



- Infections in Africa
- Hypertension: who is at risk?
- Gut genomics

International Cooperation

in EU-funded
Health Research

Address

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Science is a truly global endeavour with scientists sharing their knowledge with their colleagues around the world. Most health and bio-medical challenges are borderless and if research is to help meet those challenges, an international approach is essential.

This is why cooperative EU-funded research of the type described in this magazine is open to partners from outside the EU. I strongly believe that this openness advances competitiveness and innovation in all the countries involved. It helps Europe maintain and improve its position as a global leader in medical research and as a provider of excellent healthcare.

Cooperative research also provides invaluable development assistance for poorer regions facing specific health challenges.

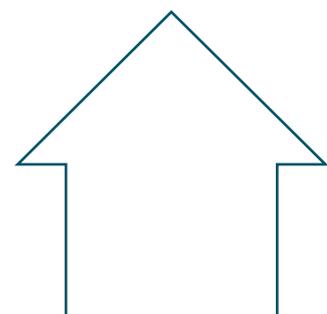
More broadly, international cooperation in research works as a kind of 'science diplomacy' helping to bring nations together, whatever their differences in culture, politics or wealth.

I am certain that international cooperation will continue in the future to be a cornerstone of our European Framework Programmes for Research and Technological Development.



Máire Geoghegan-Quinn

Máire Geoghegan-Quinn
*Commissioner for Research,
Innovation and Science
European Commission*



AROUND THE WORLD IN 36 PROJECTS



'Collaborative research...

...of the type described in this magazine has a number of benefits. The science and technology agreements which are required to allow this kind of cooperation between nations often constitute the first step towards further and closer ties. Cooperation also takes place between different types of partners; for example, between academia and industry or between the various disciplines involved in undertaking research and in translating its results into innovative treatments and improved clinical practice. Cooperative research deployed in support of health-related Millennium Development Goals reflects Europe's determination to play a major role in achieving these. As the world's biggest aid donor and its largest trading partner, the EU is ideally positioned to support the worldwide drive for a healthier future, and draws on extensive experience of healthcare systems based on the principles of solidarity and universal coverage.'

Ruxandra Draghia-Akli

Director for Health

*Directorate-General for Research
European Commission*

International cooperation, in EU-funded health research, is not an empty promise. With research partners on five continents, with project opportunities open to applicants from every country on the map, with generous funding for international teams exploring issues of relevance to the global community, the EU is fostering ambitious undertakings involving scientists and organisations from Europe and beyond.

This commitment to scientific collaboration characterises the EU's approach to research and innovation. Brilliant minds inspire each other, and their collaboration holds the keys to excellence: the opportunity to learn from the best, to disseminate and integrate outstanding methodology, to assemble top-flight expertise in order to shed new light on multi-faceted problems, to pool knowledge and resources in pursuit of a common goal and to boost competitiveness and contribute to innovation.

These interactions take the whole field forward, enabling the EU to back world-class teams performing to the highest standards. Europe's bid to tackle major research challenges at home and abroad cannot succeed without them.

The European Commission is considering further ways of boosting the impact of its research contribution. Four main areas

of action have been identified: enhancing global governance on health, promoting universal health coverage, maximising coherence between EU policies relating to global health, and increasing global health knowledge to ensure that the new products and services shaped by research and innovation are accessible and affordable, and that all diseases are taken into account.

Throughout successive Framework Programmes, international cooperation in EU-funded health research has matured into a proud tradition. The Health priority of the Sixth Framework Programme (FP6) for Research and Technological Development (RTD) had already left a notable legacy, with 214 participants from 51 third countries involved in health research for a total committed budget of EUR 30 million for non-European countries.

Further funds have been made available from other EU budgets, and all health research topics are now potentially open to applicants from any country. International cooperation is therefore expected to reach new heights under FP7, the current Framework Programme for EU research. With three more years to go,

FP7 has already funded 561 consortia which, together, involve 522 partners from 79 non-associated third countries in joint health research projects.

This publication provides an overview of the spirit and the mechanisms of EU-funded international health research and snapshots of some of the latest projects. All our projects are advancing the understanding of human health or striving to address an unmet need in prevention, diagnosis, treatment or healthcare provision. Each and every one of them may help to save or enhance the lives of several citizens. From research to market, all are contributing to innovation and to the emergence of the knowledge-based economy on which Europe's future will rely.

The projects featured here will take you around the world in a short time – without the need for suitcases, passports or travel insurance. If you would like more information about their work, please don't hesitate to contact them through their websites provided in the relevant articles, or drop us a line using the address information on page 31.

Enjoy the reading.

The ambassadors of European research

'Our main objective is to maximise the quality of the proposals that are submitted to the Framework Programme. And that includes international cooperation at all levels.' Almudena González, the coordinator of the EU-funded **Health-NCP-Net**, knows that many researchers applying for FP7-funding appreciate personalised guidance. They can rely on the support of an extensive network of National Contact Points (NCPs) which inform prospective applicants of suitable opportunities and helps them to find partners, prepare documentation and deal with contractual matters.

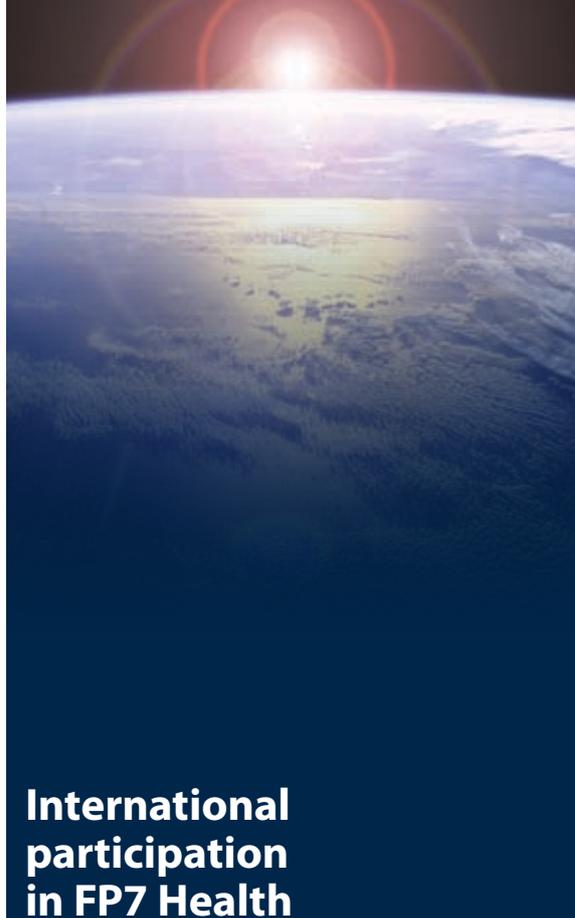
Health-NCP-Net started out with 19 partners in the core consortium, including NCPs in Egypt, Israel and South Africa. But the network is much bigger in practice, as all Health NCPs are associated with the project and the network is growing steadily. New NCPs have, for example, just been created in Taiwan, and regional contact points are being established in Africa.

Health-NCP-Net



Full name:	Coordination action for reinforcing the Health National Contact Points network
Type:	Coordination action
Start date:	01/05/2008
Project coordination:	Instituto de Salud Carlos III Madrid Spain
19 project partners from 18 countries:	Austria, Belgium, the Czech Republic, Egypt, Estonia, France, Germany, Greece, Israel, Italy, Latvia, Malta, the Netherlands, Poland, Portugal, Romania, South Africa, Spain

<http://www.healthncpnet.eu>



International participation in FP7 Health

First four calls for proposals: budget years 2007 to 2010

Participant country name	Number of participants per country*
United States	66
India	49
Russia	36
South Africa	30
China	25
Tanzania	21
Canada	18
Australia	16
Uganda	15
Burkina Faso	13
Ghana	12
Kenya	11
Argentina	10
Brazil	10
Egypt	9
Korea	8
Nigeria	8
Colombia	7
Tunisia	7
Vietnam	7
Cameroon	6
Malawi	6
Ukraine	6

* Number of participants from non-EU/non-associated countries involved in more than five projects



A disease of affluence?

Cardiovascular diseases (CVDs), diseases of the heart and the circulatory system, are Europe's greatest killers, claiming 2 million lives every year across the 27 Member States. Long regarded as diseases of affluence, they are, today, a worldwide concern: according to World Health Organization (WHO) estimates, 82% of the 17.1 million CVD-related deaths in 2004 occurred in low- and middle-income countries. CVD is a global challenge, to which the EU has already allocated EUR 123 million in research funding during the first four years of the Seventh Framework Programme (FP7).

The power of synergy

Collaborative research is particularly promising when projects tie in with an international approach. Such coordination pre-empts duplication of effort and extends the range of research activities that can be conducted simultaneously. It creates opportunities to break vast challenges down into manageable tasks. It also enables projects in areas where the research activity is less intense to pool resources and build up the required critical mass.

Programme-level cooperation

with other countries is designed to extend the potential of such synergy internationally. Research topics of common interest are defined by the European Commission in partnership with a third country and its research funding organisation. The cooperating third country and the Commission agree on a common topic and launch in parallel separate calls for proposals.

Projects selected by the two parties for funding — with each party funding its own projects — are then asked to network, establish cooperative links and take a joint approach in tackling the challenges involved in the topic wherever possible and meaningful. Such programme-level cooperation has been established mainly with industrialised countries or emerging economies that have an established research funding system and research budget.

http://cordis.europa.eu/fp7/health/international-cooperation_en.html

Hypertension: who is at risk?

Hypertension is linked to lifestyle, but the predisposition does appear to run in families. A detailed understanding of the genetic factors determining this proneness would enable health professionals to identify individuals at particular risk and could help many patients to manage their condition more effectively.

As part of the InGenious HyperCare project, 32 research organisations from 14 countries including China, Russia and Switzerland are rising to the challenge. They aim to identify genetic factors and morphological indicators, generate leads for new diagnostic tools, improve the understanding of cardiac and brain damage resulting from high blood pressure and disseminate the results.

Their work could give the medical profession a decisive edge in the fight

against high blood pressure. Insights into the underlying genetic and pathological mechanisms could boost the success of prevention programmes and inform the development of new diagnostic and therapeutic tools.

InGenious HyperCare

Full name: Integrated genomics, clinical research and care in hypertension

Type: Network of Excellence

Start date: 01/11/2006

Project coordination: Istituto Auxologico Italiano Milan, Italy

32 project partners from 14 countries: Belgium, China, the Czech Republic, Finland, France, Germany, Italy, the Netherlands, Poland, Russia, Spain, Sweden, Switzerland, United Kingdom

<http://www.hypercare.eu>

Unlocking the weighty secrets of the heart

How does body mass affect a failing heart? The SICA-HF project argues that its significance in the progression and the treatment of chronic heart failure (CHF) has been underrated, particularly in cases where patients are severely underweight. Body mass extremes and weight-related disorders such as diabetes are known to accelerate the progression of CHF, the heart's long-term inability to supply enough oxygen and nutrients to the body, but much remains to be learned about the underlying mechanisms.

The project partners are investigating the matter, and they do not plan for their work to remain theoretical. The team aims to develop tailored therapies to overcome the current one-size-fits-all approach to treatment and also hopes to improve the patients' quality of life. It places a firm emphasis on close interactions between clinicians and researchers, and on the application of its insights in clinical practice.

SICA-HF, an outstanding example of programme-level cooperation with research partners abroad, was brought to life as the result of a joint initiative between the EU and the Russian Federation. Both can lay claim to world-class expertise in heart failure research, and both welcome the opportunity to improve patient welfare and hone their competitive edge — a shared interest which suggested obvious synergies.

SICA-HF

Full name: Studies investigating comorbidities aggravating heart failure

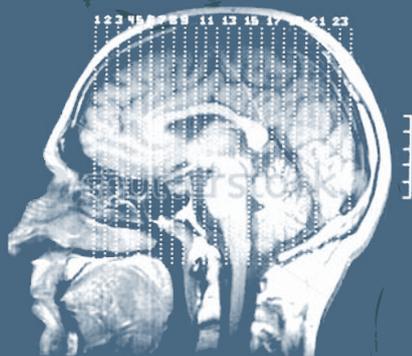
Type: Large-scale collaborative project

Start date: 01/10/2009

Project coordination: Charité – Universitätsmedizin Berlin Berlin, Germany

12 project partners from 6 countries: Germany, Italy, Poland, Russia, Slovenia, United Kingdom

<http://www.sica-hf.com>



GENETICS ON THE BRAIN

“We are trying to introduce frontline diagnostic tools to recognise genetic causes of mental retardation which could not be diagnosed before.”

In young children, mental retardation can go unnoticed for many years, depriving their parents of the chance to organise the support their offspring may need to reach their full potential. And even if the condition is diagnosed at an early stage, its causes may not always be clear, leaving one of the families' most frequently asked questions unanswered.

Sometimes, there are just no straightforward explanations. Impaired brain development can be triggered by a range of circumstances affecting children before, during or after birth. Experts estimate that the origins are genetic in approximately one case out of two. They can be due to chromosome defects, such as the additional chromosome which translates to Down's syndrome, or they can be linked to more subtle variations in individual genes.

In the Cherish project, 11 partners from Europe and Central Asia have set out to shed more light on the genetic origins of mental retardation. Project coordinator Professor Giovanni Romeo at the University of Bologna in Italy explained: 'Diagnosis is difficult because mental retardation is very heterogeneous. So we are trying to introduce frontline diagnostic tools to recognise genetic causes of mental retardation which could not be diagnosed before.'

On the same page

All participating organisations are referral centres for mental retardation, and one of the first steps in their joint endeavour will be to develop a standardised approach to diagnostics drawing on top-flight expertise and cutting-edge technology.

Training plays a central role in this respect. 'We have a very strong tradition here in Bologna of advanced training in medical genetics,' Prof. Romeo noted, referring to the work of the European School of Genetic Medicine. The school operates under the guidance of the European Genetics Foundation, a project partner.

Genetic vs hereditary

Compiling and analysing data on well-defined cases represents another crucial step. The project partners are assembling a data set of at least 1 000 case histories which should enable them to study the epidemiology of mental retardation in the participating countries. Data collection is progressing well ahead of schedule, with 400 cases documented in the project's first year alone.

These data will also feed into the project's investigations on the nature and origin of the genetic causes of mental retardation. Many of the genes involved are known, but it is likely that many more remain to be identified. New insights in this area will extend the partners' scope to determine if the genetic factors underlying individual cases of mental retardation are specific to the affected individual, or if they are likely to be hereditary – precious information for families which want to be in possession of all the facts.

Dedicated to development

Europe's health research is not just for Europeans. Many projects involve international partners and focus on health challenges of global significance. What's more, a whole range of projects investigate health threats of particular relevance to other parts of the world.

Under the current Framework Programme, projects of this type are frequently set up as **Specific International Cooperation Actions (SICAs)**. The topics for such projects are identified with respect to the relevant world region or country, and all projects must involve at least two partners located in International Cooperation Partner Countries.

Many SICA projects are deployed in support of broader development goals, reflecting the EU's dedication to cooperation with low- or middle-income countries and its commitment to the Millennium Development Goals. Central themes, for the latest generation of projects, include neglected infectious diseases; child, maternal and reproductive health; and health systems.

http://cordis.europa.eu/fp7/health/international-cooperation_en.html

Cherish



Full name:	Improving diagnoses of mental retardation in children in Eastern Europe and Central Asia through genetic characterisation and bioinformatics/statistics
Type:	SICA collaborative project
Start date:	01/02/2009
Project coordination:	Alma Mater Studiorum Università di Bologna, U.O Genetica Medica, Italy
11 project partners from 9 countries:	Armenia, Cyprus, the Czech Republic, Estonia, Italy, Lithuania, Poland, Russia, Ukraine

<http://www.cherishproject.eu>



TOGETHER... FOR FASTER DRUG DEVELOPMENT

Breaking the vicious cycle

While affluence is no protection against disease, poverty greatly increases the risk of ill health. Malnutrition and hunger, insanitary living and working conditions and limited access to clean water, healthcare services or information accelerate the spread of disease. And disease, in turn, sustains poverty, adding to the plight of afflicted households when illness translates to a lack of income or crushing medical bills. This mechanism can send whole communities into a spiral of decline and perpetuate the poverty of nations.

The EU supports the development of drugs against major poverty-related diseases as part of its commitment to the Millennium Development Goals. Medication is, however, just one of the weapons health research is honing to support this combat. Other projects backed by the EU focus on better prevention methods, improved access to healthcare and dissemination of best practices.

HIV/AIDS, malaria and tuberculosis top the list of diseases that sustain poverty and in turn are sustained by it. Together, they account for millions of deaths every year and taint the lives of millions more. Better treatment options are needed urgently for those for whom prevention has failed, but the sheer scale of the task is such that individual stakeholders stand little chance of accomplishing it alone.

As part of Europe's contribution to this global challenge, a broad alliance was brought to life in 2003 in the form of the 'European and Developing Countries Clinical Trials Partnership' (EDCTP). The aim of this partnership is to accelerate the development or improvement of drugs, vaccines and microbicides against HIV/AIDS, malaria and tuberculosis. The main emphasis, in this drive, lies on phase II and III clinical trials as it is this stage that often proves to be a stumbling block for the development of new drugs. The geographical focus is on sub-Saharan Africa, the world's worst-affected region.

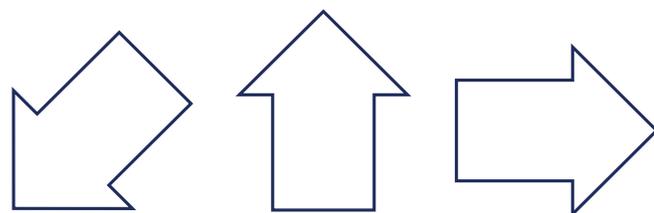
An unprecedented partnership

The EDCTP does not just aim for innovation in drug development; it is an innovative enterprise in itself. The type of cooperation on which it is built was the first of its kind under the Framework Programmes. It permits EU participation in the joint implementation of a research programme undertaken by the Member States, as part of a vast network of contributors. These include academia and the pharmaceutical industry as well as public administration.

This atypical arrangement presented the fledgling project with its first set of challenges. Successful project

management relies on sound methodology, but without the legacy of earlier endeavours of this nature to draw on, the project first had to define its own rules, processes and guidelines for implementation, governance and administration.

The partnership applies exacting standards and has also established mechanisms to validate its operations and its strategy through peer review, audits and an independent advisory structure, pioneering a new European funding mechanism in the process. Four other ventures have since been set up following this model.



Sponsoring large-scale clinical trials

The EDCTP is an autonomous entity which elaborates its own work programme and issues its own calls for proposals for the projects it intends to fund. To fuel this activity, it draws on a budget of EUR 200 million made available by the EU, matched by the same amount to be provided jointly by the European countries involved in the partnership. Private partners (industry, foundations, other public private partnerships etc.) contribute further resources by co-financing individual projects.

While it is still in its early days, first results from EDCTP-funded projects have begun to roll in. Key accomplishments to date include the creation, in Central Africa, of the first African Network of Excellence for clinical trials, the setting up of new

national ethics committees in many African countries, intensified policy dialogue with national governments in order to reinforce research agendas – and a new antiretroviral formulation for HIV-infected children. This new formulation is specifically designed for easy administration in resource-constrained settings.

Building on this promising start, the EDCTP is exploring options to extend its scope. A broader remit could encompass additional steps in the drug development process, by including stage I and stage IV clinical trials; other illnesses, such as neglected infectious diseases; and other parts of the world, notably Asia and South America. Having gathered momentum over the first few years of its operation, this unusual alliance is well positioned to foster the broad consensus among its many decision makers, which it will need to conquer new ground.

EDCTP



Full name:	European and Developing Countries Clinical Trials Partnership
Type:	Partnership funded under Art. 185 (ex-169) of the EU Treaty
Start date:	2003
Contact information:	EDCTP Secretariat The Hague P.O. Box 93015 NL-2509 AA The Hague Tel. +31 (0)70 344 08 80 Fax +31 (0)70 344 08 99 EDCTP Secretariat Cape Town P.O. Box 19070 Tygerberg 7505 South Africa Tel. +27 21 938 0819 Fax +27 21 938 0569
Project partners include:	14 EU Member States (the launch of the partnership predates the two latest rounds of EU enlargement), Norway, Switzerland and 47 sub-Saharan countries

<http://www.edctp.org>

An open invitation

Calls for health research proposals issued under the current research Framework Programme, are potentially open to any research institute, in any country. Beyond this general rule, additional provisions apply for various **categories of countries**.

These include associated countries (ACs), which have signed science and technology association agreements with the EU and contribute to the budget of the Framework Programme.

With regard to the funding of non-EU/non-AC participants in the projects, those from low- and middle-income countries are eligible for funding. But those from high-income countries are usually expected to cover their own expenses. An exception is made for US-based entities, which can receive funding in recognition of the fact that US National Institutes of Health (NIH) programmes are open to European researchers.

http://cordis.europa.eu/fp7/who_en.html

**In 2007,
33 million people were
living with HIV/AIDS .**

**Malaria claims a million
lives every year.**

**1.7 million deaths in
2006 were caused by
tuberculosis.**

Source: UN Department of Public Information, Millennium Development Goal factsheet, *Goal 6: Combat HIV/ Aids, malaria and other diseases*, DPI/2517 L, September 2008.





The complexities of co-infection

When one disease increases vulnerability to others, patients may face the grim prospect of dealing not just with one, but with several life-threatening conditions. Tuberculosis (TB), for example, is the leading cause of death for HIV/AIDS patients. Worldwide, 11 million people are thought to be infected with both.

The deadly duo is steadily gaining ground but, so far, efforts to master this twin epidemic have tended to focus on the individual diseases viewed in isolation and in specific regions. An integrated, global response might turn out to be far more effective.

The EUCCO-NET project is encouraging greater coordination between HIV/AIDS and TB management programmes and the research underpinning them. Starting from an analysis of the state-of-the-art in partner countries, the

EUCCO-NET consortium is aiming to identify global research priorities, and to boost the cooperation between leading HIV and TB experts in the EU and in the world's worst-affected areas: Africa, India, Latin America and Russia.

EUCCO-Net



Full name:	European network for global cooperation in the field of AIDS and TB
Type:	SICA
Start date:	01/11/2008
Project coordination:	Institute of Virology University of the Saarland Homburg/Saar Germany
15 project partners from 9 countries:	Argentina, Belgium, Brazil, Colombia, Germany, India, Italy, Russia, South Africa

<http://www.euco-net.eu>

Aiming for the head of the Hydra

Tackle one strain of an infectious disease and you may well find that a new one has formed to fill the gap. *Mycobacterium tuberculosis*, the bacterium which causes TB, is a case in point. Effective drugs do exist, but they were formulated in response to older strains. New, increasingly resistant strains have emerged in recent years.

The NATT project is identifying novel targets to combat the disease. Instead of focusing on the actual pathogen, it proposes to target both the bacterial machinery and the host cell machinery simultaneously in order to inhibit infection at several stages.

Compared to current treatment options, such an approach could be far more effective, faster and patient-friendly. This would eliminate several of the reasons why many sufferers fail to

actually take their medication: current treatment regimes tend to be lengthy and complex, and can also trigger significant side effects. Faster treatment and greater compliance would, in turn, help preempt the emergence of new resistant strains, leaving the Hydra little time to grow new heads.

NATT



Full name:	New approaches to target tuberculosis
Type:	SICA
Start date:	01/10/2008
Project coordination:	Laboratory for Medicinal Chemistry Katholieke Universiteit Leuven Belgium
8 project partners from 5 countries:	Belgium, Germany, India, Sweden, United Kingdom

<http://www.natt-tbc.com>

Beyond BCG

According to WHO estimates, one third of the world's population is infected with the tuberculosis bacillus. Carriers will not necessarily develop the disease; in fact, unless they are also HIV-infected, no more than 1 in 10 are likely to do so. But this still places a significant segment of the world's population potentially at risk.

Vaccination, typically through Bacillus Calmette-Gérin (BCG) inoculation, represents the first line of defence, but the efficacy of this vaccine varies considerably depending on a range of factors, such as regional variation in the predominant strains of *Mycobacterium tuberculosis*. It is further limited by the emergence of increasingly resistant strains.

The TBAdapt project has set out to analyse the interactions between TB management programmes and the genetic variability of *M. tuberculosis*. A better understanding of the mechanisms, by which the bacterium may be adapting to evade current efforts to control it, should provide valuable input for the development of a new vaccine.

TBADAPT



Full name: Effect of genetic variation in *Mycobacterium tuberculosis* on vaccine escape and the acquisition of drug resistance

Type: Specific Targeted Research Project (STREP)

Start date: 01/12/2006

Project coordination: Mycobacteria Reference Unit
Centre for infectious Disease Control
National Institute of Public Health and the Environment (RIVM)
Bilthoven
the Netherlands

10 project partners from 7 countries: Brazil, France, Mexico, the Netherlands, Norway, South Africa, Vietnam

http://www.tuberculosis.rivm.nl/TBadapt_website/

CREATING MOMENTUM

Sleeping sickness, schistosomiasis, leishmaniasis ... just three names randomly picked from the long list of neglected infectious diseases (NIDs) that blight the lives of a billion people worldwide. The needs are great, but they have not elicited a proportionate response in terms of drug development. EU funding is helping to buck this trend.

One such example is by funding research into leishmaniasis. This disease, which is caused by *Leishmania* parasites transmitted by various species of sandfly, takes two main forms. Cutaneous leishmaniasis causes severe skin lesions and can leave sufferers severely disfigured. Visceral leishmaniasis, if untreated, is fatal in the vast majority of cases – but the treatments available today are lengthy, expensive and complex. They can also produce heavy side effects. EU-funded projects around the world are formulating new treatments, improving diagnostic tools, countering emerging resistance against current drugs and developing vaccines.

A fresh look at leishmaniasis



Scientific progress over the past decades has opened up new areas of investigation, such as genomics and proteomics, the study of the proteins produced by a specific organism. The Leishdrug project, a consortium of 16 partners in 9 countries representing 4 continents, is determined to put these advances to good use.

Drawing on state-of-the-art bio-imaging, *in silico* (computer-modelled) biology, peptide chemistry and structure-based drug design, the project partners aim to advance understanding of the *Leishmania* species involved in visceral leishmaniasis and to devise better ways of tackling them.

LEISHDRUG



Full name: Targeting the *Leishmania* kinome for the development of novel anti-parasitic strategies

Project coordination: Institut Pasteur,
Paris, France

16 project partners from 9 countries: France, Germany, Israel, Italy, Spain, South Korea, Tunisia, United Kingdom, Uruguay

<http://www.leishrisk.net>



© LeishDNAVax

SLEEPING DIAGNOSIS

Handle with care

The word 'kala-azar', another name for visceral leishmaniasis, originates from the Indian subcontinent, one of the worst-affected regions on the globe. Four research organisations from this area have joined forces with partners in the EU to monitor and safeguard the effectiveness of the few drugs currently available to combat the disease.

Rationalising the use of these drugs will be central to this effort, both to maximise treatment efficiency and preempt the emergence of resistant strains. Key considerations include the availability of quality drugs, the coherence and adequacy of prescriptions, treatment compliance and effectiveness monitoring. To achieve its aims, the Kaladrug-R project will develop

monitoring tools and innovative approaches to resistance testing, collect and document clinical samples and conduct dissemination activities notably to support control programmes.

Kaladrug-R



Full name:	New tools for monitoring drug resistance and treatment response in visceral leishmaniasis in the Indian subcontinent
Project coordination:	Prins Leopold Instituut voor Tropische Geneeskunde, Antwerp, Belgium
10 project partners from 5 countries:	Belgium, Germany, India, Nepal, United Kingdom
http://www.leishrisk.net	

'The main problem with current diagnostic tools is equipment.' Sleeping sickness expert Professor Stefan Magez speaks from experience. 'Out in the field, the only thing you can count on is your 12 volt car battery. So if you want to have good field diagnostics, you need something that is very simple.'

You also want something reliable and affordable to ensure that this disease, which haunts vast stretches of rural Africa, no longer goes widely undetected in the early stages. The Nanotryp project, an international research team of African and European experts headed up by Prof. Magez, is striving to develop such tools.

Sleeping sickness is the human form of African trypanosomiasis, a parasitic infection that also affects animals. It is caused by *Trypanosoma* parasites transmitted by tsetse flies in large expanses of sub-Saharan Africa, where 60 million people are potentially at risk. If untreated, it is inevitably fatal. If treated late, some of the damage may be irreversible and the treatment itself can be lethal.

Nipped in the bud

Unfortunately, at the moment, it is not possible to vaccinate against visceral leishmaniasis, but this may soon change. The LeishDNAVax project is conducting promising research into immunisation.

The project partners are aiming to develop a safe and effective DNA vaccine. Where traditional vaccines use either the microorganisms that cause a particular disease or fragments of these microorganisms to elicit an immune response, DNA vaccines are based on strands of DNA. These strands cause the host organism to generate proteins that are recognised as pathogenic, producing the required antibody response.

DNA vaccination represents a very promising line of research, but at this stage the technique is still in its infancy. One of the key advantages of the

proposed leishmaniasis vaccine lies in the fact that it would also have therapeutic applications: it could be used not just to prevent, but also to treat or cure the disease, bringing new hope to afflicted communities worldwide.

LeishDNAVax



Full name:	Development of a DNA vaccine for visceral leishmaniasis
Project coordination:	Project management: Department of Infectious and Tropical Diseases, London School of Hygiene and Tropical Medicine, United Kingdom Scientific coordination: Drugs for Neglected Diseases Initiative, Geneva, Switzerland
9 project partners from 6 countries:	Germany, India, Israel, Switzerland, Tunisia, United Kingdom
http://www.leishdnavax.org	



SICKNESS: TICS ON THE FLY

Masters of disguise

As Prof. Magez explained, early detection could save lives and curb the crippling cost of trypanosomiasis damage to livestock, but currently this is difficult. In the early stages of infection, there may be just a few of these minute organisms present, and complex, resource-hungry equipment is needed to find them.

To defeat the invaded immune system, these parasites change as they replicate. Every new generation presents random variations on its surface, which the antibodies formed by the immune system in response to earlier generations cannot detect. The result is a war of attrition. The host's defences interpret each new wave as a fresh infection, but cannot deploy a fully effective reaction fast enough.

Some things never change

But while the surface may vary, some of its structural components remain unchanged – a weakness which Nanotryp intends to exploit with the help of nanotechnology. The project is engineering fragments of antibodies that will bind to these stable molecular structures.

Tools based on these 'nanobodies' could enable field diagnosticians to screen people and livestock. They will include fluorescent tags for fast microscopy detection, as well as a dipstick and a magnetic bead application designed to extract trypanosomes from blood samples. The beads are coated with nanobodies that latch on to the targeted parasites; mixed into a sample, they can later be pulled out with their cargo of parasites using a magnetic pen.

Picking off protozoa, one by one

This remarkable accuracy could also revolutionise treatment. 'The problem with this disease,' said Prof. Magez, 'is that you have to kill every single last parasite to treat a patient.' In advanced stages, highly toxic drugs are needed to achieve this. Targeted delivery of the drug, through nanobodies that seek out the parasites but leave other cells unaffected, could help slash the dosage and side effects.

Welcome news indeed – but, as Prof. Magez noted, 'the vast reservoir of the disease is not in humans. It's in cattle, and it's in wild animals. So unless you tackle both at the same time, you will have an eternal problem.'

To drive this message home, the partners are also conducting awareness-raising activities. From fundamental research to support for the commercialisation of diagnostic tools, this consortium of six partners on two continents mobilises an impressive range of skills in order to translate a promising idea to a robust product. A powerful alliance, which may soon turn the tables on *Trypanosoma*.

Nanotryp



Full name: Exploiting nanobodies in development of new diagnostic tools and treatment methods for trypanosomiasis

Type: SICA

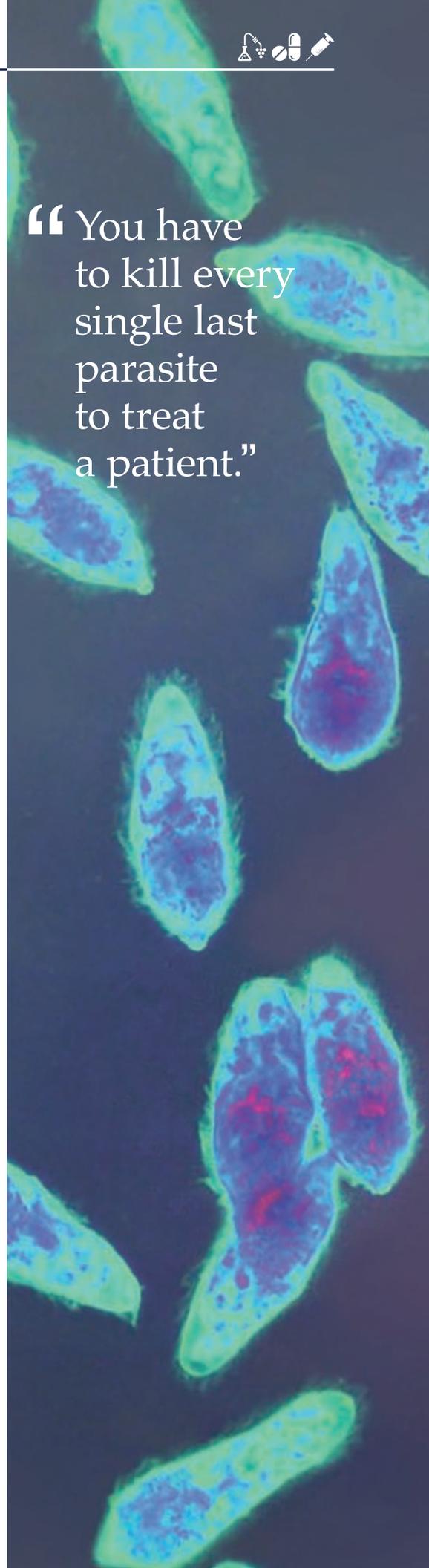
Start date: 01/01/2009

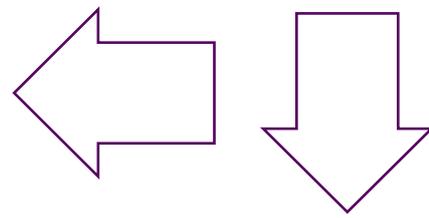
Project coordination: Laboratory for Cellular and Molecular Immunology
Department of Molecular and Cellular Interactions
Flanders Institute for Biotechnology
Gent, Belgium

6 partners from 5 countries: Belgium, Kenya, Mozambique, Spain, Switzerland

<http://www.nanotryp.org>

“ You have to kill every single last parasite to treat a patient.”





Dealing with dengue

A single encounter with a bloodthirsty *Aedes* mosquito is enough: if it carries one of the four viruses known to cause dengue, the first symptoms may appear after a week or so. Dengue is a severe flu-like disease that is rapidly gaining ground in the tropics and subtropics.

Dengue fever can escalate into dengue haemorrhagic fever (DHF), a potentially fatal complication that constitutes one of the main causes of child mortality in several Asian countries. Appropriate

medical care saves the lives of many DHF patients, but to provide this assistance, practitioners must be able to detect the cases that are likely to develop into DHF as early as possible, and know how to respond.

The DENCO project has developed an evidence-based classification and detailed case management guidelines, investigated genetic factors of virulence, and tested new ways of keeping the mosquitoes at bay. The project's outcomes have fed into the development of the WHO's global dengue guidelines.

DENCO



Full name:	Towards successful dengue control
Project coordination:	Administrative coordination: Section Clinical Tropical Medicine, University Hospital of Heidelberg, Germany Scientific coordination: Special Program for Research and Training, World Health Organization, Switzerland
9 project partners from 9 countries:	Belgium, Cuba, Germany, Philippines, Switzerland (WHO), Thailand, United Kingdom, Venezuela, Vietnam
http://www.klinikum.uni-heidelberg.de/index.php?id=113292&L=en	

VHF: A portable identity parade

Outbreaks of viral haemorrhagic fever (VHF) are becoming increasingly frequent in Africa. To manage them effectively, health practitioners need to identify the underlying virus quickly and accurately. Ebola? Marburg? Crimean-Congo? Lassa? Rift valley fever, yellow fever or dengue? Or is it maybe just a case of the common flu? In the early stages of all these diseases, it is hard to tell.

Precise identification has, so far, relied on sophisticated medical equipment rarely available at the point of care, causing delays in diagnoses and complicating containment and mitigation efforts. The partners

in the VHF Diagnostics project set out to streamline this process by developing easy-to-use detection tools for healthcare workers, bush hospitals and specialised mobile outbreak investigation teams.

VHF Diagnostics



Full name:	Development of rapid field diagnostics for identification, control and management of haemorrhagic fever outbreaks
Project coordination:	Department of Virology, University Medical Centre Göttingen, Germany
8 project partners from 7 countries:	Burkina Faso, France, Germany, Guinea, Mali, Senegal, Sweden
http://www.vhf-diagnostics.eu	

Bye bye bilharzia?

A broad alliance of research organisations in Europe and sub-Saharan Africa is taking a fresh look at the control and management of schistosomiasis, the tropical disease also known as bilharzia. A coordinated response to this disease, which is caused by worms and contracted through contact with infected freshwater, is expected to boost the outcomes of control efforts at national, regional and local levels.

The project is developing innovative molecular tools for the characterisation of the parasites and the various types of snail which serve as intermediate hosts,

elaborating spatial models for disease risk maps and prediction, promoting and evaluating local prevention and control interventions and disseminating knowledge.

Contrast



Full name:	A multidisciplinary alliance to optimise schistosomiasis control and transmission surveillance in sub-Saharan Africa
Project coordination:	Centre for Health, Research and Development, Faculty of Life Sciences, University of Copenhagen, Denmark
13 project partners from 11 countries:	Belgium, Cameroon, Denmark, Kenya, Niger, Senegal, Switzerland, Tanzania, Uganda, United Kingdom, Zambia
http://www.eu-contrast.eu	



Hounding out rabies

To protect mankind from rabies, start by protecting man's best friend: infected dogs may not be the only potential carriers, but they are far likelier to transmit the disease to humans than most. The other species that is frequently implicated in cases of human infection is the bat.

The outcomes of the Rabmedcontrol project provide vital input for the fight against rabies in several North African countries where the disease

remains endemic. Based on a comprehensive analysis of rabies epidemiology in the region, the project has developed vaccination strategies and identified the keys to successful rabies management in the participating countries.

These results represent a major step forward for public health in the areas concerned, and may also help preempt spillover to Europe, where the disease is virtually extinct in non-flying species.

Rabmedcontrol



Full name: Identifying ecological and epidemiological key factors for rabies dynamics and control in North Africa and implications for rabies status in South West Europe

Project coordination: Administrative coordination: Institut Pasteur, Paris, France
Scientific coordination: Institut Pasteur, Tunis, Tunisia

8 project partners from 7 countries: Algeria, Egypt, France, Italy, Morocco, Spain, Tunisia

<http://www.rabmedcontrol.org>

ARE YOU'RE

Influenza statistics don't make for comfortable reading. According to WHO estimates, seasonal flu epidemics claim up to 500 000 lives every year. This is an alarming figure in its own right, but it would be even higher if our immune system and healthcare services had not developed ways of coping with common strains of the virus.

But the virus changes constantly and many strains spread like wildfire: seasonal epidemics are thought to cause three to five million severe cases annually worldwide. How many more lives would be lost if a new strain were to overwhelm our defences?

This is not a rhetorical question; it is a call to action. It is also the key consideration driving the work of the AsiaFluCap project, an international team of experts analysing public health systems and ways to reinforce them.

Preparing for the next flu pandemic

Project coordinator Professor Richard Coker clarified the issue: 'In the event of pandemic influenza, do countries have sufficient health service resources to respond? Where are those resources located? And if they don't have sufficient resources, what are the public health consequences of this lack of resources in terms of number of lives lost?' The aim of this research effort, he added, is to enable countries to 'identify where their resource gaps are and where they might want to invest to fill those gaps.'

Prof. Coker and his team are focusing on public health systems in southeast Asia, a region where bird flu is endemic in poultry and which would be among the first to be affected if a highly pathogenic form transmissible among humans were to emerge. AsiaFluCap is one of 40 influenza research projects that the EU has funded since 2001, for a total

budget of EUR 100 million. It involves partners from three EU Member States cooperating with colleagues in Indonesia, Taiwan, Thailand and Vietnam. Complementary funding from the Rockefeller Foundation extends the geographical scope of the project to Cambodia and Laos.

The AsiaFluCap experts have drawn up a list of 57 key resources – infrastructure, equipment and staff – needed to respond to a pandemic, taken stock of these resources in the participating countries and translated this information to a series of maps. If the situation were to arise, this mapping exercise will complete the data supplied by national healthcare systems to provide decision makers with a vital overview of the resources at their disposal. Prof. Coker reported that it has already informed various national and international responses to the 2009 H1N1 pandemic.

FP7 > Cooperation > Health

The projects featured in this publication were funded by the EU's Framework Programmes for Research and Technological Development and Demonstration activities. FP7, the current Framework Programme, was launched in 2007 and will issue the last calls for proposals in 2013.

The priorities set out for FP7 reflect the EU's vision of a knowledge-driven future, where research and innovation have a prominent role. FP7 was designed to boost Europe's ability to develop the innovative products and services needed to compete on the global marketplace. EU-funded research also feeds into the formulation of policy by informing decision makers at local, regional, national and EU levels.

'We need to create a setting that will attract the world's most brilliant minds and support businesses investing in the development of new knowledge-based products and services. Both are prerequisites for the success of Europe's strategy for growth and jobs,' says Máire Geoghegan-Quinn, Commissioner for Research, Innovation and Science.

Under FP7, Health is a major theme of the specific programme on **Cooperation** that supports all types of research activities carried out by different research bodies from industry and academia in transnational cooperation. Scientists typically work in universities, research centres, hospitals, companies and associations, collaborating

with ambitious objectives that would be impossible to achieve for a single group or a single country,' Ruxandra Draghia-Akli, Director for Health at the Directorate-General for Health, explains. 'As global health challenges require actions at the level of the global research community, the scope for international cooperation has also been extended to improve human health.'

Major objectives for **the Health theme** include health biotechnology, translational research designed to facilitate the application of new research results in standard medical practice, and the optimisation of healthcare delivery.

<http://ec.europa.eu/research/health>

READY?

Booster shots for public health systems

Within AsiaFluCap, this information is used to establish how a pandemic is likely to unfold, identify gaps in the availability of the resources needed to mount an effective response and pinpoint the investments that would maximise the outcome of containment and mitigation efforts. The team, said Prof. Coker, aims to produce quantifiable estimates of the number of lives that could be saved by cash injections in particular areas, which will clearly indicate where investments should be going in order to protect the population.

The project may focus on pandemic influenza, but it is producing valuable methodologies and information for research and decision-making processes in other areas. 'The benefit of knowing where the resources are and how they might be mobilised to greatest effect,' noted Prof. Coker, 'is useful for future pandemics, but also for other emerging infectious diseases, for example something like SARS.'

And, of course, the project's systematic approach could also enable stakeholders and donor organisations in other parts of the world to visualise the implications of their investment decisions. How will these advances shape the way policy is made? The AsiaFluCap team is keen to find out.

“Do countries have sufficient health service resources to respond?”



AsiaFluCap

Full name: Health system analysis to support capacity development to respond to pandemic influenza in Asia

Type: SICA

Start date: 01/05/2008

Project coordination: London School of Hygiene and Tropical Medicine
Keppel Street
London
United Kingdom

7 project partners from 7 countries: Germany, Indonesia, the Netherlands, Taiwan, Thailand, United Kingdom, Vietnam

<http://www.asiaflucap.org>

A massive cash injection

The EU has set aside a budget of over **EUR 6 billion** to fund outstanding research under the Health theme of the Cooperation programme throughout the seven-year duration of FP7.

How much of this budget will be spent on international cooperation? There are no specific budget allocations or expectations at this stage. International partnership is mandatory for some projects, but the full extent of such cooperation throughout FP7 is expected to exceed these minimum requirements. The total volume will depend on the composition of the consortia that submit successful project proposals.

Prospective consortia will benefit from the fact that the EU dropped all remaining restrictions on geographical eligibility under FP7. The EU encourages cooperation with partners around the world, especially in cases where specific research topics obviously call for it. FP7 is therefore set to take international cooperation in EU-funded health research to a new level.

OVERCOMING

HERE'S YOUR CHANCE

to take a closer look at your personal body clock!

Check out the chronotype analyser on

<http://www.euclock.eu>

and make your mark on chronobiology.

“EUclock investigates the clock in the real world.”



SOCIAL JET LAG

Spend half an hour on the phone with Till Roenneberg, the coordinator of EUclock, and the urge to test-drive the project's brand new body clock monitoring device may become irresistible. The Clockwatcher, a wearable contraption involving a data acquisition module and various sensors, records a range of physiological parameters as you tackle a typical day. A series of algorithms interprets this data to tell the team what your body thinks you should have been doing at any given time.

Why bother? Because when it comes to dividing the day into windows for rest, work and play, your body has a mind of its own. And, as anybody who has ever experienced jet lag can confirm, getting your body to adjust to changing circumstances can be a struggle. Incompatibility, or desynchronisation, between people's internal clocks and the demands of their hectic schedule increases the risk of mistakes and accidents, and can affect their health in the long run.

The partners in the EUclock project study the body clock and the external cues to which it responds, and in so doing are producing new knowledge on our daily, or circadian, rhythms which will help to mitigate the risks and the consequences of desynchronisation.

Chronobiology picks up the pace

The Clockwatcher reflects EUclock's commitment to realistic conditions in chronobiology, the science of biological temporal rhythms. With 30 partners across the EU, Russia and Switzerland, with complementary expertise ranging from biochemistry to lighting technology, 'EUclock investigates the clock in the real world,' Prof. Roenneberg stated, adding that earlier experiments had generally been carried out in strictly controlled laboratory conditions. For all their merits, these experiments were unable to replicate the natural evolution of the external cues, such as variations in light and temperature, that stimulate, or entrain, our body clocks.

The Clockwatcher will notably enable the EUclock partners to fine tune their understanding of the implications of modern work patterns. As Prof. Roenneberg explained, 'Shift work, especially rotating shift work, really messes up the circadian clock,' forcing many to live permanently out of step with themselves and with society. The degree of disruption this 'social jet lag' will cause depends on the circumstances, but also on the workers' individual body clock settings – their chronotype.

A question of timing

This is where Prof. Roenneberg sees one of many key areas for future applications: 'We needed EUclock to prepare all the measurement devices and the know-how about entrainment so that we can go out into the real world and say okay, here we have a company that has to cover a 24-hour day, and here we have a staff of 1 000 workers – how can we advise them to plan the shifts to minimise the health deficits?'

The project is currently in its final year and the partners are looking for their next challenge, where they hope to apply this new know-how. 'It's a win-win-win proposition,' as Prof. Roenneberg concluded. 'The individual worker will benefit. The industry will benefit, because of higher productivity and happier staff. And society will benefit as the burden on healthcare systems is reduced.'

From policy to projects

The European Union's Research Framework Programme defines the priorities and objectives of EU-funded research throughout a given funding period. As a next step, annual work programmes outline how the Framework Programme and its sub-programmes are to be implemented.

For FP7 this approach translates into several work programmes, applicable to the various specific sub-programmes and themes. These work programmes list the priority areas for EU-funding and break these down into specific research topics to be addressed by individual projects.

On the basis of these work programmes, successive waves of calls for proposals are issued, inviting consortia to submit proposals to be evaluated by independent experts from all over the world. Proposals have to comply with exacting standards and undergo a peer review evaluation and selection process. Only excellent research proposals will be selected for funding.

http://cordis.europa.eu/fp7/find-doc_en.html

EUclock

Full name:	Entrainment of the circadian clock
Type:	Integrated project
Start date:	01/01/2006
Project coordination:	Ludwig-Maximilians-Universität München Munich, Germany
30 project partners from 10 countries:	the Czech Republic, Estonia, France, Germany, Hungary, Italy, the Netherlands, Russia, Switzerland, United Kingdom

<http://www.euclock.eu>

CRACKING THE CODE

Deciphering the genomes, or genetic codes, of organisms and understanding the function of the genes that compose them represents a massive challenge – and a fabulous opportunity to find out how our programming influences our health and wellbeing. It is also a task of such magnitude that it cannot be handled by a single laboratory, research organisation or even country acting in isolation. The EU supports large-scale international research efforts in this area, which will lay the groundwork for powerful new predictive, diagnostic and therapeutic applications.

AN INVENTORY OF MALIGNANCY

What, exactly, are the links between cancer and DNA? We know that all cancers are linked to mutations, some of which may reflect a genetic predisposition, whereas some are acquired through exposure to carcinogens. We also know that some changes drive the onset of the disease, whereas others arise as it unfolds.

Beyond that, much remains to be learned about the distinctive features of these abnormalities and the underlying mutagenic processes. Until recently, it was not possible to analyse these mutations systematically, on a large scale, for a broad range of cancer types and a significant range of tumours.

With the help of new sequencing technology, the remaining technical obstacles to such a comprehensive exploration should soon be overcome. A global alliance of funding agencies and research organisations is determined to put these technological advances to good use.

“Unless progress is made in understanding and controlling cancer, the world will be seeing 17.5 million deaths and 27 million new cases annually by 2050.”

Cancer cryptography

The International Cancer Genome Consortium (ICGC, <http://www.icgc.org>) has set itself the ambitious task of analysing 500 tumours for 50 (sub)types of cancer – a total of 25 000 tumour characterisations. To tackle this huge remit, the ICGC is mobilising skills and funds volunteered by a rapidly growing number of partners around the world.

ICGC-related projects have been launched by several research funding agencies, such as the European Commission, France's Institut National du Cancer, Genome Canada, the German Federal Ministry of Education and Research, the Government of Western Australia, the Indian Ministry of Science and Technology, the National Institutes of Health in the United States, the Spanish Ministry of Science and Innovation, and the United Kingdom's Wellcome Trust.

ICGC members undertake their own projects, but subscribe to a joint objective, methodology and code of practice. The catalogues of genomic abnormalities resulting from their work will be made available to the entire research community, giving scientists around the world a head start in their efforts to develop better predictive, diagnostic and therapeutic tools and to pinpoint the therapies to which individual patients are most likely to respond.

Crucial input from the EU

Two EU-funded projects launched in April 2010 are contributing to the work of the ICGC. The BASIS project focuses on breast cancer, whereas the CAGEKID project will be dedicated to renal cancer, a

disease for which Europe reports the highest incidence rates worldwide.

'This is the latest step in the EU's effort to tackle cancer under the Seventh Framework Programme for Research and a perfect example of the potential of EU research policy to save and improve lives,' commented Máire Geoghegan-Quinn, the EU Commissioner for Research, Innovation and Science. 'Unless progress is made in understanding and controlling cancer, the world will be seeing 17.5 million deaths and 27 million new cases annually by 2050. Cutting those numbers must be an absolute priority for the EU and the international partners we are working with.'

BASIS



Full name:	Breast cancer somatic genetics study
Type:	Collaborative Project (Large-scale integrating project)
Start date:	01/07/2010
Project coordination:	Wellcome Trust Sanger Institute, United Kingdom
13 project partners from 8 countries:	Belgium, France, Germany, the Netherlands, Norway, Sweden, United Kingdom, United States

<http://www.basisproject.eu>

CAGEKID



Full name:	Cancer genomics of the kidney
Type:	Collaborative Project (Large-scale integrating project)
Start date:	01/03/2010
Project coordination:	Fondation Jean Dausset-CEPH, France
14 project partners from 7 countries:	The Czech Republic, France, Germany, Latvia, Russia, Sweden, United Kingdom

<http://www.cng.fr/cagekid>



THE INTERNATIONAL MOUSE ARCHIVE

Genetically speaking, there is little difference between a mouse and a human: nearly 99% of our protein-coding genes are identical. While the remaining percent, in combination with gene regulation, spells out striking differences, the overlap between the two genomes creates scope to study the functions of individual genes in a living organism and their possible role in human health.

To do so, researchers investigate genetic mechanisms in mice where individual genes have been inactivated. Obtaining or creating these so-called 'knockout' mice constitutes a crucial first step, which also used to be either a time-consuming or a costly one. A reliable, affordable source of such genetic material was bound to revolutionise the field by freeing up time and resources, but with thousands of genes to process, producing knockouts for the complete mouse genome represents a challenge of epic proportions.

A knockout alliance

In March 2007, the European Commission, the US National Institutes of Health (NIH) and Genome Canada set up a joint research initiative to tackle this remit. The main objectives of the International Knockout Mouse Consortium (IKMC) are to coordinate the conditional inactivation of 20 000 mouse genes, to establish a library of the corresponding mutant embryonic stem (ES) cells

and to produce mutant mouse lines for 920 genes assumed to play a key role in human health.

Professor Wolfgang Wurst, President of the IKMC, explained that the main benefits to the research community lie in speed and availability. 'In the 20 years that the knockout technology has been around,' he said, 'the entire research community has generated between 4 000 and 5 000 mouse mutants worldwide.' Using cutting-edge, high-throughput technology, the IKMC is planning to generate five times as many in a mere six years to support promising research into the genetic origins of killer diseases such as cancer.

With its central database and repositories, the IKMC is also preempting further duplication of effort and ensuring availability to the wider research community. Without this resource, individual mutations took about a year to generate in the average lab, said Prof. Wurst, and were rarely shared with other research organisations. The IKMC is making all mutations available for a small handling fee.

Put your money where your mouse is

The IKMC's work is taken forward by projects funded separately by the partners. These include the European Conditional Mouse Mutagenesis Program (EUComm), the Knockout Mouse Project (KOMP) and the Texas A&M Institute for Genomic Medicine

(TIGM) in the United States, and the North American Conditional Mouse Mutagenesis Project (NorCOMM) in Canada. Closer ties with the Asian Mouse Mutagenesis Resource Association (AMMRA) may also be established in the near future.

Through EUComm, a team of 9 partners in 4 Member States, the EU contributes EUR 13 million to the total budget of EUR 56.6 million. Thinking back to the early days of the IKMC, Prof. Wurst notes that Europe was a driving force behind its creation: 'We had this vision that only a worldwide effort can and should provide this resource to really enhance functional genomics.' The IKMC's remit may focus on the murine system, but the tools and technologies it will deliver will enhance the whole field of functional genomics.

IKMC



Full name:	International Knockout Mouse Consortium
Type:	Programme-level cooperation
Start date:	15/03/2007
Contact information:	For the EUComm project: Helmholtz Zentrum München Institute of Developmental Genetics Neuherberg, Germany
In cooperation with partners in 6 countries:	Canada, Germany, Italy, France, United Kingdom, United States

<http://www.knockoutmouse.org>

<http://www.eucomm.org>

The hole in the virtual skirting board

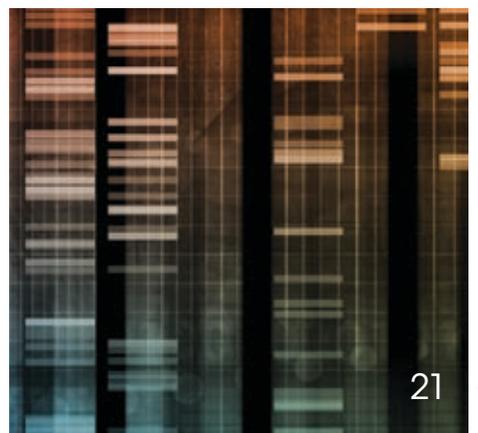
The IKMC projects are generating vast amounts of data and resources, and a single point of entry was needed to enable the wider research community access to this material. A data coordination centre for mouse genetics resources was set up in early 2009 with the aim of creating such a portal.

I-DCC



Full name:	International Data Coordination Centre
Project coordination:	Genome Research Ltd., London, United Kingdom
7 partners from 6 countries:	Canada, Germany, Greece, Italy, United Kingdom, United States

<http://www.i-dcc.org>



TEEMING WITH LIFE

If you were to search for unfamiliar life forms, where would you start? Many of us would probably look to the stars. Others might delve into the rich diversity at the centre of our personal universes. The human body is home to millions of microorganisms, including myriad bacterial species that have not yet been fully explored.

The MetaHIT project, a consortium of 15 partners in the EU and China, is searching for links between bacteria in the gut and two pathologies: obesity and inflammatory bowel disease (IBD). Project coordinator Dr Dusko Ehrlich explained that 'the bacteria that people have in their guts can represent something like 2 kg of mass, which is more than your brain or mine.' However, the composition of this microbial colony, or microbiota, which Dr Ehrlich describes as an organ in its own right, varies from one person to another.

“We operate mostly by bacterial genes, if you look at the numbers.”

The inside story

Working from a cohort of 124 Europeans, MetaHIT has compiled a catalogue of 3.3 million different bacterial genes – '150 times more than the genes coded by our own genomes,' as Dr Ehrlich noted. 'Every one of us carries on average about half a million of these genes, so we operate mostly by bacterial genes, if you look at the numbers.'

MetaHIT has developed cutting-edge tools and high-throughput technologies building on this information to determine which bacterial species combine in individual microbiota, and in what quantities. These advances are enabling the project to study the variation between lean and obese individuals on the one hand, and healthy subjects and IBD sufferers on the other. Where a link between specific genes and the targeted pathologies seems likely, MetaHIT also studies the function of these genes and the effects of their products.

Ultimately, these insights may pave the way for follow-on projects developing prognostic and diagnostic tools, or even applications optimising the composition of gut microbiota to prevent or treat disease. The participation of industrial project partners and the project's energetic approach to dissemination should ensure that MetaHIT's findings are not left to gather dust.

Gut genomics goes global

Surveys of gut bacterial genes conducted in Japan and the US have revealed up to 85% overlap with MetaHIT's gene catalogue, said Dr Ehrlich. 'But in order to generalise,' he added, 'we need access to populations from all continents and different geographical niches.'

MetaHIT's involvement in the International Human Microbiome Consortium (IHMC) provides opportunities to acquire these data and develop synergies with complementary research efforts. Founded in 2008 by the US National Institutes of Health and the European Commission, the IHMC has since grown into a truly global endeavour.

By joining the IHMC, partner organisations on five continents have agreed to release data and resources freely and openly and to coordinate their research plans in a joint investigation of the role of the human microbiome in human health. The IHMC is planning to take this effort another step ahead through shared methodologies and a web-based platform for dissemination and outreach activities.

MetaHIT



Full name:	Metagenomics of the Human Intestinal Tract
Type:	Collaborative project (Large-scale integrating project)
Start date:	01/01/2008
Project coordination:	Institut National de la Recherche Agronomique (INRA) Paris France
15 project partners from 8 countries:	China, Denmark, France, Germany, Italy, the Netherlands, Spain, United Kingdom

<http://www.metahit.eu>

<http://www.human-microbiome.org>



STRONG MEDICINE

New drugs, safer drugs, more effective drugs – top-flight research teams in the EU and beyond are investigating the scope to upgrade the content of our medicine cabinets and ensure that we make the best possible use of the products at our disposal.

One of the EU's latest international co-operation projects in this area focuses on the safety of non-steroidal anti-inflammatory drugs (NSAIDs), a class of drugs which includes a range of widely used painkillers. The SOS project draws on outstanding expertise in the EU and North America to analyse the risk of gastrointestinal and cardiovascular side effects associated with different NSAIDs. This involves reviewing information from clinical trials and observational data and analysing healthcare data from British, Dutch, German and Italian databases covering at least 35 million patients. The aim is to provide clinicians and regulatory authorities with the information and decision making support that will help them to ensure that this valuable resource is used wisely.

Many other ambitious research projects are dedicated to the safety and efficacy of existing drugs. The European and American partners in the NEMO project, for example, are evaluating the potential of bumetanide, an off-patent diuretic, to improve the treatment of neonatal seizures. These seizures are characteristic of neonatal hypoxic ischaemic encephalopathy, a condition that can be caused

when babies are starved of oxygen around the time of birth, and affect the blood flow in the brain. The drug commonly used at the moment has limited efficacy. Better ways of controlling these seizures are needed urgently, and bumetanide, which can be used to target a physiological mechanism specific to newborn babies that is thought to cause these seizures, may hold the key. NEMO is determined to find it.

While a raft of projects strives to get more mileage out of the medicines at our disposal, other international research efforts backed by the EU are developing completely new drugs to fill the gaps in our pharmacopoeia. The Pro-Kinase Research project, for example, conquered new ground in the regulation of protein kinases (PKs) for therapeutic purposes. PKs are involved in most aspects of cell life and death, and many can potentially be targeted for the development of innovative drugs and therapies. The Pro-Kinase Research project has generated promising leads and designed a range of exciting compounds that could translate into a new generation of drugs to combat diseases such as atherosclerosis, leukaemia and leishmaniasis.

Many other examples, including the EU's involvement in the 'European and developing countries clinical trials partnership' (EDCTP) which stimulates the development of drugs against HIV/AIDS, malaria and Tuberculosis (TB), are featured throughout these pages.

SOS



Full name:	Safety of non-steroidal anti-inflammatory drugs
Type:	Collaborative project
Start date:	01/11/2008
Project coordination:	Erasmus University Medical Centre, Rotterdam, the Netherlands
11 project partners from 8 countries:	Canada, France, Germany, Italy, the Netherlands, Spain, United Kingdom, United States

<http://www.sos-nsaids-project.org>

NEMO



Full name:	Treatment of neo-natal seizures with medication off-patent: evaluation of efficacy and safety of bumetanide
Type:	Collaborative project
Start date:	01/10/2009
Project coordination:	University College London, United Kingdom
14 project partners from 8 countries:	Finland, France, Germany, Ireland, the Netherlands, Sweden, United Kingdom, United States

<http://www.nemo-europe.com>

Pro-Kinase Research



Full name:	Protein kinases – novel drug targets of post-genomic era
Type:	Integrated project
Start date:	01/03/2004
Project coordination:	University of Helsinki, Finland
27 project partners from 12 countries:	Austria, Finland, France, Germany, Hungary, Israel, Italy, the Netherlands, Norway, Russia, Switzerland, United Kingdom

<http://www.proteinkinase-research.org>



BLOOD BROTHERS

'Over the past 30 years,' said Professor Alejandro Madrigal of the Anthony Nolan Trust in London, 'there has been a substantial improvement in the treatment of malignant blood disorders such as leukaemia.' However, he added, these treatments cannot yet guarantee long-term survival. Haematopoietic stem cell transplantation (HSCT) saves many patients for whom other treatments have failed, he explained, but currently the success rate does not exceed 50%, and the procedure involves significant risks.

Haematopoietic stem cells are cells that can transform into blood components. Harvested from a donor and transplanted into a patient, these cells can stimulate the development of a new immune system replacing the patient's weakened defences. If the procedure is successful, the graft can enable the patient's immune system to keep the disease at bay or to eradicate it completely. If it is not, the disease could return, infections could develop, or the grafted cells could recognise the patient as foreign and attack their new host. All of these complications are potentially life threatening.

Co-opting the defences of a donor

AlloStem, a project that mobilised world-class expertise from three continents, set out to fine-tune HSCT techniques to reduce the risk of complications and explore the method's full potential. The project's name reflects its emphasis on transplantations of donated stem cells, as opposed to stem cells collected from the patients themselves – allogeneic rather than autologous grafts.

Some people's immune systems are stronger than others' when it comes to fending off malignant diseases. The AlloStem team investigated ways of harnessing these genetic differences for the benefit of transplant patients, notably by generating selective anti-tumour responses and providing immunity against opportunistic infections.

“Haematopoietic stem cell transplantation (HSCT) saves many patients for whom other treatments have failed.”

Better chances of finding a suitable match

It also identified ways of making transplantations available to a wider population of patients. The success of transplantation depends, to a large extent, on the suitability of the donor, which is linked to a range of factors including ethnicity and gender. As some populations are underrepresented in the donor registers, the chances of finding optimal matches for some patients can be slim. The techniques developed by the AlloStem project are expected to extend the scope for successful transplantations from a donor who might not previously have been viewed as optimal.

The project ended in 2008 but, as Prof. Madrigal reported, it has produced promising leads that are being validated in clinical trials. While it would be premature to draw any conclusions at this stage, initial results indicate that the project's outcomes have significantly improved the prospects for HSCT patients.

'This platform has delivered substantial innovative developments', Prof. Madrigal concluded, 'and we now want to extend the benefits to the largest possible community and to make every transplant successful.'

AlloStem

Full name:	Development of immunotherapeutic strategies to treat haematological and neoplastic diseases on the basis of optimised allogeneic stem cell transplantation
Type:	Integrated project
Start date:	01/04/2004
Project coordination:	The Anthony Nolan Trust, London, United Kingdom
29 project partners from 14 countries:	Argentina, Brazil, the Czech Republic, France, Germany, Israel, Italy, the Netherlands, Norway, Poland, Russia, Spain, Sweden, United Kingdom

<http://www.allostem.org>



THE HCV VACCINE:

HOPE, COOPERATION, VISION

'Most people don't know that they are infected by HCV when they are infected; they only discover this through a random test or once the disease chronically affects liver function.' Professor Riccardo Cortese, Director of Merck spin-off Okairos, is referring to the hepatitis C virus, which is transmitted through contact with infected blood. 'When hepatitis C is detected at this stage,' he added, 'it is usually not very easily curable.'

HCV causes a chronic infection in four cases out of five. Many cases will respond to treatment, but this can be a rocky road as therapy can take more than a year to complete and can cause serious side effects. Add the fact that many of the world's 200 million HCV sufferers struggle with the cost, and it comes as no surprise that the disease often runs its course unchecked.

This is a tragic situation as HCV can cause life-threatening complications. A vaccine could preempt tens of thousands of new cases per year but, as Prof. Cortese explained, 'so far it has not been possible to discover an effective way to vaccinate.' Why? Because a classical vaccine would aim to trigger the production of antibodies which recognise the surface of the virus. In the case of HCV, this structural part changes constantly.

A radically new approach

An international team of researchers is rising to the challenge. Launched at the initiative of Okairos and Novartis in cooperation with universities and research organisations in seven countries, the Hepacivac project draws on world-class expertise in vaccine development.

Project coordinator Prof. Cortese explains that it is exploring a radically new approach. 'The immune system has two arms,' he noted.

'We either make antibodies against infectious agents, or we make cells that react to the presence of the infectious agents and destroy the infected cells. This second arm, the so-called cellular arm, has rarely been used to develop a vaccine.'

'The best way to elicit the cellular response,' he added, 'is to inject in the organism as vaccine the gene coding for parts of the infectious agents. So you exploit the capacity of the body to receive this genetic vaccine and manufacture the antigen in the body itself.'

Towards a therapeutic vaccine?

Hepacivac is developing a vaccine that would be based on the coding for the stable, non-structural part of the virus, possibly combined with a classical vaccine to activate both arms of the immune system. First results, said Prof. Cortese, have been highly encouraging.

A prophylactic vaccine would be a breakthrough in itself, but the approach could even be used to treat patients who are already infected. Prof. Cortese is hopeful, but insists that 'this is really uncharted territory; nobody has ever been able to make a therapeutic vaccine for hepatitis.' A product designed to tackle an infection that has already taken hold would need to address additional challenges and so would be far more complex than the prophylactic formulation.

In the shadow of the pyramids

Hepatitis C blights lives around the world, true to the adage that disease knows no borders. It is, however, particularly common in Egypt, where a local partner supplies the team with valuable data, notably about new infections among healthcare workers.

The Egyptian project partner is based in Giza, where the pyramids have been testifying to the power of ingenuity for millennia. We may never fully understand the complexities of these feats of early technology, but every medical research project brings us one step closer to unravelling the mysteries of human health.

Hepacivac



Full name:	New preventative and therapeutic hepatitis C vaccines: from pre-clinical to phase I
Type:	Integrated project
Start date:	01/02/2007
Project coordination:	Celinge Biotecnologie avanzate s.c.a.r.l., Naples, Italy
12 project partners from 7 countries:	Belgium, Egypt, Germany, Italy, the Netherlands, Poland, United Kingdom

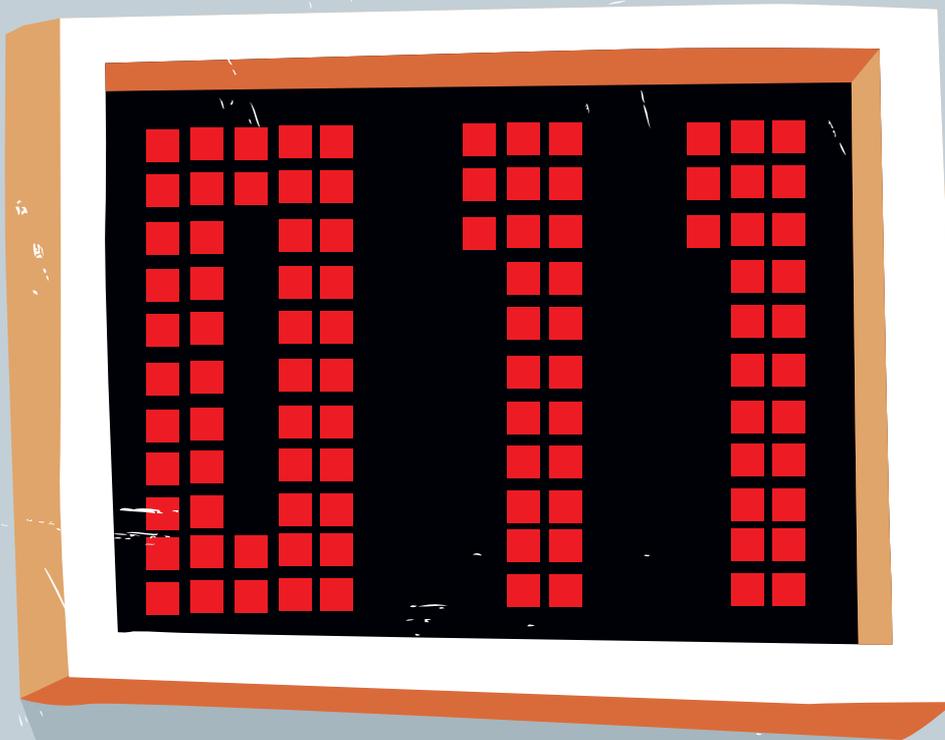
<http://www.altaweb.it/hepacivac>

“This is really uncharted territory; nobody has ever been able to make a therapeutic vaccine for hepatitis.”



BOOSTING THE DELIVERY OF HEALTHCARE SERVICES

Better ways to prevent, treat or cure disease are a vital starting point to improving public health. But once new insights have been translated into clinical practice, efficient and sustainable healthcare systems are needed to ensure that they actually benefit the health of the population. In some of the EU's health research projects, there isn't a lab coat in sight. And yet, they may be among those that make the greatest impact on public health: the EU also funds research aiming to optimise the delivery of healthcare.



BREATHING NEW LIFE INTO MATERNAL AND NEONATAL SERVICES

Pregnancy in the 21st Century remains a risky business: according to World Health Organization (WHO) estimates, more than half a million women die of complications linked to pregnancy or childbirth every year. This represents one woman every minute – and many more are injured in the process.

Better maternal and neonatal care (MNC) would help to keep more mothers and their babies safe, but unfortunately the provisions remain patchy in many parts of the world. Where resources or infrastructures do exist, they may not be utilised to best effect due to a lack of funds, guidance, equipment, supplies and skills. But beyond such structural issues, which should indeed be addressed as a matter of urgency, a key driver of optimal healthcare delivery may be lacking: the determination to perform to the highest standards at all times.

One more push

While some MNC services strive to do their best even in difficult circumstances, observers report that others, which may be even better equipped than their more proactive peers, are held back by staff which has all the necessary qualifications and knowledge but lacks the motivation to apply it. The Qualmat project is analysing this particular aspect of healthcare provision in three sub-Saharan countries: Burkina Faso, Ghana and Tanzania. The project strives to develop tools and incentives that will inspire staff to pull out all the stops.

Qualmat is attacking the issue from several angles. One of these will involve a thorough investigation of the reasons affecting staff motivation. Another will focus on possible solutions. A computer-

assisted decision-support system will enable the participating organisations to standardise care decisions, facilitate treatment and referrals, particularly in the case of emergencies, and generally support logistics and administration. It will also help to assess the performance of individual staff members. The results will be linked to an incentive scheme.

Keeping an eye on the prize

Financial incentives tend to lift morale, but they may not be sustainable in settings where money is scarce or where human resources policies don't allow for them. So while extra cash remains an option, there are plenty of other ways to reward outstanding performance.

The nature of the incentives will vary depending on the financial, legal and cultural context of the participating countries, but the project partners are striving to develop a range of attractive options. The information technology system will also be used to monitor the success of this large-scale motivational drive – for the benefit of mothers and babies facing one of the biggest challenges of their lives.

Qualmat



Full name:	Quality of maternal and prenatal care: bridging the know-do gap
Type:	SICA
Start date:	01/05/2009
Project coordination:	University of Heidelberg, Germany
6 partners from 6 countries:	Belgium, Burkina Faso, Germany, Ghana, Sweden, Tanzania

<http://www.qualmat.net>

Healthcare systems on the move

For nomadic peoples, access to healthcare systems can be especially difficult. The Bedouin Health project has set out to analyse and enhance the quality of the healthcare provision for mobile and newly sedentary Bedouin populations in Jordan and Lebanon, with a special emphasis on reproductive and child health.

Bedouin Health



Full name:	Improving access to and quality of reproductive and child health care to marginal peoples: Bedouin in Jordan and Lebanon
Project coordination:	Institute of Health, School of Health and Social Studies, University of Warwick, Coventry, United Kingdom
6 project partners from 5 countries:	France, Jordan, Lebanon, Sweden, United Kingdom

<http://www.bedouinhealth.org>

Health insurance for all

The Shield project is placing three very different African healthcare systems under the microscope. Ghana, South Africa and Tanzania have all set up ambitious health insurance programmes and are striving to improve the coverage, equity and sustainability of these schemes. The project interacts with policy and decision makers at the national level to clarify the options and identify the best solutions.

Shield



Full name:	Strategies for health insurance mechanisms to address health system inequities in Ghana, South Africa and Tanzania
Project coordination:	Department of Public Health and Policy, London School of Hygiene and Tropical Medicine, London
7 project partners from 6 countries:	Ghana, the Netherlands, South Africa, Sweden, Tanzania, United Kingdom

<http://web.uct.ac.za/depts/heu/SHIELD/about/about.htm>



HOW INCLUSIVE IS YOUR SYSTEM?

Does your health system provide the same standard and quality of care for all? Does it strive to be equally accessible to all its users? Is it able to address the specific needs of particularly vulnerable user groups? Answer 'yes' to all three and you may be looking at a system that has truly mastered the principle of equity in healthcare.

But the answers are unlikely to be straightforward. The Equitable project, a consortium of partners in the EU and Africa, is putting the healthcare systems of Malawi, Namibia, South Africa and Sudan to the test in order to identify the barriers they may need to overcome on the road to genuine equity. The example of these developing systems is yielding valuable insights for emerging and established healthcare systems everywhere.

Cartography of an obstacle course

As Project Coordinator Professor Mac MacLachlan explained, 'There is a lot of rhetoric around the idea that healthcare should be equitable, but that's really not possible unless health services are equally accessible to everyone.' And there are many reasons why that may not be the case. The barriers may be physical, psychological, administrative, financial or cultural, to name but a few. They may be linked to the distance patients must travel to receive treatment, or to the fact that they are displaced, minority or otherwise vulnerable groups that often struggle to obtain the services they need.

These challenges affect different systems to varying degrees, but there is one indicator that can be applied to all: their ability to address the needs of system users with disabilities. All health system users should have equal

access to crucial services such as immunisation, dentistry or antenatal care, but only a system specifically *designed for equity* will be able to offer this level of inclusiveness.

Paving the way for equity

A mud road to an immunisation clinic, for instance, can become an insurmountable obstacle to a wheelchair user. 'If you can get the health provision for people with disabilities right and they are able to access services,' said Prof. MacLachlan, 'then you're probably also going to be getting it right for the rest of the population, because you'll be concerned to maximise the intersectoral relationships between education, transport, healthcare and so on, on which peoples' health depends.'

This may be a tall order even in affluent settings, let alone the resource-constrained context of many low-income countries. But as Prof. MacLachlan noted, political determination goes a long way to ensure that available means are deployed equitably. Equitable is assessing health systems and the policies on which they build. To do so, it has developed its very own methodology: EquiFrame, an analytic tool for evaluating and developing inclusiveness in healthcare policies.

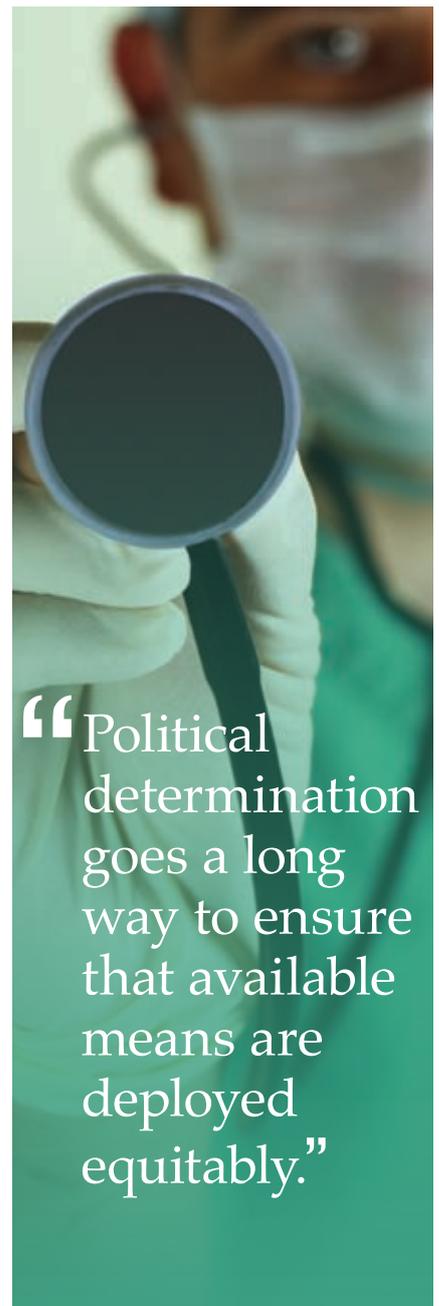
The project is also profiling system users and conducting a survey of 8 000 households to analyse their uptake of healthcare services. One of the aims is to identify people who do not use such services at all, and to establish why. Due to be published by the end of 2012, these case studies will give non-users of the healthcare system a voice, and should give policymakers ample food for thought.

Equitable



Full name:	Enabling universal and equitable access to healthcare for vulnerable people in poor resource settings
Type:	Collaborative project
Start date:	01/03/2009
Project coordination:	Centre for Global Health & School of Psychology Trinity College Dublin Dublin, Ireland
8 project partners from 6 countries:	Ireland, Malawi, Namibia, Norway, South Africa, Sudan

<http://www.equitableproject.org>



“Political determination goes a long way to ensure that available means are deployed equitably.”

A HEALTHY DOSE OF INFORMATION

When faced with a challenge, decision makers must be able to identify the best course of action quickly and reliably. Bad choices are likely to waste time and resources, and could even be counterproductive. Is this a risk worth taking when lives are at stake?

In public health, there often are lives at stake. 'The problem now,' said Professor Andy Oxman of the Norwegian Knowledge Centre for the Health Services, 'is that often we're not using the research evidence we have to inform important decisions about how to organise, finance and govern our health systems.'

Where's your evidence?

This could be due to a number of reasons. The information may be hard to find, for instance, it may not seem to apply, or it may reach the stakeholders at a stage where insufficiently informed decisions are already being implemented.

The SURE project, which draws on the expertise of seven African project partners supported by colleagues from Canada, France, Norway, Sweden and the WHO, has set out to bridge this gap in 11 countries in Africa. Headed up by Prof. Oxman, the project cooperates closely with two organisations dedicated to the use of research evidence in health policy: the Evidence-Informed Health Policy Network (EVIPNet) and the Regional East African Community Health Policy Initiative (REACH).

The fact finders

The SURE team sources and supplies reliable research evidence to inform decisions about African healthcare systems. To do so, it produces research syntheses and develops strategies for their dissemination. These include virtual clearing houses and rapid response systems

designed to provide policymakers with the relevant facts and figures in a matter of days, or even hours.

The aim is to help African policymakers ensure that healthcare resources are used wisely and to support their efforts to improve access to high-quality healthcare for all. The team will also fine-tune strategies to boost the use of research evidence in low and middle-income countries – an outcome that could be of interest to health systems beyond the scope of SURE. Where budgets are tight, said Prof. Oxman, 'you actually need more research, not less, because you want to make sure that you are using the few resources you have well.'

What policymakers need to know

Prof. Oxman is not, however, hoping for universally applicable answers, and noted that SURE is developing policy for individual countries, based on a thorough analysis of their specific health challenges. Why are malaria prevention efforts failing in some countries, for example, why is maternal mortality high in others, and what can be done to tackle these issues?

'There is probably not any one thing that works everywhere.' But, he said, his project provides opportunities to 'learn, to get a better sense of what works, and of the contextual factors that determine what works where.'

“You want to make sure that you are using the few resources you have well.”



SURE



Full name: Supporting the use of research evidence for or policy in African health systems

Type: SICA

Start date: 01/06/2009

Project coordination: Prevention and International Health Unit
Nasjonalt Kunnskapssenter for Helsetjenesten
Oslo, Norway

12 project partners from 12 countries: Burkina Faso, Cameroon, Canada, Central African Republic, Ethiopia, France, Mozambique, Norway, Sweden, Switzerland, Uganda, Zambia

<http://www.evipnet.org/sure>





An African coordinator: Next Generation of researchers from disease endemic countries

"Our project brings African and European scientists together and trains them in understanding operational issues in health and development. Thus science and biology become more relevant in resolving contemporary problems of the community." Prof. Wilfred Mbacham from University of Yaounde knows from his own experience that early stage collaboration reinforces sustainable networks for collaborative research in Africa and Europe.

PRD College is an interactive programme in BioMedicine and development, a virtual institute and a network that connects young African and European biomedical scientists and their institutions. By training PhD Students and Post-Docs from Africa and Europe to perform research on diseases such as HIV/AIDS, malaria and tuberculosis and applying it to sustainable development, the programme bridges the gap between science and development in Africa. The impact of this programme is the creation of a research environment, where highly innovative ideas are conceived and new approaches can be developed to manage diseases in endemic countries.

PRD College

Full name:	Poverty Related Disease College - An International Programme on Biomedicine and Development
Type:	Coordination action
Start date:	01/07/2009
Project coordination:	University of Yaoundé I, Yaoundé, Cameroon
10 project partners from 9 countries:	Cameroon, Germany, Italy, Kenya, the Netherlands, South Africa, Sweden, Tanzania, Zambia.

<http://www.prd-college.eu>

WHAT ELSE WOULD YOU LIKE TO KNOW?

Online resources with further information on international cooperation in EU-funded health research include:

- Dedicated Web pages:
http://cordis.europa.eu/fp7/health/home_en.html
http://ec.europa.eu/research/health/index_en.html
- An e-Library with publications:
http://ec.europa.eu/research/health/e-library_en.html
- EU-funded projects in health research:
http://ec.europa.eu/research/health/ongoing_en.html
- An interactive platform on European health research:
<http://www.healthcompetence.eu>
- National Contact Points and other support structures:
http://cordis.europa.eu/fp7/health/get-support_en.html
- A mailbox for your comments or questions:
RTD-HEALTH@ec.europa.eu

How does body mass affect a failing heart? Body mass extremes and weight-related disorders such as diabetes are known to accelerate the progression of chronic heart failure, but much remains to be learned about the underlying mechanisms of this frightening disease, especially in overweight people.

Twelve international research groups across Europe and Russia are investigating the matter together, and they do not plan for their work to remain theoretical. The team aims to develop tailored therapies to overcome the current one-size-fits-all approach to treatment and also hopes to improve the patients' quality of life.

SICA-HF, an outstanding example of programme-level cooperation with research partners abroad, was brought to life as the result of a joint initiative between the EU and the Russian Federation.



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