order to correct for recognized inequalities: a boost has been given to the younger professors, to the humanities, and to the provincial universities. The total share of the humanities has been pushed from 15 to 25% of a budget that itself increased by more than 30% between 1989 and 1992. In much the same way, we have tried to correct for the historical concentration of funding in the capital city. It is a difficult problem to avoid, particularly in the humanities: Claude Allègre has called it the "law of inverse square distance from the Pantheon" since it seems that the only aim of certain professors is to end their career as close as possible to the Pantheon (even if not eventually being buried there—recall that the Pantheon is where our national heroes are buried). Parisian budgets have therefore been increased by 11%, whereas provincial ones were receiving a +18% boost. Another idea has been to create the Institut Universitaire de France (IUF) to which 15 senior and 25 junior members, outstanding professors from all fields, are appointed each year. They are awarded a special bonus for their research (FFr500,000 to be used over a 5-year period), are given a promotion, and are relieved from two-thirds of their teaching duties. In addition, the university in which they are elected gets a "free" additional full professor position in the same field, permanently. Only one condition: that the appointed IUF member remains for the 5-year period in the university in which he or she established his or her reputation. Moving from the province to Paris, which often in the past has led to the death of lively teams in provincial universities, would cause one to lose membership. Creating the IUF is a clear message that one can address both quantity and quality in renovating and promoting graduate studies and academic research.

Remaining problems lie with student and professor mobility at all scales (within France, within Europe, and outside of it). Mobility is traditionally and unfortunately low within France. In 1988, out of 2000 recruitments or advancements, only 10% occurred with a change in university! In 1992, 5000 recruitments or advancements will take place and there are indications that mobility has increased quite significantly. European programs such as ERASMUS and now Human Capital and Mobility should encourage the flow of students and academics. It is interesting to note differences in the relative numbers of Ph.D.'s awarded to national and foreign students by several countries (see Table 1). France and the United Kingdom appear to produce much larger relative numbers of "foreign" Ph.D.'s than the United States and Germany. As far as postdocs are concerned, a small program has been launched under which 150 positions are offered to students from OECD countries coming for 1-year stays in French laboratories. Several countries have already indicated their interest and willingness to reciprocate (first Australia, now possibly the United Kingdom and the United States). This program comes in addition to others jointly funded with the ministry of foreign affairs and the ministry of research and technology aimed among others at African countries, and also at the new Eastern and Central European countries.

Academic leaders in many Western European countries seem to share the same concerns: shortages in certain areas of research considered to be of strategic importance and a need to ensure flows of innovation into industry and to improve efficiency in training graduates. What has been achieved in France has been based on the recognition by the highest authorities that education and research are the topmost priorities and the basis for any investment toward the future (particularly for a country with no large natural resources). This priority has held for 4 years during which the total budget of the ministry of education has increased by more than 50%. It has involved the buildup of a new, largely international evaluation scheme: this harsh evaluation was not always easily swallowed at first but is now steadily gaining acceptance. Another asset has been the will to accept making choices and to largely redirect financing, rather than following a more traditional policy of marginal evolution (where one thinks that a 1% change in trend or budget is a great achievement). However the future of this renovation rests on very stringent conditions: a steady continuation of efforts during this whole decade and an opening to European countries, which are expected to eventually follow the same trend. Should these not be met, France could easily find itself beginning the 21st century a loser in the race toward the future.

Genome Research in Europe

Sir Walter Bodmer

The idea that polymorphic genetic markers and linkage analysis could be used to study human diseases goes back to J. B. S. Haldane and R. A. Fisher in the 1920s and 1930s. The development of recombinant DNA technology and of increasingly powerful techniques for long-range physical analysis of DNA has made it possible to clone genes for phenotypically defined human variation simply from a knowledge of their map position and so to elucidate the functional defect of many diseases. All this requires the availability of polymorphic markers spaced throughout the genome at a high density and physical maps that show the locations of the functionally expressed genes and their sequences. The aim of the Human Genome Project is to provide this resource as a basis for the elucidation, and eventual prevention and cure, of human diseases. The same approach applies to the study of normal human variation and to the analysis of variation in other organisms of economic or fundamental interest. But the major impetus for all genome projects is undoubtedly the drive to understand the human organism.

The Human Genome Project is too large for any one laboratory, funding agency, or country sensibly to undertake on its own. Furthermore, the information it will provide is a common good that should not be the property of any one organization, however large. The wide availability of the materials and resources needed for human genome analysis provides the opportunity for many scientific groups worldwide to participate in the project.

Collaboration works best when those involved see that they are going to get at least as much out as they put in. Participants, whether laboratories, whole countries, or even regions such as Europe, must be convinced that working together for the common cause is more efficient than going it alone, competitively, and without coordination. Collaboration also works best when the partners are well balanced in terms of their respective contributions to the overall project. For all these reasons, I believe it to be essential that Europe develop a coordinated genome program that can be an effective partner to the ones developing in the United States and in Japan and elsewhere. For the European contribution to be effective, I believe that each country should have a well-developed program of its own, both as a basis for participating in international collaboration and in order to exploit genome

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analysis effectively nationally. Only in this way will it be possible to remain at the forefront of disease control and other areas of cultural and economic importance, in particular the pharmaceutical industry.

European countries, especially the United Kingdom and France, have made major contributions to the scientific underpinnings of the Human Genome Project. An analysis of genome research carried out for the European Science Foundation (ESF) just over a year ago (ESF Report on Genome Research, 1991) showed that the percentage of the world share for 1990 from European Community (EC) countries was just under 30 percent, compared with 50 percent for the United States. The United Kingdom provided about a third of the total, followed by France and Germany. International comparisons of expenditure are always difficult, and the Human Genome Project is no exception. It is hard to draw the boundary between new resources specifically devoted to the project and the contribution of general support through conventional funding mechanisms. The ESF report suggested that overall EC expenditure was at that time about a third of that of the United States. The EC expenditure is less visible than that from the combined National Institutes of Health and Department of Energy program in the United States because it is so fragmented among countries. Only the EC program itself, funded from 1990 to 1992 at approximately $6.5 million per year, with an increase for the following 2½ years to approximately $13.5 million per year, stands out as a clearly defined European contribution. Thus, although Europe still lags behind the United States in terms of overall activity, it is making a respectable and effective contribution.

The United Kingdom, Denmark, France, Germany, and Italy have established national genome programs with others, for example, in Sweden, being developed. The former Soviet Union's program seems to be surviving, in spite of the current horrendous economic problems. Of all these, the United Kingdom's national program, funded by the Medical Research Council, is probably the most highly developed. The main support is for a resource center that provides specialist services to the community; collects, maintains, and distributes reagents, material, and data generated in the community; and carries out sustained and systematic programs of data generation, for example, in a complementary DNA sequence database initiated by Sydney Brenner. A "directed program" provides grants and contracts for research directly relevant to genome analysis. Nongovernmental sources also make significant contributions to the national and international genome efforts: the Imperial Cancer Research Fund has a substantial involvement in human genome analysis and the Wellcome Trust provides the major support for the London-based European office of the Human Genome Organisation, HUGO.

CEPH (Centre d'Etude du Polymorphism Humain), based in Paris and supported by a mixture of government and private sources, has been a major contributor to international collaboration in the construction of human gene maps. More recently, the French Muscular Dystrophy Association (AFM) has funded a large project called Genethon designed to coordinate disease gene mapping on a large scale, together with organized genomic sequencing. The major activity in Germany is so far based in Heidelberg, where the European Molecular Biology Laboratory has a strong tradition in genetic analysis and makes a specific contribution to DNA databases, while the German Cancer Center (DKFZ) is developing a broadly based human genome program with a particular interest in general integrated database developments for genome research.

The EC genome support comes from Brussels (through DG12, the Research Directorate) and, as in all such programs, requires participation of two or more EC countries. The programs are defined by means of a work plan, are targeted, provide research contracts, are able to pay by results (as with the fruitful project to sequence chromosome 3 of *Saccharomyces cerevisiae*), and have an emphasis on infrastructure, the provision of resources through centers and networking. The initial program supported a consortium of 23 laboratories in ten countries (EUROGEM) that aimed to improve the human linkage map to a resolution of three to five centimorgans. Collaborations for physical mapping of particular chromosomes, namely 11, 17, 21, and X, through exchange of cosmid libraries, support for technological developments, data handling and databases, consideration of ethical, legal, and social issues, and sponsorship of Single Chromosome Workshops were also included. A new program starting this summer will expand these developments and includes support for the distribution of yeast artificial chromosome (YAC) and complementary DNA libraries, the improvement of DNA sequencing methodology, and the improvement of coordination between and accessibility to existing databases, in particular the future of the Genome Database (GDB) and other international genome databases. Additional programs have supported the yeast sequencing project and analyses of the *Arabidopsis*, *Caenorhabditis elegans*, *Bacillus subtilis*, *Drosophila melanogaster*, mouse, and pig genomes. A particularly noteworthy example of international cooperation is the *C. elegans* project initiated by John Sulston from Cambridge and supported jointly by the Medical Research Council and the National Institutes of Health, with a possibility of additional funding from the EC.

The EC funding makes a particularly important contribution, as it coordinates programs such as EUROGEM and encourages collaboration between countries. It provides an ideal mechanism for top-down coordination, where this is appropriate and useful. The ideal situation is to have well-developed national programs, each with one or more resource centers, which can then be organized into an effective collaboration through EC funding. This is the basis, for example, for research on integrated genome database developments by a consortium of laboratories from the United Kingdom, France, and Germany. It is this group then that should collaborate with the United States' databases, GDB, and their parallels in Japan.

The role of HUGO, with members in 32 countries, is to establish a bridge between the working scientists, who wish to collaborate internationally and have clearly formulated views on how this should be done from the bottom up, and the national and international funding agencies which necessarily provide the resources from the top down. HUGO has had a difficult gestation. As it has been perceived by the scientific community and by government agencies to be important, it has been subject to considerable demands for support and organization, while commanding only minute resources. I believe, however, that HUGO is now coming out of an inevitable lag phase—as evidenced by the contract that the EC has awarded to HUGO to assist in the coordination of Single Chromosome Workshops, which lie at the heart of future international collaboration. The scale of support needed for the Human Genome Project necessitated the initial, direct involvement of funding agencies in the planning and the implementation of the science. In the absence of HUGO, or some other comparable organization, the Human Genome Project would inevitably become a fragmented activity, with the risk that one, or a few, countries dominate.

A considerable challenge for the future is to bring the European countries together "from the Atlantic to the Urals." Hopefully, well before 2001 the newly developing democracies of Central and Eastern Europe, including Russia and other states of the former Soviet Union, will have established themselves sufficiently to mount effective national genome programs. Then the challenge of Europe-wide coordination will become even greater. But Europe must be a major collaborator in the Human Genome Project with its other world partners.