



GENERAL

Tuberculosis research in the European Union: Past achievements and future challenges

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SUMMARY

The European Commission (EC) supports a large number of research activities in tuberculosis through the EU Framework Programmes for Research and Development (FP). By utilizing a variety of funding instruments, the EC has established a mixed portfolio of research projects, ranging from small discovery projects to large multidisciplinary consortia with sufficient critical mass to undertake translational and clinical research. The European investments in TB research have generated promising results with new vaccine candidates, drug leads, diagnostic markers and basic research results starting to emerge. In the light of a rapidly changing global research environment it has therefore become timely to review and update the priorities for TB research. To facilitate this process, a high-level conference on “Challenges for the future: research on HIV/AIDS, Malaria and Tuberculosis” was convened in Brussels on November 2008. This review gives an overview of the present portfolio of EC funded TB research, and summarises the conclusions from the conference on future perspectives for TB research in Europe and beyond.

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1. Introduction

Tuberculosis (TB) remains one of the most devastating infectious diseases with more than 9 million cases annually and with more than 1.7 million fatalities.¹ During the last 10 years there has been a renewed global interest for research in TB, and this has resulted in the launch of several new initiatives by national and international organisations, private charities and pharmaceutical companies. The new focus on TB has partly been triggered by the persistent high number of TB cases in poor countries, and partly by the increased occurrence of multidrug and extensively drug-resistant TB (MDR- and XDR-TB).² In HIV-positive individuals, XDR-TB has been associated with very high mortality.³ On the political level, global support to combating TB was expressed in the United Nations *Millennium Declaration* in 2000, and has subsequently been confirmed on a number of occasions at high-level summits such as the annual G8 meetings and the Berlin declaration on TB.⁴ “The global plan to stop TB: 2006–2015” was endorsed in 2005 by the Stop TB Partnership.⁵ It launched a number of specific targets: the target for 2005 was to detect 70% of new sputum smear-positive cases and cure at least 85% of these cases. For 2015, it established to sustain or exceed those indicators and reduce the prevalence and death rates of TB by 50% relative to the 1990 level; and for 2050, to eliminate TB as a public health problem.⁶

Since these goals will be difficult to reach, political leaders, non-governmental organisations and prominent personalities have followed up by calling for more resources being allocated to the fight against TB. Responding to the political climate, the European Commission (EC) launched the ‘Programme for action on HIV/AIDS, Malaria and TB’ in the context of poverty reduction (2001–2006).⁷ It provides a broad framework for trade, development and research policies in order to improve the access, affordability and availability of treatments for poverty related diseases (PRDs) in developing countries. The Programme for Action, which has subsequently been confirmed and extended under a new formula for the period 2007–2011, includes a firm commitment to incentivise the development of new public goods for TB through the Framework Programme (FP) for Research and Development.⁸

The FPs are the EU’s mechanism to support research with a major scientific and societal impact. They are multi-annual programmes agreed by the EU Member States and the European Parliament and implemented by the EC. The FPs are characterised by a strong emphasis on collaborative research between scientists in different nations and different sectors. Since the introduction of the first FP in 1984, they have become the main tool to fund cooperative research in Europe under the EU Treaty with the goal of boosting European competitiveness and solving societal problems.

In order to provide feedback on achievements and setting future priorities for research in HIV/AIDS, malaria and TB, the EC brought together a large number of stakeholders to an international conference in November 2008. The conference comprised more than

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350 leading scientists, research managers, decision-makers, funding agencies and relevant international NGOs from 63 countries, including representatives from many resource poor countries.⁹

The present article gives an overview of the recent EC efforts and achievements on TB research and summarizes the results of the EC conference with respect to suggestions for research priorities on TB.

2. TB research funded by EC

Research activities with relevance to TB have been supported throughout the FPs, albeit sporadic in the early FPs. Under FP5 (1998–2002), the EC initiated a more dedicated approach to the area of TB research and provided financial support to 21 projects with a total budget of €30 million. These projects covered a wide range of activities, covering basic research in, e.g. mucosal immunology, structural and functional genomics, host-parasite relationship and *Mycobacterium tuberculosis* population studies, as well as applied research for vaccine development, drugs and diagnostics. Many of these projects generated important scientific results, but lacked sufficient critical mass and financial strength to translate the findings into applicable health solutions. Another special feature of FP5 was the division of TB projects across two separate programmes, the Quality of Life Programme and the International Cooperation Programme, which also addressed issues related to science policy and capacity building in developing countries.¹⁰

With the introduction of FP6 (2002–2006), the TB activities were merged and grouped with activities in HIV/AIDS and malaria into a single dedicated activity line under health research. This was done to highlight the importance of the three major poverty related diseases (PRDs) and to exploit possible synergies between them. Importantly, the introduction of FP6 was accompanied by a quadrupling of funding to research in PRDs from €105 to 457 million. Out of this, more than €68 million was allocated to discovery and translational TB research (Table 1). FP6 introduced a new funding instrument, the integrated projects (IP), which made it feasible for the first time for the EC to support large projects with a focus on translational research. This became an important element of the dedicated strategy for European TB research. Translational research was thus supported by a total contribution of €43 million to three large IPs. The three IPs are addressing TB vaccine development (TB-VAC), TB drug development (NM4TB) and mucosal vaccines (Muvapred).¹¹ Each of the IPs comprises a critical mass of high-level and complementary research groups that can jointly move promising drug and vaccine candidates from discovery phase to early human testing. The three consortia have received an EC contribution between €11 and 17 million to undertake translational research activities during a 5-year period and each of them comprise more than 20 different research teams. Furthermore, they all comprise small- and medium-sized biotech companies, large pharmaceutical enterprises as well as research

groups from disease-endemic countries outside Europe.¹² Approximately €25 million was channelled to early stage research through Specific Targeted Research Projects (STREP). These projects are mostly exploring new concepts for drug, vaccine or diagnostic development, or generating information about basic biological mechanisms. They are mostly small projects with a typical duration of 3 years and an EC contribution of €1–3 million. Finally, a few well-defined activities such as harmonization of research standards, conferences and training were supported with the smallest projects, namely the Strategic Support Actions (SSA).

In addition, the EC has supported the European and Developing Countries Clinical Trials Partnership (EDCTP) with a contribution of €200 million. The EDCTP is an independent legal entity with the objective to support late-stage clinical trials and capacity building in the area of PRD in sub-Saharan Africa. The contribution to the EDCTP has made it possible for the EC to support late-stage clinical activities for TB, and it is anticipated that a significant proportion of the EDCTP grants will be earmarked to support TB research activities. So far, the EDCTP has earmarked support to 16 TB trials with a total budget of €85 million. In addition, several non-disease-specific projects for capacity building have been initiated, which will also contribute to clinical TB research.¹³

3. The current portfolio of TB research

Continuity and sustainability have been the guiding principles for health research in the transition from FP6 to FP7 (2007–2013). The purpose has been that FP7 should retain and expand the most successful elements of the previous FPs. In line with this, TB has been maintained as one of the priority areas of research. During the first 3 years of FP7, approximately €48 million have been committed to support collaborative research projects on TB (Table 1). Two large-scale collaborative projects have been selected for funding, one for establishing a European network for clinical management of TB drug resistance (TB PAN-NET), and one for development of new vaccine candidates for TB (NEWTBAC), which will continue and expand the work initiated by the TB-VAC project during FP6. In addition, several small scale projects on host-pathogen interaction, innovative drug development and diagnosis of MDR-TB have been funded.

The portfolio of EC supported TB projects from FP6 and the first 3 years of FP7 are presented in Table 2. This reveals a fairly broad portfolio of research activities with the largest EC contribution being allocated to vaccine research, and the remaining EC contributions being fairly evenly distributed between basic research, drug discovery, diagnostics and clinical research and epidemiology (Figure 1). An analysis of the projects reveals that the globalisation of research in recent years has been embraced by FP6 and FP7 through an increased openness and eagerness to attract research teams from all over the world. In the field of TB, it has been a particular goal to include research teams of high quality from disease-endemic countries in resource poor regions of the world. Although European research teams are still contributing with the largest number of participants, the number of non-European participants in the TB projects has been steadily increasing and constitutes about 15% of all participants in the currently active projects.

New collaborations between multiple stakeholders in different sectors have been put forward by many analysts as essential for developing new and affordable health products.¹⁴ The pharmaceutical R&D process is complex, risky and expensive, and developing a new medicine or vaccine for low-income countries is unlikely to occur without significant support and brokering from the public sector. An additional strategic goal for TB research in the FPs has therefore been to establish links between private and public research institutions in order to create synergy between the two

Table 1
The EC contribution to TB research in recent Framework Programmes.

	FP5 (1998–2002)	FP6 (2002–2006)	FP7 (2007–2013)
EC contribution to PRD* (million €)	105	457 [†]	
EC contribution to TB (million €)	30	68 [§]	48 ^{**}
Annual average for TB (million €)	7.5	17.1 [§]	17.7 ^{**}

* Poverty related diseases.

[†] Including an EC contribution of €200 million to the European Developing Countries Clinical Trials Partnership (EDCTP).

[§] Not including EDCTP.

** Only the first 3 years of FP7.

Table 2

Overview of EC funded TB research projects in FP6 (2002–2006) and during the first 3 years of FP7 (2007–2013).

Acronym	Project title	EC contribution	Partners	FP	Instrument	Keywords
MUVAPRED	Mucosal vaccines for poverty related diseases	15.250.000	29	FP6	IP	Vaccine
TB-VAC	An integrated project for new vaccines against tuberculosis	17.000.000	33	FP6	IP	Vaccine
MM-TB	Molecular markers of <i>M.tb</i> early interactions with host phagocytes	976.000	5	FP6	STREP	Basic
scrINSILICO	Finding promising drug candidates against tuberculosis with multidisciplinary protocol based non-conventional search	1.000.000	7	FP6	STREP	Drug
TB-DRUG OLIGOCOLOR	Development of a molecular platform for the simultaneous detection of <i>Mycobacterium tuberculosis</i> resistance to rifampicin and fluoroquinolones	770.856	6	FP6	STREP	Diagnostic
TB treatment marker	Establishing a TB treatment efficacy marker	375.104	2	FP6	SSA	Diagnostic
Tuberculosis China	The diversity of <i>Mycobacterium tuberculosis</i> strains in China: tracing the origins of the world-wide dispersion of the multidrug-resistant Beijing genotype	150.000	2	FP6	SSA	Clinical and epidemiology
VACCINES4TB	Genome- and HLA-wide scanning and validation of cytotoxic CD8 T cell responses against <i>Mycobacterium tuberculosis</i>	1.053.445	4	FP6	STREP	Vaccine
NM4TB	New medicines for tuberculosis	11.070.000	21	FP6	IP	Drug
NEOTIM	Innate and adaptive immunity in clinical and experimental mycobacterial infection in neonates and infants	2.000.000	8	FP6	STREP	Basic
New-TBDrugs	New drugs for persistent tuberculosis: exploitation of 3-D structure of novel targets, lead optimisation and functional in-vivo evaluation	1.800.000	5	FP6	STREP	Drug
CSI-LTB	The role of chromosome stability in persistence, latency and reactivation of <i>Mycobacterium tuberculosis</i>	1.000.000	5	FP6	STREP	Basic
FASTEST-TB	Development and clinical evaluation of fast tests for tuberculosis diagnosis	1.217.800	8	FP6	STREP	Diagnostic
Immuno VacTB	A new approach for developing a less immunosuppressive vaccine for tuberculosis	857.298	4	FP6	STREP	Vaccine
MILD-TB	Immunogenicity of <i>Mycobacterium tuberculosis</i> lipids in the non-replicating status of latency	1.099.794	4	FP6	STREP	Basic
MYCOMANCY	Transcriptional regulation and cellular localisation of Mycobacterial cell cycle proteins during dormancy	835.875	5	FP6	STREP	Basic
TBADAPT	Effect of genetic variation in <i>Mycobacterium tuberculosis</i> on vaccine escape and the acquisition of drug resistance	1.794.956	11	FP6	STREP	Clinical and epidemiology
TB-DRUG	A SME-STREP for tuberculosis drug development	1.945.000	5	FP6	STREP	Drug
TBMACS	Identification and characterisation of <i>Mycobacterium tuberculosis</i> virulence genes involved in macrophage parasitism	734.713	3	FP6	STREP	Basic
TB-trDNA	Evaluation of transrenal-DNA detection to diagnose tuberculosis	2.000.000	8	FP6	STREP	Diagnostic
SERO-TB	Development of a specific serological kit for the diagnosis of TB	827.313	4	FP6	STREP	Diagnostic
TBIRIS	Pathogenesis and identification of predictive factors of TB-IRIS in HIV patients under HAART	2.475.482	6	FP6	STREP	Clinical and epidemiology
INNOVAC	Highly innovative strategies for vaccination to PRDs	2.000.000	7	FP6	STREP	Vaccine
HOMITB	Host and Mycobacterial molecular dissection of immunity and pathogenesis of tuberculosis	2.998.251	9	FP7	FRP	Basic
TB-EURO-GEN	Genetic analysis of the host-pathogen interaction in tuberculosis	2.838.624	4	FP7	FRP	Basic
NOVSEC-TB	Novel secretion systems of <i>Mycobacterium tuberculosis</i> and their role in host-pathogen interaction	2.821.726	8	FP7	FRP	Basic
TB-VIR	<i>Mycobacterium tuberculosis</i> W-Beijing genetic diversity and differential virulence and host immune responses	2.967.000	12	FP7	FRP	Basic
StopLATENT-TB	LATENT TUBERCULOSIS: New tools for the detection and clearance of dormant <i>Mycobacterium tuberculosis</i>	2.716.003	7	FP7	FRP	Diagnostic
TM-REST	A new platform for fast molecular detection of MDR and XDR resistant strains of <i>M. tuberculosis</i> and of drug-resistant malaria	2.983.207	9	FP7	FRP	Diagnostic
FAST-XDR-DETECT	Development of a two-approach plate system for the fast and simultaneous detection of MDR and XDR <i>M. tuberculosis</i>	2.695.565	8	FP7	FRP	Diagnostic

(continued on next page)

Table 2 (continued).

Acronym	Project title	EC contribution	Partners	FP	Instrument	Keywords
TB PAN-NET	Pan-European network for the study and clinical management of drug-resistant tuberculosis	10.998.270	27	FP7	IP	Clinical and epidemiology
Tbsusgent	Sustaining research momentum over the coming decades: mentoring the next generation of researchers for tuberculosis	999.909	7	FP7	Coordination actions	Basic
ESI-TBVI	Establishment, strategy and initial activities of the tuberculosis vaccine initiative: coordination of European efforts with global research initiatives	429.601	5	FP7	Support actions	Vaccine
NATT	New approaches to target tuberculosis	2.994.478	8	FP7	SICA Collaborative project	Drug
NEWTBVAC	Discovery and pre-clinical development of new generation tuberculosis vaccines	11.996.730	35	FP7	IP	Vaccine
TOTAL		115.673.000	331			

sectors. A particular effort has been made to attract small- and medium-sized biotech companies to the FP funded projects, and currently more than 20 such enterprises are participating in EC funded TB research. This is complemented by the participation of several larger pharmaceutical companies. Taken together, a significant proportion of all activities in the TB projects are now performed by industry participants, demonstrating that the FPs have become a useful tool for bringing together research teams from different sectors as well as from different nations.

4. Report on the EU conference

The increased global interest for research in TB has resulted in a boost for the entire field, which is now both expanding and changing in the light of new scientific discoveries. The European investments in TB research in previous FPs are also beginning to generate important results, with new vaccine candidates, new drug leads and new diagnostic markers starting to appear. It has therefore become timely to review and update the European research priorities for TB. To facilitate this process, the EC convened a high-level conference in Brussels in November 2008 on “Challenges for the future: research on HIV/AIDS, Malaria and Tuberculosis”.⁹ The objective of the conference was to establish an inventory of recent research results and to set research priorities on PRDs for the remainder of FP7. More precisely, the conference goals were to: (i) regain political momentum for continuing and intensifying research addressing the “big three” global killer diseases; (ii) set the scene by reporting on research efforts supported by the EC since 2002, when HIV/AIDS, malaria and TB first became a separate research focus under FP6; and (iii) gather input from relevant stakeholders in order to set research priorities on PRDs for the remainder of the FP7 and beyond. The conference, that was lead by a series of preparatory meeting, comprised a mix of plenary sessions for all PRDs, and separate breakout sessions for each of the three diseases. The specific recommendations for TB research were formulated during the TB breakout session, where approximately 100 scientific experts and stakeholders gathered to ponder about

four key areas in TB research: diagnostics, drugs, vaccines and global coordination of research activities. The deliberations and key recommendations are summarised below, while the full details are available on the EC website.¹⁵ The results are listed on Table 3.

4.1. Diagnostics and biomarkers

Improved diagnostics are imperative to TB care and control.¹⁶ Investments should be significantly increased in TB diagnostics, drug susceptibility testing and biomarker development to help to detect TB disease activity, cure and relapse.¹⁷ On the positive side, several new diagnostic tests are under development including culture-based tests to identify *M. tuberculosis* and to determine drug resistance, as well as molecular assays to detect antigens or DNA from the TB pathogen and antibodies from the patient's immune response. These developments work towards the high priority issue, which is to change the current gold standard test, sputum microscopy with more sensitive tests that can be applied at point of care since sputum culture is inadequate for extra pulmonary TB and for TB in children who do not produce sputum.

Biomarkers can be used in a broad context, e.g. for monitoring treatment, cure and relapse. Particularly, identification of suitable biomarkers can significantly facilitate diagnostics. TB biomarkers should be used for development of both diagnostic tests which differentiates between healthy individuals with a latent infection from patients with active TB and for development of prognostic tests which allows prediction of the risk of develop TB in latently infected individuals. Diagnostic tests should also be developed for serving as surrogate endpoint of disease for monitoring drug and vaccine trials in TB.

More resources than are available at the moment are required to support diagnostics-oriented basic science in pathogen biology, biomarker discovery, systems biology and point of care test development. Many diagnostic companies have become interested in working with academia and established project-driven public-private partnerships (PPPs) to develop diagnostic tests for developing countries. Such new concepts have led to the development of several technologies with interesting potential and should be supported by the EC.¹⁸

4.2. Vaccines

The classical BCG vaccine was developed in the first decades of 1900s, but it does not induce good protection in all geographic areas, particularly against adult pulmonary TB. After a long period of modest interest in TB vaccine research, there is now a rich pipeline of candidate vaccines, the majority of which has been developed in Europe. The most advanced vaccine candidate is MVA-85A, currently in phase II under a prime-boost strategy with

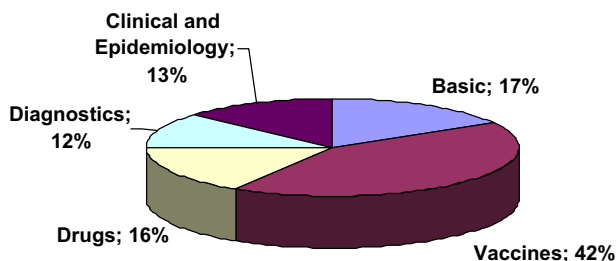


Figure 1. Distribution of EC funding in FP6 and the first 3 years of FP7.

Table 3
Recommendations from the EC PRDs conference.

VACCINES
1. Invest in 2nd generation pre-exposure TB vaccines able to achieve sterile eradication
2. Invest in 2nd generation post-exposure vaccines preventing disease in latently infected individuals
3. Combined vaccine strategies for 1st and 2nd generation vaccine antigens
4. Select vaccines that protect against broad spectrum of strains
5. Invest in centralised facilities for animal models
6. Invest in capacity for (late phase) clinical trials
7. Invest in advocacy to increase the global funding for TB vaccine R&D
8. Deliver affordable vaccines
DRUGS
1. Invest in new drugs and treatment regimens for eradicating latent infections
2. Prevent dormant <i>Mycobacteria</i> from re-activating in HIV-infected individuals
3. More efforts in phenotypic screening, new targets and ways of action, models of different physiological stages of <i>Mycobacteria</i>
4. Increase availability of and access to compound libraries with wider diversity and more drug-like properties
5. Increase industrial commitment to drug development in infectious diseases
6. Invest in infrastructure
7. Invest in clinical trials, and fill the gap between pre-clinical and clinical development
DIAGNOSTICS
1. Development of new tools should be prioritized to meet global needs, which are led by case detection and, secondarily, by detection of drug resistance
2. Change the current gold standard test, sputum microscopy with more sensitive tests that can be applied at point of care
3. Identify biomarkers to facilitate diagnostics
4. Invest in diagnostics-oriented basic science in pathogen biology, biomarker discovery, systems biology and point of care test development
GLOBAL COORDINATION
1. Strengthen the role of EC as a leader in TB research
2. Translate high-level political will into clearly articulated and timed pledges
3. Integrate and coordinate funding between EU countries and the EC
4. Articulate bolder vision for potential of targeted and integrated programmes
5. Develop a coherent and comprehensive research agenda, with balance between basic and translational research

BCG. Several products are in phase I (e.g. 72f, Hybrid 1, Aeras 402, rBCG-UreC-Hly), and many of these candidates are results from the EU FP6 projects TB-VAC and Muvapred, where valuable progress has been achieved.^{13,19} Several other candidates are in the pre-clinical phase; in a *M. tuberculosis* strain, mutation of virulence genes produced a TB strain conferring potentially greater protection with fewer side effects than BCG, and an improved, recombinant BCG vaccine with a higher efficacy and a better safety profile has just moved into phase I clinical trials.

Current vaccine candidates have been developed for pre-exposure administration. One of the important properties for these TB vaccine candidates is the ability to achieve sterile eradication. However, there is the need for a post-exposure vaccine for those who are already infected (currently 2 billion people) in order to prevent reactivation. In a next stage of research, combination vaccines should be considered in which the current first generation booster vaccines are associated with a second generation prime vaccine in order to deal with primary, active pulmonary TB and prevention of TB in latently infected individuals.

Vaccine testing should be conducted mainly in a naïve stage on *M. tuberculosis* uninfected individuals, and strategies should be developed to get vaccines from the research bench to the bedside and into the community. Apart from the protective effect of novel vaccine candidates, priority should be given to their delivery route, formulation (storage, shelf-life and distribution) and utility for HIV-infected individuals.²⁰ Another focus of vaccine development should be protection against the broad spectrum of *M. tuberculosis*

strains, ensuring effectiveness in different geographical regions. In the evaluation of all these vaccine strategies, confounding factors such as prior BCG vaccination or HIV status will be considerably complicating the clinical and epidemiological picture. For vaccination of HIV-infected individuals *M. vaccae* could be considered for further development or post-exposure prophylaxis.

Investment in global partnerships for vaccine development would help to sustain structures and organisations which are capable to strengthen the pipeline of next TB vaccines, including clinical trials in different geographical areas. Further advances towards a new generation of TB vaccines can only be made if policy-makers, funding agencies and scientists act in concert to remove barriers to cooperative research and development. Cross-cutting issues need also be addressed, including centralised facilities for animal models, novel imaging technologies and post-exposure models, and clinical trials capacity building, particularly phases IIb and III. Partnering current networks of trial sites and starting developing GMP production capacity for TB vaccines in developing countries should also be on the agenda.

4.3. Drugs

There is a wide agreement in the TB research community that the desired qualities of new TB drugs contain the following: (i) rapidly acting and potent; (ii) allowing shorter treatment regimens; (iii) effective against MDR-TB; (iv) safer than existing treatments; (v) allowing co-administration with anti-retrovirals; (vi) easy use in the field; and (vii) action against latent as well as active forms.

While there are still gaps at different stages of TB drug development, the number of candidates in the discovery and pre-clinical pipeline is increasing. Many different mechanisms of action and drug targets have been identified, and the most common aim is at increasing efficacy and/or reducing treatment duration (to 1–3 months). However, only a few target dormant bacteria and can therefore not be used for eradicating latent infections. The need for research into new drugs and treatment regimens which can achieve this therapeutic objective remains therefore urgent.²¹

Another priority is drugs that can prevent dormant mycobacteria from re-activating in HIV-infected individuals. They should avoid the therapeutic problems associated with co-infections, such as the antagonistic effect of Rifampicin on anti-retroviral drugs. Improvements in these areas would allow to further enhance patient acceptability, compliance, and adherence and to reduce new infections.²² Despite a 95% efficacious 6-month treatment, the TB problem is still expanding world-wide, among others due to emergence of MDR-TB and XRT-TB.

In the field of TB drug discovery, innovation may be expected from more efforts in phenotypic screening, seeking new targets and ways of action against mycobacteria, and developing models of different physiological stages. A coordinated effort should be made to further increase the availability of and access to compound libraries with a wide diversity of molecules and with optimal pharmacological documentation.

4.4. Global coordination and sustainability

The fragmentation of TB funding for research and development is a true problem, as well as the varying degrees of territoriality of the research groups. The time has come to play the same tune and to move forward together. The EC is in a good position to orchestrate global coordination in TB research funding, and has come at a critical juncture on which more focus and investment is needed. The EC should translate high-level political will into clearly articulated and timed pledges; integrate and coordinate funding between EU countries, the EC and other funders. Europe can play

a crucial role in innovation and discovery in the field of TB research. The EC, in particular through the EDCTP, should continue and increase its efforts to assist endemic countries in strengthening and harmonising the regulatory environment. The EDCTP's clinical research programme has now started off, including development of regulatory and ethical frameworks. It would be highly desirable to extend the current emphasis of the EDCTP from phases II to III drug trials to include also phases I and IV.⁹

The EC should aim to enhance and sustain TB research and development to accelerate a coherent and comprehensive agenda for research, development and capacity building. The right balance between basic, translational and applied research, including sustained and increased support to EDCTP is important; as well as taking on the responsibility to develop research and laboratory capacities for TB (including infrastructure, training and quality assurance) in countries with lesser resources.

Within the EU, national programmes, scientific institutions and funding bodies, transnational and non-governmental organisations must be encouraged to align and contribute to such a common agenda. In order to refute undue fragmentation and competition, the above agenda should be coordinated at the level of major global institutions. Europe needs to exploit its strengths in a global context together with the scientific community. We must define clear strategies for the control of TB in all settings; help to develop research and laboratory capacities world-wide, and support capacity building in clinical and public health research.²³

The EU is still lagging behind the USA in TB research funding and this gap could be closed. Despite the economic recession, the EC and Member States must sustain and increase funding for TB research, while improving its instruments to focus joint priorities and to facilitate the translation of research into new or improved diagnostics, biomarkers, drugs and vaccines.

Significant and concrete outputs of research and development on TB require long-term efforts. Continued funding is therefore a major issue, and the current project or programme funding from 3 to 5 years might not meet the expectations. The EU should join forces with other funders to create new funding mechanisms which ensure sustainable, transparent and pooled resources.

5. Concluding remarks

The European programmes for TB research have significantly contributed to advancing science and developing new vaccines, drugs and diagnostics against TB. The emphasis on transnational and trans-sectorial collaboration has been instrumental in achieving these results as well as building solid international partnerships. Despite the economic recession, it is important for the European Commission and its Member States to continue funding a multitude of TB research – basic, translational, clinical, and clinical trials – and develop better processes to identify, agree and coordinate research priorities. In the international landscape of TB research, with exciting novel technological developments in hand, investments and partnerships can pay off more than ever before. Maintaining and accelerating momentum is therefore important. Further coordination and alignment within Europe, with global organisations and most of all with the endemic countries can lead to great results which will lighten the heavy burden of TB throughout the world.

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