PARTNERS

PoC-HCV is a three year European project (Collaborative Research Project), which started in September 2013 and is coordinated by the French National Institute for Health and Medical Research (Inserm, Professor Matthew Albert, based at Pasteur Institute in Paris, France). Our consortium brings together five complementary partners, including three small medium sized enterprises, one technology transfer/management company and the coordinator, a public research organisation. The partners are based in four European Member States (France, Portugal, Sweden and the United Kingdom) and the project is supported by the European Commission under the Health Priority of the 7th Framework Programme.

Inserm anRS Agence nationale de recherches sur le sida et les hépatites virales

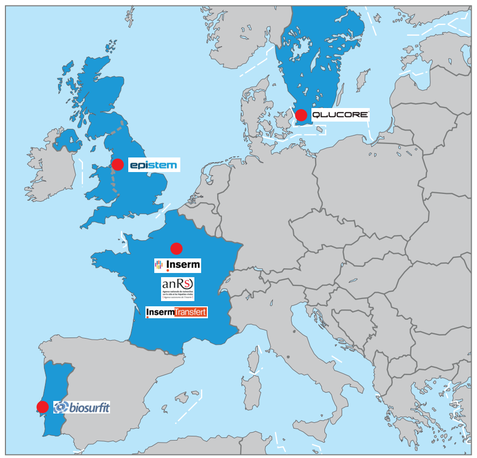
INSERM is the French National Institute of Health and Medical Research. It is a public scientific and technological institute, which operates under the joint authority of the French Ministry of Health and French Ministry of Research. The ANRS is the French Agency for Research on HIV/AIDS and viral hepatitis which since 2012 has been an autonomous agency within Inserm.
(France) **www.inserm.fr - www.anrs.fr**

epistem

Epistem's Biomarker Division specialises in providing gene expression information using their proprietary GenetRx™ platform and genetic polymorphism and genotype tests using their proprietary point-of-care platform, GeneDriveTM. (UK)
www.epistem.co.uk

InsermTransfert

Inserm Transfert is specialised in technology transfer, legal affairs & business negotiation with industry, as well as EU project management.
(France) **www.inserm-transfert.fr**



biosurfit

biosurfit developed spinit®, a proprietary technological platform for the point-of-care testing market. Their goal is to deliver results in a matter of minutes translating into fast and accurate predictive tests and improved patient care. (Portugal)
www.biosurfit.com

QLUCORE

Qlucore is an industry driver in the development of user- friendly software tools for analysing and integrating complex data sets. (Sweden)
www.qlucore.com

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We are actively seeking strategic partnerships with national health agencies, development agencies and NGOs to help implement these point of care tests. If you are interested in such a partnership please contact us.

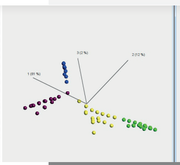
For further information, please visit our website at:
www.poc-hcv.eu

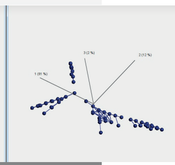
POC HCV

Point-Of-Care

tests to revolutionise the clinical management of patients infected by

Hepatitis C Virus





COOPERATION

PoC-HCV is a European research network (Collaborative Project) supported by the European Commission under the Health Cooperation Work Programme of the 7th Framework Programme, under the Grant Agreement n°601851.

CONTEXT

PoC-HCV will capitalise and translate promising discoveries made in the context of the SPHINX FP7 project (http://www.sphinx-hcv.eu), which identified biomarkers useful in the management of patients infected by hepatitis C virus (HCV), thus establishing a foundation for the migration of assays onto Point-of-Care (PoC) technologies. As detailed herein, genetic and protein biomarkers tested on PoC devices, will be united by new predictive mathematical algorithms, taking advantage of leading-edge biomarker discoveries to help overcome challenges for patient management in resource-poor countries. In Western settings the new PoC tests will assist health agencies and physicians, allowing for cost optimised treatment strategies while minimising adverse side-effects of new therapies.

Viral hepatitis C

Hepatitis C is an infectious disease affecting the liver, caused by the hepatitis C virus (HCV). Chronic infection may result in life-threatening liver failure or cancer. About 170 million people worldwide are chronically infected with hepatitis C virus, representing a 15 billion euro / year economic burden. More than 350 000 people die every year from hepatitis C-related liver diseases. In Europe alone, estimates for hepatitis C incidence are 8.7 per 100 000, with much higher prevalence in injecting drug users (reference: European Centre for Disease Prevention and Control).

Current treatment options against HCV

Clinical management decisions include questions of whether, when, and how to treat patients with chronic HCV. Until recently, and still the case in resource limited settings, treatment for chronic hepatitis C involves th combination of pegylated interferon and ribavirin. The effectiveness of this therapy depends on many factors, and only achieves a 50% response rate. New direct acting anti-viral drugs, called protease inhibitors, have recently been approved for clinical use. Protease inhibitors block the effects of enzymes that viral cells need to reproduce and when combined with conventional bi-therapy give increased cure rates. Next generation direct anti-virals targeting other viral proteins promise even more effective cure rates.

PERSONALISED MEDICINE

Personalised medicine (PM), a strategy for customization of healthcare based on individual phenotyping of profiles rather than the long established 'one-size-fits-all' approach, identifies elements that predict the individuals' response to treatment and their predisposition to disease.

Personalised medicine approaches are already been utilised for the management of HCV patients, for example the Fibrotest and FibroMax biomarker panels and viral genotype help to influence treatment decisions.

The PoC-HCV project will extend this approach combining well established genetic and protein biomarkers to help predict patient outcome when required. These point of care tests will be performed from single blood droplets with results delivered in 30 minutes enabling real time treatment decisions. The point of care technologies will also be applied to monitor in treatment responses and to identify early indicators of adverse reactions. In addition they may enable the detection and diagnosis of previously undetectable HCV infected cases. The newly developed PoC assays will enable maximisation of health resources in all clinical settings.

CONCEPT & OBJECTIVES

This Consortium federates the expertise of three SMEs and one academic partner, having a shared commitment to establish a stable, long-term mechanism to support "genetic-protein" biomarker development for the implementation of predictive and prognostic tests.

Point-of-care (PoC) medical devices have the potential to revolutionise clinical practice. SMEs within our Consortium (Epistem & biosurfit) have developed genetic and protein PoC devices to deliver on this promise. Results from these enabling technologies will be integrated using novel bioinformatics tools and algorithms (Qlucore) allowing for bedside analysis. This integrated genetic-protein approach will exploit recent biomarker discoveries from the FP7 project SPHINX, to improve the management of hepatitis C virus (HCV) infected patients. We will focus on two public health problems: (i) addressing the need to predict, pre-treatment, individuals in resource poor countries who will benefit from conventional treatment; and (ii) helping to limit treatment costs globally, where new therapies for HCV are anticipated to significantly increase health care expenditures.

TECHNOLOGY INTEGRATION

- Quantification and genotyping of plasma HCV
- Host genetic polymorphisms
- Host protein and cellular responses

To date, the technologies required for the implementation of genetic and protein biomarkers have been developed as stand-alone assays. These technologies require integration in order to address key medically relevant questions with simple-to-use algorithms, and ensure rapid uptake by the medical community.

The technologies include: (i) a hand-held CE-IVD marked PCR platform, called GenedriveTM that enables single nucleotide polymorphism (SNP) testing (Epistem); and (ii) a microfluidics system, called spinit®, which enables fluid management in a spinning compact disc format, applied for protein immunoassays (biosurfit). In each case, biomarker datasets and clinical data will be integrated using novel bioinformatics tools and algorithms, implemented on a mobile device application (Qlucore).

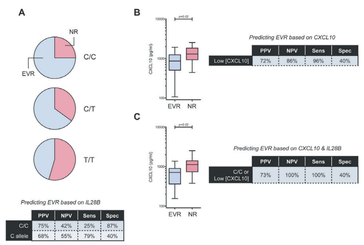


Figure 1. Stratification of HCV patients based on the combination of genetic (IL28B SNP) and protein (plasmal P-10) biomarkers show 100% negative predictive value for viral clearance in response to therapy. (A) IL-28B C/C SNP used alone gave 42% negative predictive value. (B) High plasma levels of IP-10 used alone gave 86% negative predictive value. (C) A mixed model using both IL28B SNP and IP-10 resulted in 100% negative predictive value.

[EVR, early virologic responders: indicates patients who achieve a 2-log reduction in their serum viral load at week 12; NR, non virological responders: patients who fail to respond to therapy and remain chronically infected.]

Albert, Fontanet & Pol, Hepatology. 2011 Apr;53(4):1410-11

EXPECTED OUTCOMES

The proposed PoC-HCV tests will generate and report biomarker results in less than 30 minutes, putting clinicians in a position to make treatment decisions during a single patient visit. The results obtained from the PoC tests will be easy to perform, easy to interpret and will be more cost effective than competing approaches. By providing PoC predictive and prognostic tests, PoC-HCV will enable tangible improvements in the health and quality of life of chronic hepatitis C patients, while simultaneously helping to manage the rising cost of medical treatment through a more efficient use of available resources. It is an approach that capitalises on our combined expertise in leading edge miniaturised molecular tests, lab-on-a-chip systems, treatment algorithm design and cost-effectiveness studies. These enabling technologies will permit the development and delivery of the first integrated "genetic-protein" biomarker tests, applied here to hepatitis C disease for:

- making the decision to treat;
- response-guided monitoring;
- selection of therapy;
- and clinical research practices.

CAPACITY DEVELOPMENT & LONG TERM SUSTAINABILITY OF PUBLIC/PRIVATE EFFORTS

The value of personalised approaches for managing patients with HCV infection is rooted in positive outcomes for the patient: saving lives and improving the quality of life. Other stakeholders will also benefit: physicians will realise easier decision-making, and better prediction of treatment outcome. Payers will benefit from optimised use of resources: initiating early treatment for those who are likely to respond; discontinuing treatment when risk of failure or adverse reactions is high; and permitting rapid modifications of treatment plans. Regulators and policymakers will find a stronger basis for the development of cost-effective and/or cost-saving treatment guidelines. Simply stated, point-of-care testing for the management of HCV patients makes sense. Our Consortium will work closely with government officials, leaders in academia, non-governmental organisations (NGOs) and industry in order to forge a plan for the financing and use of our predictive and prognostic tests.