

A new global strategy for the life sciences in Europe

The challenges of the post-genomic era require new ways of organizing and funding biological research in the European Union

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Since the mid-1990s, the life sciences have undergone a major revolution. The systematic sequencing of the human and other genomes has triggered major changes in biological research, which was previously based on the traditional bottom-up philosophy of individual investigators contributing knowledge piecemeal. But technological advances and large-scale approaches to knowledge production require new ways to plan, fund and conduct research. These developments have also raised enormous interest not only from industry but also from politicians who count on the life sciences to create new jobs and economic developments. "Life sciences and biotechnology are widely recognized to be [...] the next wave of knowledge-based economy, creating new opportunities for our societies and economies," the European Commission (EC) stated in a strategy document (EC, 2002). This is testament to the political and economic importance of the 'omics' revolution—the use of high-throughput technologies to generate huge amounts of sequence, expression, protein and metabolic data.

It is against this background that the EC held a conference in Brussels entitled "Funding basic research in the life sciences: exploring opportunities for European synergies," a few days before Christmas 2004. The aim of the conference was to define a common European research strategy that would achieve one of the EC's *raison d'être*: encouraging the member states of the European Union (EU) to pull together the financial means and expertise that are

required to be competitive in the global economy. To this end, the EC proposes establishing a forum of high-level representatives from funding organizations to develop synergies and address the new challenges for biological research in a coordinated and cost-effective manner.

Although once a pioneer in genomics—thanks to the EC-sponsored sequencing of the yeast genome—Europe is now a minor player on the global scale, despite plethoric ambitions in most European countries to establish Silicon Valley-like bioscience parks. Victor de Lorenzo, chair of the European Group of Life Sciences (EGLS) that advises the European Commissioner for Research, recently warned of the economic consequences if Europe were unable to carry out research in genomics and its offspring. "While ownership of the information present in the human genome has triggered all social and political alarms," he wrote, "it is shocking that the factual monopoly of the exploration of the global genetic contents of the biosphere (which is yielding around one million new genes per year) by the USA is being left unchecked by Europe. [This] will mean that massive genetic resources will be owned by the few who get there first. Researchers on our continent have the ability and vision to implement ambitious metagenomic projects on a large scale, but lack funding and appropriate structure" (de Lorenzo, 2004). But it is not limited to the USA: Europe faces exacerbated competition from Japan and other emerging

economies in Asia, which are massively investing in the life sciences with the ultimate goal of acquiring proprietary data and reaping the economic benefits.

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Although the mass generation of data through 'omics' programmes must continue and be amplified, as pointed out by de Lorenzo, the next challenge is to translate this information into knowledge and eventually therapies, products and services. In this context, the investigator-driven approach, which is particularly strong in the life sciences, is still valid. But to assemble a larger picture of the mechanisms of life from huge data sets, more ambitious and comprehensive research strategies are needed. This so-called goal-orientated research relies on systematic and multi-disciplinary approaches in which intelligent systems harness individual units of information and integrate them into a larger context. One such example is systems biology, which requires an integrated vision and multi-disciplinary expertise that is often not available at a single location. Scientists from various institutions and research fields must therefore cooperate, which means making decisions on a common research strategy and research goals,

and establishing timetables and criteria for acceptance (Gannon, 2003). In addition, funding for such large and distributed projects must come from many different sources. Such an approach differs from the current Framework Programme consortia that join people with similar interests, albeit with a rather narrow focus.

Both post-genomics and goal-orientated programmes are integral dimensions of basic research, but they require long-term financial support and a restructuring of research communities. Furthermore, they share a common salient feature: an increasing reliance on infrastructures, such as databases and bio-computing facilities, mutant collections, bio-banks and archives. This includes infrastructures that were built primarily for the physics and engineering sciences, such as cyclotrons and advanced spectroscopy, but that are now becoming crucial for disciplines such as structural biology. This dependency on scientific infrastructure and the continued development of high-throughput technologies has led to an exponential increase in research costs in the life sciences during the past decade.

The question therefore arises: How can this new type of research be organized and funded? Hypothesis-driven research is primarily the responsibility of national funding agencies, which are geared for this purpose. In the future, they may be joined by a European Research Council (ERC) as the EC has proposed in its plans for Framework Programme 7. By contrast, major 'omics' programmes and the development of goal-orientated projects rely on critical mass in terms of human and financial resources, expertise and infrastructures, which are often beyond the capabilities of individual countries.

In this context, the goal of the December conference was legitimate and laudable, in particular as basic research slowly becomes a priority for the EC. Octavi Quintana Trias, Head of Health Research with the

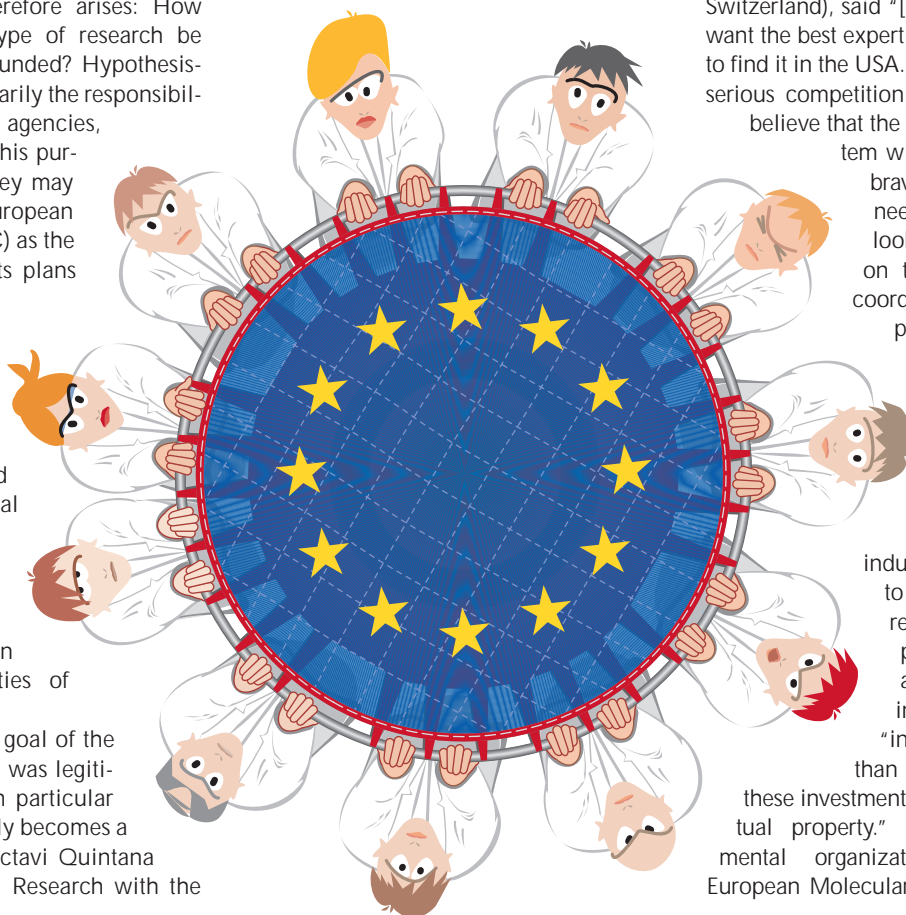
EC Directorate General for Research, even claimed during the conference—scientists, listen up—that “one of our main responsibilities as a funding agency is to fund basic research.” But it cannot be tackled through EC funding alone, which represents only 5% of the total investment in European research and development (R&D) in all disciplines. Europe as a whole invests some €30 billion in the life sciences each year. For ‘omics’ and goal-orientated research to succeed, the full potential of the European research area must be mobilized.

Today, the European science funding structure encompasses a great variety of parties and systems: national research councils and agencies, private foundations and charities, intergovernmental organizations, the EC and industry. This diversity, which reflects the parallel evolution of national systems as well as cultural differences, is a source of richness for Europe. But it is also a cause of redundancy in some areas and deficiency in others, especially where a critical mass of expertise and financial means is required.

The lack of political will and coordination at the European level has so far prevented the launch of joint large-scale programmes, which greatly affects the competitiveness of European research. Common efforts are also hampered by legal hurdles and national cultures and practices. For instance, eligibility criteria and evaluation procedures are often not compatible between various countries. To face this challenge, there is a need to confront existing funding systems and define common standards and practices. It also requires more exchange of information on programmes and priorities as well as prospective studies on issues with a European dimension. National agencies and other funding organizations must all be involved. This is the scope of the forum as envisaged by the EC, which should ultimately identify and decide on coordinated research strategies and actions.

Most participants in the conference were very supportive of this new EC initiative. Speaking for industry, Jonathan Knowles, President of Global Research at Hoffmann-LaRoche (Basel, Switzerland), said “[For the moment] if you want the best expertise, you are more likely to find it in the USA. And we will soon have serious competition in Asia. [...] I do not believe that the current [European] system will allow answering the brave question. What we need is a different way to look at science.” He went on to stress the need for coordinated approaches that put more emphasis on multidisciplinary research and the interface between basic biological research and other disciplines.

However, European industry would not be likely to contribute to a basic research fund, despite politicians' hopes and anticipations. “Pharma industry,” Knowles said, “invests more in R&D than other industries, but these investments are driven by intellectual property.” Similarly, intergovernmental organizations, such as the European Molecular Biology Organization



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(EMBO) or the Human Frontier Science Programme (HFSP), would not be helpful either. Their scope is often restricted to fellowship programmes and they could therefore not directly commit money to large-scale research projects. However, these organizations usually set standards in terms of quality and best practice and, building on their expertise and membership, they could have a major role in advising the forum. More support for joint initiatives could come from charities and private foundations, which in some countries represent a major source of research funding. The UK's Wellcome Trust, for instance, has been a key player in the sequencing of the human and other genomes and, at one point, represented the only substantial European contribution to these endeavours. Furthermore, charities and foundations are instrumental in advocating science and linking with the public and policy makers. However, their financial contributions would most likely be restricted to specific research topics and geographical areas. Obviously, the main targets of the forum are national research councils and agencies. To their credit, they increasingly cooperate in the development of joint programmes. However, the scope of these cooperations is rather limited and usually depends on additional 'networking funds' provided by the EC. As a sign of the times, most of the high-level decision makers were absent at the Brussels meeting—coincidence or a lack of interest?

Another impediment to international collaboration is the very contrasted situation among EU member states with respect to the priority of research and development in each country, the level of public funds available for research and research performance. Furthermore, national councils have their own policies and political agendas: to promote research niches, foster education, contribute to regional development and enhance research. Hence, agreeing on common priorities and providing money for joint initiatives may turn out to be difficult for some. All of this points to future

collaborations that involve only a subset of countries. All the better because it could save us from transnational approaches that pursue European cohesion for the sake of it, rather than being driven by scientific needs and arguments.

Whether countries that participate in joint programmes will then pool money, organize joint calls and evaluation and fund research projects from a common pot is doubtful. Although in a strict sense scientifically desirable, this could result in countries with less competitive teams sponsoring research in more advanced ones. An example, on a very small scale, is the Young Investigator Awards of the EU Research Organization's Heads Of Research Councils (EUROHORCs). Several participating countries had no young investigator awarded during the first round of selection, and it will be interesting to see whether these countries extend their participation should the next rounds of application lead to a similar result.

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So, could the forum bring about some of the much needed changes in the European scientific landscape? This will depend on a combination of factors. First, scientists must be closely involved in all aspects of the discussions and in the identification of priority areas. Second, it requires the political will and the right conditions for efficient decision-making. To this end, policy makers and administrators at the highest level must be engaged, for they are the ones who will give the necessary impulse and commit resources. This could probably not be achieved in the framework of a big stakeholders' conference in which hundreds of participants debate until the cows come home. It would be more likely to succeed if all decision makers were locked in a small room until white smoke comes out of the chimney similar to the election of a new pope. Third, the scope of the joint initiatives and the money committed to them must be commensurate with the scale of the problem. Finally, the long-standing problem of

creating and supporting research infrastructures must be tackled. Altogether, these are reasons enough to be sceptical, but one has to take the chance, as it is probably the only one left. On a more positive note, the Brussels conference showed a sense of frustration, chiefly among the countries that recently joined the EU and who seem particularly eager to be involved in shared initiatives. Therefore, even if it is not successful in terms of joint ventures, the forum may become useful for including those who feel excluded and may help to build a research community in Europe.

All these plans, however, do not address another important factor for biological research in the 'omics' era: research infrastructures. Although the topic was a recurrent theme at the Brussels conference, their funding does not seem to be the task of a forum as foreseen by the EC. The need to create and support infrastructures is obvious to every scientist, as highlighted by Fotis Kafatos, Director-General of the European Molecular Biology Laboratory (EMBL) in Heidelberg, Germany. "Infrastructures," he said, "are not equal to research, but they are absolutely needed; they are an integral part of any agenda of research in the life sciences." Kafatos listed bioinformatics, archives, tissue collections, genome reagents, structural biology infrastructures, clinical trial infrastructures, high-throughput and sequencing platforms, and added that these infrastructures must be embedded within excellent research centres in order to make them responsive to the needs of scientists.

But the concept of infrastructures is probably not so easy to grasp for politicians, especially given the specific requirements of the life sciences. Indeed, biological infrastructures differ substantially from the big infrastructures in the physical sciences, not only in terms of costs, but also because by their nature, they evolve. The lion's share of the investment is not made up front, but must be available for ongoing developments. The question is complicated further by the fact that the scientists behind these infrastructures often pursue their own research programmes for which they should be funded through competitive schemes. Theoretically, one should be able to distinguish between institutional funding for the maintenance, development and services for the scientific community on the one hand, and on the other hand, research

per se. But the overlap between the two tasks, and the failure to secure adequate research funding, often leads to problems, such as those repeatedly experienced by the European Bioinformatics Institute in Hinxton, UK, over the past few years.

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Kafatos therefore called for the creation of a European programme to create and support life science infrastructures based on an ongoing evaluation of requirements. This is to become the task of the European Strategy Forum on Research Infrastructures (ESFRI), commissioned by the EC and the EU member states (ESFRI, 2004). Its mission is to "support a coherent approach to policy-making on research infrastructures in Europe and to act as an incubator for international negotiations about concrete initiatives [...] for new research infrastructures of pan-European interest" (www.cordis.lu/era/esfri_home.htm). But even if the scientific and technical criteria for establishing new infrastructures can be agreed on, the question of their sustainable financing will remain the key issue. Research infrastructures in the life sciences are less prestigious than, say, CERN or the European Space Agency, and their return on investment is close to nothing, because none of the life sciences' infrastructures could successfully develop a sustainable business model. Consequently, individual European countries are reluctant to invest in these infrastructures. Even worse, until recently, EU member states prohibited the EC from investing directly in new research infrastructures, and allowed the commission only to facilitate access to existing infrastructures with hard currency in order to relieve their own financial burden. The solution may be to provide all the money centrally, whether through an intergovernmental agency or directly from the EC budget. But intergovernmental agencies would draw their money from national research agencies, with obvious consequences and expectable opposition, and EC funds are allocated through the framework programmes, which have a lifespan of only four years.

Be it research infrastructures, large 'omics' programmes or goal-orientated projects of common European interest and dimension, the main problem is, and will remain, the political will and the funding. Some scientists naively advocate the merging of national research councils. But even if it were desirable, Europe is not, and may never be, ready for that. In the long term, the solution may come from a European research agency, possibly the ERC with an enlarged mandate, whose budget would be provided by the EC. To ensure continuity and avoid the traditional bargaining and instability that characterize the framework programmes, this agency should be established as an EU agency in its own right. Its actions should only respond to scientific needs and be measured against scientific criteria; however, it could contribute to European cohesion by establishing new infrastructures throughout the member states.

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Given the current negotiations on the EU's future financial perspectives—during which, net contributors opposed budget hikes requested by the EC, notably to amplify its R&D—an alternative financing mechanism may be needed. The Commission has already suggested that contributions from member states could, at least in part, be replaced by a European tax, thereby disconnecting the EU budget from the budgetary situation of the member states. Although this was rejected by the EU member states, the debate has been launched and will certainly reappear. More cynically, further enlargements of the Union may eventually lead to a reorientation of EU policies in line with the Lisbon objective of knowledge-based society and the recommendations of the Sapir report (Sapir *et al*, 2004) that both call for higher investments into R&D. The large net contributors and the beneficiaries of the Common Agricultural Policy (CAP), who feared that a large chunk of this money would go to Central European countries at their detriment, already agreed to freeze the CAP budget before the recent EU enlargement in May 2004. The perspective that more Eastern countries and Turkey could

join the EU may well reinforce the trend towards a more science-friendly policy.

In the meantime, scientists will have to accommodate the present situation, lobby policy makers and seek more public support; and learn a thing or two from their US colleagues. At the conference, Mary Woolley, President of the lobbying organization Research!America (Alexandria, VA, USA), explained how instrumental they had been in maintaining the trust of the public and policy makers in order to make health and medical research a higher national priority. Research!America was even given credit by *The Wall Street Journal* for their role in doubling the budget of the National Institutes of Health. She concluded her presentation by citing Mary Lasker, who established the Lasker Foundation (New York, NY, USA) to increase the public awareness, appreciation and understanding of medical science in order to create public support for research: "If you think research is expensive, try disease." May this wisdom penetrate the minds of our policy makers.

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