3.4 RNA Biomarkers

In contrast to the very stable DNA biomarkers, the versatile transcriptome with all its different components like mRNA, microRNA, and short and long noncoding RNAs is the next level on which dynamic changes on the molecular level can occur. Some of the methods used to detect biomarkers at the RNA expression level include quantitative reverse transcription polymerase chain reaction (RT-qPCR), serial analysis of gene expression (SAGE), differential display, bead-based methods, and microfluid card and microarray analysis. Comparative analysis of RNA expression in terms of heat maps, supervised algorithms, and snapshots are eventually linked with diagnosis and prognosis.

The major attraction in transcriptomics as a starting point for biomarker identification is the ability to measure mRNA concentrations of all genes under any condition that allow studying regulation of gene expression at a genome-wide scale. The genome-wide search for mRNA biomarkers is since more than 20 years an established method in different life science fields. In pharmacogenomics mRNA expression levels were successfully applied to establish treatment prediction with specific drugs. In most studies, a number of genes whose expression was influenced by treatment could be identified. Hence the identification of a biomarker pattern consisting of various expressed genes will be more promising than finding standalone single markers. Despite the impressive number of publications aiming on the detection of mRNAs that predict disease progression or indicate the appropriate use of a specific drug treatment, the current FDA list of pharmacogenomic biomarkers in drug labeling does not even count ten different mRNA-based assays.

3.5 microRNA

Instead of the classical analysis of mRNA, the quantitative analysis of microRNA (miRNAs) is more and more used for biomarker identification and establishment. miRNAs are small noncoding RNA molecules with 20–22 nucleotides which are involved in posttranscriptional processing of mRNA. They are able to regulate physiological pathways and metabolic processes and therefore impact the entire cellular physiology, organ development, and tissue differentiation. Most miRNAs are known to be expressed in a physiological-, tissue-, and disease-specific manner. Due to their short length, they are less sensitive to RNase exposure and hence are more stable than the longer mRNA with an average length of 2 kb. It is already proven that miRNAs have the potential in the diagnosis of specific types of cancer. For example, tissue derived from gastrointestinal cancer can be differentiated from non-gastrointestinal cancer tissue by analyzing specific miRNA profiles. As also described for mRNA, the miRNA profile characterization gives insights in the progression of specific diseases or the response to a given therapeutic approach, e.g., in breast cancer, miR-210 levels correlate with sensitivity to trastuzumab (Herceptin®) and miR-125b is predictive of chemoresistance (Roosbroeck et al. 2013).