Bioluminescent Bioreporter Integrated Circuits (BBICs) for Tumor-Specific Protein Detection

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A promising approach for advanced identification of cancerous or precancerous cells is the detection of tumor-specific secreted proteins in body fluids. This represents a unique approach as it allows for the detection of cancer cells based on signature protein secretions rather than on the identification of a distinguishable tumor mass or other major physiological change. We believe that a sentry of reporter cells can be developed that will emit bioluminescent signals in response to signature tumor protein molecules. Thus, cancer cells can be accurately recognized before tumor development initiates and appropriate preventative medical treatment can be effectively administered on an early basis.

These reporter cells, referred to as bioluminescent biosensors, represent a line of living cellular organisms that bioluminesce in response to specific analytes within their environment. By coupling the bioluminescent organism to an analytic measuring instrument, the bioluminescent signal can be specifically detected and monitored. Recently, we reported on novel biosensor devices that combine bioluminescent bioreporters with integrated circuits (ICs) to produce miniaturized (4 mm^2) detection units [1]. These bioluminescent bioreporter integrated circuits (BBICs) represent a revolutionarily new class of highly sensitive biosensors that can be effectively utilized for the routine detection and monitoring of a wide variety of molecular compounds and characteristic chemical signatures. We have developed BBIC prototypes that detect toluene and naphthalene in ppb concentrations [1-3]. Although our previous work has typically concentrated on environmental chemical monitoring, we are currently advancing BBIC technology into medical applications. We are presently developing a eukaryotic bioluminescent bioreporter that will specifically respond to glucose. Ultimately, we envision an implantable BBIC that can be incorporated into diabetic therapies for continuous monitoring of blood glucose levels. Inclusion of an on-chip radio frequencing transmitter will allow the BBIC to remotely communicate with an insulin delivery system. We believe that this technology is fully adaptable to tumor-specific protein detection and monitoring as well.

References

1. Simpson, Michael L., Gary S. Sayler, Steven Ripp, David E. Nivens, Bruce M. Applegate, Michael J. Paulus, and Gerald E. Jellison Jr. "Bioluminescent Bioreporter Integrated Circuits Form Novel Whole-Cell Biosensors". *Trends in Biotechnology*, Vol. 16, August 1998, pp. 332-338.

2. Simpson, M. L., G. Sayler, S. Ripp, M. J. Paulus and G. E. Jellison. "Bioluminescent Bioreporter Integrated Circuits (BBICs)". In *Smart Structures and Materials 1998: Smart Electronics and MEMS*, Vijay K. Varadan, Paul J. McWhorter, Richard A. Singer, Michael J. Vellekoop, Editors, Proceedings of SPIE, Vol. 3328, 202-212 (1998).

3. Simpson, Michael, Michael Paulus, Gerald Jellison, Gary Sayler, Bruce Applegate, Steven Ripp, and David Nivens. "Bioluminescent Bioreporter Integrated Circuits (BBICs): Whole-Cell Chemical Biosensors". *Technical Digest of 1998 Solid-State Sensors and Actuators Conference*, Hilton Head Isl., SC, pp. 354-357.