P-MEDICINE NEWSLETTER

ISSUE NO 1

European Commission

eHealth
Better Healthcare for Europe

EDITORIAL

by Norbert Graf, p-medicine coordinator

"Time flies when you are having fun", so it doesn't come as a surprise that the first year of our p-medicine project has come to an end, although it seems that we have just returned from the kick-off meeting in February 2011.

The preparation of this first of a total of four yearly p-medicine newsletters as well as the upcoming first official p-medicine report represent a good opportunity for a look behind and also for a preview of activities to come.

In this first issue we will give an overview of the project, the very special VPH community and will introduce a number of very special people who are part of both. Attention is also given to several closely related FP7 VPH projects, such as VPH-Share or CONTRACT, with all of whom p-medicine shares partners, visions and synergies.

In fact, such synergies are considered essential by the p-medicine consortium, which is reflected by the achievements of the first project year in this respect. Close cooperations have already been established with *CONTRACT* and *TUMOR*.

Most important is the collaboration with the FP7 project *VPH-Share* which aims to build a global infrastructure for other VPH projects so that other projects can become clients of them, which is intended also for p-medicine. A joint technical review of the two projects in Brussels in November 2011 demonstrated successfully how both projects, if acting in concert, will produce added value for the VPH domain and at the same time will avoid the creation of different and independent infrastructures.

In this connection, special thanks go to Rod Hose, coordinator of the VPH-Share project, who was not only been so kind as to contribute to this newsletter (see page 6), but also gave us the opportunity to contribute to their newsletter, which was prepared in parallel.

The *p-medicine website* which has been available since the very start of the project, is our window to the world and I herewith encourage partners and interested readers to make use of it. Don't hesitate to communicate your comments and contributions to us so that we can provide up-to-date information at any time.

In addition, we would like to draw your attention to the *Summer School in 'Computational Oncology'* which is organised by p-medicine and will take place at Schloss Dagstuhl in Saarland/ Germany from June 23 – 28, 2013. The summer school will be the second one in a series, the first of which was organised by our friends from FORTH in June 2011.

However, all of this doesn't mention the ultimate goal of our efforts: to place patients into the centre of interest of medicine and to offer tailor-made therapies for as many people as possible.

Knowing that we are working for the benefit of patients suffering from severe illness will certainly help us to cope with the hard work that is lying ahead of us – and with the disturbances that come naturally with such a large project.

Saying this I am quite confident that we will find the time to enjoy our joint work, to cultivate existing friendships and to build new ones.

Norbert Graf
p-medicine coordinator

CONTENTS

Editorial 2
About p-medicine 3
Comment by David Ingram 5
VPH-Share and p-medicine 6
Related projects 8
Partners in depth "ecancer" 9
Interview on p-medicine 10
Upcoming events 14

THE P-MEDICINE PROJECT

An innovative approach on medicine

For many years, healthcare has been a reactive discipline. In recent years, however, medicine has undergone a revolutionary shift gradually transforming this reactive treatment into a preventive and predicitive approach. This change is possible due to major advances in molecular biology, bioinformatics and system biology, leading to a better understanding of diseases, and the increased ability of computers to handle vast amounts of heterogeneous data. These achievements will advance personalized medicine tremendously, a medicine where diagnosis and treatment of diseases will be based on an integrated approach of using and analysing all possibly available data of patients.

p-medicine – From data sharing and integration via VPH models to personalized medicine – is a 4-year large-scale integrating project funded under the EU's 7th Framework Programme which aims at developping new tools, an IT infrastructure and VPH models to accelarate the steps to be taken to achieve advanced personalized medicine. In p-medicine, 19 partners from 9 European countries and Japan have dedicated themselves to create, support and sustain new knowledge and innovative technologies to overcome current problems in clinical research and pave the way for a more individualized therapy. The complex p-medicine Consortium, including partners from the IT, basic research, clincial medicine and legal area, is best-suited to produce excellent results for the benefit of patients and the entire scientific community.

What is the approach taken in p-medicine to create an infrastructure that facilitates the development from current medical practices to personalized medicine?

In general, the project itself is scenario-based. In this respect, two categories of scenarios will be addressed:

1. The composition of large, pseudo-/anonymized datasets from multiple sources, used for the development of VPH tools;

2. The use of data obtained from a single patient to run a simulation workflow in support of an individual clinical decision making process.

The infrastructure of p-medicine will consist of an IT and a clincial research infrastructure that are smoothly interconnected. The system architecture will be modular, such that switching to the p-medicine system is not an all-or-nothing decision. We will ensure that privacy, non-discrimination, and access policies are aligned to maximize protection of and benefit to the patients. The legal and ethical framework to be implemented in p-medicine will specifically address this. The infrastructure itself guarantees data security and safety without storage of personal data within the p-medicine platform.

The pseudo-/anonymized data and tools will be stored in repositories and will be open to access by other researchers and end-users under binding contracts. The data warehouse serves as a data collection to be used for running VPH simulations (*in silico* oncology) and for testing developed tools, for which standardization and semantic interoperability is a key issue. It is a major goal that the developed tools will meet requirements to be used in large, international multicentre clinical GCP-conform trials. They should be easily integrated into existing infrastructures such as ECRIN (European Clinical Infrastructures Network), a task which UDUS as p-medicine partner will undertake.

p-medicine – From data sharing and integration via VPH models to personalized medicine

Acronym
p-medicine

Instrument
Large-scale integrating project

Grant Agreement No.
270089

Duration
01 February 2011 – 31 January 2015

Clinical trials and available data are the heart of the p-medicine project.

The clinical trials incorporated in p-medicine focus on three cancer types and three different aspects of the developed framework:

- The Wilms tumour trial will be used to employ the newly developed and validated tools of p-medicine. The trial also provides data for the Oncosimulator which will test a specific Wilms tumour scenario (continuation of the ACGT project funded under FP6);
- The breast cancer trials will be used for the validation of decision making tools and data acquisition, sharing, joining and analysis. In addition, the breast cancer neoadjuvant pharmacodynamic phase II trial will extend the VPH tools;
- The leukaemia trial and the breast cancer neoadjuvant pharmacodynamic phase II trial will be used to run system biology and postgenomic dynamic scenarios to find individual risk factors for decision making and to validate the proposed models.

Data from clinical information systems will be made available by a 'push' model where data owners initiate data transfers. Access to biobanks will help to answer research questions without running new trials. Allowing patients to decide at any time what kind of research can be done with their data and their biomaterial supports patient empowerment, a key element of p-medicine.

A special focus of the p-medicine project in all its research activities is on creating collaborations and synergies with other projects and initiatives and to learn from previous work done. In this respect the FP6 project *ACGT* (Advancing ClinicoGenomic Trials in cancer) is drawn on as a reference and basis for p-medicine. Interaction has already successfully started with other ongoing FP7 projects such as *TUMOR* (Transatlantic Tumour Model Repositories), *CONTRACT* (CONsent in a TRial And Care EnvironmenT) and, first and foremost, *VPH-Share* (Virtual Physiological Human: Sharing for Healthcare) and will be further developed over the next years.

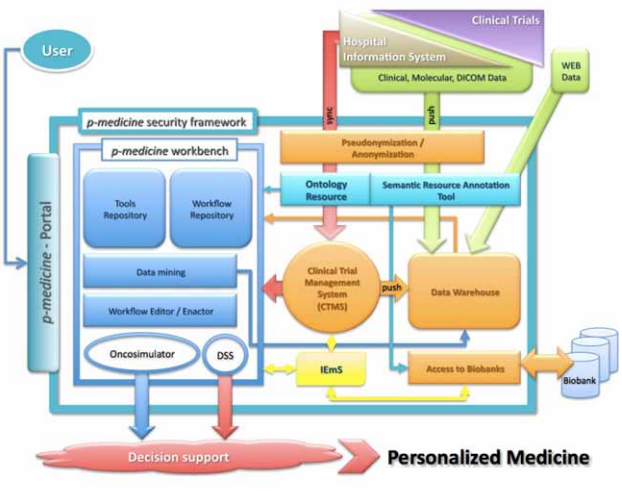
A close cooperation will be established with important stakeholders in healthcare, including IT researchers and the industry, to give them the opportunity to learn about the p-medicine environment, tools and services via eLearning tools and training workshops.

Their feedback is of vital interest to improve and optimize these tools and services over the next years of the project's duration.

More information:
www.p-medicine.eu

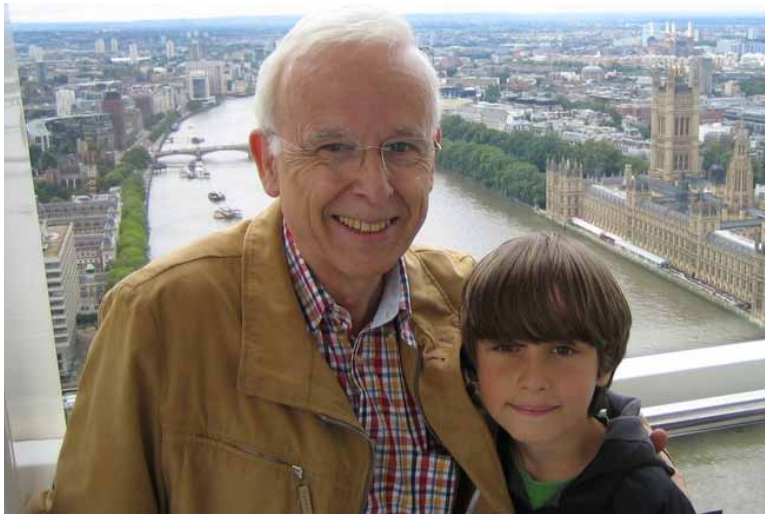
Overview of p-medicine's objectives:

- Create a collaborative environment facilitating clinically driven multi-scale VPH modelling
- Combine clinical, molecular biological and genomic data in individual patients
- Deploy clinical trials for VPH adaptation and validation purposes leading to decision support
- Build a data warehouse and p-medicine workbench to run VPH simulations
- Exploit the potential of high-performance computing and cloud storage
- Increase the quality of data mining in biomedical research
- Establish a service framework for accessing biomaterial resources
- Further develop the legal & ethical framework
- Link the p-medicine environment with important European Research Infrastructure Initiatives
- Develop training and educational eLearning tools
- Develop a business plan to further develop p-medicine into a self-sustaining entity



"Some personal reflections on Personalised Medicine"

Comment by David Ingram, member of the p-medicine External Advisory Board



David Ingram and his eldest grandchild Jake.

I well remember the first Dean of Medical School that I encountered when I started my academic career. A wily, somewhat ageing politician, he was completely bemused when his newly appointed Professor of Medicine (each School only had one in those days) arrived at his 12th century-established Hospital and announced that he wanted to appoint me, his former PhD student, as his one and only new lecturer appointee, in a new-fangled discipline that he proposed to call Medical Computing. The Dean used to spot me around the Campus and would exchange greetings as we passed – *'Ah Ingram'*, he would say, *'remind me to ask you what medical computing is one day.'* Pausing for a slightly sardonic grin of amusement at his wit, he swept on. I expect Norbert faces this kind of challenge with his crusty peers – *'Well really, Graf, surely all medicine is personalised, isn't it?'* The problem I faced, and my innovative sponsor Professor as well, was that I wasn't sure exactly what medical computing was, either. But that didn't alter the fact that I knew that the interaction of medicine and computation was going to matter and need academic discipline that was as yet unexplored, and that, as with any ground-breaking innovations, it was bound to be a bit threatening to the status quo.

Personalised medicine is today's paradigm challenging mission at the heart of clinical practice. It absolutely depends on good people, like all of the p-medicine team, committing to the long haul of exploring its theoretical, experimental and clinical underpinnings. It's going to be a hard slog. In his book *'What remains to be discovered?'*, the ex-Editor of Nature, John Maddox, wrote at the end of the 20th century that unravelling the clinical implications of genomics for patients would be the stuff of many careers for many years, at least ten times more work than that of identifying and sequencing the genes themselves.

But what is this I see in today's mail box – an invitation to a forthcoming conference on Personalised medicine, to be chaired by the President of the Royal College of Physicians of London, and addressed by luminaries of healthcare, pharma and academia! So the subject is clearly on the radar of the powers that be, and progress in your project is fundamental to shaping policy for its support at national and industrial levels.

Adjusting treatment regimens to meet the needs and achieve proven effectiveness for individual patients opens up huge requirements for new, more science based management of clinical data. That message is appearing in national broadsheet headlines, balanced by tales of woe about wastage of government money on failed large scale infrastructure projects. IT is truly shaking many foundations. Elsewhere in the healthcare IT world, there is huge change afoot seeking to establish a new experimental and open source ecosystem for clinical records, adopting key architectural outputs from the openEHR Foundation. National sections of openEHR are bursting into life in Japan, New Zealand and Brazil and government programmes, major health provider organisations and companies are sitting up and taking very careful notice, including the recently announced GE/MicroSoft alliance.

p-medicine must keep itself in the experimental vanguard of medical science and informatics to ensure that its insights and innovations can quickly be shared and replicated at scale, worldwide. It needs to choose wisely in selecting the right framework for standardisation of its IT.

David Ingram is a member of the p-medicine External Advisory Board, Emeritus Professor of Health Informatics at UCL and President of the openEHR Foundation.

He has recently established Charing Systems, a spinout company of UCL committed to helping health care providers and suppliers of health IT systems develop and exploit an open source software framework for standardised clinical records, based on the open EHR architecture.

"VPH SHARE AND P-MEDICINE"

Interview with Rod Hose, project coordinator of VPH-Share on the cooperation with p-medicine

What is VPH-Share trying to achieve?

In a nutshell, *VPH-Share* is seeking to develop an infostructure that will facilitate interactions between VPH researchers by making it easy to share, and to find, models, tools and data. It will also facilitate access to and use of computational resources in a cloud environment. Because these goals are very abstract, the first target is to facilitate the operation of four flagship workflows developed in previous European projects, with a view to sharing the technology with new research partners thus fostering 'virtual collaborations'. The idea is that researchers who are expert, for example, in computational fluid dynamics and wish to test their code and algorithms in a VPH environment can access (anonymised) medical scan data and the requisite image processing tools to convert them into a model without having to become expert in all components of the workflow.

VPH-Share will provide an environment in which new workflows can be built from a series of independent services. One of the first goals is to decompose some of the complex flagship workflows into a series of atomic services, or discrete tools, to support new compositions. The four flagship workflows are @neurIST (cerebral aneurysms), euHeart (cardiac), Virolab (HIV) and VPH-OP (osteoporosis). VPH-Share has a development cycle that envisages a first release of a set of prototypes to the VPH community at the end of its second year, and it is keen to engage external collaborators in a series of funded workshops.

VPH-Share focuses on a key bottleneck: the interface with the wealth of data from medical research infrastructures and from clinical processes.

How does VPH-Share differ from p-medicine?

My first reaction is that the projects are chalk and cheese! Each project has very different goals. VPH-Share seeks to support the whole VPH Community, and to make the minimum demands and enforce minimum constraints on those who wish to engage with its services, and its whole architecture is designed accordingly. VPH-Share has a positive mandate to engage with external partners to demonstrate take-up of its services. This comes, of course, at a cost. VPH-Share will have no control over the models, tools and data that are shared through its services. Whilst it can ensure that its services are secure, and that it provides robust processes and procedures to ensure that contributors can maintain control over who accesses the resources that they provide, it cannot provide any assurances as to the quality of the material that is made available by external contributors. VPH-Share is very concerned with issues of governance and process in the management of data, but not directly per se with ethics. Issues of data quality, as well as ethical considerations, must remain the responsibility of the provider (the formal data controller). The use of material accessed through VPH-Share is at the discretion of the end user.

VPH-Share targets the research community. It is not envisaged, for example, that its services would be used directly in clinical trials. p-medicine, in contrast, is much more

tightly controlled. At least during the funded lifetime of the project it focuses on specific communities in the cancer domain. It has strong focus on data quality, curation and integration and on data security. It offers direct support for clinical trial quality studies, with all necessary and appropriate legal and regulatory constraints. The primary target is the clinical user, not only for research but possibly also directly in the context of patient care. Both projects, of course, have ambition to encompass some of the areas addressed by the other. p-medicine envisages that the infrastructure that it develops will be readily transportable to other clinical domains. VPH-Share envisages that its core IT infrastructure can be adopted in a tightly-controlled clinical environment, but the point is that neither project has these spin-off developments as core targets during its first phase of funding.

What do the two projects have in common?

Both VPH-Share and p-medicine are Integrated Projects, funded under FP7-ICT-2009-6 and the objective ICT-2009.5.3 Virtual Physiological Human, Target Outcome b). It is extraordinary that both completely address both the text and the spirit of the Call, but from diverse perspectives. Their common goal is to develop ICT infrastructures to share data, tools and models, but for very different target client bases and therefore with very different constraints.

You have recently had a joint review in Brussels, in what way do you feel this has enabled the projects to collaborate?

It is not surprising that the ICT for Health Unit wishes to see strong collaboration between two major Integrated Projects funded and operating under its remit. Whilst we might originally have been perceived, and indeed regarded ourselves, as competitors during the evaluation phase, both projects approached the joint review with a real spirit of co-operation and a genuine desire to learn from each other. We had had the opportunity to become more closely acquainted during the negotiation process, and I believe that there is a strong mutual respect between the projects. Although the original focus was on potential synergies afforded by the fact that both projects have work packages on cloud computing, our discussions rapidly escalated to cover a much wider perspective encompassing much of the breadth of activity of both projects. We have held two joint, whole day, meetings of those most directly affected and following these we were able to assemble a comprehensive plan for our collaborations, including further joint meetings and workshops.

Both projects have new deliverables reflecting interactions in their approach to cloud computing services. p-medicine offers a very strong use case, with a clear exploitation plan, to support VPH-Share's evaluation of the impact of VPH technologies, and furthermore is an obvious client for some of VPH-Share's services. p-medicine committed to explore whether some of their data, tools or models might be catalogued and shared more widely through VPH-Share, and will engage with VPH-Share's dissemination workshops. VPH-Share will examine closely the security models enacted by p-medicine, and will be a potential client for p-medicine's workflow composition software. These plans were well-received by the appointed expert reviewers, and indeed their primary comment was that they would be very satisfied if we did what we said we would do, and that they would be monitoring our actions against our words!

What can VPH-Share learn from p-medicine (and vice versa)?

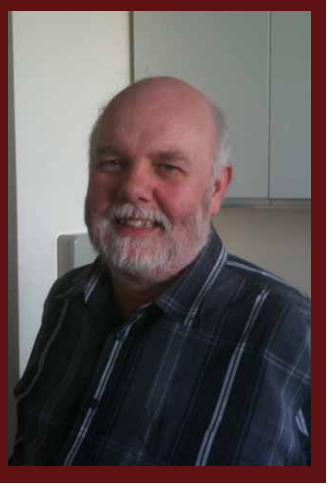
I think that I've already answered this in answering the previous section, but in particular on technical level VPH-Share is very interested in p-medicine's security model and in its workflow composition software. We are also keen to explore the degree to which p-medicine can be a client for VPH-Share's services, and whether we can assist p-medicine with its technology impact evaluation and dissemination processes, even including identifying new clients for the resources that it might be able to offer more widely (subject to ethical and legal constraints).

More information on VPH-Share

Prof. Rod Hose
University of Sheffield

Phone +44 (0) 114 27 13147
Fax +44 (0) 114 27 11863

d.r.hose@sheffield.ac.uk
www.vph-share.eu



P-MEDICINE – OTHER RELATED PROJECTS AND INITIATIVES

TUMOR – Transatlantic Tumour Model Repositories

TUMOR aims at implementing an EU cancer model/data repository, and developing/providing specific tools and methods for the collection, curation, validation and customization of existing EU and US cancer models, by linking the most significant relevant EU VPH projects on cancer modelling (ContraCancrum, ACGT), and the US project (CViT).

The key expected results of the project can be summarized as follows: Facilitated access to and utilization of internationally available models can lead to the development of "higher-order" multi-level cancer models which will address more aspects of the natural phenomenon of cancer. Moreover, an EU cancer model repository based on mutual exchange of model and tool executables will emerge, thus facilitating international cancer research interaction and compatibility. In addition, a signifcant expansion of the VPH interoperability efforts will evolve beyond the EU boundaries (EU-US cancer model interoperability). Several partners of the p-medicine project (FORTH, ICCS, USAAR, UOXF) are involved in both projects. p-medicine can profit from a cooperation with TUMOR in various aspects. Co-development of models in complementary areas can speed up progress and avoid duplication of work that needs to be done. TUMOR has done significant work in mark-up languages from which p-medicine can benefit directly and TUMOR has also shown results in advanced clinical workflows that can serve as paradigms for p-medicine scenarios.

TUMOR and p-medicine will also collaborate on legal and ethical issues invoking non-EU partners since MGH Harvard is a partner of TUMOR and significant discussions and actions have been initiated in the direction of transatlantic collaboration and sharing of models.

CONTRACT – CONsent in a TRial And Care EnvironmenT

CONTRACT is about consent. The project focuses on analysing how the legal (and underlying ethical) concepts of informed consent in the European Data Protection Directive and in the Clinical Trials Directive have had and continue to have an impact on the success of translational research. The project predominantly deals with vulnerable patients as their consent is of utmost complexity. The concept of informed consent in the two mentioned Directives is analysed from a legal, ethical, IT-related and clinical perspective. The European approach on the matter is being compared with national concepts of informed consent in chosen Member States.

CONTRACT aims at supporting the European Commission and other policymakers in achieving a clear Community framework by providing clarity on different concepts of informed consent on European and national level. CONTRACT s approach is based on legal analysis and an empirical survey, which was conducted at the project start. As an outcome CONTRACT produces an analysis of the national and European legal framework on consent. Finally this analysis will become a part of the CONTRACT helpdesk on consent issues – a tool which will support relevant stakeholders in balancing patient's and research interests by helping to produce informed consent documents. In achieving these objectives the project has put together an internationally recognised interdisciplinary team of individuals and organisations with significant expertise and know-how on all areas of relevance to the project, it has drawn-up an ambitious – yet achievable – workplan.

LUH, leader of the Legal and Ethical Framework work package in p-medicine is the coordinator of CONTRACT. In addition, Custodix, USAAR and FORTH are members of the CONTRACT consortium. But CONTRACT and p-medicine do not only have consortium members in common. The matters of informed consent, which are in the main focus of CONTRACT, and so also the outcomes of the project, are of extreme relevance in p-medicine, given that a valid consent for the processing of his/her data is an indispensable prerequisite for the patient's participation in the project. Hence the CONTRACT Helpdesk on questions of Informed Consent and the IC Generator will be used as a competence center whenever questions of consent arise in p-medicine. The CONTRACT Helpdesk may also be further developed and enhanced by additional functions useful for the p-medicine project.

If you are interested in the project and its outcomes please contact its coordinator – Institut für Rechtsinformatik, Leibniz Universität Hannover: *Prof. Nikolaus Forgó* or *Ms. Magdalena Góralczyk*.

P-MEDICINE PARTNERS IN DEPTH

This section is dedicated to individual p-medicine partners. Since the p-medicine consortium is very large and composed of many different partners from various scientific fields, this section offers some of the partners with core tasks in the project a platform to present themselves in more detail. ecancer is leading the way in this first newsletter issue.

ECANCER – THE LEADING ONCOLOGY CHANNEL

ecancer is a leading oncology channel committed to improving cancer communication and education with the goal of optimising patient care and outcomes. Employing the latest technologies, ecancer works closely with leading oncologists to inform and educate the global cancer community.

ecancer enhances cancer communication by running a free to publish, open access journal called ecancermedicalscience. Our journal is wholly online and is the official journal of the European Institute of Oncology and the Organisation of European Cancer Institutes. ecancer also gives key researchers from the latest conferences a global platform by interviewing them about their work. We currently host over 1,200 videos which have been viewed 1.4 million times, helping the latest developments in cancer to be shared quickly and effectively all over the world. We have 7,000 registered oncology professionals with the website enjoying 40,000 unique visits per month.

For more information, please visit www.ecancer.org

The website provides you with the latest information in the cancer domain

ECANCER AND P-MEDICINE

The ecancer team leads two work packages within p-medicine, WP14- Patient Empowerment and WP16- Education and Training.

For the patient empowerment elements we are working alongside a team from the Interdisciplinary Research Centre on Decision Making Processes (IRIDe) within the University of Milan. IRIDe was founded in 2007 with the aim of creating an institutional research centre on decision making. By studying the processes which cancer patients go through while making choices about their treatment, we

Empowering patients through improved communication

aim to increase the understanding of how different factors affect these choices. This is achieved through a series of questionnaires covering individuals' perceived health state and psychological, psycho-social and cognitive aspects. Data from the questionnaires will be used to create a patient's personal psychological profile that will facilitate the doctor taking these factors, which directly relate to quality of life, into account when making joint decisions about treatment. By combining medical and psychological considerations p-medicine will deliver truly personalised care for an empowered patient.

ecancer has been educating the cancer community since 2007. By creating and hosting online learning

Sharing knowledge to improve patient care

resources and running educational events we ensure that our learners have a long term understanding that reinforces good practice and/or results in behaviour change as appropriate. Through the effective education of oncology professionals, ecancer helps deliver real and significant benefit to cancer patients across the world.

LINKS

www.ecancer.org

Dr Simona Rossi interviewed at the WIN meeting

WIN Conference Report, S. Rossi et al.

To be interviewed at a conference or publish for free contact danny@ecancer.org

INTERVIEW ON KEY ASPECTS OF P–MEDICINE

with Manolis Tsiknakis (FORTH) and Benjamin Jefferys (UCL)

It is a great pleasure that Manolis Tsiknakis from the Foundation for Research and Technology – Hellas (FORTH) and Benjamin Jefferys from University College London (UCL), two core partners in p–medicine, kindly agreed to participate in this interview to explain and talk about key aspects of p–medicine.

First of all, please let us know something about your main research interest and why p–medicine is an important project for you.

Manolis Tsiknakis: I am a principal researcher at the Computational Medicine Laboratory of the Institute of Computer Science of FORTH, Greece. The Computational Medicine Laboratory has two main research directions. These are Biomedical Informatics in support of individualized medicine and ambient intelligence eHealth environments.

In the domain of Biomedical Informatics, the Lab is focusing its research on various computational aspects of biomedical informatics, such as (a) ontology based integration and analysis of genetic and medical information for health applications; (b) grid–based approaches to demanding molecular–biomedical applications; (c) analysis, simulation and modeling of complex biomedical processes, and (d) design and development of novel and prototypical DM/KDD methods, techniques, algorithms, tools and systems. All these activities are directly in line with the core research and development activities of the p–medicine project.

Benjamin Jefferys: My scientific background is in computational biochemistry: I worked on modelling of proteins, specifically protein synthesis and folding. So p–medicine is a significant change in direction for me. My interest in the project was to move away from theoretical work, which has a small chance of making a big impact, towards more practical work, which has a smaller impact, but a bigger chance of success. I'm also interested in the power of large quantities of data as compared to refined analytical and modelling techniques. I have found the balance between these two a recurring theme in many domains, and is nicely encapsulated in Rutherford's infamous quote about stamp collecting versus mathematics. Finally, many close family members and some friends and colleagues have

Short CV Manolis Tsiknakis

Manolis Tsiknakis received the B. Eng. degree in Electric and Electronic Engineering in 1983, the MSc degree in Microprocessor Engineering in 1985, and the PhD degree in Systems Engineering from the University of Bradford, Bradford, U.K. in 1989, where he worked as a teaching research assistant until 1991.

Since 1992, he has been with the Institute of Computer Science, Foundation for Research and Technology – Hellas, Greece, where he is currently a Principal Researcher. He has coordinated many collaborate EU–funded research projects, and has been the technical coordinator of a large scale national effort for the development of HYGEIAnet, the regional health information network of Crete. Recently, Dr Tsiknakis has been the scientific coordinator of an EU–funded integrated project (ACGT – Advancing Clinico–Genomic Trials on Cancer) focusing on the development of innovative ICT solutions supporting large scale translational research on Cancer. He is also involved in a series of R&D projects in the domain of cancer biomarker discovery and translational medicine. He has been the initiator and chair of the Biomedical Informatics Working Group of the European Research Consortium in Informatics and Mathematics (ERCIM). Manolis Tsiknakis is a member of the Editorial Board of the Open Medical Informatics Journal and the International Journal of Telemedicine and Applications, and a member of the program committee in numerous high–profile conferences. He has been a key note speaker in important IEEE conferences, and also acts as a regular reviewer for a number of scientific journals and conferences. He has been a member of the Advisory Board in several FP6 and FP7 projects; currently he is chairing the Advisory Board to the EHR4CR project funded by the Innovative Medicine Initiative (IMI) programme. Manolis has published extensively – over 200 papers in refereed scientific journals and conferences – on issues related to the application of innovative Information and Communication Technologies in the domain of clinical and translational research, care and wellness management.

His current research interests include biomedical informatics and engineering; service oriented SW architectures and their application in biomedicine; approaches for semantic health data integration; enterprise integration strategies and patterns; smart eHealth and mHealth service platforms; managing technological change and socio–economic aspects of eHealth technologies and services.

suffered from cancer, which gives me a more personal motivation. I am sure this is true for most other p-medicine collaborators.

What are you and your institution exactly doing in the project?

Tsiknakis: FORTH has an important role in p-medicine. We lead two central work packages of the p-medicine workplan, i.e. WP3-IT Architecture and WP8-p-medicine workbench. In addition a member of our staff has undertaken the role of the integration manager, which is important in making sure that a coordinated and managed process of technical implementation takes place and that an integrated technical platform results from the p-medicine workplan.

Jefferys: Our main role in the Centre for Computational Science at UCL is in managing WP7, constructing a data warehouse for collecting clinical and other data from diverse sources in a standardised form defined by our partners in WP4. We are also involved in requirements gathering, IT architecture (particularly in researching relevant standards), the workbench (particularly our relationship with VPH NoE), molecular modelling of drug-virus interactions, clinical decision support, patient empowerment, quality assurance, training and dissemination. Our colleagues at Great Ormond Street Hospital, affiliated to UCL, are involved in one of the Wilms' tumour clinical trials, from which we will gather data for analysis. We seem to touch most parts of the project!

p-medicine is a VPH Infrastructure project and depends on the sharing of huge amounts of heterogeneous data. Can you explain where these data come from?

Tsiknakis: p-medicine is indeed an infrastructure development project. Its ultimate vision is to architect and deliver an open, state-of-the-art computational platform supporting the notion of translational medicine and personalized medicine. Testing and validating such a platform requires availability of large, multilevel and temporal data sets. The management team of p-medicine has made every effort to include in the project a number of clinical research groups, academic medical centers and trials coordinators who have committed to provide and make available such multilevel data sets.

Jefferys: That's right. Initially, the primary source of data in p-medicine will be from previous clinical trials conducted by our clinical partners. Those same partners will be conducting clinical trials as part of p-medicine, and will feed data to us from their work. Finally, it would be wonderful to see data coming from clinicians outside of p-medicine, since the more data we collect, the more powerful the analytical methods will be.

This brings us to an important question. How will these data be made available for the research community by guaranteeing data privacy and data security?

Tsiknakis: These data sets – following an elaborate data protection framework that the project has established, which guarantees full adherence to the European data protection requirements – will be made available to the p-medicine research community and the wider community in due time.

Jefferys: Privacy is ensured primarily through pseudonymisation, replacing personally identifiable information with a unique identifier, which can only be traced to a particular individual through a trusted third party. Data will be kept secure with a bespoke authentication and authorisation system which allows access only by people who have signed contracts which constrain how they can use the data.

The data warehouse plays a central role in the project. In your opinon, what needs to be done that physicians and basic researchers trust in the infrastructure of p-medicine so that they will share their data in the future?

Tsiknakis: This question touches a very sensitive issue indeed. Trust on ICT infrastructures has over time been a key factor influencing adoption.

Short CV Benjamin Jefferys

Benjamin Jefferys graduated in 1999 with a degree in software engineering from Imperial College London, and started as a software engineer working on social networking websites (before anyone was interested in them), and then software for film and TV special effects. In 2003 he retrained in biochemistry and bioinformatics, then completed a PhD and his first postdoc in protein structure modelling at Imperial College, before joining UCL in February 2011 to work on p-medicine.

UCL was established in 1826 in order to open up education in England for the first time to students of any race, class or religion. Its founding principles of academic excellence and research aimed at addressing real-world problems, inform the university's ethos to this day. UCL is ranked seventh in the world's top ten universities by the QS World University Rankings (2011). More than 4,000 academic and research staff at UCL are dedicated to research and teaching of the highest standards.

The process will inevitably be gradual since it also involves changing attitudes – but the project has defined a set of outreach activities with the objective to reach out to the community and demonstrate the ethical, legal and security framework in place – which is more than simply technology – which guarantee the complete trust on the infrastructure.

Jefferys: I think that the pseudonymisation process goes a long way to reassuring data providers that their data will be handled safely. I also think that the provision of auditing facilities in the data warehouse, which allow an independent third party to check that data is only being accessed by those with permission, is also a good method of earning their trust. As important as trust is, however, I think that clinicians will be encouraged to give us data by offering them solid benefits, in the form of improved decision-making based upon a large database and state-of-the-art analytical techniques.

There are many issues dealing with standardization and semantic interoperability in p-medicine. How are these issues addressed?

Jefferys: This is primarily being addressed by our colleagues in WP4, which deals with semantics. The data warehouse must support their work, however. We are doing this by providing a very modern data storage facility which is based around ontologies and "dynamic" schemas – meaning that the structure of the database doesn't have to be fixed ahead of time, and it can accommodate many heterogeneous data sources. The old table-based relational database has been replaced by a triplestore, which represents data as a set of objects and a set of relationships between them. We are also supporting constant alteration of the mapping from data sources to the standardised p-medicine data warehouse, so we can correct errors and ensure tight semantic integration.

Tsiknakis: Bringing together and integrating large datasets, which relate to various levels of the biological system or the disease and which evolve over time presents very complex issues regarding semantic interoperability. In responding to these challenges the project has adopted two complementary approaches, a) mapping of data to a shared domain model – through the use of a Health Data Ontology been developed; and b) extension and optimizing of semantic resources against the background of evolving data pushed into the system through the use of reach metadata. Both these areas pose significant research questions, which in p-medicine are studied by dedicated internationally recognized research groups.

p-medicine will develop tools, services and models for decision support. Can you give an example of such a tool and explain it?

Tsiknakis: A major objective of p-medicine is the design and implementation of a computational platform able to seamlessly integrate multilevel clinico-genomic data and support the development of complex models. Within such a context, simulating disease evolution and/or disease outcome is a milestone for the technological advancement of predictive medicine based decision support. An example of such a tool is an integrated oncosimulator (IOS) tool simulating in vivo tumour response to therapeutic modalities within the clinical trial context.

In the context of the project two neoadjuvant clinical trials on nephroblastoma and breast cancer have been considered, respective simulation components are been developed and critical validation work is planned. The ultimate objective is the validation and clinical translation of such innovative predictive medicine tools that have the potential to optimize therapy outcome, reduce patient suffering and healthcare costs related to unnecessary treatment.

In addition, a number of focused decision support scenarios are currently being considered including for example adverse event prediction decision support. These require models and corresponding tools which are being developed based on analyzing/modelling of retrospective clinical information from the EHRs.

Jefferys: The data warehouse will be at the core of most decision support, however it will not be a decision support tool in itself. The simplest use of the data warehouse would be for physicians to search for patients who have a similar phenotype and condition to a patient the clinician is treating. They can look at this data and learn from other physicians on how to treat the patient - what worked, what didn't work? This is a simple but powerful use of data.

From your perspective, what do you think is the role of patients and clinicians in this IT project?

Tsiknakis: As earlier stated, p-medicine seeks to develop a platform, and tools to support personalized medicine. The ultimate users of these tools will be the clinicians and the patients. Therefore – as many years of research have indicated – their involvement at every step of the analysis, specification, implementation and validation of these tools is of paramount importance in making sure that the solutions respond to real user needs. In parallel their active involvement at every step of the development process will ease the difficulties of adoption we talked about earlier on. So, in conclusion their role is very important and the project has made sure that a strong representation of patient groups and clinicians does indeed exist.

Jefferys: As already stated by Manolis, patients and clinicians are at the core of the project, they should be the focus of everything we do. Anything which does not contribute to serving their needs should be regarded as a peripheral activity. I previously worked in several industrial positions: our customers were the motivation for every task and goal, because if they weren't, we didn't sell products and we lost our jobs. Sometimes it seems like the European Commission are the customers of p-medicine! But really patients and clinicians should be our customers. This ruthless pursuit of serving the end user might not seem like the best way to foster basic research, which is quite a different activity to making saleable products. However, I personally think that a focus on making tools that contribute to our final goal of curing cancer and other diseases is more likely to produce high quality research than a more liberal goal of furthering IT research in general.

Usability and validation of tools are major tasks in p-medicine. How are these processes triggered in p-medicine?

Jefferys: I hope that they are triggered as soon as the first user-facing tool is ready for testing, and continues as long funding is available to do so. Validation is clearly a crucial process and should start before the tool is deployed, and then be ongoing, because even if the tool itself remains the same, the data driving it will change over time. So validation is a continuous process. Since we are supposed to be producing tools which support clinical decision-making, then validation is important not only to ensure the advice given is beneficial, but also to ensure it isn't detrimental. Usability can be more reactive, but clearly the two are intimately linked – a tool that is not validated is not useful or usable. There is a subtler edge to usability though, and it is tough to assess it independently prior to deployment. Therefore I think that usability should be continuously assessed by encouraging feedback from users and monitoring usage. We should aim to have some minimum number of users by some point, and to increase that number over time. This is the real test of usability!

Tsiknakis: Usability and validation of tools are indeed key tasks in the p-medicine workplan, for the simple reason – as we already said – that user adoption depends upon and is influenced by these ICT quality attributes. Dedicated tasks – coordinated by experienced researchers in the domain – provide the means for the execution and coordination of these activities. Regarding validation of tools, it is worth pointing out that, apart from the technical validation of the tools which are coordinated by the Integration Manager of the project, we place emphasis on the clinical validation of such tools – a more challenging and time consuming process, which however is a crucial step for the clinical translation of such innovative predictive medicine tools.

LINKS

For further information on our two interview partners and their institutions you may visit the p-medicine website or the institution's official homepage:

FORTH: *p-medicine page*
official homepage

UCL: *p-medicine page*
official homepage

Visit us at our building in Biomed Town. Soon to come!

Biomed Town is a free community open to all those who have a professional or educational interest in biomedical research & technology.

Meet us at our Biomed Town Building!

ANNOUNCEMENT OF UPCOMING EVENTS

INBIOMEDvision Training Challenge 2012

April 23–27, 2012
Monastery of Les Avellanes
Lleida, Spain

The Challenge is an innovative training experience that gathers two groups of 5 advanced students with expertise on different biomedical informatics fields (bioinformatics, medical informatics, biology, medicine, chemistry, etc.), who will collaboratively work on a case study related to a research problem. The objective of this training activity is to promote the dialogue between disciplines, which is key for the future development of Biomedical Informatics.

More information

3rd VPH study group on VPH Toolkit

May 7–11, 2012
Barcelona, Spain

The event will take place on the premises of Universitat Pompeu Fabra the week after the IEEE International Symposium on Biomedical Imaging (ISBI 2012). The organisers invited three groups of world-recognised experts, typically leading large VPH projects, to submit a proposal for a grand challenge in the area of musculoskeletal, cardiovascular, and oncology research. Norbert Graf, USAAR, Saarbrücken, coordinator of the p-medicine project, and Georgios Stamatakos, ICCS, Athens, coordinator of the Oncosimulator project and partner in p-medicine, organise a working group entitled "Multiscale cancer models and oncosimulators for clinical use" dealing with ontology research in VPH.

More information

25th IEEE – International Symposium on COMPUTER-BASED MEDICAL SYSTEMS (CBMS 2012)

June 20–22, 2012
Rome, Italy

Grid for the Life Sciences is an environment that allows sharing of resources, in which heterogeneous and dispersed health data as well as applications can be accessed by all users as a tailored information providing system according to their authorization. The main goal of the track is to exchange ideas and results related to ongoing grid and cloud computing research in Biomedicine, Life Sciences and correlated disciplines, such as Climate Change, that impact on human health, focusing on different aspects of middleware, technologies and applications.

More information is available on the *conference website*

MIE 2012 – The 24th European Medical Informatics Conference

August 26–29, 2012
Pisa, Italy

The theme of the conference is Quality of Life through Quality of Information. MIE 2012 will provide a unique platform for a fruitful exchange of ideas and experiences among the actors and stakeholders of ICT supported healthcare since the opinion and experiences of both the designers/planners and the addresses/users of eHealth systems are of great importance when the target is the global improvement of the quality of life, at personal and public level.

More information

VPH 2012 – The Virtual Physiological Human Conference

September 18–20, 2012
London, UK

The Virtual Physiological Human Network of Excellence (VPH NoE) will hold the second of a series of VPH Conferences (VPH 2012) on September 18–20, 2012 in London.

VPH2012 will be an international conference on computational biomedicine, with a clear focus on the integrative aspects of VPH. Special attention will be given to the 'Digital Patient' as well as 'health forecasts'. VPH2012 aims at reaching outside of the VPH community to other equally important communities: systems biology and genomics. In this respect, our vision is to have a conference that truly encompasses all possible scales to model physio/pathology with a clear ICT focus.

More information is available on the *conference website*

Since the section of the website on upcoming events is regularly updated we invite you to visit our *website* for most recent changes.

SUBSCRIPTION

The p-medicine newsletter is published once a year by the p-medicine consortium and is distributed free of charge.

All issues of the newsletter will be available on our website.

For subscription to the newsletter please go to
www.p-medicine.eu/news/newsletter

RSS FEED

An RSS feed is available on the p-medicine website. For more information please go to *www.p-medicine.eu/news/rss-feed*

DISCLAIMER

The p-medicine project (Project Identifier: 270089) is funded by the European Commission under the Seventh Framework Programme.

The content of this newsletter cannot be considered as the European commission's official position and neither the European Commission nor any person acting on behalf of the European Commission is responsible for the use which might be made of it; its content is the sole responsibility of the p-medicine project partners.

Although the p-medicine consortium endeavours to deliver high quality, no guarantee can be given regarding the correctness and completeness of the content of this newsletter due to its general informational character.

The p-medicine consortium is not responsible and may not be held accountable for any loss suffered as a result of reliance upon the content of this newsletter.

EDITORIAL BOARD

NEWSLETTER TEAM

CONSORTIUM MEMBERS

GUEST AUTHORS