MicroActive

Automatic Detection of Disease Related Molecular Cell Activity

MicroActive will develop an instrument for molecular diagnostics intended for use in the doctors' office. The instrument will in the first instance be used to screen patients for a group of viruses, known as human papilloma virus, which is implicated in cervical cancer. Microfluidics and biotechnology form the basis for the development.

Objectives of the project

Currently many common diseases require that samples are sent to remote labs for diagnosis. This is costly, time consuming, increases patient anxiety and delays the start of treatment. **MicroActive** will make it feasible to carry out automatic, accurate diagnosis at the local doctor's office. **MicroActive** will achieve this by using bio-marker mRNA detection. Compared to commonly used approaches (e.g. PCR amplification and immunoassay methods), mRNA detection avoids false positive results and has a high sensitivity. This approach is currently used to detect cervical pre-cancer, cancer, STDs and a range of respiratory diseases, to mention a few. In addition, recent advances in the field of molecular biology and high throughput technologies are generating hundreds of potential biomarkers every day. **MicroActive**e will:

- Develop an integrated system based on microtechnology and biotechnology for automated diagnosis of a wide range of diseases. The system will analyze biological samples and be specifically designed for use in primary health care.
- Validate the sensitivity of the system using cytological samples from women at risk of developing cervical cancer (the second most common female cancer) as test cases. Results from the new, automated system will be compared with gold standard hospital lab tests for human papilloma viruses (HPV).
- Prepare for industrial production of the system.

Project Description

Within the **MicroActive** project the partners will:

- Develop one chip for sample preparation with all the necessary liquid reagents integrated.
- Develop a second chip for amplification and detection of HPV with dried spotted reagents stored in micro-channels.
- Develop disposable chips so there will be no risk of contamination between samples.
- Develop manufacturing methods for spotting and drying of reagents, surface coating, patterning, and polymer chip lamination that will not inhibit the biomolecular processes.
- Perform multi target detection from a single sample. This is possible due to simultaneous amplification and detection in separate parallel detection channels.

"A low-cost, fully automated diagnosis system will widen the availability of advanced diagnostics for all citizens"

Scenario

Year 2009: Anne visits her doctor for her cervical smear test. Three years ago she had to wait for weeks while the pap-smear was analyzed at a central laboratory. This time the doctor selects a polymer chip for cervix screening from his fridge. A droplet of a solution containing Anne's epithelial cells is applied to the polymer chip and the chip is inserted into the **MicroActive** instrument on his desk. Two hours later the doctor tells her that her test is negative; no mRNA activity was found for the 5 markers of high cancer risk human papilloma virus types. This result has a lower probability for false positive results than those obtained from traditional tests.

- Test more than 5 different bio-markers (in the first instance biomarkers of HPV infection) from one sample droplet.
- Test the performance of the system. At early stages of the project, perform tests on clinical samples. This is already underway, using test-chips for separate functions.
- Develop an instrument without manual protocols.
- Test the instrument on clinical specimens and compare to gold standards
- Address factors such as reliability, usability and cost of the total instrument which are crucial to acceptance by health care professionals.

Expected Results & Impacts

A low-cost, fully automated diagnosis system will widen the availability of advanced diagnostics for all citizens. The end result will reduce the time from patient testing to diagnosis, lessen patient anxiety and facilitate earlier treatment.

Using an automatic diagnosis system as an alternative to today's diagnostic testing will imply cost savings for the public health authorities.

The result of the **MicroActive** project is an automated diagnostics instrument that will be unique because:

- It is based on sensitive detection of RNA biomarkers. This method offers high clinical sensitivity to cellular activity related to disease, and largely avoids false positive results.
- It provides a generic technology platform, consisting of a re-usable instrument and two disposable chips:
  - o The chips are disposable to avoid contamination between samples.
  - o Chip no. 1 will include reservoirs with all necessary reagents to perform sample preparation consisting of cell concentration, lysis and nucleic acid purification.
  - o Chip no. 2 will include all reagents to perform multiplex amplification and fluorescent detection of mRNA. The enzymes and primers will be stored in a dry state for long-term stability. The primers are disease specific.
- It provides new methods for spotting and drying of enzymes and primers for storage in the microchannels.
- It provides the repeatable and stable fluid control required by a commercial system through use of simple pumps in combination with surface modification.

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- IMTEK, University of Freiburg (DE)
- BioFluidix GmbH (DE)
- The Coombe Lying-in Hospital (IE)

Timetable: from 12/05 – to 11/08

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EC funding: € 1.600.000

Instrument: STREP

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