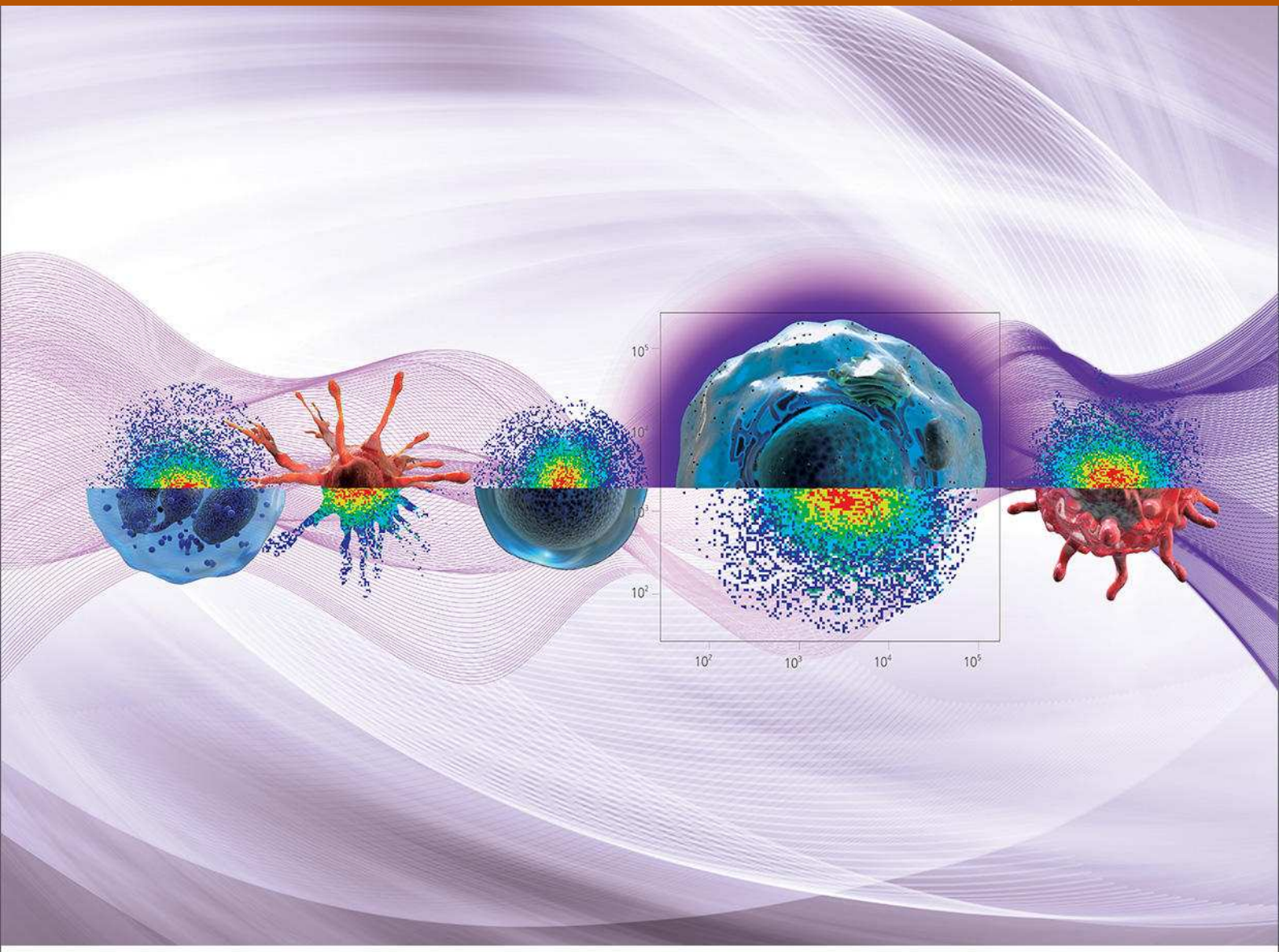

Millions of dots:
violet makes your plot more interesting

New eBioscience™ Super Bright antibody conjugates for flow cytometry

Learn more ›

invitrogen
by Thermo Fisher Scientific

PROSPECTS
Journal of Cellular Biochemistry 9999:1–8 (2017)

Journal of Cellular Biochemistry

MicroRNAs-Based Imaging Techniques in Cancer Diagnosis and Therapy

Maryam Keshavarzi,[1] Saba Sorayayi,[2] Mohammad Jafar Rezaei,[3] Mohsen Mohammadi,[4] Amir Ghaderi,[5] Ayoob Rostamzadeh,[6] Aria Masoudifar,[7] and Hamed Mirzaei [8]*

[1]*Department of Oral and Maxillofacial Radiology, School of Dentistry, Lorestan University of Medical Sciences, Khorramabad, Iran*

[2]*Faculty of Medicine, Department of Clinical Biochemistry, Ardabil University of Medical Sciences, Ardabil, Iran*

[3]*Cellular and Molecular Research Center, Department of Anatomical Sciences, Faculty of Medicine, Kurdistan University of Medical Sciences, Sanandaj, Iran*

[4]*Faculty of Pharmacy, Department of Pharmaceutical Biotechnology, Lorestan University of Medical Sciences, Khorramabad, Iran*

[5]*Faculty of Pharmacy, Department of Pharmaceutical Biotechnology, Tehran University of Medical Science, Tehran, Iran*

[6]*Faculty of Medicine, Department of Anatomy and Neuroscience, Shahrekord University of Medical Sciences, Shahrekord, Iran*

[7]*Department of Molecular Biotechnology, Royan Institute for Biotechnology, Cell Science Research Center, ACECR, Isfahan, Iran*

[8]*Department of Medical Biotechnology, School of Medicine, Mashhad University of Medical Sciences, Mashhad, Iran*

ABSTRACT

Cancer is one of the most serious global health concerns in different populations. Several studies indicated that there are many potentially promising cellular and molecular targets for cancer therapy within cancer cells and their microenvironment. Among different cellular and molecular targets involved in cancer pathogenesis, microRNAs (miRNAs) are well known as key targets for cancer therapy. miRNAs are one of main classes of non-coding RNAs. These molecules play important roles in different critical processes of cancer pathogenesis. Hence, this makes miRNAs as a suitable tool for cancer diagnosis and therapy. There are different approaches for monitoring miRNAs in cancer patients. Some conventional approaches including next-generation sequencing, real-time polymerase chain reaction (PCR), northern blotting, and microarrays could be used for assessment of miRNAs expression. Some studies revealed that the utilization of these approaches associated with various limitations. Recently, it has been revealed that molecular imaging techniques are powerful tools for monitoring of different cellular and molecular targets involved in various diseases such as cancer. These techniques help investigators to investigate and monitor miRNAs functions through assessing different targets by fluorescent proteins, bioluminescent enzymes, molecular beacons, as well as various nanoparticles. Therefore, utilization of molecular imaging techniques could assist investigators to better monitor and more effectively treat patients during different phases of malignancy. Here, we give a review on the current state of miRNAs-based imaging techniques in cancer diagnosis and therapy. J. Cell. Biochem. 9999: 1–8, 2017.

KEY WORDS: MOLECULAR IMAGING; MicroRNA; CANCER; DIAGNOSIS; THERAPY

To date, cancer has been emerged as one of main health problems in worldwide [Faghihloo et al., 2016; Mirzaei et al., 2016a–c]. Despite of recent advances in cancer therapy (such as gene therapy, cell therapy, and molecularly-targeted therapies), this disease has remained as one of the major public health issues worldwide [Mirzaei et al., 2016d–f, 2017a; Mohammadi et al., 2016a]. Hence, the identification of new targets and molecules involved in cancer, from initiation to progression and treatment, could contribute in understanding of the pathways involved in cancer pathogenesis [Arabpour et al., 2016; Mirzaei et al., 2016e; Simonian et al., 2016]. These finding could lead to development of new and effective treatments in this field. One of the most important mediators in cancer pathogenesis is microRNAs (miRNAs) [Fathullahzadeh et al., 2016; Mohammadi et al., 2016b; Gholamin et al., 2017; Mirzaei et al., 2017b; Moridikia et al., 2017].

Conflicts of interest: None.

*Correspondence to: Hamed Mirzaei, Department of Medical Biotechnology, School of Medicine, Mashhad University of Medical Sciences, Mashhad 91779-48564, Iran. E-mail: h.mirzei2002@gmail.com

Manuscript Received: 21 March 2017; Manuscript Accepted: 22 March 2017

Accepted manuscript online in Wiley Online Library (wileyonlinelibrary.com): 29 March 2017

DOI 10.1002/jcb.26012 • © 2017 Wiley Periodicals, Inc.

MiRNAs are well known as a class of non-coding RNAs which play key roles in a wide range of biological processes including development, cellular differentiation, proliferation, and apoptosis in living organisms [Ryoo et al., 2013; Gholamin et al., 2016; Rashidi et al., 2016]. The lengths of these molecules are almost ~22 nucleotides [Mirzaei et al., 2016b]. Several studies indicated that miRNAs have a central role in pathogenesis of various diseases such as cancer [Gholamin et al., 2017; Mirzaei et al., 2017a; Moridikia et al., 2017]. Hence, detection and profiling of these molecules could contribute to the better understanding of cancer pathogenesis and, thereby, developing more precise strategies for early detection and/or treatment of cancer [Zubakov et al., 2010; Salarini et al., 2015; Gholamin et al., 2016; Mirzaei et al., 2016c]. So far, various conventional approaches such as microarray and RT-PCR have been used for miRNAs detection in different living systems [Li and Ruan, 2009; Momin et al., 2009; Hernandez et al., 2013]. These approaches are associated with some limitations. For example, these approaches are time-consuming and laborious and required to fix or lyse the cells and thus cannot monitor dynamic functions of miRNAs in living cells and organisms (In vivo) [Fang et al., 2006; Lu and Tsourkas, 2009; Ryoo et al., 2013]. To overcome the limitations, developing new and more efficient, particularly noninvasive repeated quantitative, methods are the most highly demanded. Recently, some imaging techniques have been emerged as effective tools for monitoring of miRNAs [Wang et al., 2009; Hernandez et al., 2013]. Imaging techniques are well known as powerful tools in monitoring of various targets and genes in many diseases such as cancer [Wang et al., 2009; Hernandez et al., 2013]. These techniques could provide new avenue in diagnosis and treatment of cancer. Various imaging techniques such as magnetic resonance imaging (MRI), florescence imaging, and bioluminescence imaging (BLI) could be used for monitoring and detection of miRNAs in patients with cancer [Wang et al., 2009; Hernandez et al., 2013]. In the present review, we will not only focus on a variety of miRNAs involved in cancer pathogenesis but also highlight some recently developed imaging methods which assist investigators to detect miRNAs in a high throughput profiling and noninvasive repeated quantitative manner in preclinical and clinical cancer studies.

MicroRNA AND CANCER

MiRNAs are one of main class of non-coding short RNAs that are highly conserved [Mirzaei et al., 2016e,b; Mohammadi et al., 2016b]. These RNAs regulate gene expression at different levels (protein and RNA) [Rashidi et al., 2017; Salarini et al., 2015]. MiRNAs have multiple biological roles in different processes within living organisms [Mirzaei et al., 2017a; Rashidi et al., 2017]. Figure 1 illustrate a scheme of miRNA biogenesis. Multiple lines of evidence indicated that miRNAs play important roles in initiation and progression of various cancers [Mirzaei et al., 2016f,g; Mohammadi et al., 2016b]. These molecules regulate different cellular and molecular pathways including Wnt, Notch, TGF-β and play putative roles in epithelial–mesenchymal transition (EMT). It is plausible that some expression aberrations of miRNAs might lead to initiation and/or development of a variety of cancers [Mirzaei et al., 2016g,h; Mohammadi et al., 2016b] (Table I). Various studies have been revealed that miRNAs could be used as diagnostic, prognostic and therapeutic biomarkers for various cancers. Therefore, monitoring of miRNA expression patterns can assist the elucidation of the biogenesis and biological function of miRNAs in different phases of cancers.

MicroRNA AND MOLECULAR IMAGING IN CANCER

The miRNAs are known to regulate the expression of genes involved in many cellular/and molecular pathways. The aberration of these

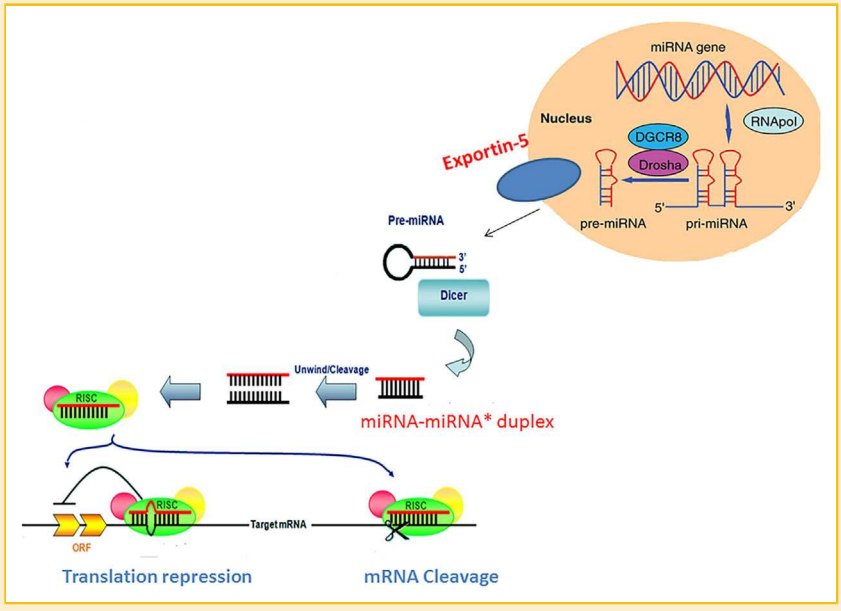

Fig. 1. A scheme of miRNA biogenesis.

TABLE I. Various MiRNAs Involved in Cancer Pathogenesis

Type of cancer	miRNA	Expression in cancer	Target gene	Stage/patient sample	Citation
Melanoma	miR-200c	Down regulation	ZEB1, DEF1, Nil-2-A	I, II, III, IV/41	Xu et al, [2012]
	miR-211	Down regulation	MITF, AP1S2, SOX11, IGFBP5	I, II, III, IV/41	Xu et al. [2012]
	miR-205	Down regulation	E2F1, E2F5	I, II, III, IV/41	Xu et al. [2012]
	miR-203	Down regulation	E2F3	I, II, III, IV/41	Xu et al. [2012]
	miR-33a	Up regulation	Pim-1, CDK6, cyclin D1	I-III/140	Friedman et al. [2012]
	miR-33a	Up regulation	p53, c-Myc	IIIB, IIIC, IV/59	Segura et al. [2010]
Lung	miR-193b	Up regulation	MAPK, PI3K-AKT, p53, ErbB	I, II/107	Nadal et al. [2015]
	miR-301	Up regulation	MAPK, PI3K-AKT, p53, ErbB	I, II/107	Nadal et al. [2015]
	miR-141	Up regulation	MAPK, PI3K-AKT, p53, ErbB	I, II/107	Nadal et al. [2015]
	miR-200b	Up regulation	MAPK, PI3K-AKT, p53, ErbB	I, II/107	Nadal et al. [2015]
Breast	miR-21	Up regulation	PDCD4, HIF1A	17	Qi et al. [2009]
	miR-10b	Up regulation	HOXD10	23	Ma et al. [2007]
	miR-155	Up regulation	SOCS1, FOXO3	15	Jiang et al. [2010]
	miR-373	Up regulation	CD44	11	Huang et al. [2008]
	miR-520c	Up regulation	CD44	11	Huang et al. [2008]
	miR-125b	Up regulation	EPO, EPOR	42	Ferracin et al. [2013]; van Schooneveld et al. [2015]
Liver	miR-18	Up regulation	–	22	Murakami et al. [2006]
	miR-20	Up regulation	–	22	Murakami et al. [2006]
	miR-195	Down regulation	–	22	Murakami et al. [2006]
	miR-21	Up regulation	–	20	Li et al. [2009]
	miR-101	Down regulation	–	20	Li et al. [2009]
	miR-92	Up regulation	–	4	Connolly et al. [2008]
Ovarian	miR-21	Up regulation		38	Resnick et al. [2009]
	miR-155	Down regulation		38	Resnick et al. [2009]
	miR-30c-1-3p	Up regulation		24	Häusler et al. [2010]
	miR-342-3p	Down regulation		24	Häusler et al. [2010]
	miR-16	Up regulation		35	Suryawanshi et al. [2013]
	let-7f	Down regulation		360	Zheng et al. [2013]
Oral	miR-21	Up regulation		60	Zahran et al. [2015]
	miR-184	Up regulation		60	Zahran et al. [2015]
	miR-145	Down regulation		60	Zahran et al. [2015]
	miR-26a	Down regulation	*TMEM184B*	36	Fukumoto et al. [2015]
	miR-26b	Down regulation	*TMEM184B*	36	Fukumoto et al. [2015]
	miR-375	Down regulation		51	Lajer et al. [2011]
	miR-31	Up regulation		51	Lajer et al. [2011]
Glioblastoma	miR-23	Up regulation	Mdm2, TSC1	Cell line	Tang et al. [2011]
	miR-10b	Up regulation	HOXD10, RhoC	20	Guessous et al. [2013]
	miR-25	Up regulation	Mdm2, TSC1	9/I, III	Ciafre et al. [2005]
	miR-16	Up regulation	BCL2	Cell line	Chaudhry et al. [2010]
	miR-19a	Up regulation		118	Jia et al. [2013]
	miR-451	Down regulation	PI3K/AKT	Cell line	Gal et al. [2008]
	miR-145	Down regulation	Oct4, SOX2	Cell line	Koo et al. [2012]
Retinoblastoma	*miR-373*	Up regulation		3	Yang and Mei, 2015]
	miR-181a	Down regulation	*CDKN1B*	3	Yang and Mei, 2015]
	miR-125b	Down regulation	*CDK6, CDC25A*	3	Yang and Mei, 2015]
	let-7b	Down regulation	*CDK6, CDC25A*	3	Yang and Mei, 2015]
	miR-25	Up regulation	*BCL2L1*	3	Yang and Mei, 2015]
	miR-18a		*BCL2L1*	3	Yang and Mei, 2015]
	miR-20a	Up regulation	*BCL2L1*	3	Yang and Mei, 2015]
Prostate	*miR-141*	Up regulation		102	Kelly et al. [2015]
	miR-145	Up regulation		102	Kelly et al. [2015]
	miR-155	Up regulation		102	Kelly et al. [2015]
	let7a	Down regulation		102	Kelly et al. [2015]
	miR-375	Up regulation		102	Kelly et al. [2015]
Colon	*let-7*	Down regulation	*KRAS*	Cell line	Graziano et al. [2010]
	miR-29	Down regulation	*MMP2, DNMT3A/B*	Cell line	Ding et al. [2011]
	miR-30a-5P	Down regulation	*DTL*	Cell line	Baraniskin et al. [2012]
	miR-34a	Down regulation	*FRA1, SIRT1, MYC, BCL2*	Cell line	Schetter et al. [2012]
	miR-17-92 cluster	Up regulation	*E2F1*	Cell line	Yu et al. [2012]
	miR-95	Up regulation	*SNX1*	Cell line	Huang et al. [2011]
	miR-135a/b	Up regulation	*APC*	Cell line	Luo et al. [2011]
Gastric	miR-21	Up regulation	RECK	59/I, II, III, IV	Zhang et al. [2008]; Tsujiura et al. [2010]; Zheng et al. [2010]
	miR-17-5p	Up regulation		87/I, II, III, IV	Tsujiura et al. [2010]; Wang et al. [2012]
	miR-1	Up regulation	MET	116/I, II, III, IV	Liu et al. [2011]
	miR-421	Up regulation		141/I, II, III, IV	Zhou et al. [2012]; Wu et al. [2014]
	miR-34	Up regulation	MET	141/I, II, III, IV	Zhou et al. [2012]; Wu et al. [2014]
	miR-195-5p	Down regulation		In vivo	Gorur et al. [2013]
	miR-196a	Down regulation	Annexin A1, HMGA2, HOXA8	In vivo	Tsai et al. [2012]
	miR-203	Down regulation	EMT activators	130/I, II, III, IV	Imaoka et al. [2015]
	let-7a	Down regulation		69/I, II, III, IV	Arabpour et al. [2016]
Hepatocellular carcinoma	miR-373	Up regulation	PPP6C	110	Wu et al. [2011]
	miR-381	Up regulation		110	Murakami et al. [2013]

(*Continued*)

TABLE I. (*Continued*)

Type of cancer	miRNA	Expression in cancer	Target gene	Stage/patient sample	Citation
	miR-130b	Up regulation	TP53INP1	57	Liu et al. [2012]; Wei et al. [2013]
	miR-20a	Up regulation		110/I, II, III	Fan et al. [2013]; Wei et al. [2013]
	miR-21	Up regulation	C/EBPb, RhoB, PDCD4, PTEN	137/I, II, III	Ura et al. [2009]; Xu et al. [2011]; Wei et al. [2013]; Zhou et al. [2011]
	miR-122	Down regulation	c-Myc, Bcl-w, ADAM-1, Wnt-1, MTTP	90/B, C, D, A	El-Garem et al. [2014]
	miR-223	Down regulation	STMN1	110/I, II, III	Ura et al. [2009]; Xu et al. [2011]; Wei et al. [2013]; Zhou et al. [2011]

genes could contribute to cancer initiation and progression. In respect to the magnitude of miRNA genes in the pathogenesis and progression of cancer, the utilization of suitable methods for assessing miRNAs provide insight into new opportunities for cancer treatment by modulating miRNA pathways and activities [Lee et al., 2008; Hernandez et al., 2013].

There are various conventional miRNA detection strategies including microarray, RT-PCR, and Northern blotting. Conventional

TABLE II. Various Techniques for Detecting MiRNAs in Cancer

Technique	miRNA	Type of cancer	Expression in cancer	Citation
BLI	miR-21	Breast	Up regulation	Hernandez et al. [2013]
	miR-221	Papillary thyroid carcinoma	Up regulation	Kim et al. [2008]
	miR-9	Embryonic carcinoma	Down regulation	Ko et al. [2008]
	miR-9	Embryonic carcinoma	Down regulation	Ko et al. [2008]
	miR-124a	Embryonic carcinoma	Up regulation	Ko et al. [2009a]
MB	miR-155	Lung	Up regulation	Yao et al. [2012]
	miR-10b	Breast	Up regulation	Yigit et al. [2013]
	miR-10b	Adenocarcinomas	Up regulation	Yigit et al. [2013]
	miR-1	–	Up regulation	Kang et al. [2015]
	miR-26a	–	Down regulation	Kang et al. [2015]
	miR124a	–	Up regulation	Kang et al. [2015]
	miR-126	–	Up regulation	Kang et al. [2015]
	miR-206	–	Up regulation	Kang et al. [2015]
	miR-221	–	Up regulation	Kang et al. [2015]
	miR-9		Down regulation	Kang et al. [2015]
Microarray	miR-136	Oral cancer	Down regulation	Momen-Heravi et al. [2014]
	miR-147	Oral cancer	Down regulation	Momen-Heravi et al. [2014]
	miR-1250	Oral cancer	Down regulation	Momen-Heravi et al. [2014]
	miR-148a	Oral cancer	Down regulation	Momen-Heravi et al. [2014]
	miR-632	Oral cancer	Down regulation	Momen-Heravi et al. [2014]
	miR-646	Oral cancer	Down regulation	Momen-Heravi et al. [2014]
	miR-668	Oral cancer	Down regulation	Momen-Heravi et al. [2014]
	miR-877	Oral cancer	Down regulation	Momen-Heravi et al. [2014]
	miR-503	Oral cancer	Down regulation	Momen-Heravi et al. [2014]
	miR-220a	Oral cancer	Down regulation	Momen-Heravi et al. [2014]
	miR-323-5p	Oral cancer	Down regulation	Momen-Heravi et al. [2014]
	miR-24	Oral cancer	Up regulation	Momen-Heravi et al. [2014]
	miR-27b	Oral cancer	Up regulation	Momen-Heravi et al. [2014]
	let-7 family	Breast	Down regulation	Litman et al. [2007]
	miR-21	Breast	Up regulation	Litman et al. [2007]
	miR-505-5p	Breast	Down regulation	Matamala et al. [2015]
	miR-125b-5p	Breast	Down regulation	Matamala et al. [2015]
	miR-21-5p	Breast	Up regulation	Matamala et al. [2015]
	miR-96-5p	Breast	Up regulation	Matamala et al. [2015]
	miR-576-5p,	Glioblastoma	Up regulation	Dong et al. [2014]
	miR-340	Glioblastoma	Up regulation	Dong et al. [2014]
	miR-626	Glioblastoma	Up regulation	Dong et al. [2014]
	miR-320	Glioblastoma	Down regulation	Dong et al. [2014]
	let-7g-5p	Glioblastoma	Down regulation	Dong et al. [2014]
	miR-7-5P	Glioblastoma	Down regulation	Dong et al. [2014]
RT-PCR	miR-223	Gastric	Up regulation	Gorur et al. [2013]
	miR-106b	Gastric	Up regulation	Gorur et al. [2013]
	miR-147	Gastric	Up regulation	Gorur et al. [2013]
	miR-34a	Gastric	Up regulation	Gorur et al. [2013]
	miR-130b	Gastric	Up regulation	Gorur et al. [2013]
	miR-638	Gastric	Down regulation	Gorur et al. [2013]
	miR-37	Gastric	Down regulation	Gorur et al. [2013]
	miR18a	Colon	Up regulation	Giráldez et al. [2013]
	miR19a	Colon	Up regulation	Giráldez et al. [2013]
	miR15b,	Colon	Up regulation	Giráldez et al. [2013]
	miR29a	Colon	Up regulation	Giráldez et al. [2013]
NGS	miR-574-3p	Breast	Down regulation	Krishnan et al. [2015]
	miR-660-5p	Breast	Down regulation	Krishnan et al. [2015]

BLI: bioluminescence imaging, MB: molecular beacon, NGS: Next Generation Sequencing, RT-PCR: Reverse transcription polymerase chain reaction.

detection methods are associated with some limitations which indicate a necessity for devising and deploying high-throughput noninvasive repetitive and real-time imaging systems for the detection of miRNAs in preclinical and clinical settings [German et al., 2008; Ko et al., 2009a; Sun et al., 2010]. In the following section, we will describe recently developed miRNA imaging strategies such as the various bioluminescence systems, fluorescent imaging approaches, as well as magnetic resonance imaging. In addition, both the advantages and inherent inefficiencies of various imaging systems are also described.

Recent significant advancement in reporter-based optical imaging systems has provided the opportunities of noninvasive and repeated real-time analysis of the miRNA gene expression in living cells. These miRNA imaging approaches offer a better elucidation of the biogenesis and biological function of miRNAs in vivo as well as miRNAs expression profile in human diseases [Gambhir et al., 1999; Blasberg, 2003; Wang et al., 2003]. These imaging techniques could, for example, provide better data on intact biological context than the "snapshots" provided by in vitro assays [Lee et al., 2008; Hernandez et al., 2013].

Several studies indicated that there are different categories for miRNA imaging. One of the main categories is based on nanoparticles, Bioluminescent imaging (BLI), fluorescent proteins (FPs), and molecular beacon (MB) imaging.

Despite of much advancement in the field of imaging for detecting of miRNAs, this field is still in its infancy. Modern and new imaging techniques provide a new horizon for the study of various targets and molecules in different levels in living cells [Ottobrini et al., 2006; Lee et al., 2008; Hernandez et al., 2013].

Some studies have been used bioluminescent reporter proteins such as Firefly luciferase (Fluc) and Gaussia luciferase (Gluc) for the imaging of various miRNAs in living cells [Ottobrini et al., 2006]. Gaussia luciferase utilizes coelenterazine as a substrate and emits light with a peak at 480 nm with a broad spectrum extending to 600 nm. Firefly luciferase emits light with a peak at 562 nm. D-luciferin serves as a good substrate for Firefly luciferase [Gould and Subramani, 1988; Tannous et al., 2005].

Other systems are reporter-based miRNA detection imaging systems. In the presence of miRNA, these systems demonstrate a dropping in reporter signals which is correlated with translational repression of its target mRNA [Ko et al., 2008, 2009b; Kim et al., 2009]. These imaging systems could facilitate potential applications for assessing of miRNA levels during biological processes such as cell growth and differentiation and the cell cycle in living animals [Ko et al., 2009b]. For instance, these techniques could be utilized to detect and monitor differentiation patterns of stem cells by miRNA (cell-specific) expression in vivo or to detect miRNAs involved in cancer progression, for example, miR-221 and miR-21 [Ko et al., 2009b]. Table II represents a variety of miRNAs which are detected by various techniques.

CONCLUDING REMARKS

MicroRNAs are a class of small non-coding RNA species, known as miRNAs, which control gene expression across various physiological and pathological processes. Their aberrant expression may be involved in human diseases. Among human diseases, it has been shown that miRNAs are aberrantly expressed or mutated in cancer, indicating that they may play a role as a new class of oncogenes or tumor suppressor genes. As the miRNA field continues to grow and evolve, it is an important step to develop efficient tools for rapid, specific, sensitive, and noninvasive imaging detection of miRNAs toward understanding the functions of miRNAs in various regulatory pathways in vivo, which consequently effect on the development of miRNA-based diagnostic and therapeutic assays at molecular level and new targets in drug discovery. In contrast to conventional imaging systems, new molecular imaging systems such as reported-based optical imaging systems are multiplex and have high specificity against other family RNAs and minimum sample manipulation and could be utilized for studying living systems. However, once new generations of imaging systems (i.e., reporter-based imaging) involve genetic modification in studied subjects; there are still some concerns regarding their translation into clinical practice. In conclusion, molecular imaging techniques are robust tools for high-throughput noninvasive repetitive and real-time monitoring of biogenesis, localization patterns, and biological function of miRNAs in vivo as well as miRNAs expression profile in human diseases particularly cancer. Such imaging systems will deepen our knowledge of miRNAs expression patterns and their biological functions in various tumorigenic regulatory networks in vivo, which eventually effect on the development of miRNA-based diagnostic and therapeutic assays and new targets in cancer drug discovery.

REFERENCES

Arabpour M, Mohammadparast S, Maftouh M, ShahidSales S, Moieni S, Akbarzade H, Mirhafez S, Parizadeh S, Hassanian S, Avan A. 2016. Circulating microRNAs as potential diagnostic biomarkers and therapeutic targets in gastric cancer: Current status and future perspectives. Curr Med Chem.

Baraniskin A, Birkenkamp-Demtroder K, Maghnouj A, Zöllner H, Munding J, Klein-Scory S, Reinacher-Schick A, Schwarte-Waldhoff I, Schmiegel W, Hahn SA. 2012. MiR-30a-5p suppresses tumor growth in colon carcinoma by targeting DTL. Carcinogenesis 33(4):732–739.

Blasberg RG. 2003. In vivo molecular-genetic imaging: Multi-modality nuclear and optical combinations. Nucl Med Biol 30(8):879–888.

Chaudhry MA, Sachdeva H, Omaruddin RA. 2010. Radiation-induced microRNA modulation in glioblastoma cells differing in DNA-repair pathways. DNA Cell Biol 29(9):553–561.

Ciafre S, Galardi S, Mangiola A, Ferracin M, Liu C-G, Sabatino G, Negrini M, Maira G, Croce C, Farace M. 2005. Extensive modulation of a set of microRNAs in primary glioblastoma. Biochem Biophys Res Commun 334(4):1351–1358.

Connolly E, Melegari M, Landgraf P, Tchaikovskaya T, Tennant BC, Slagle BL, Rogler LE, Zavolan M, Tuschl T, Rogler CE. 2008. Elevated expression of the miR-17–92 polycistron and miR-21 in hepadnavirus-associated hepatocellular carcinoma contributes to the malignant phenotype. Am J Pathol 173(3):856–864.

Ding Q, Chang C-J, Xie X, Xia W, Yang J-Y, Wang S-C, Wang Y, Xia J, Chen L, Cai C. 2011. APOBEC3G promotes liver metastasis in an orthotopic mouse model of colorectal cancer and predicts human hepatic metastasis. J Clin Invest 121(11):4526–4536.

Dong L, Li Y, Han C, Wang X, She L, Zhang H. 2014. MiRNA microarray reveals specific expression in the peripheral blood of glioblastoma patients. Int J Oncol 45(2):746–756.

El-Garem H, Ammer A, Shehab H, Shaker O, Anwer M, El-Akel W, Omar H. 2014. Circulating microRNA, miR-122 and miR-221 signature in Egyptian patients with chronic hepatitis C related hepatocellular carcinoma. World J Hepatol 6(11):818–824.

Faghihloo E, Araei Y, Mohammadi M, Mirzaei H, Mohammadi H, Mokhtari-Azad T. 2016. The effect of oxamflatin on the E-cadherin expression in gastric cancer cell line. Cancer Gene Ther.

Fan MQ, Huang CB, Gu Y, Xiao Y, Sheng JX, Zhong L. 2013. Decrease expression of microRNA-20a promotes cancer cell proliferation and predicts poor survival of hepatocellular carcinoma. J Exp Clin Cancer Res 32(1):21.

Fang S, Lee HJ, Wark AW, Corn RM. 2006. Attomole microarray detection of microRNAs by nanoparticle-amplified SPR imaging measurements of surface polyadenylation reactions. J Am Chem Soc 128(43):14044–14046.

Fathullahzadeh S, Mirzaei H, Honardoost M, Sahebkar A, Salehi M. 2016. Circulating microRNA-192 as a diagnostic biomarker in human chronic lymphocytic leukemia. Cancer Gene Ther.

Ferracin M, Bassi C, Pedriali M, Pagotto S, D'Abundo L, Zagatti B, Corrà F, Musa G, Callegari E, Lupini L. 2013. MiR-125b targets erythropoietin and its receptor and their expression correlates with metastatic potential and ERBB2/HER2 expression. Mol Cancer 12(1):1.

Friedman EB, Shang S, de Miera EV-S, Fog JU, Teilum MW, Ma MW, Berman RS, Shapiro RL, Pavlick AC, Hernando E. 2012. Serum microRNAs as biomarkers for recurrence in melanoma. J Transl Med 10(1):1.

Fukumoto I, Hanazawa T, Kinoshita T, Kikkawa N, Koshizuka K, Goto Y, Nishikawa R, Chiyomaru T, Enokida H, Nakagawa M. 2015. MicroRNA expression signature of oral squamous cell carcinoma: Functional role of microRNA-26a/b in the modulation of novel cancer pathways. Br J Cancer 112(5):891–900.

Gal H, Pandi G, Kanner AA, Ram Z, Lithwick-Yanai G, Amariglio N, Rechavi G, Givol D. 2008. MIR-451 and Imatinib mesylate inhibit tumor growth of Glioblastoma stem cells. Biochem Biophys Res Commun 376(1):86–90.

Gambhir S, Barrio J, Herschman H, Phelps M. 1999. Assays for noninvasive imaging of reporter gene expression. Nucl Med Biol 26(5):481–490.

German MA, Pillay M, Jeong D-H, Hetawal A, Luo S, Janardhanan P, Kannan V, Rymarquis LA, Nobuta K, German R. 2008. Global identification of microRNA-target RNA pairs by parallel analysis of RNA ends. Nat Biotechnol 26(8):941–946.

Gholamin S, Miezaei H, Razavi SM, Hassanian SM, Saadatpour L, Masoudifar A, ShahidSales S, Avan A. 2017. GD2-targeted immunotherapy and potential value of circulating micrornas in neuroblastoma. J Cell Physiol.

Gholamin S, Pasdar A, Sadegh Khorrami M, Mirzaei H, Reza Mirzaei H, Salehi R, Ferns GA, Ghayour-Mobarhan M, Avan A. 2016. The potential for circulating microRNAs in the diagnosis of myocardial infarction: A novel approach to disease diagnosis and treatment. Curr Pharm Des 22(3):397–403.

Giráldez MD, Lozano JJ, Ramírez G, Hijona E, Bujanda L, Castells A, Gironella M. 2013. Circulating microRNAs as biomarkers of colorectal cancer: Results from a genome-wide profiling and validation study. Clin Gastroenterol Hepatol 11(6):681–688.e683.

Gorur A, Fidanci SB, Unal ND, Ayaz L, Akbayir S, Yaroglu HY, Dirlik M, Serin MS, Tamer L. 2013. Determination of plasma microRNA for early detection of gastric cancer. Mol Biol Rep 40(3):2091–2096.

Gould SJ, Subramani S. 1988. Firefly luciferase as a tool in molecular and cell biology. Anal Biochem 175(1):5–13.

Graziano F, Canestrari E, Loupakis F, Ruzzo A, Galluccio N, Santini D, Rocchi M, Vincenzi B, Salvatore L, Cremolini C. 2010. Genetic modulation of the Let-7 microRNA binding to KRAS 3′-untranslated region and survival of metastatic colorectal cancer patients treated with salvage cetuximab-irinotecan. Pharmacogenomics J 10(5):458–464.

Guessous F, Alvarado-Velez M, Marcinkiewicz L, Zhang Y, Kim J, Heister S, Kefas B, Godlewski J, Schiff D, Purow B. 2013. Oncogenic effects of miR-10b in glioblastoma stem cells. J Neurooncol 112(2):153–163.

Häusler S, Keller A, Chandran P, Ziegler K, Zipp K, Heuer S, Krockenberger M, Engel J, Hönig A, Scheffler M. 2010. Whole blood-derived miRNA profiles as potential new tools for ovarian cancer screening. Br J Cancer 103(5):693–700.

Hernandez R, Orbay H, Cai W. 2013. Molecular imaging strategies for in vivo tracking of microRNAs: A comprehensive review. Curr Med Chem 20(29):3594–3603.

Huang Q, Gumireddy K, Schrier M, Le Sage C, Nagel R, Nair S, Egan DA, Li A, Huang G, Klein-Szanto AJ. 2008. The microRNAs miR-373 and miR-520c promote tumour invasion and metastasis. Nat Cell Biol 10(2):202–210.

Huang Z, Huang S, Wang Q, Liang L, Ni S, Wang L, Sheng W, He X, Du X. 2011. MicroRNA-95 promotes cell proliferation and targets sorting Nexin 1 in human colorectal carcinoma. Cancer Res 71(7):2582–2589.

Imaoka H, Toiyama Y, Okigami M, Yasuda H, Saigusa S, Ohi M, Tanaka K, Inoue Y, Mohri Y, Kusunoki M. 2015. Circulating microRNA-203 predicts metastases, early recurrence, and poor prognosis in human gastric cancer. Gastric Cancer 19(3):744–753.

Jia Z, Wang K, Zhang A, Wang G, Kang C, Han L, Pu P. 2013. MiR-19a and miR-19b overexpression in gliomas. Pathol Oncol Res 19(4):847–853.

Jiang S, Zhang H-W, Lu M-H, He X-H, Li Y, Gu H, Liu M-F, Wang E-D. 2010. MicroRNA-155 functions as an OncomiR in breast cancer by targeting the suppressor of cytokine signaling 1 gene. Cancer Res 70(8):3119–3127.

Kang HJ, Lee J, Ali BA, Al-Khedhairy AA, Kim S. 2015. Bioimaging of miRNA biogenesis using a color-tunable molecular beacon. RNA Dis 2(3):e697.

Kelly BD, Miller N, Sweeney KJ, Durkan GC, Rogers E, Walsh K, Kerin MJ. 2015. A circulating microRNA signature as a biomarker for prostate cancer in a high risk group. J Clin Med 4(7):1369–1379.

Kim HJ, Chung J-K, Lee DS, Kim S. 2009. In vivo imaging of miR-221 biogenesis in papillary thyroid carcinoma. Mol Imaging Biol 11(2):71–78.

Kim HJ, Kim YH, Lee DS, Chung J-K, Kim S. 2008. In vivo imaging of functional targeting of miR-221 in papillary thyroid carcinoma. J Nucl Med 49(10):1686–1693.

Ko HY, Lee DS, Kim S. 2009a. Noninvasive imaging of microRNA124a-mediated repression of the chromosome 14 ORF 24 gene during neurogenesis. FEBS J 276(17):4854–4865.

Ko HY, Lee DS, Kim S. 2009b. A reporter gene imaging system for monitoring microRNA biogenesis. Nat Protoc 4(11):1663–1669.

Ko MH, Kim S, Hwang DW, Ko HY, Kim YH, Lee DS. 2008. Bioimaging of the unbalanced expression of microRNA9 and microRNA9* during the neuronal differentiation of P19 cells. FEBS J 275(10):2605–2616.

Koo S, Martin GS, Schulz KJ, Ronck M, Toussaint LG. 2012. Serial selection for invasiveness increases expression of miR-143/miR-145 in glioblastoma cell lines. BMC Cancer 12(1):1.

Krishnan P, Ghosh S, Wang B, Li D, Narasimhan A, Berendt R, Graham K, Mackey JR, Kovalchuk O, Damaraju S. 2015. Next generation sequencing profiling identifies miR-574-3p and miR-660-5p as potential novel prognostic markers for breast cancer. BMC Genomics 16(1):1.

Lajer C, Nielsen F, Friis-Hansen L, Norrild B, Borup R, Garnaes E, Rossing M, Specht L, Therkildsen M, Nauntofte B. 2011. Different miRNA signatures of oral and pharyngeal squamous cell carcinomas: A prospective translational study. Br J Cancer 104(5):830–840.

Lee JY, Kim S, Jeong JM, Chung J-K, Lee MC, Lee DS. 2008. Development of a dual-luciferase reporter system for in vivo visualization of MicroRNA biogenesis and posttranscriptional regulation. J Nucl Med 49(2):285–294.

Li S, Fu H, Wang Y, Tie Y, Xing R, Zhu J, Sun Z, Wei L, Zheng X. 2009. MicroRNA-101 regulates expression of the v-fos FBJ murine osteosarcoma viral oncogene homolog (FOS) oncogene in human hepatocellular carcinoma. Hepatology 49(4):1194–1202.

Li W, Ruan K. 2009. MicroRNA detection by microarray. Anal Bioanal Chem 394(4):1117–1124.

Litman T, Jacobsen N, Nørholm M, Glue C, Stahlberg N, Møller S. 2007. MicroRNA profiling of breast cancer tissue using an LNA-based microarray. Nat Meth | Application Notes.

Liu AM, Yao TJ, Wang W, Wong KF, Lee NP, Fan ST, Poon RT, Gao C, Luk JM. 2012. Circulating miR-15b and miR-130b in serum as potential markers for detecting hepatocellular carcinoma: A retrospective cohort study. BMJ Open 2(2):e000825.

Liu R, Zhang C, Hu Z, Li G, Wang C, Yang C, Huang D, Chen X, Zhang H, Zhuang R. 2011. A five-microRNA signature identified from genome-wide

serum microRNA expression profiling serves as a fingerprint for gastric cancer diagnosis. Eur J Cancer 47(5):784–791.

Lu J, Tsourkas A. 2009. Imaging individual microRNAs in single mammalian cells in situ. Nucleic Acids Res 37(14):e100.

Luo X, Burwinkel B, Tao S, Brenner H. 2011. MicroRNA signatures: Novel biomarker for colorectal cancer? Cancer Epidemiol Biomarkers Prev.

Ma L, Teruya-Feldstein J, Weinberg RA. 2007. Tumour invasion and metastasis initiated by microRNA-10b in breast cancer. Nature 449(7163):682–688.

Matamala N, Vargas MT, González-Cámpora R, Miñambres R, Arias JI, Menéndez P, Andrés-León E, Gómez-López G, Yanowsky K, Calvete-Candenas J. 2015. Tumor microRNA expression profiling identifies circulating microRNAs for early breast cancer detection. Clin Chem 61(8):1098–1106.

Mirzaei H, Gholamin S, Shahidsales S, Sahebkar A, Jafaari MR, Mirzaei HR, Hassanian SM, Avan A. 2016a. MicroRNAs as potential diagnostic and prognostic biomarkers in melanoma. Eur J Cancer 53:25–32.

Mirzaei H, Naseri G, Rezaee R, Mohammadi M, Banikazemi Z, Reza Mirzaei H, Salehi H, Peyvandi M, Pawelek JM, Sahebkar A. 2016b. Curcumin: A new candidate for melanoma therapy? Int J Cancer 139(8):1683–1695.

Mirzaei H, Sahebkar A, Jaafari M, Hadjati J, Javanmard S, Mirzaei H, Salehi R. 2016c. PiggyBac as a novel vector in cancer gene therapy: Current perspective. Cancer Gene Ther 23:45–47.

Mirzaei H, Sahebkar A, Jaafari MR, Goodarzi M, Mirzaei HR. 2016d. Diagnostic and therapeutic potential of exosomes in cancer: The beginning of a new tale? J Cell Physiol.

Mirzaei H, Khataminfar S, Mohammadparast S, Sales SS, Maftouh M, Mohammadi M, Simonian M, Parizadeh SM, Hassanian SM, Avan A. 2016e. Circulating microRNAs as potential diagnostic biomarkers and therapeutic targets in gastric cancer: Current status and future perspectives. Curr Med Chem 23(36):4135–4150.

Mirzaei H, Yazdi F, Salehi R, Mirzaei HR. 2016f. SiRNA and epigenetic aberrations in ovarian cancer. J Cancer Res Ther 12(2):498–508.

Mirzaei HR, Mirzaei H, Lee SY, Hadjati J, Till BG. 2016g. Prospects for chimeric antigen receptor (CAR) γδ T cells: A potential game changer for adoptive T cell cancer immunotherapy. Cancer Lett 380(2):413–423.

Mirzaei HR, Sahebkar A, Salehi R, Nahand JS, Karimi E, Jaafari MR, Mirzaei H. 2016h. Boron neutron capture therapy: Moving toward targeted cancer therapy. J Cancer Res Ther 12(2):520–525.

Mirzaei H, Fathullahzadeh S, Khanmohammadi R, Darijani M, Momeni F, Masoudifar A, Goodarzi M, Mardanshah O, Stanveng J, Jaafari MR. 2017a. State of the art in MicroRNA as diagnostic and therapeutic biomarkers in chronic lymphocytic leukemia. J Cell Physiol.

Mirzaei H, Momeni F, Saadatpour L, Sahebkar A, Goodarzi M, Masoudifar A, Kouhpayeh S, Salehi H, Mirzaei HR, Jaafari MR. 2017b. MicroRNA: Relevance to stroke diagnosis, prognosis and therapy. J Cell Physiol.

Mohammadi M, Goodarzi M, Jaafari M, Mirzaei H, Mirzaei H. 2016a. Circulating microRNA: A new candidate for diagnostic biomarker in neuroblastoma. Cancer Gene Ther 23(11):371–372.

Mohammadi M, Jaafari M, Mirzaei H, Mirzaei H. 2016b. Mesenchymal stem cell: A new horizon in cancer gene therapy. Cancer Gene Ther 23(9):285–286.

Momen-Heravi F, Trachtenberg A, Kuo W, Cheng Y. 2014. Genomewide study of salivary microRNAs for detection of oral cancer. J Dent Res. 0022034514531018.

Momin MA, Okochi K, Watanabe H, Imaizumi A, Omura K, Amagasa T, Okada N, Ohbayashi N, Kurabayashi T. 2009. Diagnostic accuracy of cone-beam CT in the assessment of mandibular invasion of lower gingival carcinoma: Comparison with conventional panoramic radiography. Eur J Radiol 72(1):75–81.

Moridikia A, Mirzaei H, Sahebkar A, Salimian J. 2017. MicroRNAs: Potential candidates for diagnosis and treatment of colorectal cancer. J Cell Physiol.

Murakami Y, Tamori A, Itami S, Tanahashi T, Toyoda H, Tanaka M, Wu W, Brojigin N, Kaneoka Y, Maeda A, Kumada T, Kawada N, Kubo S, Kuroda M. 2013. The expression level of miR-18b in hepatocellular carcinoma is associated with the grade of malignancy and prognosis. BMC Cancer 13:99.

Murakami Y, Yasuda T, Saigo K, Urashima T, Toyoda H, Okanoue T, Shimotohno K. 2006. Comprehensive analysis of microRNA expression patterns in hepatocellular carcinoma and non-tumorous tissues. Oncogene 25(17):2537–2545.

Nadal E, Truini A, Nakata A, Lin J, Reddy RM, Chang AC, Ramnath N, Gotoh N, Beer DG, Chen G. 2015. A novel serum 4-microRNA signature for lung cancer detection. Sci Rep 5.

Ottobrini L, Ciana P, Biserni A, Lucignani G, Maggi A. 2006. Molecular imaging: A new way to study molecular processes in vivo. Mol Cell Endocrinol 246(1):69–75.

Qi L, Bart J, Tan LP, Platteel I, van der Sluis T, Huitema S, Harms G, Fu L, Hollema H, van den Berg A. 2009. Expression of miR-21 and its targets (PTEN, PDCD4, TM1) in flat epithelial atypia of the breast in relation to ductal carcinoma in situ and invasive carcinoma. BMC Cancer 9(1):1.

Rashidi B, Hoseini Z, Sahebkar A, Mirzaei H. 2016. Anti-atherosclerotic effects of vitamins D and E in suppression of atherogenesis. J Cell Physiol.

Rashidi B, Malekzadeh M, Goodarzi M, Masoudifar A, Mirzaei H. 2017. Green tea and its anti-angiogenesis effects. Biomed Pharmacother 89:949–956.

Resnick KE, Alder H, Hagan JP, Richardson DL, Croce CM, Cohn DE. 2009. The detection of differentially expressed microRNAs from the serum of ovarian cancer patients using a novel real-time PCR platform. Gynecol Oncol 112(1):55–59.

Ryoo S-R, Lee J, Yeo J, Na H-K, Kim Y-K, Jang H, Lee JH, Han SW, Lee Y, Kim VN. 2013. Quantitative and multiplexed microRNA sensing in living cells based on peptide nucleic acid and nano graphene oxide (PANGO). ACS Nano 7(7):5882–5891.

Salarini R, Sahebkar A, Mirzaei H, Jaafari M, Riahi M, Hadjati J, Asrami M, Fdaee S, Salehi R, Mirzaei H. 2015. Epi-drugs and Epi-miRs: Moving beyond current cancer therapies. Curr Cancer Drug Targets.

Schetter AJ, Okayama H, Harris CC. 2012. The role of microRNAs in colorectal cancer. Cancer J (Sudbury, Mass) 18(3):244.

Segura MF, Belitskaya-Lévy I, Rose AE, Zakrzewski J, Gaziel A, Hanniford D, Darvishian F, Berman RS, Shapiro RL, Pavlick AC. 2010. Melanoma MicroRNA signature predicts post-recurrence survival. Clin Cancer Res 16(5):1577–1586.

Simonian M, Mosallayi M, Mirzaei H. 2016. Circulating miR-21 as novel biomarker in gastric cancer: Diagnostic and prognostic biomarker.

Sun W, Julie Li Y-S, Huang H-D, Shyy JY, Chien S. 2010. MicroRNA: A master regulator of cellular processes for bioengineering systems. Ann Rev Biomed Eng 12:1–27.

Suryawanshi S, Vlad AM, Lin H-M, Mantia-Smaldone G, Laskey R, Lee M, Lin Y, Donnellan N, Klein-Patel M, Lee T. 2013. Plasma microRNAs as novel biomarkers for endometriosis and endometriosis-associated ovarian cancer. Clin Cancer Res 19(5):1213–1224.

Tang H, Liu X, Wang Z, She X, Zeng X, Deng M, Liao Q, Guo X, Wang R, Li X. 2011. Interaction of hsa-miR-381 and glioma suppressor LRRC4 is involved in glioma growth. Brain Res 1390:21–32.

Tannous BA, Kim D-E, Fernandez JL, Weissleder R, Breakefield XO. 2005. Codon-optimized Gaussia luciferase cDNA for mammalian gene expression in culture and in vivo. Mol Ther 11(3):435–443.

Tsai KW, Liao YL, Wu CW, Hu LY, Li SC, Chan WC, Ho MR, Lai CH, Kao HW, Fang WL. 2012. Aberrant expression of miR-196a in gastric cancers and correlation with recurrence. Genes Chromosomes Cancer 51(4):394–401.

Tsujiura M, Ichikawa D, Komatsu S, Shiozaki A, Takeshita H, Kosuga T, Konishi H, Morimura R, Deguchi K, Fujiwara H. 2010. Circulating microRNAs in plasma of patients with gastric cancers. Br J Cancer 102(7):1174–1179.

Ura S, Honda M, Yamashita T, Ueda T, Takatori H, Nishino R, Sunakozaka H, Sakai Y, Horimoto K, Kaneko S. 2009. Differential microRNA expression between hepatitis B and hepatitis C leading disease progression to hepatocellular carcinoma. Hepatology (Baltimore, Md) 49(4):1098–1112.

van Schooneveld E, Wildiers H, Vergote I, Vermeulen PB, Dirix LY, Van Laere SJ. 2015. Dysregulation of microRNAs in breast cancer and their potential role as prognostic and predictive biomarkers in patient management. Breast Cancer Res 17(1):1.

Wang J, Chen J, Chang P, LeBlanc A, Li D, Abbruzzesse JL, Frazier ML, Killary AM, Sen S. 2009. MicroRNAs in plasma of pancreatic ductal adenocarcinoma patients as novel blood-based biomarkers of disease. Cancer Prev Res 2(9):807–813.

Wang M, Gu H, Wang S, Qian H, Zhu W, Zhang L, Zhao C, Tao Y, Xu W. 2012. Circulating miR-17-5p and miR-20a: Molecular markers for gastric cancer. Mol Med Rep 5(6):1514–1520.

Wang X, Rosol M, Ge S, Peterson D, McNamara G, Pollack H, Kohn DB, Nelson MD, Crooks GM. 2003. Dynamic tracking of human hematopoietic stem cell engraftment using in vivo bioluminescence imaging. Blood 102(10):3478–3482.

Wei R, Huang GL, Zhang MY, Li BK, Zhang HZ, Shi M, Chen XQ, Huang L, Zhou QM, Jia WH, Zheng XF, Yuan YF, Wang HY. 2013. Clinical significance and prognostic value of microRNA expression signatures in hepatocellular carcinoma. Clin Cancer Res 19(17):4780–4791.

Wu J, Li G, Yao Y, Wang Z, Sun W, Wang J. 2014. MicroRNA-421 is a new potential diagnosis biomarker with higher sensitivity and specificity than carcinoembryonic antigen and cancer antigen 125 in gastric cancer. Biomarkers 20(1):58–63.

Wu N, Liu X, Xu X, Fan X, Liu M, Li X, Zhong Q, Tang H. 2011. MicroRNA-373, a new regulator of protein phosphatase 6, functions as an oncogene in hepatocellular carcinoma. FEBS J 278(12):2044–2054.

Xu J, Wu C, Che X, Wang L, Yu D, Zhang T, Huang L, Li H, Tan W, Wang C, Lin D. 2011. Circulating microRNAs, miR-21, miR-122, and miR-223, in patients with hepatocellular carcinoma or chronic hepatitis. Mol Carcinog 50(2):136–142.

Xu Y, Brenn T, Brown E, Doherty V, Melton D. 2012. Differential expression of microRNAs during melanoma progression: miR-200c, miR-205 and miR-211 are downregulated in melanoma and act as tumour suppressors. Br J Cancer 106(3):553–561.

Yang Y, Mei Q. 2015. MiRNA signature identification of retinoblastoma and the correlations between differentially expressed miRNAs during retinoblastoma progression. Mol Vis 21:1307.

Yao Q, Zhang A-M, Ma H, Lin S, Wang X-X, Sun J-G, Chen Z-T. 2012. Novel molecular beacons to monitor microRNAs in non-small-cell lung cancer. Mol Cell Probes 26(5):182–187.

Yigit M, Ghosh S, Kumar M, Petkova V, Kavishwar A, Moore A, Medarova Z. 2013. Context-dependent differences in miR-10b breast oncogenesis can be targeted for the prevention and arrest of lymph node metastasis. Oncogene 32(12):1530–1538.

Yu G, Tang JQ, Tian ML, Li H, Wang X, Wu T, Zhu J, Huang SJ, Wan YL. 2012. Prognostic values of the miR-17-92 cluster and its paralogs in colon cancer. J Surg Oncol 106(3):232–237.

Zahran F, Ghalwash D, Shaker O, Al-Johani K, Scully C. 2015. Salivary microRNAs in oral cancer. Oral Dis 21(6):739–747.

Zhang Z, Li Z, Gao C, Chen P, Chen J, Liu W, Xiao S, Lu H. 2008. MiR-21 plays a pivotal role in gastric cancer pathogenesis and progression. Lab Invest 88(12):1358–1366.

Zheng H, Zhang L, Zhao Y, Yang D, Song F, Wen Y, Hao Q, Hu Z, Zhang W, Chen K. 2013. Plasma miRNAs as diagnostic and prognostic biomarkers for ovarian cancer. PLoS ONE 8(11):e77853.

Zheng Y, Cui L, Sun W, Zhou H, Yuan X, Huo M, Chen J, Lou Y, Guo J. 2010. MicroRNA-21 is a new marker of circulating tumor cells in gastric cancer patients. Cancer Biomark 10(2):71–77.

Zhou H, Xiao B, Zhou F, Deng H, Zhang X, Lou Y, Gong Z, Du C, Guo J. 2012. MiR-421 is a functional marker of circulating tumor cells in gastric cancer patients. Biomarkers 17(2):104–110.

Zhou J, Yu L, Gao X, Hu J, Wang J, Dai Z, Wang JF, Zhang Z, Lu S, Huang X, Wang Z, Qiu S, Wang X, Yang G, Sun H, Tang Z, Wu Y, Zhu H, Fan J. 2011. Plasma microRNA panel to diagnose hepatitis B virus-related hepatocellular carcinoma. J Clin Oncol 29(36):4781–4788.

Zubakov D, Boersma AW, Choi Y, van Kuijk PF, Wiemer EA, Kayser M. 2010. MicroRNA markers for forensic body fluid identification obtained from microarray screening and quantitative RT-PCR confirmation. Int J Legal Med 124(3):217–226.