Project no: STRP 016833

Project acronym: SNiP2CHIP

Project title: Development of a complete integrated SNP analysis system

Instrument: STREP

Thematic Priority: Sixth Framework Programme Priority 3: Nanotechnologies And Nanosciences, Knowledge-Based Multifunctional Materials, And New Production Processes And Devices

Year 1 – Executive Summary

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Start date of project: 01-02-2006 Duration: 36 Months

Project coordinator name: Dr. Paul Galvin

Organisation name of lead contractor for this deliverable: Tyndall

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1. Project overview

The requirement to screen for known SNPs (single nucleotide polymorphisms) has become one of the key challenges to be addressed to enable the exploitation of the human genome sequence, where approximately 3 million SNPs are responsible for all of the variation within the human population. Several methods and technologies are currently available for detection of SNPs, but no single platform exists which can deliver 100% accuracy, in a low cost, versatile, and easy-to-use integrated system. The SNIP2CHIP project is focused on the development of integrated SNP detection platforms to include modules for DNA extraction and purification from biological samples, DNA amplification, DNA characterisation (including SNP detection), signal transduction, interpretation and data analysis. Integration of the modules on a single platform is being implemented using a transport mechanism based on electrowetting actuation (EWOD). Two alternative SNP detection platforms are being developed based on optical and magnetic sensing respectively. The whole system is being integrated as a single automated functional system with a simplified GUI interface, based on end-user specifications. The systems development will focus on ultimate delivery of a product customised for low to medium throughput, low cost, point-of-care applications, with emphasis on providing very rapid and accurate results. Within the project, the systems will be benchmarked for screening of SNPs in the CFTR gene that are associated with cystic fibrosis. CF patient samples will be used to verify the accuracy and reproducibility of the system in a clinical diagnostics laboratory.

2. Project Objectives

The overall objective of the SNiP2CHIP project is to develop a fully integrated system for genetic analysis, capable of providing genotypic data directly from a biological sample. The research is based on the vision to enable point-of-care genetic analysis (e.g. in a physician / GP surgery), by integrating DNA extraction, amplification and analysis modules onto a single miniaturised system with an easy-to-use interface for unambiguous genotype interpretation. Central to this vision will be a system that delivers genotypic data with very high accuracy at low cost, such that it provides a novel affordable technology solution for point-of-care genetic analysis.

The key science and technology objectives of the project are being implemented through seven workpackages as detailed below:

1. Development of a novel miniaturised DNA extraction and purification module.
2. Development of a novel PCR-on-a-chip module based electrowetting actuation.
3. Development of novel DNA analysis modules based on optical and magnetic sensors for SNP detection.
4. Development of an easy to use system control module with a graphic user interface.
5. Integration of all modules together in a single functional system, which will be validated in a clinical laboratory for CFTR SNP detection.

Workpackage list
WP1. DNA extraction & purification module
WP2. DNA amplification module
WP3. Magnetic sensor module for SNP detection
WP4. Development of an optical sensor module for SNP detection
WP5. System integration
WP6. System validation
WP7. Project management

The final integrated genetic analysis system will provide a novel solution for point-of-care genetic analysis. However, the different modules which are being developed within the system are also highly innovative, and the potential to protect associated IP is being evaluated. .

- The DNA extraction module comprises a novel microsystem for automated DNA extraction using established paramagnetic bead-based protocols for DNA extraction and purification in a lab-on-chip format.
- The PCR amplification module comprises a novel microsystem for PCR amplification using channel-free transport of microdroplet reactions across temperature zones using electrowetting actuation (EWOD).
- The magnetic sensor based DNA microarray platform will be a novel, rapid and potentially low cost solution for highly parallel SNP detection
- The optical flow-through platform will be a rapid, low-cost solution for low to medium throughput SNP detection

However, the core originality of this technology will be the integration of DNA sample preparation and multiple SNP analysis in a single automated system. Despite the growing demand for accurate SNP data for clinical diagnosis of monogenic diseases, no products currently exist which enable multiple SNPs to be screened directly from a blood sample in a fully integrated system. This project will deliver two alternative original integrated systems for rapid identification of multiple SNPs.

The availability of an automated and rapid integrated system for genetic analysis of patient samples has the potential to form the basis of a "disruptive technology", which could significantly improve healthcare delivery. By affording the possibility for near-realtime (e.g. <60 minutes) analysis of patient DNA for specific traits, on-site at their local medical clinic / general practitioner, the duration of anxiety of the patient can be greatly reduced. This technology would simplify the delivery of a universal high standard of genotyping for clinical diagnosis, which currently requires specialist clinicians and a range of expensive equipment usually found in only one or a few laboratories in each state. The integration of the processes into a single system will eliminate a significant source of error in terms of mistyping of patient samples due to either technical or clerical errors (e.g. mixing of samples during the different steps of the analysis process). In the longterm, SNP screening technology such as that proposed will be essential for personalised medicine to enable selection of the drugs and dosages appropriate to each patient.

3. Participant list

Participant name	**Participant short name**	**Country**
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Commissariat à l'Energie Atomique	CEA-LETI	France
Instituto De Engenharia De Sistemas E Computadores Microsistemas e Nanotecnologias	INESC-MN	Portugal
Centro De Investigacao Em Genetica Molecular Humana, Fundaçao Da Faculdade De Ciencias Da Universidade De Lisboa	FFCUL	Portugal
Czech Natl. Center for Diagnosis & Treatment of CF	UCPRA.2SM.CFC	Czech Republic
National Centre For Medical Genetics, National University Of Ireland	NUID/UCD	Ireland
Asper Biotech	Asper Biotech	Estonia

4. Impact

In the post genomic era, together with many technical and scientific advances of the last twenty years of the 20th century, there has been a dramatic increase in the demand and provision of genetic testing both in the EU and also in rest the developed world. The use of genetic tests for humans – for diagnostic, confirmatory and predictive purposes – is expanding in all European countries. Laboratories face a proliferation of demand for molecular genetic testing for a wider range of diseases. Following the completion of the first draft of the human genome sequence, the results are being translated into medical applications including diagnostics and therapy and promote new concepts in predictive medicine. Several hundred hereditary diseases have already been assigned to specific genes and their mutations. The number of diseases for which genetic tests are available will continue to increase in the coming years. Additionally, genetic testing for predisposition to numerous human malignancies and to multifactorial diseases is being considered, opening up the possibility of making personalized or targeted disease prevention a new paradigm of medicine. Pharmacogenetics based on common genetic variants influencing effectiveness of pharmaceuticals and aimed at developing and prescribing the right medicine for the right patient signifies another line of future possible applications of SNP detection in medicine.

The SNiP2CHIP project consortium includes examples of initial end-users of the technology i.e. clinical laboratories in both the design specification and validation of the system, to ensure that the system developed will be appropriate for the requirements of the clinical diagnostics market. The inclusion of an SME in the consortium will help facilitate the development of clear exploitation strategies for all outputs of the research

The SNiP2CHIP project is targeting the development of a low cost easy-to-use system accessible to the non-specialist. By ensuring that both operation of, and data interpretation from the system will be compatible with the non-specialist, and that the system could deliver a genotype within 1-2 hours of collecting the sample, a market among general practitioners and physicians is easily envisaged, especially in the case of the larger medicentres with greater resources.

5. S&T prospects and dissemination policy and plans

The main goal of the research is the development of new IP in the form of a novel integrated SNP analysis system, together with each of its modules with innovative solutions for DNA extraction and amplification, as well as the DNA microarray with either optical or magnetic detection. All research outputs are therefore being initially screened for novel IP and will be patented if feasible.

Once each research output has been screened for IP (and protected if applicable), dissemination proceeds via high profile international peer-reviewed journals, seminars and international conference presentations, and via the project website (www.tyndall.ie/projects/snip2chip). Where appropriate, dissemination via the mainstream media such as daily newspapers will also be used to showcase the research to the public.