cancer. The Mammostrat® test measures the levels of five genes in breast cancer cells. These measurements are used to calculate a risk index score. The higher the risk index, the more likely the cancer is to come back. The Prosigna™ test was developed based on the signature of 50 genes. The expression of these PAM50 genes is an accepted standard for subtyping breast cancer and used to classify tumors into 4 different subtypes.

2.5 Is This Biomarker Unique to Disease Status?

Diagnostic biomarkers are biomarkers that help defining a disease in a group of similar diseases. These biomarkers are used to identify a disease, a subtype of a disease, or a specific condition. Typical examples are elevated blood glucose levels and increased glycosylated hemoglobin (HbA1c) as indicators of diabetes.

2.6 Does This Biomarker Guide Treatment Decisions?

Predictive biomarkers are biomarkers that are used for patient stratification, predicting response to a specific treatment, which may increase the chance for a successful treatment. These biomarkers are used to predict whether or not a patient is likely to respond to a specific therapy or treatment regimen. The expression of the drug target is, for example, used in this respect for targeted therapies in oncology. A well-known example is the detection HER2 overexpression in patients suffering from, e.g., breast cancer predicting a likely response to trastuzumab (Herceptin®). Two additional biomarkers that are used to determine treatment decisions for patients that have been diagnosed with advanced stage non-small cell lung cancer are epidermal growth factor receptor (EGFR) and anaplastic lymphoma kinase (ALK). Whether or not these biomarkers contain a mutation or a gene rearrangement determines if patients will be treated with either the drugs erlotinib (Tarceva®) or crizotinib (Xalkori®), respectively.

3 Biomarker Technologies

3.1 Technology Trends and Applications

For the last 10 years, biomarkers (nucleic acid, mutation presence, gene panels/signatures, gene rearrangements, and protein expression patterns) have gained a great deal of attraction and application into clinical trials. This goes in parallel with the increasing number of new targeted approaches in drug discovery and a broad range of new technologies that have helped facilitate these applications. As a consequence of new technological platforms, a significant drop in costs for pharmacogenomics and pharmacogenetic testing has occurred leading to more deep sequencing of patient tumors and large uncombed data sets. In turn, the