Autoimmunity Reviews 11 (2012) 305–314

Contents lists available at ScienceDirect

Autoimmunity Reviews

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

Review

MicroRNAs in autoimmunity and inflammatory bowel disease: Crucial regulators in immune response

Marisa Iborra [a], Francesca Bernuzzi [b], Pietro Invernizzi [b,c,*], Silvio Danese [d,*]

[a] Fundacion Hospital Universitari La Fe. Department of Gastroenterology, Hospital Universitari La Fe. Valencia, Spain
[b] Division of Internal Medicine and Hepatobiliary Immunopathology Unit, IRCCS Istituto Clinico Humanitas, Rozzano, Milan, Italy
[c] Division of Rheumatology, Allergy and Clinical Immunology, University of California, Davis, CA, United States
[d] Division of Gastroenterology, IRCCS Istituto Clinico Humanitas, Rozzano, Milan, Italy

ARTICLE INFO

Article history:
Received 1 July 2010
Accepted 8 July 2010
Available online 11 July 2010

Keywords:
Autoimmune disease
MicroRNA
Inflammation
Inflammatory bowel disease
Crohn's disease and ulcerative colitis

ABSTRACT

MicroRNAs (miRNAs) have recently emerged as a new class of modulators of gene expression at the post-transcriptional level. The function of miRNA is the control of protein production by targeting mRNAs for translational repression or degradation. MiRNAs play a critical role in many biological processes such as cellular proliferation and maturation, apoptosis, regulation of chronic inflammation and development of cancer. It has recently been discovered that miRNAs are differentially expressed in autoimmune diseases (AID) and miRNA regulation may impact in the development or prevention of AID. In this paper we review the importance of miRNAs in AID in particular in inflammatory bowel disease (IBD). IBD is an AID whose pathophysiology remains uncertain. It is generally hypothesized that IBD is caused by the enteric microflora in genetically predisposed patients with an immune dysregulation in the gastrointestinal tract. Knowing the typical miRNA pattern of IBD will improve our knowledge of the pathogenesis of this disease and will lead to future well-focused projects to study the regulatory function of such miRNAs. Furthermore, it is possible that some miRNAs are specific to IBD and could serve as biomarkers with clinical applications for the diagnosis or assessment of disease activity.

Contents

1. Introduction . . . 306
2. Micro-RNA. . . . 306
   2.1. Concept of microRNA . . . 306
   2.2. Biogenesis of miRNA . . . 306
   2.3. Characteristics of miRNA. . . . 307
3. miRNA and inflammation. . . . 307
4. miRNA and cancer . . . 307
   4.1. Inflammation and cancer . . . 308
   4.2. miRNA and gastrointestinal cancer . . . 308
5. miRNA and autoimmune disease . . . 308
   5.1. Rheumatoid arthritis . . . 309
   5.2. Systemic lupus erythematosus . . . 309
   5.3. Primary Sjogren's syndrome . . . 310
   5.4. Multiple sclerosis . . . 310

Abbreviations: IBD, inflammatory bowel disease; CD, Crohn's disease; UC, ulcerative colitis; miRNA, micro-RNA; UTR, untranslated regions; AID, autoimmune disease; RA, rheumatoid arthritis; SLE, systemic lupus erythematosus; PSS, primary Sjogren's syndrome; MS, multiple sclerosis; PS, psoriasis; PBC, primary biliary cirrhosis; ITP, idiopathic thrombocytopenic purpura.

* Corresponding authors. Invernizzi is to be contacted at Hepatobiliary Immunopathology, Division of Internal Medicine, Istituto Clinico Humanitas, Via Manzoni 56, 20089, Rozzano, Milan, Italy. Danese, IBD Unit, Division of Gastroenterology, Istituto Clinico Humanitas, Via Manzoni 56, 20089, Rozzano, Milan, Italy.
E-mail addresses: pietro.invernizzi@humanitas.it (P. Invernizzi), Silvio.danese@humanitas.it (S. Danese).

1568-9972/$ – see front matter © 2010 Elsevier B.V. All rights reserved.
doi:10.1016/j.autrev.2010.07.002

5.5. Psoriasis. . . . 311
5.6. Primary biliary cirrhosis . . . 311
5.7. Idiopathic thrombocytopenic purpura . . . 311
6. miRNA and inflammatory bowel disease . . . 311
6.1. Genetic and epigenetic factors in IBD . . . 311
6.3. miRNA and IBD . . . 312
7. Conclusion and future perspectives . . . 312
Take-home messages . . . 313
References . . . 313

1. Introduction

MicroRNAs (miRNAs) are recently discovered small non-coding RNA molecules. MiRNAs bind to complementary sequences in the 3' untranslated region (UTR) of specific target mRNAs and can prevent protein synthesis [1]. MiRNAs are believed to play a crucial role in the regulation of many biological processes, such as cellular proliferation, differentiation and apoptosis, as well as in the induction of several disorders (e.g. immunity, inflammatory and autoimmune disease (AID), cancer) [2,3].

The majority of studies are focused on the potential role of miRNAs in the development of cancer, in contrast much less is known about how miRNAs may impact AID. Currently studies have revealed that few miRNAs including miR-155, miR-181a, miR-17–92, miR-146, and miR-223 may be involved in the development and function of the immune system [4–10].

Researchers worldwide are interested in miRNAs as potential therapeutic targets and potential diagnostic biomarkers mainly in cancer. This review is focused on miRNA expression patterns in AID specifically in inflammatory bowel disease (IBD) in order to determine whether miRNAs could be used as biomarkers for the diagnosis of disease or the determination of disease activity in AID. MiRNAs may open new opportunities for the non-invasive tests for IBD patients.

2. Micro-RNA

2.1. Concept of microRNA

Currently, a new class of post-transcriptional regulators has been discovered in diverse studies of genetic expression. This includes a class of small (about 18–24 nucleotides in length), endogenous, single-stranded, non-coding RNAs, called miRNAs, which regulate gene expression by targeting the 3' UTR of specific mRNAs for degradation or translational repression [1].

In 1993, Ambros et al., reported the first description of a miRNA, lin-4, in *Caenorhabditis elegans* [11,12]. However, the first study that discovered abnormalities in miRNA expression was performed in patients affected by B-cell chronic lymphocytic leukaemia (B-CLL) in 2002. They documented the down-regulation and frequent deletions of the following miRNA genes miR-15 and miR-16 in B-CLL patients [13].

2.2. Biogenesis of miRNA

The biogenesis of miRNA remains still unknown and is carried out in a multistep process (Fig. 1). MiRNA transcription depends on the localization within the genome. Over 50% of known miRNAs are located within the intronic regions of either coding or noncoding

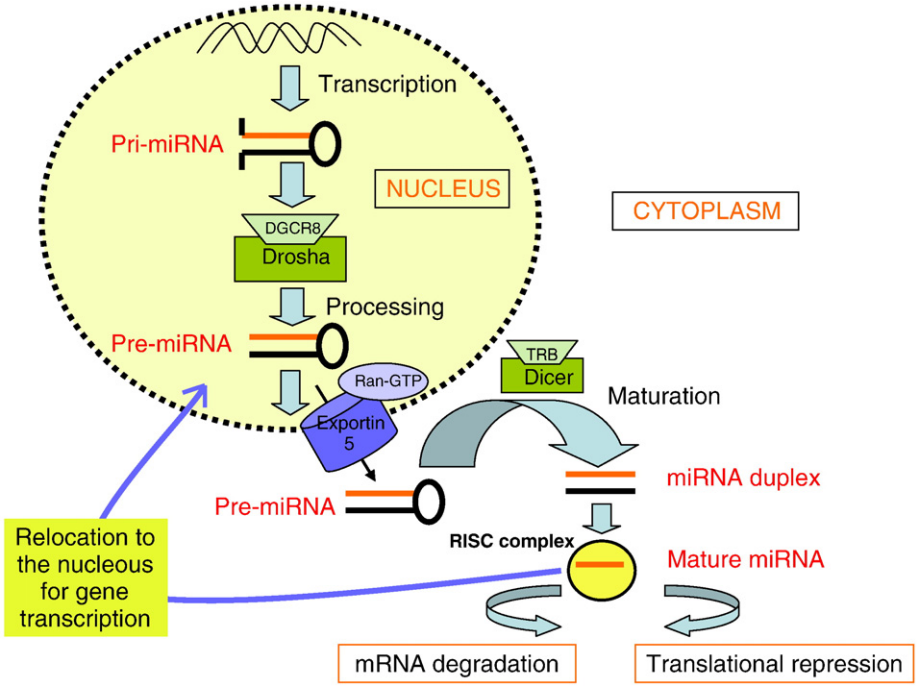

Fig. 1. Biogenesis of miRNA (view the test).