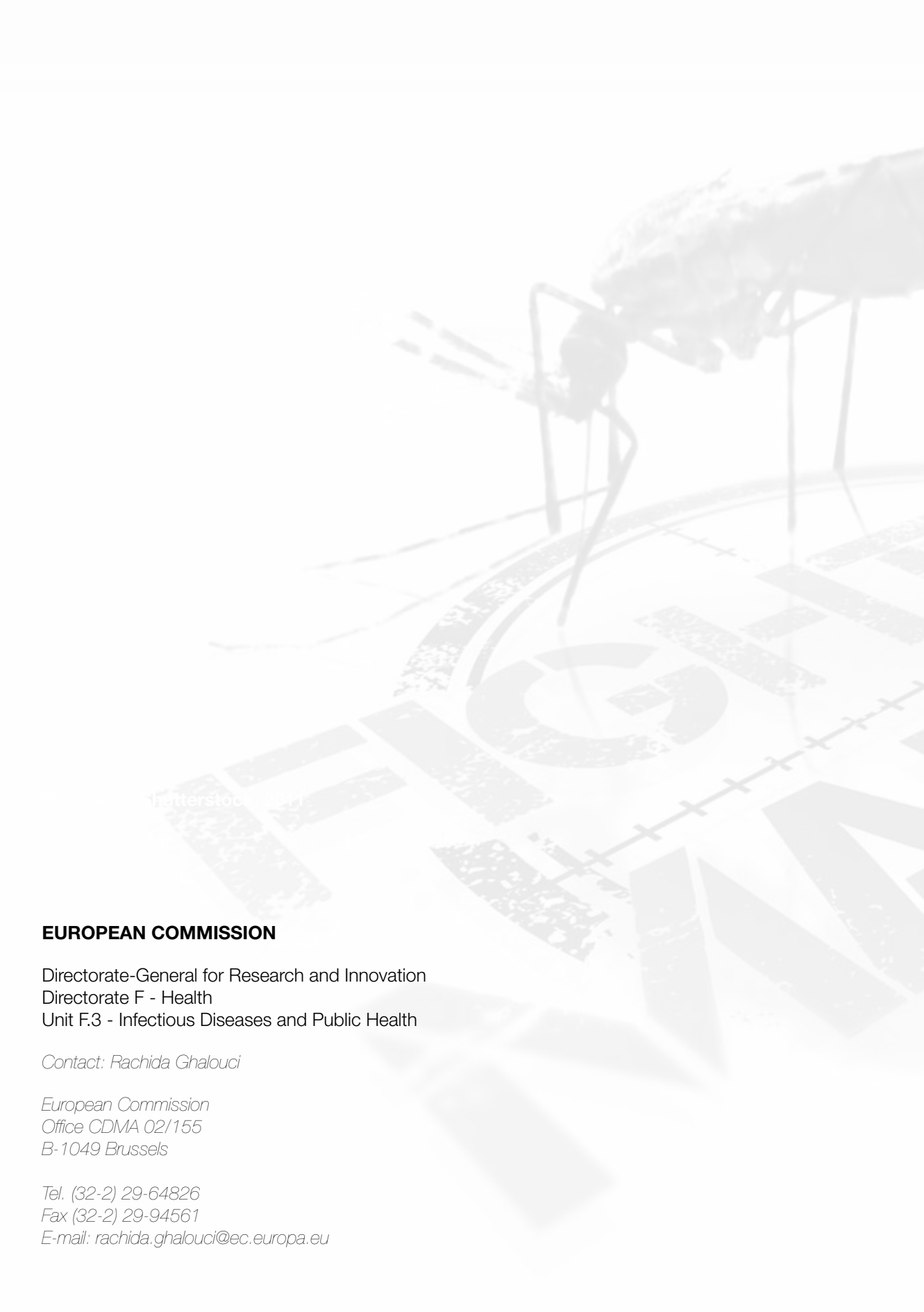




Fighting Malaria:

EU Research and Innovation role



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Directorate-General for Research and Innovation
Directorate F - Health
Unit F.3 - Infectious Diseases and Public Health

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“We cannot let this momentum slip. Significant recent gains, though fragile, must be sustained. The international community needs to ensure sufficient and predictable global funding to meet ambitious targets set for malaria control as part of the drive to reach the health-related Millennium Development Goals by 2015”.

Dr Margaret Chan,
Director-General World Health Organization
(2010 World Malaria Report)





“This brochure shows the added value both of EU-funded research and innovation in general and of collaboration with researchers in developing countries in particular.

The ultimate goal is the complete eradication of the global scourge of malaria and collaborative work across many borders is the only way of confronting such global challenges effectively”.

Directorate-General for Research and Innovation
Commissioner Máire Geoghegan-Quinn

A handwritten signature in blue ink, reading "Máire Geoghegan-Quinn", is positioned below the printed name. The signature is written in a cursive, flowing style.

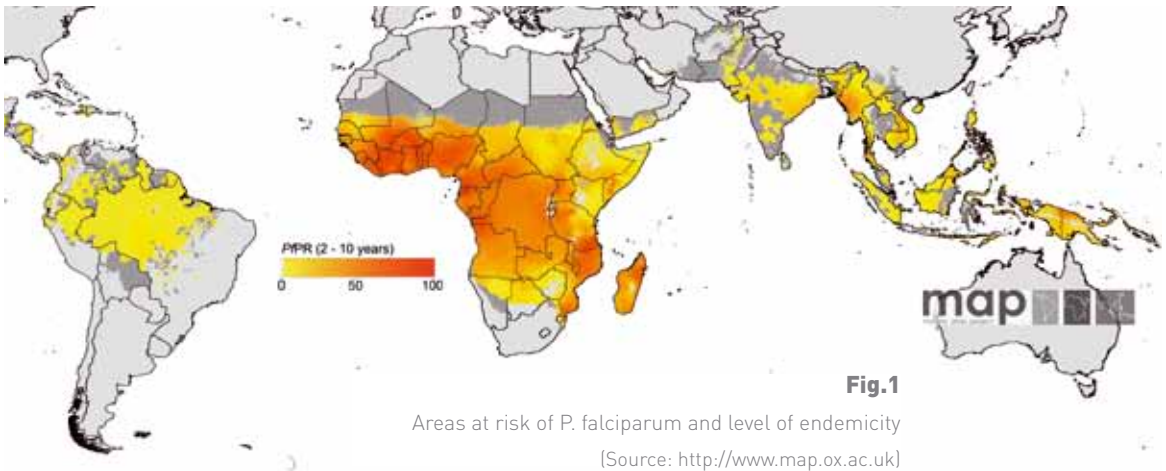


Fig.1

Areas at risk of *P. falciparum* and level of endemicity

[Source: <http://www.map.ox.ac.uk>]



1. THE GLOBAL BURDEN OF MALARIA

What is malaria?

Malaria is a severe febrile, vector-borne disease caused by parasites of the genus *Plasmodium* which is transmitted to humans through the bite of female *Anopheles* mosquitoes. The most lethal of the malaria parasites that infect humans is *Plasmodium falciparum*, which is especially common in Sub-Saharan Africa. The disease is also present in tropical and subtropical areas of Central and South America, Asia and the Middle East, there, however, often with another predominant species, *P. vivax*.

One of the world's most important public health concerns

The World Health Organization (WHO) estimates that the parasite infected around 225

million and killed nearly 800 000 people worldwide in 2009, mostly among children under 5 years old and pregnant women. Africa is the most affected continent.

Malaria versus development

According to the World Bank, it is estimated that malaria reduces GDP (Gross Domestic Product) growth globally by approximately 1 full percentage point per year. The lower rates of economic growth shown by malaria-endemic countries (Fig. 1) hamper their development. The reduction of the malaria burden is clearly targeted in the United Nation's Millennium Development Goals and many initiatives have recently been taken to try to eradicate the disease. Among them is the Global Malaria Action Plan (GMAP), ↗

the roadmap for malaria control and elimination worldwide which has been developed by the Roll Back Malaria Partnership (WHO, UNICEF, UNDP, the World Bank, the Bill & Melissa Gates Foundation and many other partners).

The parasite causing malaria is a sophisticated organism with a complex life cycle (Fig.2). It is present in human liver and blood cells for much of this cycle and hence well-adapted to outsmart the human immune system and, equally so, medical prevention and treatment devices. Sexual proliferation of the parasite ↗

requires passing through a mosquito-borne life stage, to which the parasite is equally well adapted.

While in certain geographical areas progress in malaria control has been remarkable due to the use of insecticide-treated bed nets and the availability of effective treatment, potential threats demand increased attention: the development of resistance to insecticides and to antimalarial medicines, as well as precarious health systems characteristic of many of the most vulnerable regions of the world.

2. RESEARCH NEEDS FOR EFFICIENT MALARIA CONTROL

The knowledge gaps and research needs are multiple, especially when the ultimate goal is the complete eradication of malaria, where therefore the efficacy and efficiency of prevention, treatment and diagnostic tools need to be raised significantly. Significant research investments are also needed to most efficiently deploy implementation schemes in the context of the poor health-system conditions.

Preventing

Malaria can be prevented by different means, e.g. by fighting the mosquito using physical or chemical barriers (e.g. insecticide treated bed nets, repellents) to prevent infected mosquitoes from

biting and infecting humans, by killing or debilitating the mosquitoes (spraying insecticides, biological pest control), or by preventing their proliferation (e.g. sterile insects technology).

In addition other new tools directed at blocking the transmission of parasites are under investigation, such as a transmission blocking vaccine.

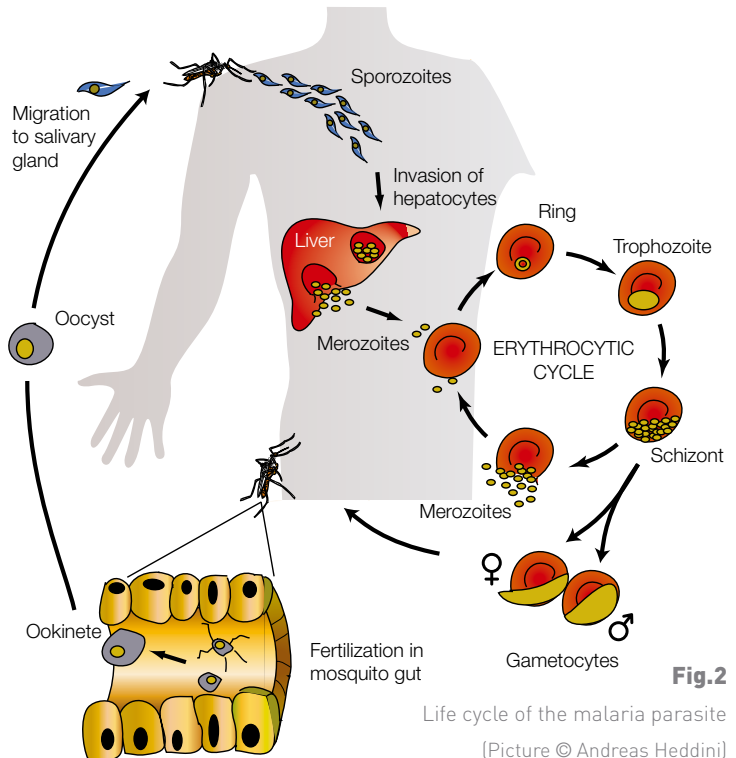


Fig.2

Life cycle of the malaria parasite
(Picture © Andreas Hedding)

Research concerned with studying the resistance of mosquitoes to insecticides, studying the toxicity of insecticides and their impact on ecological balances, must be underpinned, in order to have application impact, this needs a profound understanding of vector epidemiology and the behaviour of mosquito vectors.

Protecting from malaria through use of an efficacious and efficient vaccine, would probably be the most powerful prevention tool. Such a vaccine does not exist yet, but a promising vaccine candidate product (RTS'S, developed by GSK Biologicals) is presently in phase 3 trials ongoing at several sites in Africa (<http://www.malariaivaccine.org>). If an anti-infection vaccine becomes available in the near future, it will need to be highly effective since natural immunity to the disease may be lowered in vaccinated populations in endemic regions.

Research into developing a highly efficacious vaccine would be facilitated if the mechanisms of naturally acquired immunity of exposed populations were better understood, and a broadly efficacious malaria vaccine will probably need to integrate multiple antigens into a multi-component vaccine.

Prevention in risk groups is also possible through intermittent preventive drug treatment (IPT), e.g. for pregnant women and small

children, with some possible safety issues concerning giving certain antimalarial drugs in early pregnancy, and the issue of potential development of drug resistance due to large-scale application.

remedies represent resources that deserve to be tapped into on a larger scale.



Treating

Treatment of malaria patients with drugs requires continuous research and development efforts to generate new anti-malaria drugs, and preferably acting on new biological targets, since expanded use of drugs triggers the rapid development of resistance. Research is also needed to reveal the mechanisms of such resistance development, and how these can be circumvented. The large molecule libraries now being available from industry and from collections of traditional

Diagnostics

Efficient treatment in malaria-endemic regions requires differentiating febrile diseases with tools for rapid diagnosis which are not only sensitive and specific, but also affordable, reliable and robust, since the traditional microscopic analysis of blood films is not always feasible and accurate, especially in resource-poor settings. In addition, high-throughput molecular tools are needed as surveillance tools, e.g. for monitoring drug resistance markers. And large scale diagnostics of asymptomatic carriers will be a particular challenge for elimination and eradication efforts.

3. HOW EUROPEAN RESEARCH TACKLES MALARIA

The European Commission, since 2002 and up to 2010, has supported malaria research through its successive Framework Programmes for Research and Development FP6 and FP7 (~ €180 million). Under the EU's previous Framework Programme for Research (FP6, 2002-2006), a total of 18 cooperative malaria research projects were supported to the tune of about €100 million (Fig.3). These include three large projects which have helped greatly to structure the European Research Area (ERA) in the field of malaria research (Fig.4): (1) a strong malaria basic research network (BioMalPar), (2) an Integrated Project to develop new anti-malarial drugs (ANTIMAL) and (3) the European Malaria Vaccine Development Association (EMVDA), the latter coordinated by EMVI (European Malaria Vaccine Initiative, now EVI). EU malaria research support is also given through the European and Developing Countries Clinical Trials Partnership (EDCTP), a programme which supports phase 2 and 3 trials as well as capacity building related to malaria, HIV/AIDS and tuberculosis research in Africa.

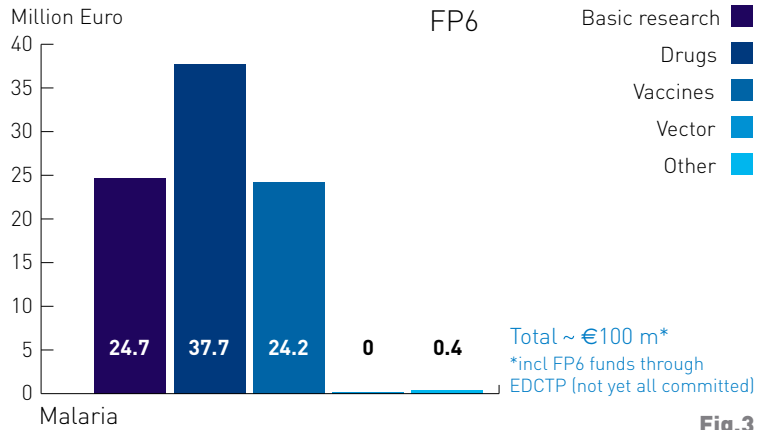


Fig.3
Malaria research under EU's FP6 (2002-2006)

Under FP7 (2007-2013), European research, in the field of malaria, is being consolidated and reinforced with continuity of funding of basic research in malaria (Fig.5). The EU has also tackled identified gaps in certain sub-areas of malaria

research, for example, malaria in pregnancy, was covered by a specific topic under FP7's first call for proposals, in addition a major project on controlling the malaria mosquito vector is going to be financed, half way through the FP7.



Future FP7 calls will address other research topics pertinent to sustaining efficient control of malaria and global malaria eradication efforts. They will focus on improvements to diagnostics, providing sound rationales for optimised vaccines, and, under the public health pillar of the health

research programme, will address aspects of efficient implementation of intervention measures, in particular to assess how different types of malaria control may be best implemented under the existing conditions of local health systems. In addition a new funding round of the EDCTP programme is

presently being discussed.

Particularly noteworthy is the remarkable progress in the self-organisation of the respective malaria research areas that has been achieved under FP6, and that has been pursued under the first three calls of FP7 (Fig.4).



Fig.4
New partnerships and new products for Global Health: The examples of EU Funded Malaria Research



Virtually the entire European malaria research community, complemented by many African partner groups and more non-EU researchers, have come together under a number of key umbrella projects on basic malaria research, drugs, vaccines and, on vector research. These projects complement each other in many ways, most prominently in a jointly undertaken European Malaria Graduate School which has already produced a new generation of more than 50 European and African PhD students in the field of malaria.

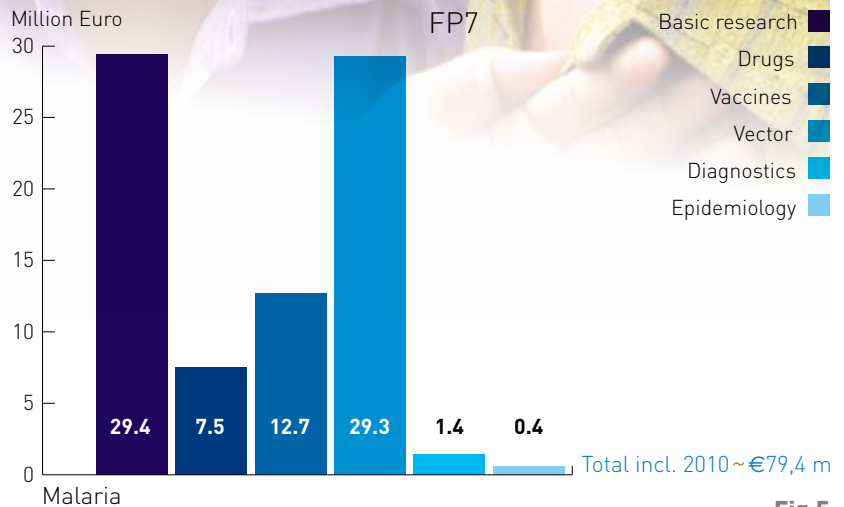


Fig.5

Malaria research under EU's FP7 (2007-2010)

The overall approach for the future should be to capitalise on these structural advances, which need to be sustained, as they allow European malaria

research to more actively take on its due share of the global research agenda for malaria.

4. THE EUROPEAN AND AFRICAN MALARIA RESEARCH COMMUNITIES HAVE THEIR SAY

The consultation of the EU and African malaria research communities that took place in the conference “Challenges for the Future”, organised by the European Commission in Brussels, 13-14 November 2008, resulted in the following recommendations for EU-funded research.



→ Malaria vaccine development still requires new immunogenic antigens, possibly in combination with current leads. Pre-clinical assays and selection criteria should be based on a more thorough understanding of immune responses. As falciparum and vivax malaria are co-prevalent in many places, an anti-vivax component for combination vaccines should be explored. A pregnancy vaccine was considered amenable to a straight-forward approach since a functional target has been identified.

→ The search for new anti-malarial drugs should make use of chemical libraries and promising leads in ethnic pharmacology.

Malaria drug development should also include medicinal chemistry and Structure-Activity Relationships (SARs) should be pursued. Research frameworks should ensure that interesting leads are handed over to Private-Public Partnerships (PPPs) and/or industry at an early phase for further development.

→ Treatment without prevention is not a sustainable approach to controlling transmission. In addition to vaccines, effective vector control tools are also greatly in need. Research on vector control should span the range from vector and

population biology to new insecticides and implementation strategies. Operational research into malaria control and eradication should include rapid diagnostics and a comparative assessment of intervention tools and strategies.

The forthcoming annual, health-research work programmes under FP7 will strive to meet the above recommendations as comprehensively as possible and represent a continuation of EU efforts over the past years: to contribute to the common fight to reduce the global burden of malaria, and possibly eradicate malaria altogether.

FIND OUT MORE ABOUT:

- FP6-funded malaria projects in the FP6 catalogue for Poverty-Linked Diseases:
www.ec.europa.eu/research/health/infectious-diseases/poverty-diseases/projects/l_fp6_en.htm
- FP7-funded malaria projects:
www.ec.europa.eu/research/health/infectious-diseases/poverty-diseases/projects/l_fp7_en.htm
- Conference Challenges for the Future, research on HIV/IADS, Malaria and Tuberculosis:
www.ec.europa.eu/research/conferences/2008/poverty-related-diseases/index_en.html

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- EDCTP
www.edctp.org
- Malaria basic research network (BioMalPar)
www.biomalpar.org
- Integrated Project to develop new anti-malarial drugs (ANTIMAL)
www.antimal.eu
- European Malaria Vaccine Development Association (EMVDA), coordinated by EVI (European Vaccine Initiative)
www.emvda.org ; www.euvaccine.eu
- 2010 World Malaria Report
http://whqlibdoc.who.int/publications/2010/9789241564106_eng.pdf
- EU-funded malaria research under the 6th and 7th Framework Programmes for research and technological development
www.malariajournal.com/content/10/1/11

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Malaria is an old infectious disease that still kills nearly one million people every year, mostly children and women in developing countries. While in certain geographical areas malaria control has been remarkable, thanks to insecticide-treated bed nets and effective treatment; the development of resistances to insecticides, to medicines and the quality of the health systems in these regions are threats that demand increased research efforts. Europe has been traditionally strong in malaria research. More recently, targeted and sustained support for malaria research at EU level, through the 6th and 7th Framework Programmes for research and technological development (FP6 (2002-2006) and FP7 (2007-2013)), has contributed to better structure the malaria research, under complementary research projects and networks, around few key areas: fundamental research on the malaria parasite, development of new drugs, research and development of a vaccine, research to control the malaria-transmitting mosquito vector, research for better diagnostic tests and operational research for better control intervention tools and strategies. Considerable efforts are being undertaken to ensure adequate participation of research groups from endemic countries, in particular from Africa, aiming at strengthen research capacities in these countries.

