Biomarkers can take the form of an array or collection of genes. Because the device that contains this array is small, it is called a microarray. Any given microarray contains between about 50 and 5,000 genes or more. With use for any given patient, the number of genes that gives a positive signal, and the identities of the genes that give a positive signal, is likely to be unique, in a manner somewhat reminiscent of a fingerprint. Because of this fingerprint quality, the term *personalized medicine* is used to refer to the use of microarray data for guiding diagnosis and treatment. Microarrays have the utility of correlating the patient's fingerprint with a go/no-go decision to treat the patient with a specific type of therapy. Researchers developing microarrays conduct research that is used to establish the correlation. Once the microarray is widely accepted or marketed, physicians can take advantage of the established correlation, and use the microarray to make go/no-go decisions.

In clinical trials, biomarkers can be used to dictate subgroups used in the stratification of study subjects. In the alternative, biomarkers can be used for purely exploratory purposes.

The utilities of biomarkers include:

- Identifying patients with a good prognosis (in absence of medical treatment) or poor prognosis (in absence of medical treatment);
- Identifying patients likely to respond to a given drug versus patients unlikely to respond to that drug; and
- Identifying patients likely to experience adverse drug reactions to a given drug versus patients unlikely to experience adverse drug reactions.

a. Predictive markers versus prognostic markers

The most common uses for biomarkers are to predict outcome of disease, that is, a disease in absence of therapy, and to determine if a given drug is likely to be effective against that disease. According to Mandrekar and Sargent (10) these two uses are referred to by the terms *prognostic* marker, where marker is associated with disease outcome, and *predictive* marker, where marker is associated with drug response. These concepts are illustrated below with data on breast cancer and colorectal cancer.

Overexpression of HER2 by breast cancer cells increases invasiveness and tumorigenicity of breast cancer, where the oncogenic effects of HER2 result from gene amplification rather than from mutations (11). Trastuzumab (Herceptin®), an antibody that binds to HER2, generally mediates the killing only of tumors that overexpress HER2

[10] Mandrekar SJ, Sargent DJ. Clinical trial designs for predictive biomarker validation: theoretical considerations and practical challenges. *J Clin Oncol*. 2009;27:4027–4034.

[11] Purdie CA, Baker L, Ashfield A, et al. Increased mortality in HER2 positive, oestrogen receptor positive invasive breast cancer: a population-based study. *Br J Cancer*. 2010;103:475–481.