

# CD-MEDICS

## Coeliac Disease Management Monitoring and Diagnosis using Biosensors and an Integrated Chip System

A disposable polymer microsystem and portable desktop instrument with embedded communication abilities, will allow the cost-effective diagnosis and management of coeliac disease, detecting genetic and immunomarkers in a single drop of blood, avoiding the need to carry out invasive biopsies for disease confirmation.

### Objectives of the Project

**Problem or Context:** Coeliac Disease is an autoimmune condition which affects 1 in 100 people in Europe. It is characterised by an intolerance to dietary gluten found in wheat, rye and barley. This manifests itself in varied symptoms, many of which are quite debilitating, which makes it very difficult to diagnose. Some estimates show that it can take over 10 years for a diagnosis to be made. The only treatment is a gluten free diet.

**Project:** CD-MEDICS will develop a point of care instrument that will both test for the genetic predisposition to the disease as well as the levels of auto-antibodies related to it. These antibody levels can then be used for monitoring and management of the disease, following withdrawal of gluten from the diet. This will be performed on a disposable microsystem using a single drop of blood within a portable instrument in a primary care setting.

### Key Project Goals

- Improved sensitivity and specificity of autoantibody assays and multi-plex HLA typing protocols for diagnosis and management of coeliac disease
- Nanostructured biosensor arrays to realise ultrasensitive levels of detection
- Individual micromodules for sample treatment, mixing, metering, nucleic acid amplification, HLA typing and autoantibody detection
- Microsystem integrating sample treatment, handling and detection with biosensor arrays
- Portable instrument embedded with communication abilities for connectivity with electronic patient record systems
- Dissemination and training of public and healthcare professionals

### Project Description

The overall objective of CD-Medics is the development of a portable device for multi-analyte screening of coeliac disease. The system will be built around a Lab-on-a-Chip platform capable of simultaneous detection of nucleic acids (*HLA typing*) as well as proteineous molecular markers (*auto-antibodies*), and will provide information as to the genetic predisposition as well as the early diagnosis of the coeliac disease patient. This platform will be developed in a modular format, which will allow the instrument to be used in a variety of locations and enable various instrument configurations to be realised.

Thus, the combined integrated device could be used for general population screening, or just the HLA typing microsystem could be used for neonatal screening; or alternatively just the auto-antibody microsystem could be used for monitoring compliance with the identified diet, or recurrence of the disease due to non-compliance.

The proposed combination of serology and HLA-typing is the only definitive way to screen for coeliac disease; a combined diagnosis accounting for symptomatic, silent and latent CD patients aims for **100% specificity and sensitivity**.

A core component of the diagnosis system is a lab-on-a-chip disposable. This enables the user to introduce a drop of blood to the device, insert it in the instrument and run the diagnostic test. The *lab-on-a-chip* device looks like a simple piece of plastic but incorporates comprehensive intelligence: including a microstructured fluidic network allowing for a precisely controlled flow of reagents, a specifically adapted surface for capture the target biological markers, and finally electrochemical *biosensor arrays*, to enable an integrated and extremely fast detection.

#### CASE STUDY

Mary is a 30 year old woman who has spent the past 10 years being treated by a variety of doctors for fatigue, joint pain, anaemia, hair loss, infertility and depression amongst other symptoms. To date, no successful diagnosis has been made and Mary has an appointment with her new GP. After he reviews Mary's file, he takes a disposable microsystem, inserts it in the CD-MEDICS instrument and adds a drop of Mary's blood from a fingerprick. After 15 minutes, the display shows the test has been successfully executed and the results have been encrypted and transferred to Mary's electronic health record (EHR). The doctor informs Mary that she has a genetic predisposition to coeliac disease, and has tested positive for elevated levels of autoantibodies, leading to a clear diagnosis of coeliac disease, and advises her to completely remove gluten from her diet. Following advice from her local coeliac disease society, Mary starts her new life on a gluten-free diet, and a month later she returns to see her GP, feeling a rejuvenated and happier person. The doctor accesses Mary's EHR, then takes a fingerprick blood sample and in less than 10 minutes, the results are displayed, and the EHR updated, her antibody levels are vastly reduced, and she is responding well to her new diet.

The project also aims to incorporate communications that are capable of seamlessly operating in all point-of-care-driven environments (e.g. clinical laboratories, hospitals, physicians' offices) and transparently *communicating with existing Hospital Information Systems (HIS) and patient's Electronic Health Record (EHR)*. This approach will allow for the integration of the information collected by the PoC device with the patient's EHR content, and better analysis and interpretation of the measurement results. A fully functional prototype device will be tested in the clinical environment with real patient samples and interfaced to the hospitals electronic patient record system.

## Expected Results & Impacts

- Improvement in the quality of life for coeliac disease sufferers
- Reduction in health care provision costs
- Generic Technological platform that is transferrable to a plethora of other applications

Reducing the time for diagnosis and regular monitoring will enable a considerable improvement in the quality of life for CD sufferers. Many suffer for decades with irrecoverable complications. Studies have shown that the cost of undiagnosed CD is very high. In Holland 5 of the long term implications of CD cost €9 million to the healthcare system. The technology under development has considerable applications outside of coeliac disease. Indeed almost any genetic or serology test could be run on the platform with appropriate assays, making the technology very powerful and commercially viable.

### Achievements in Project Year 1

- Requirements specification for instrument and microfluidics
- Deamidation protocols for HMW glutenins
- Isolation of IgA and IgG antibodies and quantification for identification of clinically relevant range and standards
- Identification of deamidated gliadin peptides and testing with specific patient cohorts
- On-chip DNA extraction protocol
- Multiplex SSO and SSP amplification protocols and probes for low and medium resolution typing
- Prototypes of amperometric and impedance sensors
- Design of the microsystem and prototyping of functional elements
- Design of communication protocols for HIS and EPR
- Training and dissemination including a virtual school of excellence and over 100 press, television and radio items
- Business planning process together with an understanding of the regulatory issues in taking a product to market
- Four potential patent applications



### CD-MEDICS

**Coeliac Disease Management Monitoring and Diagnosis using Biosensors and an Integrated Chip System**

#### Project co-ordinator:

Universitat Rovira i Virgili

#### Contact person:

Dr Ciara O' Sullivan

Tel: +34 977 558740/8722

Email: ciara.osullivan@urv.net

Website: www.cdmedics.eu

#### Partners:

- Universitat Rovira i Virgili (Spain)
- Institut für Mikrotechnik Mainz (Germany)
- Microfluidic Chip Shop (Germany)
- University Newcastle upon Tyne (United Kingdom)
- Intracom S.A. Telecom Solutions, Clemens GmbH (Germany)
- Microsystems-Microfluidics for Genetic Tests S.A. (Greece)
- Eurospital SPA (Italy)
- King's College London (United Kingdom)
- Inno-Train Diagnostik GmbH (Germany)
- TATAA Biocentre (Sweden)
- MULTI-D Analysis (Sweden)
- Finish Red Cross Blood Service (Finland)
- Fondazione IRCCS Policlinico San Matteo (Italy)
- Maribor General Hospital (Slovenia)
- Valentia Technologies (Ireland)
- Association of European Coeliac Societies (Malta)
- Coeliac UK (United Kingdom)
- Asociacion de Celiacos de Madrid (Spain)
- iXscient Ltd (United Kingdom)

**Timetable:** from February 2008 to January 2012

**Total cost:** € 9,500,000

**EC funding:** € 12,796,599

**Instrument:** IP

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### KEYWORDS

Coeliac Disease diagnosis, Managing and monitoring, Point-of-care diagnostics, Serology profile, HLA Typing, Anti-gliadin antibodies, Anti-glutenin antibodies, Anti-tissue transglutaminase antibodies, Coeliac Disease electrochemical sensors