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Review

Meta-analysis of microRNA-183 family expression in human cancer studies comparing cancer tissues with noncancerous tissues

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ABSTRACT

MicroRNA-183 (miR-183) family is proposed as promising biomarkers for early cancer detection and accurate prognosis as well as targets for more efficient treatment. The results of their expression feature in cancer tissues are inconsistent and controversy still exists in identifying them as new biomarkers of cancers. Therefore, to systemically evaluate the most frequently reported cancers in which miR-183 family members were up- or down-regulated is critical for further investigation on physiological impact of its aberrant regulation in specific cancers. The published studies that compared the level of miR-183 family expression in cancer tissues with those in noncancerous tissues were reviewed by the meta-analysis with a vote-counting strategy. Among the 49 included studies, a total of 18 cancers were reported, with 11 cancers reported in at least two studies. In the panel of miR-183 family members' expression analysis, colorectal cancer and prostate cancer ranked at the top among consistently reported cancer types with up-regulated feature. Bladder cancer, lung cancer and hepatocellular carcinoma were the third most frequently reported cancer types with significant over-expression of miR-96, miR-182 and miR-183 respectively. Breast cancer and gastric cancer were presented with inconsistent regulations and the members of this family had their own distinct regulated features in other different cancers. MiR-183 family, either individually or as a cluster, may be useful prognostic markers and/or therapeutic targets in several cancers. Further studies and repeat efforts are still required to determine the role of miR-183 family in various cancer progressions.

Contents

Abbreviations: miRNA, miR, microRNA; qRT-PCR, quantitative real-time reverse transcription polymerase chain reaction; FC, fold change; UC, bladder urothelial carcinoma; BCC, basal cell carcinoma; CIS, carcinoma in situ cells of the testis; HCC, hepatocellular carcinoma; SCC, lung squamous cell carcinoma; NSCC, non-small cell lung cancer; HG-SOC, high-grade serous ovarian carcinoma; PDAC, pancreatic ductal adenocarcinoma; PanINs, pancreatic intraepithelial neoplasms; MPM, Malignant pleural mesothelioma; HMCs, human normal pleural mesothelial short-term cell cultures.

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1. Introduction

Cancer is one of the most common causes of death worldwide, and has become a major public health challenge. Based on the GLOBOCAN 2008 estimates, about 12.7 million cancer cases and 7.6 million cancer deaths are estimated to have occurred (Jemal et al., 2011). Hence, early detection and precise diagnosis are critical for the patients to receive proper therapeutic treatment. Accompanied with the advance of research on carcinogenesis, more and more studies focus on novel strategies for early detection and prevention (Fan et al., 2012). Emerging evidence has suggested and proposed microRNAs (miRNAs) as promising biomarkers for early cancer detection and accurate prognosis as well as targets for more efficient treatment (Vosa et al., 2013).

MicroRNAs are a class of endogenous, small (approximately 22 nucleotides in length), non-coding functional RNAs (Bartels and Tsongalis, 2009). MicroRNA gene family is constituted by the gene miRNA clusters which have high homogeneity. The miRNA-183 family is highly conserved consisting of miR-96, miR-182, miR-183 three members (Pierce et al., 2008). Several studies demonstrated that members are abnormally expressed in various tumors and directly involved in human cancer processes, such as cellular differentiation, tumorigenesis, proliferation, apoptosis and metabolism (Abraham et al., 2011; Lin et al., 2012; X. Xu et al., 2012). Moreover, many studies have focused on searching for biomarkers by identifying differences in miRNA expression between cancer tissues and paired neighboring noncancerous tissues. The published evidence suggested that miR-183 family members abnormally expressed, either up- or down-regulated, in various cancers depending on their target downstream genes. However, the results of their expression feature are inconsistent and controversy still exists in identifying them as new biomarkers of cancers. No review focuses on associations between miR-183 family expression especially with various cancers, and summary on consistently reported cancers and statistical significant frequency of the level of expression is not considered in multiple independent cancer expression profiling studies.

Therefore, to systemically evaluate the most frequently reported cancers in which miR-183 family members were consistently up- or down-regulated is critical for further investigation on physiological impact of its aberrant regulation in specific cancers. A logical method to identify the cancers with the miR-183 family consistent expression is to search for the intersections of miR-183 family expression in multiple independent studies. It is strenuous to collate the results of those studies when the researchers employed different profiling platforms, and adopted different methods to ascertain differential expression. Then a vote-counting strategy proposed by Griffith and Chan to identify consistent results when raw data are unavailable (Chan et al., 2008; Griffith et al., 2006), this kind of meta-review has been proved to be useful in exploring candidate miRNA biomarkers in human cancers (Guan et al., 2012; Ma et al., 2012), which gave us insights into the meta-analysis of miR-183 family expression in human cancer studies to present and rank the frequently reported cancer types for further investigations on the miRNA-183 family as biomarkers.

2. Material and methods

2.1. Study selection

To identify relevant literature, we search PubMed, Web of Science and ELSEVIER ScienceDirect (SDOS) for cancer expression profiling studies of miR-183 family using search term ((microRNA 96) OR (microRNA 182) OR (microRNA 183)) AND (cancer OR tumor OR neoplasms OR carcinoma). The last search was performed in January 2013. Studies were included if: (1) they were miR-183 family expression studies in cancer patients; (2) they used tissue samples obtained from surgically resected tumor and neighboring noncancerous or normal tissues in human for comparison; (3) validation method and validation sample set reported. Therefore, the miR-183 family expression studies using the serum, or cancer cell lines were excluded. Review articles were also excluded.

2.2. Data abstraction

Two authors (Q.H. Zhang and H.M. Sun) independently evaluated and extracted the data with the inclusion criteria. Any disagreements were resolved through discussion between the authors. From the full text and corresponding supplement information, the following eligibility items were collected and recorded for each study: author, year of publication, location of study, selection and characteristics of recruited cancer patients, validation method and validation sample, the members of miR-183 family with abnormal expression, up-/down- regulated feature, and their corresponding fold change (if available).

2.3. Ranking

Each included study comparing miR-183 family expression between cancer tissues and corresponding noncancerous or normal tissues provided a list of different cancer types. Then the following vote-counting strategy based method of ranking potential molecular biomarkers by Griffith et al. (2006) and Chan et al. (2008), was adopted in the meta-analysis. The different cancer types reported were ranked according to the following order of importance: (1) number of the studies that reported the same cancer type with a consistent direction of change; (2) total number of samples for comparison in agreement; (3) average fold change reported by the studies in agreement (if the studies with available fold change information). Total sample size was considered more important than average fold-change because many studies do not report a fold-change. Therefore, average fold-change was based solely on the subset of studies for which a fold-change value was available. And the ranking was performed by Statistical Product and Service Solutions Version 13 (SPSS 13.0).

3. Results

3.1. Independent studies for data extraction

In total, 272 studies were searched. Following the inclusion and exclusion criteria, only 50 independent studies were included in the analysis (Balatti et al., 2011; Cekaite et al., 2012; Cho et al., 2009; Dettmer et al., 2013; Donnem et al., 2012; Earle et al., 2010; Giricz et al., 2012; Goeppert et al., 2010; Han et al., 2011; Hannafon et al., 2011; Jiang et al., 2010; Kong et al., 2012; Larne et al., 2013; Lee et al., 2012; Lehmann et al., 2010; Li et al., 2010, 2011; Li et al., 2012a, 2012b; Lin et al., 2010, Z. Liu et al., 2012, A.M. Liu et al., 2012; Lowery et al., 2010; Q. Ma et al., 2011; L. Ma et al., 2011; Mihelich et al., 2011; Motoyama et al., 2009; Myatt et al., 2010; Novotny et al., 2012; Pignot et al., 2012; Pineau et al., 2010; Sand et al., 2012; Sarver et al., 2009; Schaefer et al., 2010; Siva et al., 2009; Slaby et al., 2010; Szafranska et al., 2007; Tan et al., 2011; Tang et al., 2013; Tsuchiyama et al., 2012; Y. Wang et al., 2012; J. Wang et al., 2012; Wang et al., 2013; X.M. Xu et al., 2012; Yamada et al., 2011; Yu et al., 2010, 2012; Zheng et al., 2012; Zhu et al., 2011, 2012). Among the 50 studies, two studies (Li et al., 2012a, 2012b) reported the same results in different languages, then we picked the English one (Li et al., 2012b) for further analysis. The characteristics of these studies are listed in Table 1 in alphabetical order of the cancer types. Among the 49 included studies, a total of 18 cancers were reported, with 11 cancers reported in at least two studies. Four studies focused on bladder cancer, seven studies focused on colon and rectal cancers, five studies were about HCC, breast cancer, lung cancer and prostate cancer for each, three studies were respectively related to gastric cancer