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# Point-of-care biosensor systems for cancer diagnostics/prognostics

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**Abstract**

With the growing number of fatalities resulting from the 100 or so cancer-related diseases, new enabling tools are required to provide extensive molecular profiles of patients to guide the clinician in making viable diagnosis and prognosis. Unfortunately with cancer-related diseases, there is not one molecular marker that can provide sufficient information to assist the clinician in making effective prognoses or even diagnoses. Indeed, large panels of markers must typically be evaluated that cut across several different classes (mutations in certain gene fragments—DNA; over/under-expression of gene activity as monitored by messenger RNAs; the amount of proteins present in serum or circulating tumor cells). The classical biosensor format (dipstick approach for monitoring the presence of a single element) is viewed as a valuable tool in many bioassays, but possesses numerous limitations in cancer due primarily to the single element nature of these sensing platforms. As such, if biosensors are to become valuable tools in the arsenal of the clinician to manage cancer patients, new formats are required. This review seeks to provide an overview of the current thinking on molecular profiling for diagnosis and prognosis of cancers and also, provide insight into the current state-of-the-art in the biosensor field and new strategies that must be considered to bring this important technology into the cancer field.


*Keywords:* Biosensors; Cancer; Point-of-care

## 1. Introduction

Cancers arise as a result of the disruption of normal cell signaling pathways, which can produce cells (cancer cells) that exhibit a decisive growth advantage compared to their neigh-

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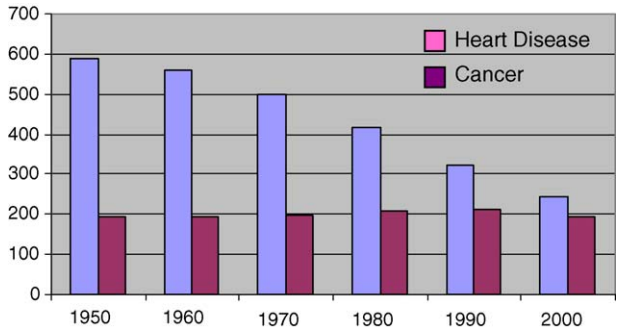


Fig. 1. Age-adjusted death rates from heart disease and all cancer-related diseases from 1950 to 2000.

bors. These growth advantages are typically produced from a number of different genetic and/or epigenetic changes, which result in the activation of oncogenes and the inactivation of tumor suppressor genes. Unfortunately in terms of diagnosis, no single oncogene or tumor suppressor gene has been discovered to be universally altered in all adult cancers. In addition, patterns of genetic and/or epigenetic changes differ not only in terms of tumor location (i.e., organ), but also among tumors from the same location. Besides genome-related changes, other complex molecular alterations result during the course of tumorigenesis, such as gene over/under-expression (mRNA changes) or protein over/under-expression. As such, a plethora of molecular biomarkers can potentially be analyzed via different sensing platforms for tumor classification to guide diagnosis, prognosis, monitoring treatment and disease recurrence.

As depicted in Fig. 1, the age-adjusted death rate for heart disease has dramatically declined over the last 50 years, while in the case of cancer this same trend has not occurred (Leaf, 2004). In 2004, nearly 563,700 patients were diagnosed with one or several of the 100 diseases belonging to the cancer family with one in two and one in three men and women, respectively, expected to contract one of these diseases during their lifetime. It is interesting to note that ~90% of all cancer-related deaths occur from metastasis and not directly from the primary tumor site.

In spite of the rapid explosion of new technology platforms and biomarkers that have been discovered and reported in the literature for cancer diagnostics, prognostics, therapeutics and monitoring disease recurrence, few of these technologies or biomarkers have transitioned into the clinical arena. The common method for cancer diagnosis and prognosis relies heavily on technologies that are over 100 years old (paraffin fixation of tissues with visual inspection of cell morphology by a pathologist). Therefore, in spite of the significant investment by a number of agencies into discovery of new molecular markers and the technologies to utilize these biomarkers, most have not entered the clinic. The major fundamental question then arises: Why have the incidence and survival rates of cancers not shown marked decreases in line with the large financial and time investments that have been waged against this disease? In this paper, information will be presented that provides information on potentially new technologies in the form of point-of-care (POC) biosensors for biomarker analysis and the merging of new biomarkers with the appropriate technology platform to develop systems that provide clinically relevant information to assist the physician and clinician in disease diagnosis, prognosis, treatment and recurrence. The major technology platform that will be the focus of this discussion is biosensors, and their integration into POC systems for the analysis of clinically significant cancer biomarkers.

## 2. Biosensors and point-of-care technologies

### 2.1. Description of technology area

A biosensor (see Fig. 2) in the traditional sense is defined as: bioanalytical device incorporating a biological material or a biomimic (e.g., tissue, microorganisms, organelles, cell receptors, enzymes, antibodies, nucleic acids, etc.), intimately associated with or integrated within a physicochemical transducer or transducing microsystem, which may be optical, electrochemical, thermometric, piezoelectric or magnetic. The usual aim of a biosensor is to produce either discrete or continuous digital electronic signals, which are proportional to a single analyte or a related group of analytes.

POC systems are viewed as integrated systems that can process clinical samples for a number of different types of biomarkers in a variety of settings, such as clinical laboratories, doctors' offices and eventually, at home. *Basically*, *POC systems make state-of-the-art technology platforms accessible to a large population pool*. From a diagnostic or prognostic perspective, POC systems provide the clinician the ability to have access to a wealth of molecular information for providing profiles of cancers using novel technology platforms that in the past have been accessible to only major cancer centers. The development of POC technologies will provide opportunities for better screening of at-risk patients, tighter surveillance of disease recurrence and better monitoring of treatment. In addition, POC technologies are by their very nature, low cost in their implementation making large scale screening for disease prevention more attractive to health care insurers.

### 2.2. Biomarkers for cancer

The utility of any biosensing platform is intimately dependent on the viability of biomarker(s) for producing diagnoses with high confidence. In particular, biomarkers must not only signal the presence of a tumor or cancer, but should also predict the

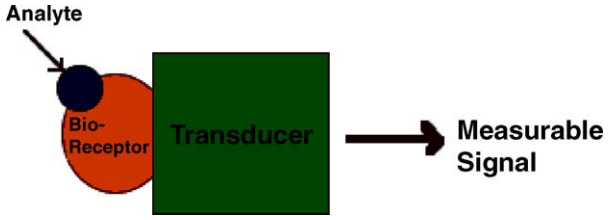


Fig. 2. Schematic representation of a single element biosensor containing the biorecognition element, transducer and the physical output whose magnitude is related to the concentration of the analyte of interest.