MicroRNAs are Emerging as Most Potential Molecular Biomarkers

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Broadly biomarker word is defined as quantifiable indicator of disease conditions or physiological changes of living organisms. Biomarker field is very old, only few specific biochemical and molecular biomarkers are identified. Discovery of novel and specific biomarkers is still facing several challenges [1]. Based on the methods of quantification, biomarkers can be classified in three types 1) Imaging biomarkers (like X-ray, ultra sound, CT scan, PET, MRI), 2) Biochemical biomarkers (transaminases, bilirubin, alkaline phosphatase, serum creatinine) and 3) Molecular biomarkers. Molecular biomarkers are defined as markers which are measured based on genomic and proteomic approaches. Molecular biomarkers are most recent development in biomarker field, which is still in early developmental stage and needs tremendous amount of research to identify the specific biomarkers which can help in detection of disease before onset of physio; pathological changes or symptoms.

Discovery of small regulatory RNA molecules known as miRNAs (miRNAs), dramatically fasten the speed of development in the field of molecular biomarkers [2]. MiRNAs are small (around 20bp), non-protein coding RNA molecules, which controls protein synthesis in sequence specific manner [3]. Identification of miRNA expression in the circulating fluids including whole blood, serum, plasma, and other body fluids provides an opportunity to develop them as novel biomarkers. Identification of crucial regulatory role of miRNAs in almost every physiological or cellular process, positions them ahead of other molecules in race for biomarkers [3-6]. Relatively higher half-life or stability of miRNAs in comparison to mRNAs probably due to their shorter size provides additional benefits in their detection and biomarker development [7]. Moreover, total number of identified miRNAs (~2000) is around 5% of total number of known protein coding mRNAs, so it is relatively easy to profile their expression. With rapid advancement in sequencing and expression profiling techniques, in future clinicians will be able to have look on global miRNA profiling data of patients before prescribing drugs to patients. Diseases like cancer and neurological disorders can be treated successfully if they are detected in their early phases. Both cancer and neurological disorders needs identification of reliable and early biomarkers based on changes which precedes pathological symptoms of these diseases. Regulation of miRNAs and their target miRNAs provides best option for development of novel biomarkers in these diseases.

Pubmed is overfilled with research papers on identification of circulatory miRNAs in one or another disease and equally good number of reviews are also available compiling their details [8-11]. A summary of same have been provided in Tables 1 and 2. Studies of Yanaihara et al. seems to be first report, which described regulation of miRNA expression as indicator of lung cancer, for diagnostic and prognastic purposes [12]. Their studies have found that high miR-155 and low let-7a-2 expression correlates with poor survival in lung cancer patients [7]. Developing miRNA based biomarkers can also help in differentiating cancer types and stages of cancer development, which is a major issue in their treatment [10-13]. Interestingly miRNAs are also detected in microvesicles and exosomes, which act as communicator between cells [13-15]. As these extracellular vesicles are secreted from different kind of cells like cancer cells, lymphocytes, immune cells, dendritic cells, and regulation of miRNA expression in these cells can provide crucial information about molecular changes happening inside the tissue of origin. Most of the studies carried out on development of miRNA based biomarkers used blood or tissue samples from patients carrying disease [16]. However for identification of early biomarkers, studies are needed which involves expression kinetics of miRNAs between non-disease stage to disease stage. Long term studies, which involve unbiased expression profiling of miRNAs in large populations over long time can identify the miRNAs which are altered before onset of disease. In conclusion, miRNAs can act as better molecular biomarkers than existing biomarkers and development of specific biomarkers for cancer or neurological disorders will help in managing these diseases.

### Table 1: List of miRNAs targeted as biomarker in different type of cancers.

<table>
<thead>
<tr>
<th>MiRNA</th>
<th>Disease</th>
</tr>
</thead>
<tbody>
<tr>
<td>miR-21</td>
<td>Breast cancer [17], Colorectal cancer [18], Gastric cancer [19]</td>
</tr>
<tr>
<td>miR-143</td>
<td>Non-small cell lung cancer [20], Bladder cancer [21], colorectal cancer [22]</td>
</tr>
<tr>
<td>miR-375</td>
<td>Esophageal squamous cell carcinoma [23], Head and neck squamous cell [24], Prostate cancer [25]</td>
</tr>
<tr>
<td>miR-155</td>
<td>Colorectal cancer [26], Non-small cell lung cancer [27],breast cancer [28], diffuse large B-cell lymphoma [29].</td>
</tr>
<tr>
<td>miR-125b</td>
<td>Breast cancer [30], HBV-positive hepatocellular carcinoma [31].</td>
</tr>
<tr>
<td>miR-107</td>
<td>Esophageal cancer [32]</td>
</tr>
<tr>
<td>miR-31</td>
<td>Oral cancer [33]</td>
</tr>
<tr>
<td>miR-141</td>
<td>Colon cancer [34]</td>
</tr>
<tr>
<td>miR-184</td>
<td>Squamous cell carcinoma of tongue [35]</td>
</tr>
<tr>
<td>miR-17</td>
<td>Nasopharyngeal carcinoma [36], lung cancer [37]</td>
</tr>
<tr>
<td>miR-92</td>
<td>Acute leukemia [38], breast cancer [39]</td>
</tr>
<tr>
<td>miR-18a</td>
<td>Colorectal cancer [40]</td>
</tr>
<tr>
<td>miR-18b</td>
<td>Rectal Cancer [41]</td>
</tr>
<tr>
<td>miR-20a</td>
<td>Rectal Cancer [41], nasopharyngeal carcinoma [36].</td>
</tr>
<tr>
<td>miR-218</td>
<td>Gastric cancer [19], Colorectal cancer [42]</td>
</tr>
<tr>
<td>miR-1 R-196a/b</td>
<td>Oral cancer [43].</td>
</tr>
<tr>
<td>miR-10b</td>
<td>Breast cancer [44], Oral cancer [45].</td>
</tr>
<tr>
<td>miR-221</td>
<td>Colorectal cancer [46], Pancreatic cancer [47].</td>
</tr>
<tr>
<td>miR-181</td>
<td>Breast cancer [48]</td>
</tr>
<tr>
<td>miR-126</td>
<td>T-cell leukemia [49].</td>
</tr>
</tbody>
</table>

**Table 1: List of miRNAs targeted as biomarker in different type of cancers.**

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Table 2: List of miRNAs targeted as biomarker in different neurodegenerative disorders.

Conflict of Interest

The authors declare no conflict of interest.

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