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MicroRNA Regulated Macrophage Activation in Obesity

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Abstract

Obesity and many other metabolic disorders, including type 2 diabetes and atherosclerosis, have conventionally been viewed as lipid storage disorders caused by over nutrition. Research has demonstrated that the obesity associated chronic low-grade tissue inflammation and oxidative stress is crucial factors in the initiation, propagation, and development of these metabolic disorders. Disruption in the normal functioning of the immune system and its interaction with host tissue cells makes it difficult to treat these diseases. Macrophages play critical roles in the development of insulin resistance and tissue inflammation, particularly through a unique shift in polarized activation status from an anti-inflammatory M2 function in lean adipose tissues to proinflammatory M1 activation in adipose tissues of obese individuals. Compelling evidence demonstrated the significance of microRNAs as important regulators in the immune system network. Our recent research has demonstrated that microRNA-223 is a crucial regulator of obesity associated insulin resistance through regulation of macrophage polarization in adipose tissue. This review highlights the importance of various microRNAs and their roles played in the polarization of macrophages which could be targeted for development of new therapeutic strategies to treat obesity associated diseases.

Keywords: MicroRNA; Obesity; Insulin Resistance; Macrophage; Macrophage Polarization; M1; M2

Introduction

In the last several decades, lack of balanced diet both in terms of quality and quantity has led to a rapid progression of obesity throughout the world; resulting in a major pandemic situation attracting the attention of many nations. The severity of obesity has been tightly associated with many chronic diseases. Obese patients are prone to conditions like inflammation and insulin resistance which is a causal factor in the pathogenesis of life threatening diseases like Type II Diabetes Mellitus, cardiovascular diseases and many more [1-3]. Recently studies demonstrated that obesity is a disease status characterized with chronic, low-degree tissue inflammations, which can result from elevated infiltration of macrophages into obese tissues, and more importantly, activation status shift from an anti-inflammatory to a proinflammatory status [1,4-9]. Impairment in the immune system makes it more difficult to treat these disease conditions.

Macrophages are key cellular components in the innate immune system. They play an essential role in responding to invading pathogens by triggering elaborate immuno-inflammatory reactions that ultimately results in the elimination of the pathogen and reinstatement of normal conditions. In response to microenvironmental cues like pathogenic and tissue-derived molecules, macrophages undergo profound phenotypic changes and provide appropriate responses by adapting to their microenvironment [4,10,11]. Understanding these 'adaptive' changes' will provide pivotal information to open the gate for development of new clinical therapies for in treating chronic diseases within the proper context. Recent studies have shown that microRNAs have a profound influence on immune cell functions, including macrophage activation [12,13]. Results of our previous studies provide new evidence to support an essential role for microRNA in regulating Adipose Tissue Macrophage (ATM) polarization [14]. In this review, we will discuss the importance of macrophage polarization in obesity and related disorders and the newly discovered regulatory network governed by microRNAs.

Macrophage Polarization and its Diverse Functions

Macrophages play several pivotal roles in innate and adaptive immune response, tissue repair and remodeling and many more. Of the many key traits of macrophages, a major one is their functional diversity [15,16]. This key feature could be attributed to their capability of responding to diverse stimuli and in turn exhibit diverse phenotypes and functional roles. Macrophages undergo two unique activation programs, classical (M1) and alternate (M2) activation, and a full spectrum of intermediate phenotypes between those two extremes in status [10,15,16]. In response to stimuli provided by bacterial infections like lipopolysaccharide (LPS) and interferon-

γ (IFN-γ), or palmitate fatty acid in the context of obesity, macrophages adopt a classical activation strategy and a proinflammatory phenotype and become highly phagocytotic, as well as exerting the bactericidal activity, and secreting proinflammatory cytokines and chemokines to further protect against invading pathogens. On the other hand, signals from interleukins (IL) like IL-4 and IL-13 promote alternative activation of macrophages which have role in parasite elimination, tissue remodeling and repair, and inhibition of tumor progression [6,15,17,18]. The phenomenon of activation of M1and M2 macrophage polarization has been investigated intensively in recent decades as it could lead into pathways for treatment of many important disease conditions.

Genomic and transcriptional studies and other phenotypic analyses of M1 and M2 macrophages provided immense knowledge on several distinct characteristics extending from traits inherent in their chemokinome to metabolome [19]. For example, M1 macrophages express the Th1-attracting chemokines such as CXCL9 and CXCL10,

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whereas M2 macrophages express the chemokines CCL17, CCL22 and CCL24 [10,19-24]. In the same fashion, M1 and M2 macrophages display different functional phenotypes in response to glucose, amino acid, lipid and iron metabolism [10,15,16]. Even though the macrophage polarization was originally studied and defined *in vitro* using conventional methods, numerous studies have shown such polarization states *in vivo*, under physiological and pathological conditions. Of note, macrophages stimulated in response to parasite infections, allergy and in many tumor types resemble to a large extent an M2-or M2-like phenotype [25,26]. But it is to be considered that, *in vivo* conditions are often complex to interpret as other cues involved both M1 and M2 macrophages which may show a mixture of multiple functional phenotypes [4,18,27]. Further, many studies that cues which induce polarization *in vivo* are due to interactions among various immune and non-immune cell types like lymphocytes, dendritic cells, fibroblasts, and mesenchymal stem cells [7,10,18,28] and several other factors including non-coding RNA [14,29,30]. These factors make the study on macrophage polarization in relation to these diverse cell types important.

As mentioned, macrophages show functional diversity ranging from inflammation, phagocytosis, immunoregulation, tissue remodeling and even metabolism. The contribution of macrophages to inflammation is one of its most well-documented functions. In contrast to its proinflammatory functions, macrophages also contribute to the dampening of inflammation through their immunoregulatory properties [16,31,32]. Phagocytosis is a defining feature of macrophages. Macrophages not only play roles in killing pathogens but also in elimination of dead cells and remnants of cells which is important for resolution of inflammation. In fact, it is known that phagocytosis of apoptotic cells polarize these cells into an anti-inflammatory mode that supports their immunoregulatory functions [33].

Adipose Tissue Macrophages are Major Contributor to Obesity Associated Inflammation

The central feature of obesity which aggravates the progression of insulin resistance is chronic low-grade inflammation due to the infiltration of adipose tissue by macrophages [1,4-9]. The dysfunction of adipose tissue with respect to maintaining energy homeostasis is associated with obesity, inflammation and metabolic complications [34]. In addition, in the case of obese persons, weight loss is linked to improved insulin sensitivity and their risk of cardiovascular diseases is decreased. The inflammatory condition in obese patients is different from inflammation caused by classical activated macrophages which are stimulated by pathogens. In response to nutrient excess and is relatively chronic in nature, adipose tissue in obese individuals has an enhanced production of proinflammatory cytokines, infiltration by immune related cells, especially ATMs and the formation of crown like structures where apoptotic or soon to be apoptotic adipocytes and their remnants accumulate and cluster around phagocytic macrophages [5,35,36]. In lean mice, the ATMs are mainly the alternatively activated M2 macrophages and when these mice were subjected to high fat diet there is seen a phenotypic switch in macrophage polarization towards a proinflammatory type in mouse adipose tissue [28]. Polarized macrophages play an important role in lipid metabolism and homeostasis. Studies showed ATMs from tissues of lean subjects and ATMs during weight loss to resemble M2 macrophage and found to express high levels of the anti-inflammatory cytokine IL-10 [20,37,38]. It is believed that these ATMs maintain adipose tissue homeostasis by protecting from inflammation in response to high fat concentrations [39].

As explained, obesity is associated with increased accumulation of macrophages as well as with enhanced switching in polarization of ATMs from an anti-inflammatory (M2) to a proinflammatory (M1) state [6]. This change in polarization could be related to pathogen interference and could be specified by the targeted grouping of M1 macrophages around adipocytes which are apoptotic and having necrotic like structures [40]. Interestingly, some studies suggested that in people who are experiencing weight loss, there is a reduction in the infiltration of inflammatory macrophages into the adipose tissue and an improvement in the inflammatory response and oxidant profile of adipocytes as well as the circulating monocytes [30].

MicroRNAs are Important for Adipose Tissue Function

Compelling evidence suggest critical roles of microRNAs in regulating adipose tissue function in the context of obesity [41]. The discovery of microRNAs, a class of 21-23-nucleotide non-coding RNAs revealed a new layer of gene regulation in almost every aspect of biological processes, including those of the immune systems [12,13]. MicroRNAs are short non-coding RNAs that are approximately 22-nucleotide in length and bind to target mRNAs and regulate gene expression. The microRNA pairs to its target mRNAs typically result in their degradation and/or repression of translation [42].

MicroRNAs are expressed in a tissue- and cell-type specific manner and play important roles in many molecular and biological processes, including proliferation, apoptosis, development, and differentiation [12,42-44]. During adipogenesis, microRNAs are modulating the formation and function of adipose tissue from various aspects. MicroRNA-33a and microRNA-33b target genes are related to metabolism [45,46] and microRNA-103 and microRNA-107 regulate insulin sensitivity and glucose homeostasis by modulating the abundance of caveolin-1 in adipocytes [47,48]. Furthermore, microRNAs have been associated with inflammation, oxidative stress, impaired adipogenesis and insulin signaling, and apoptosis and angiogenesis in relation to obesity. All of these processes contribute to the development of type 2 diabetes, atherosclerosis, and associated cardiovascular disorders [30,41,49-51]. However, their association with these processes does not necessarily imply a causal role. Each microRNA can have different roles under various conditions. For instance, microRNA-17-92 cluster, microRNA-21, microRNA-103, miR-143, microRNA-371, and miR-378/378* have shown to increase adipogenesis [47,48,52-57]. This is evidenced by increased concentrations of triglycerides in the circulation and enhanced expression of adipogenic markers [33,52,54,56,57]. The microRNA-17-92 cluster induces and accelerates adipocyte differentiation by suppressing expression of the pivotal cell cycle regulator Rb2/p130 [52]. In addition, let-7, microRNA-27, microRNA-130, microRNA-138, microRNA- 369-5p, and microRNA-448 inhibit adipogenesis which results in a decrease in triglycerides and down-regulation of adipogenic factors [53,58-60]. Similarly, microRNA-21 stalls adipogenesis by inhibiting the TGF-β signaling pathway and microRNA-143 acts in the similar fashion through down-regulating ERK-5 function [54]. The let-7 microRNA inhibits adipogenesis by targeting high-mobility group AT-hook 2 (HMGA-2) [53], whereas microRNA-27 and microRNA-130 function through suppressing peroxisome proliferator activated receptor γ directly [61,62].

Significance of MicroRNAs in Regulating Adipose Tissue Macrophage Activation

MicroRNAs are now accepted as important posttranscriptional

regulators of gene expression in immune cells like monocytes and macrophages [12,13]. Variety of inflammatory signals stimulate microRNA expression induction like LPS, TNFα or IL-1β and these tune down TLR4/IL-1R signaling pathways in macrophages/monocytes [12,13]. A decrease in microRNA-17, microRNA-92a and microRNA-155 is associated with an increase in monocyte/macrophage proliferation and enhanced TLR-4 activation [63-65]. Similarly, microRNA-424 expression in endothelial cells is increased by hypoxia and switches on a pathway to regulate monocyte/macrophage differentiation [66,67]. For example, different studies have shown that microRNA-146, microRNA-125b, microRNA-155 and microRNA-9 are induced by LPS and subsequently inhibiting TLR4/IL-1R signaling pathway by posttranscriptional regulation of the pathway components' levels [68-71]. In a similar fashion, some studies suggested microRNAs can directly regulate production of type 2 cytokine productions during macrophage activation, for example, microRNA-98 and microRNA-21 can control the expression of IL-10 in macrophages and monocytes that in turn inhibit induction of expression of inflammatory genes [60,72]. Recent study found that let-7c regulates bactericidal and phagocytic activities of macrophages, two functional phenotypes implicated in macrophage polarization [29].

Based on these evidences, it may be hypothesized that, in the context of obesity, the switching of inflammatory macrophages to an anti-inflammatory phenotype could be promoted by microRNAs. A study by Zhuang et.al identified that microRNA-223 acts as an important regulator of ATMs polarization and further demonstrated that it plays a significant role in modulating obesity associated insulin resistance [14]. MicroRNA-223 is differentially expressed during macrophage polarization, and microRNA-223–deficient macrophages were hypersensitive to LPS stimulation and exhibited delayed responses to IL-4 compared with controls. Furthermore, there is increase in M1 and decreases in M2 polarization biomarkers in microRNA-223 deficient macrophages indicated a suppressive effects on activation of pro-inflammatory macrophages and stimulatory effect on anti-inflammatory activation. MicroRNA-223–deficient mice displayed enhanced adipose tissue inflammatory responses and decreased adipose tissue insulin signaling accompanied by inappropriate adipokine expression, which are indicators for adipose tissue dysfunction. These results support the hypothesis that microRNA-223–regulated macrophage polarization, likely acting through suppressing a proinflammatory gene Pknox1, is important for adipose tissue function. These studies provided profound knowledge in the complex interaction in the macrophage-mediated adipose tissue inflammatory response and metabolic regulation as well as indicating the possibility of targeting microRNAs for treatment of metabolic disorders and disease resulting from insulin resistance.

Conclusion

Thus this review collectively signifies the importance of microRNAs in diverse roles of macrophage polarization with specific focus on the dysfunction of adipose tissue and its disorders. Impairment in the normal functioning of adipocytes leads to an inflammatory phenotype, with enhanced expression of proinflammatory adipocytokines and down regulation of expression of anti-inflammatory adipocytokines. The roles played by polarized macrophages are immense and the significant contribution by microRNAs could not be ignored as well. Future research a profound understanding of the complex network of interactions among different factors involved in state of polarization of macrophages in health and disease.

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References

1. Ohman MK, Shen Y, Obimba CI, Wright AP, Warnock M, et al. (2008) Visceral adipose tissue inflammation accelerates atherosclerosis in apolipoprotein E-deficient mice. Circulation 117: 798-805.
2. Berg AH, Scherer PE (2005) Adipose tissue, inflammation, and cardiovascular disease. Circ Res 96: 939-949.
3. Hotamisligil GS, Arner P, Caro JF, Atkinson RL, Spiegelman BM (1995) Increased adipose tissue expression of tumor necrosis factor-alpha in human obesity and insulin resistance. J Clin Invest 95: 2409-2415.
4. Furuhashi M, Fucho R, Görgün CZ, Tuncman G, Cao H, et al. (2008) Adipocyte/macrophage fatty acid-binding proteins contribute to metabolic deterioration through actions in both macrophages and adipocytes in mice. J Clin Invest 118: 2640-2650.
5. Weisberg SP, McCann D, Desai M, Rosenbaum M, Leibel RL, et al. (2003) Obesity is associated with macrophage accumulation in adipose tissue. J Clin Invest 112: 1796-1808.
6. Lumeng CN, Bodzin JL, Saltiel AR (2007) Obesity induces a phenotypic switch in adipose tissue macrophage polarization. J Clin Invest 117: 175-184.
7. Kang K, Reilly SM, Karabacak V, Gangl MR, Fitzgerald K, et al. (2008) Adipocyte-derived Th2 cytokines and myeloid PPARdelta regulate macrophage polarization and insulin sensitivity. Cell Metab 7: 485-495.
8. Meng ZX, Wang GX, Lin JD (2012) A microRNA circuitry links macrophage polarization to metabolic homeostasis. Circulation 125: 2815-2817.
9. Olefsky JM, Glass CK (2010) Macrophages, inflammation, and insulin resistance. Annu Rev Physiol 72: 219-246.
10. Biswas SK, Mantovani A (2010) Macrophage plasticity and interaction with lymphocyte subsets: cancer as a paradigm. Nat Immunol 11: 889-896.
11. Rodríguez-Prados JC, Través PG, Cuenca J, Rico D, Aragonés J, et al. (2010) Substrate fate in activated macrophages: a comparison between innate, classic, and alternative activation. J Immunol 185: 605-614.
12. Lodish HF, Zhou B, Liu G, Chen CZ (2008) Micromanagement of the immune system by microRNAs. Nat Rev Immunol 8: 120-130.
13. Baltimore D, Boldin MP, O'Connell RM, Rao DS, Taganov KD (2008) MicroRNAs: new regulators of immune cell development and function. Nat Immunol 9: 839-845.
14. Zhuang G, Meng C, Guo X, Cheruku PS, Shi L, et al. (2012) A novel regulator of macrophage activation: miR-223 in obesity-associated adipose tissue inflammation. Circulation 125: 2892-2903.
15. Gordon S, Taylor PR (2005) Monocyte and macrophage heterogeneity. Nat Rev Immunol 5: 953-964.
16. Mosser DM, Edwards JP (2008) Exploring the full spectrum of macrophage activation. Nat Rev Immunol 8: 958-969.
17. Odegaard JI, Chawla A (2008) Mechanisms of macrophage activation in obesity-induced insulin resistance. Nat Clin Pract Endocrinol Metab 4: 619-626.
18. Lumeng CN, Deyoung SM, Saltiel AR (2007) Macrophages block insulin action in adipocytes by altering expression of signaling and glucose transport proteins. Am J Physiol Endocrinol Metab 292: E166-174.
19. Martinez FO, Gordon S, Locati M, Mantovani A (2006) Transcriptional profiling of the human monocyte-to-macrophage differentiation and polarization: new molecules and patterns of gene expression. J Immunol 177: 7303-7311.
20. Mantovani A, Sica A, Sozzani S, Allavena P, Vecchi A, et al. (2004) The chemokine system in diverse forms of macrophage activation and polarization. Trends Immunol 25: 677-686.
21. Porta C, Rimoldi M, Raes G, Brys L, Ghezzi P, et al. (2009) Tolerance and M2 (alternative) macrophage polarization are related processes orchestrated by p50 nuclear factor kappaB. Proc Natl Acad Sci U S A 106: 14978-14983.

22. Yamashita U, Kuroda E (2002) Regulation of macrophage-derived chemokine (MDC, CCL22) production. Crit Rev Immunol 22: 105-114.

23. Kurowska-Stolarska M, Stolarski B, Kewin P, Murphy G, Corrigan CJ, et al. (2009) IL-33 amplifies the polarization of alternatively activated macrophages that contribute to airway inflammation. J Immunol 183: 6469-6477.

24. Tighe RM, Liang J, Liu N, Jung Y, Jiang D, et al. (2011) Recruited exudative macrophages selectively produce CXCL10 after noninfectious lung injury. Am J Respir Cell Mol Biol 45: 781-788.

25. Loke P, Nair MG, Parkinson J, Guiliano D, Blaxter M, et al. (2002) IL-4 dependent alternatively-activated macrophages have a distinctive in vivo gene expression phenotype. BMC Immunol 3: 7.

26. Biswas SK, Sica A, Lewis CE (2008) Plasticity of macrophage function during tumor progression: regulation by distinct molecular mechanisms. J Immunol 180: 2011-2017.

27. Mantovani A, Locati M (2009) Orchestration of macrophage polarization. Blood 114: 3135-3136.

28. Lumeng CN, Deyoung SM, Bodzin JL, Saltiel AR (2007) Increased inflammatory properties of adipose tissue macrophages recruited during diet-induced obesity. Diabetes 56: 16-23.

29. Banerjee S, Xie N, Cui H, Tan Z, Yang S, et al. (2013) MicroRNA let-7c Regulates Macrophage Polarization. J Immunol 190: 6542-6549.

30. Hulsmans M, De Keyzer D, Holvoet P (2011) MicroRNAs regulating oxidative stress and inflammation in relation to obesity and atherosclerosis. FASEB J 25: 2515-2527.

31. Lawrence T, Gilroy DW, Colville-Nash PR, Willoughby DA (2001) Possible new role for NF-kappaB in the resolution of inflammation. Nat Med 7: 1291-1297.

32. Serhan CN, Yang R, Martinod K, Kasuga K, Pillai PS, et al. (2009) Maresins: novel macrophage mediators with potent antiinflammatory and proresolving actions. J Exp Med 206: 15-23.

33. Weigert A, Johann AM, von Knethen A, Schmidt H, Geisslinger G, et al. (2006) Apoptotic cells promote macrophage survival by releasing the antiapoptotic mediator sphingosine-1-phosphate. Blood 108: 1635-1642.

34. Sethi JK, Vidal-Puig AJ (2007) Thematic review series: adipocyte biology. Adipose tissue function and plasticity orchestrate nutritional adaptation. J Lipid Res 48: 1253-1262.

35. Xu H, Barnes GT, Yang Q, Tan G, Yang D, et al. (2003) Chronic inflammation in fat plays a crucial role in the development of obesity-related insulin resistance. J Clin Invest 112: 1821-1830.

36. Wellen KE, Hotamisligil GS (2003) Obesity-induced inflammatory changes in adipose tissue. J Clin Invest 112: 1785-1788.

37. Clément K, Viguerie N, Poitou C, Carette C, Pelloux V, et al. (2004) Weight loss regulates inflammation-related genes in white adipose tissue of obese subjects. FASEB J 18: 1657-1669.

38. Odegaard JI, Chawla A (2011) Alternative macrophage activation and metabolism. Annu Rev Pathol 6: 275-297.

39. Red Eagle A, Chawla A (2010) In obesity and weight loss, all roads lead to the mighty macrophage. J Clin Invest 120: 3437-3440.

40. Lumeng CN, DelProposto JB, Westcott DJ, Saltiel AR (2008) Phenotypic switching of adipose tissue macrophages with obesity is generated by spatiotemporal differences in macrophage subtypes. Diabetes 57: 3239-3246.

41. Rottiers V, Näär AM (2012) MicroRNAs in metabolism and metabolic disorders. Nat Rev Mol Cell Biol 13: 239-250.

42. Bartel DP (2009) MicroRNAs: target recognition and regulatory functions. Cell 136: 215-233.

43. Bartel DP, Chen CZ (2004) Micromanagers of gene expression: the potentially widespread influence of metazoan microRNAs. Nat Rev Genet 5: 396-400.

44. Bartel DP (2004) MicroRNAs: genomics, biogenesis, mechanism, and function. Cell 116: 281-297.

45. Rayner KJ, Sheedy FJ, Esau CC, Hussain FN, Temel RE, et al. (2011) Antagonism of miR-33 in mice promotes reverse cholesterol transport and regression of atherosclerosis. J Clin Invest 121: 2921-2931.

46. Rayner KJ, Suárez Y, Dávalos A, Parathath S, Fitzgerald ML, et al. (2010) MiR-33 contributes to the regulation of cholesterol homeostasis. Science 328: 1570-1573.

47. Xie H, Lim B, Lodish HF (2009) MicroRNAs induced during adipogenesis that accelerate fat cell development are downregulated in obesity. Diabetes 58: 1050-1057.

48. Trajkovski M, Hausser J, Soutschek J, Bhat B, Akin A, et al. (2011) MicroRNAs 103 and 107 regulate insulin sensitivity. Nature 474: 649-653.

49. Ling C, Groop L (2009) Epigenetics: a molecular link between environmental factors and type 2 diabetes. Diabetes 58: 2718-2725.

50. Wei Y, Nazari-Jahantigh M, Chan L, Zhu M, Heyll K, et al. (2013) The microRNA-342-5p fosters inflammatory macrophage activation through an Akt1- and microRNA-155-dependent pathway during atherosclerosis. Circulation 127: 1609-1619.

51. Wei Y, Schober A, Weber C (2013) Pathogenic arterial remodeling: the good and bad of microRNAs. Am J Physiol Heart Circ Physiol 304: H1050-H1059.

52. Wang Q, Li YC, Wang J, Kong J, Qi Y, et al. (2008) miR-17-92 cluster accelerates adipocyte differentiation by negatively regulating tumor-suppressor Rb2/p130. Proc Natl Acad Sci U S A 105: 2889-2894.

53. Sun T, Fu M, Bookout AL, Kliewer SA, Mangelsdorf DJ (2009) MicroRNA let-7 regulates 3T3-L1 adipogenesis. Mol Endocrinol 23: 925-931.

54. Kim YJ, Hwang SJ, Bae YC, Jung JS (2009) MiR-21 regulates adipogenic differentiation through the modulation of TGF-beta signaling in mesenchymal stem cells derived from human adipose tissue. Stem Cells 27: 3093-3102.

55. Esau C, Kang X, Peralta E, Hanson E, Marcusson EG, et al. (2004) MicroRNA-143 regulates adipocyte differentiation. J Biol Chem 279: 52361-52365.

56. Bork S, Horn P, Castoldi M, Hellwig I, Ho AD, et al. (2011) Adipogenic differentiation of human mesenchymal stromal cells is down-regulated by microRNA-369-5p and up-regulated by microRNA-371. J Cell Physiol 226: 2226-2234.

57. Gerin I, Bommer GT, McCoin CS, Sousa KM, Krishnan V, et al. (2010) Roles for miRNA-378/378* in adipocyte gene expression and lipogenesis. Am J Physiol Endocrinol Metab 299: E198-206.

58. Lee EK, Lee MJ, Abdelmohsen K, Kim W, Kim MM, et al. (2011) miR-130 suppresses adipogenesis by inhibiting peroxisome proliferator-activated receptor gamma expression. Mol Cell Biol 31: 626-638.

59. Lin Q, Gao Z, Alarcon RM, Ye J, Yun Z (2009) A role of miR-27 in the regulation of adipogenesis. FEBS J 276: 2348-2358.

60. Liu Y, Chen Q, Song Y, Lai L, Wang J, et al. (2011) MicroRNA-98 negatively regulates IL-10 production and endotoxin tolerance in macrophages after LPS stimulation. FEBS Lett 585: 1963-1968.

61. Karbiener M, Fischer C, Nowitsch S, Opriessnig P, Papak C, et al. (2009) microRNA miR-27b impairs human adipocyte differentiation and targets PPARgamma. Biochem Biophys Res Commun 390: 247-251.

62. Kim SY, Kim AY, Lee HW, Son YH, Lee GY, et al. (2010) miR-27a is a negative regulator of adipocyte differentiation via suppressing PPARgamma expression. Biochem Biophys Res Commun 392: 323-328.

63. Ventura A, Young AG, Winslow MM, Lintault L, Meissner A, et al. (2008) Targeted deletion reveals essential and overlapping functions of the miR-17 through 92 family of miRNA clusters. Cell 132: 875-886.

64. Xiao C, Srinivasan L, Calado DP, Patterson HC, Zhang B, et al. (2008) Lymphoproliferative disease and autoimmunity in mice with increased miR-17-92 expression in lymphocytes. Nat Immunol 9: 405-414.

65. Fontana L, Pelosi E, Greco P, Racanicchi S, Testa U, et al. (2007) MicroRNAs 17-5p-20a-106a control monocytopoiesis through AML1 targeting and M-CSF receptor upregulation. Nat Cell Biol 9: 775-787.

66. Ghosh G, Subramanian IV, Adhikari N, Zhang X, Joshi HP, et al. (2010) Hypoxia-induced microRNA-424 expression in human endothelial cells regulates HIF-Î± isoforms and promotes angiogenesis. J Clin Invest 120: 4141-4154.

67. Rosa A, Ballarino M, Sorrentino A, Sthandier O, De Angelis FG, et al. (2007) The interplay between the master transcription factor PU.1 and miR-424 regulates human monocyte/macrophage differentiation. Proc Natl Acad Sci U S A 104: 19849-19854.

68. Taganov KD, Boldin MP, Chang KJ, Baltimore D (2006) NF-kappaB-dependent induction of microRNA miR-146, an inhibitor targeted to signaling proteins of innate immune responses. Proc Natl Acad Sci U S A 103: 12481-12486.

69. O'Connell RM, Rao DS, Chaudhuri AA, Boldin MP, Taganov KD, et al. (2008) Sustained expression of microRNA-155 in hematopoietic stem cells causes a myeloproliferative disorder. J Exp Med 205: 585-594.

70. Tili E, Michaille JJ, Cimino A, Costinean S, Dumitru CD, et al. (2007) Modulation of miR-155 and miR-125b levels following lipopolysaccharide/TNF-alpha stimulation and their possible roles in regulating the response to endotoxin shock. J Immunol 179: 5082-5089.

71. Bazzoni F, Rossato M, Fabbri M, Gaudiosi D, Mirolo M, et al. (2009) Induction and regulatory function of miR-9 in human monocytes and neutrophils exposed to proinflammatory signals. Proc Natl Acad Sci U S A 106: 5282-5287.

72. Sheedy FJ, Palsson-McDermott E, Hennessy EJ, Martin C, O'Leary JJ, et al. (2010) Negative regulation of TLR4 via targeting of the proinflammatory tumor suppressor PDCD4 by the microRNA miR-21. Nat Immunol 11: 141-147.

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