Biophysica Acta 1850 (2015) 708–721

Contents lists available at ScienceDirect

Biochimica et Biophysica Acta

journal homepage: www.elsevier.com/locate/bbagen

MiR-143 and rat embryo implantation

Shi Tian [a,1], Xing Su [b,c,1], Lu Qi [b,1], Xiao-Hua Jin [b,c], Yi Hu [b], Chun-Ling Wang [d], Xu Ma [b,c,*], Hong-Fei Xia [b,c,*]

[a] Haidian Maternal & Child Health Hospital, Beijing 100080, China
[b] Reproductive and Genetic Center of National Research Institute for Family Planning, Beijing 100081, China
[c] Graduate School, Peking Union Medical College, Beijing 100730, China
[d] Cadre Ward, China Mei-Tan General Hospital, Beijing 100028, China

ARTICLE INFO

Article history:
Received 5 June 2014
Received in revised form 26 November 2014
Accepted 29 November 2014
Available online 5 December 2014

Keywords:
miR-143
Embryo implantation
Uterus
Rat
Lifr

ABSTRACT

Background: To study the role of *miR-143* during embryo implantation in rat.
Methods: MiR-143 expression in rat early pregnancy was detected by Northern blot. The relation between *miR-143* and *Lifr* predicted and confirmed by bioinformatics method, dual-luciferase activity assay, Western blot and immunohistochemistry. The role of *miR-143* was detected by MTS, Edu and *ranswell* chamber assays.
Results: The expression level of *miR-143* on gestation day 5–8 (g.d. 5–8) was higher than on g.d. 3–4 in uteri of pregnant rat. *MiR-143* was mainly localized in the superficial stroma/primary decidual zone, luminal and glandular epithelia. The expression of *miR-143* was not significantly influenced by pseudopregnancy, but the activation of delayed implantation and experimentally induced decidualization significantly promoted *miR-143* expression. Over-expression of *miR-143* in human endometrial stromal cells (ESCs) inhibited cell proliferation, migration and invasion. Knockdown of *miR-143* promoted cell proliferation and invasion. The results of recombinant luciferase reporters showed that *miR-143* could bind to the 3¢-untranslated region (UTR) of *leukemia inhibitory factor receptor* (*Lifr*) to inhibit *Lifr* translation.
Conclusions: Uterine *miR-143* may be involved in the successful pregnancy, especially during the process of blastocyst implantation through regulating *Lifr*.
General significance: This study may have the potential to provide new insights into the understanding of ***miR-143*** function during embryo implantation.

1. Introduction

Mir-143 is a short non-coding RNAs molecule and located on chromosome 5 position 33 in the human genome [38]. *MiR-143* is highly conserved in vertebrates and function to regulate the expression levels of their target genes by binding to their 3′-untranslated regions (3′-UTR) [11,12,38]. *MiR-143* also down-regulates the expression levels of their target genes through targeting their coding regions [43].

MiR-143 is thought to play an important role in tumorgenesis. Decreased expression of *mir-143* has been observed in diversified cancer samples, such as bladder cancer, cervical cancer, colorectal cancer, liposarcomas, prostate carcinomas, non-small cell lung cancer, breast cancer, endometrioid carcinomas, renal cell carcinoma and so on [1,9,13,18,19,30,44–47]. Loss of *miR-143/145* cluster enhanced cancer cell migration and invasion in prostate cancer through directly regulating Golgi membrane protein 1 (GOLM1) [22]. The chemically modified *miR-143* duplex showed a significant tumor-suppressive effect on xenografted tumors of human colorectal cancer DLD-1 cells and may be a candidate for an RNA medicine for the treatment of colorectal tumors [21]. There are striking similarities present between the behavior of invasive placental cells during embryo implantation and that of invasive cancer cells [29]. Implantation of the embryo is one of the last great mysteries of reproductive biology. *MiR-143* was found to be upregulated at implantation sites in mouse uterus on day 5 of pregnancy compared with inter-implantation sites [15]. Our previous study also showed that *miR-143* was differentially expressed in rat uteri between pre-receptive and receptive phase via microRNA (miRNA) microarray analysis [40]. However, the roles of *miR-143* during embryo implantation remain unclear.

In the present study, we measure the expression and regulation of *miR-143* in uterus during peri-implantation in rat. Additionally, we analyze the effects of *miR-143* on cell viability, migration and invasion, and investigate the regulatory target of *miR-143*.

2. Materials and methods

2.1. Experimental animals and protocols

Sexually mature female Sprague Dawley rats (220–260 g body weight) were purchased from the Laboratory Animal Center of the

* Corresponding authors at: Genetic Center of National Research Institute for Family Planning, Beijing 100081, China. Tel.: +86 1 62178932; fax: +86 1 62179059.
E-mail addresses: chinawang2007@163.com (C.-L. Wang), genetic@263.net.cn (X. Ma), hongfeixia@126.com (H.-F. Xia).
[1] These two authors contributed equally to this work.

http://dx.doi.org/10.1016/j.bbagen.2014.11.023
0304-4165/

Academy of Military Medical Sciences (Beijing, China). Rats were housed in a temperature- and humidity-controlled room with a 12/12 h light/dark cycle. All animal procedures were approved by the Institutional Animals Care and Use Committee of the National Research Institute for Family Planning. Rats were caged overnight with fertile males of the same strain. The presence of a vaginal plug or sperm was considered