lasting effects that could damage US science in the long run. Even if Bush's presidency is limited to one term, and Kerry is elected to office later this year, US science may not immediately recover, Waxman fears. "Some of the effects will reverse themselves once the administration changes," he said, "but I am concerned that many will be long term. The scientific integrity of federal agencies is at stake. If expert scientists are driven from public service, it will be more difficult to craft the best policies to protect the health and well-being of the American people."

While much of the talk and debate surrounding this presidential election is about domestic issues and the war in Iraq, it misses the important influence of American research enterprise on global policy and attitudes. As Democrats and Republicans debate the validity of criticisms aimed at the science policies of the Bush administration, scientists have more pressing concerns. Changes in science policy and the administration of federal research have also affected international health programmes for AIDS and women's health, which have suffered over the past four years from the Bush administration's reluctance to fund and support such efforts (Walgate, 2004; Germain, 2004). "My greatest concern is that we'll lose time because of this," said Keusch, who is now Dean and Provost for Global Health at Boston University (MA, USA). "And as I look at the crises of health in the developing world, there is no time to lose. We need to be acting now."

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Accession without concession

The ten new EU member states have an uphill battle to improve their science base, but would prefer not to play by different rules from the rest

On 1 May this year, the European Union celebrated its expansion to 25 member states, having welcomed 10 new countries, mainly from Eastern Europe, or to be geographically more accurate, central Europe (Fig 1). EU membership creates many opportunities for these countries, but with it come challenges, including the future of their life sciences research. The state of scientific knowledge, research and development in many of the new Eastern member states is the legacy of more than 50 years of misguided investment. Under Communism, an unhealthy bias towards strategically useful sciences—mathematics, physics and chemistry—came at the expense of biology, which for military purposes was of little interest. In Poland, for instance, as little as 20% of the entire research and development (R&D) budget is invested in the life sciences even today. What is lacking are certainly not brains and motivation, but rather the research infrastructure, which boils down to new laboratories, equipment and centres of excellence in certain disciplines.

While recognition and funding of scientists by external organizations, such as the Howard Hughes Medical Institute

and the European Molecular Biology Organization (EMBO), has certainly helped to lever more government funding in molecular biology, the degree to which recovery and convergence with the larger Western countries is possible differs widely. Among the so-called CC-10 countries one finds everything from large, slow-to-change countries, through smaller countries with excellent research in niche areas, to other small countries that have rapidly capitalized in the industry sector. Their current economic situation and investment in R&D vary considerably (Table 1). The disparities among the new member states themselves, and between them and the old EU members, have been debated hotly in European Commission (EC) circles. Proposals range from using some of the EU infrastructure funds to establish and maintain new research infrastructure in the East, to creating a two-tier system in the soon-to-be-established European Research Council (ERC) that would mainly benefit new members. However, scientists in the East have their own ideas on how to become competitive in the EU, despite acknowledging that their countries have to implement special measures to draw level with countries such as France, Finland, Germany or the UK in terms of research systems and performance. Most of the adjustments must be made at home, not on the international scene.

Most of the adjustments must be made at home, not on the international scene

Fig 1 | Expanding borders: existing, new and candidate countries of the EU

For instance Poland—the largest new member of the EU—puts a heavy emphasis on applied research, not unlike some older member states. According to Maciej Zylicz, Head of the Department of Molecular Biology at the International Institute for Molecular and Cell Biology in Warsaw, about 70% of the entire R&D budget goes into applied research, and only 30% into basic science. This focus on applied research remains a large problem: of the 240 research institutes created under Communist rule to make the link between science and industry, 220 are still open and, according to Zylicz, do nothing. “If you see the titles of these institutes, they make you laugh; some of the named industries don’t even exist anymore.” Polish scientists, on the whole, are therefore worried that they may not be able to compete successfully for EU basic research grants. But far from favouring a two-tier system, they would rather level the playing field gradually by using infrastructural money from the EC for scientific infrastructures instead of, say,

better roads. But as Zylicz pointed out, “It’s a tough decision when you consider that Poland doesn’t have any motorways.” Other funding from outside the EU does not make a large difference—important as it may be in particular fields, it tends to be very targeted.

“It would be useful to have a one-off injection of money for new instrumentation to boost us up to the same capabilities [as older EU states]”

While Poland may be bogged down by its over-concentration on applied research, Andres Metspalu—Director of the Estonian Genome Project, based in Tartu—complains of the opposite problem. “We have too much basic research, mostly funded from the government budget (two-thirds), and not so much from the private sector (one-third).” In Finland, Estonia’s neighbour, the balance of funding is reversed, and while Finland has

thriving technology-based industries, Metspalu laments that there are no industries in Estonia that really invest in science. To help budding entrepreneurs, the recently formed Estonian Enterprise Foundation offers financial support—part loan, part grant—to scientists who can team up with a private company to develop an idea. The other two components of government funding, from the Estonian Science Foundation, amount annually to €5.3 million for individual researcher grants, and €16 million for laboratory funding across all sciences.

Estonian life-science research is dominated by genetics, molecular biology and biotechnology. Despite the fact that many professors with degrees from the Soviet era are not competitive when it comes to obtaining EC funding, a positive legacy of the Soviets is the Estonian Biocentre in Tartu, which was established five years before independence after lobbying from Estonian scientists. This, and the emergence of private funding just before and during the 1990s, to some extent stemmed the dramatic brain drain seen in

other former Soviet block countries at the time of independence. EU monies also helped, but as Metspalu remarked, "The George Soros Foundation was probably more important than the EU in these difficult times."

Today, however, EU money is a "very substantial component of the funding of molecular biology and genetics research," according to Metspalu, accounting for up to half of the national budget in this area. "We're getting more out than we put in," he commented, continuing, "in a comparison of international peer-reviewed publications and grants, we're doing very well." In the 7th Framework Programme of the EC (FP7), Metspalu is looking forward to the promised inclusion of biobanking in the thematic priorities, which will allow Estonia to integrate its research into mainstream Europe. He hopes that the government will take the necessary steps to convert its recognition of biotech on paper into concrete measures in order to promote this sector.

Indeed, biotechnology is an area of intense focus for several new member states. Many of Hungary's institutes are part of a national programme for biotechnology (www.biotechnology.hu) and partners in the EU's 'cell factory' priority area. Furthermore, a recently passed innovation fund law requires all companies either to invest in their own R&D, or to pay an equivalent sum into a national innovation fund, which is matched by an equal contribution from the government. As Dénes Dudits, Head of the Institute of Plant Biology at the Hungarian Academy of Sciences in Szeged, pointed out, "there has been a decision at the political level to support biotechnology and genomics, but the total capacity for spending is low." Across all sciences, the country is struggling to creep up from 0.9% GDP spending on R&D.

But the recent bias towards applied research comes at the expense of a basic research sector that desperately needs new instrumentation in order to compete internationally for external funding. Although Dudits snubs the notion of a two-tier system, he concedes "It would be useful to have a one-off injection of money for new instrumentation to boost us up to the same capabilities [as older EU states]." Indeed, the €1 million that Hungary received in the 5th EU

Table 1 | GDP and investments on R&D in the new EU members

	GDP (millionUS\$)*	Population (1,000)*	Average income per capita (US\$)*	R&D (% of GDP) †
Cyprus§	8,900/1,217	776	16,000/5,600	0.25
Czech Republic	160,500	10,246	15,700	1.24
Estonia	17,370	1,342	12,300	0.75
Hungary	139,700	10,032	13,900	0.69
Latvia	23,770	2,306	10,100	0.41
Lithuania	40,170	3,608	11,200	0.60
Malta	7,082	396	17,700	Not available
Poland	426,700	38,626	11,000	0.75
Slovak Republic	72,290	5,424	13,300	0.66
Slovenia	36,890	2,011	18,300	1.51
EU-15	10,055,610	381,517	26,360	1.93
USA	10,980,000	293,028	37,800	2.7

*Source: CIA World Factbook. 2003 estimates for GDP and average income. 2004 estimates for population size. www.cia.gov. †Source: EC (2002) Science Technology and Innovation, Key Figures. European Commission, Brussels. §Numbers are for Greek Cypriot area and Turkish Cypriot area respectively. Data for 2001. Source: Science and Engineering Indicators 2004. US National Science Foundation. www.nsf.gov

Framework Programme (FP5) was put to very good use in preparing centres of excellence in time for accession. But the Szeged researcher complains that participation by Hungary in FP6 is much lower because the consortia are too large, and the chances of Hungarian researchers being successful are small. As an EMBO evaluation of molecular biology in Hungary in 1999 showed, the country is particularly strong in basic research in plant molecular biology, *Drosophila* developmental biology and neurobiology. However, materials science still dominates, and the proportional support of life sciences does not match that in the old EU states, according to Dudits.

Whereas Hungary has enshrined biotechnology at the political and legal level, the Czech Republic is still fighting legislation that does not support investments in research by the private sector, according to Vaclav Paces, Director of the Institute of Molecular Genetics of the Czech Academy of Sciences in Prague. This clearly pains him when he sees a "flourishing classical pharmaceutical industry"—represented by companies such as the American-owned Zentiva—taking advantage of highly trained, relatively cheap labour and low overheads. In comparison, he noted, "modern biotechnology, based on genetic engineering, transgenesis etc is performing very poorly." But a new programme of research centres to be started in 2005 will specifically address the link

between academic research and spin-off enterprises. In total R&D spending, the Czech Republic seems to be holding its own with the rest of Europe—1.5% of its GDP, of which 0.6% is spent on basic research—and Paces reports a government system of science funding that is very similar to the rest of the EU. But when it comes to EC grants, he is clearly concerned that the Czech Republic and other CC-10 countries might get a less than fair return in an ERC: "I am afraid that these countries will finance research in better developed and richer countries."

The brain drain from Eastern Europe has long been a thorn in the flesh of scientists who want to build up the system at home, and in biology it has been frighteningly high

Some economies are already racing forwards, economically speaking. Slovenia, for instance, ranks above Germany in a recent Price Waterhouse analysis of economic vitality, and has an expenditure of 1.51% of GDP on R&D—the highest among the new countries. A former republic of Yugoslavia, it broke with the Soviet Union in 1948 as a result of the split between Stalin and Tito, and hence has none of the baggage of the old Soviet science academies. Yugoslavia had no visa requirements, and was geographically and

ideologically on the doorstep of classical Western Europe, making it particularly open to investment. This has further been capitalized on by independent Slovenia, which has a booming pharmaceuticals sector, albeit in generics produced by foreign companies.

However, this is small consolation to scientists like Vito Turk, Director of the Jozef Stefan Institute in Ljubljana, who thinks that in basic and applied research, it could do much better. In total, 26% of government funding goes to the life sciences, which Turk describes as "a misunderstanding of [their] impact in the whole of research", continuing "today, you need excellent basic research if you want to make any kind of progress in applied research." As elsewhere, infrastructural funds will be diverted to establishing centres of excellence. Furthermore, nepotism and lack of objective peer review—problems common to many accession countries—need to be replaced by scientific evaluation at an international level. But while that very feature of the ERC is welcomed by Turk—admittedly with some kind of allowance for inferior infrastructures and a historical lag—he is convinced that the answer to competitiveness is to invest first nationally, rather than into a large EU pot.

For those who play the game in worn out shoes, the opening up of the labour markets and increasing mobility in Europe bring the overwhelming temptation to join a better equipped team in the West. The brain drain from Eastern Europe has long been a thorn in the flesh of scientists who want to build up the system at home, and in biology it has been frighteningly high. As Zyllicz lamented, "When I was teaching biotechnology in Gdansk, almost 100% of my students left for the USA or Germany after graduation." Although greater freedom to leave the new EU states is accompanied by greater ease of reintegration upon return, sufficient incentive to return is currently lacking in many countries. And it may be wise if the rest of the EU puts up some of this money. After all, as Turk pointed out, it is not generally to Western Europe that the brains flee, but rather out of Europe altogether, to the USA.

Brain drain is not a problem everywhere. Metspalu reported that qualified people in Estonia do not leave: of the 50 students graduating in biotechnology

each year in Tartu, most stay in Estonia, he said. Dudits also noted "a lot of our good postdocs return" despite the fact that after a PhD all students in Hungary are encouraged to go abroad. In general he thinks that brain drain from the East has been overemphasized. So too does Paces from the Czech Republic, who commented, "It is less serious than we expected. Czechs are probably rather conservative and like to stay at home."

Brain drain or not, changing the rules of participation in EC grants for new EU member states is not an option in the opinion of most scientists in those countries. A two-tier system would, as Zyllicz put it, "be a disaster." In his view, if the EC wants a more unified situation, it needs to invest more money in the infrastructure rather than changing the criteria. He continued, "In the case of Greece and Portugal [setting different criteria] was a disaster; we should not repeat this mistake. We joined Europe not to have two Europes, but to have one Europe," that is a Europe that dispenses money for basic research on the basis of merit—the antithesis of the old Soviet-style academies.

Brain drain or not, changing the rules of participation in EC grants for new EU member states is not an option in the opinion of most scientists in those countries

The ERC is, therefore, understandably supported by the new EU states—even if some see themselves not getting a '*juste retour*'—because it will put their scientists into direct competition with the best in Europe. As Zyllicz remarked, "Even if for the first few years Polish scientists don't do very well, this is the only way to adjust the average level of science in these countries." This element of 'standard-raising' competition is seen by him and others as the most important element of the ERC. But Dudits, also very pro-ERC, is anxious that its funding should come from a common EU budget and not from already creaky national funds; indeed, if the latter happens, it will not just be Hungary that ends up paying more into the EU than it gets back.

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Hormone therapy for the ageing

Despite the negative results of recent trials, hormone replacement therapy retains enticing promises for the elderly

Last year, two large trials in the USA and the UK dealt major blows to hormone replacement therapy (HRT), which was being used by millions of women to ease the effects of the menopause. The US Women's Health Initiative (WHI) and the UK Million Women Study (MWS) both showed that HRT increases the risks of breast cancer, dementia and stroke and other cardiovascular diseases (Brower, 2003). Both the US National Institutes of Health (NIH) and the British Medical Research Council halted the trials even before completion and

recommended that all women should abandon taking oestrogen and progesterone to reduce menopausal symptoms, such as hot flashes, sleep disruption and vaginal atrophy. Earlier this year, the NIH also stopped the oestrogen-only arm of the WHI trial because of a greater incidence of stroke among its participants. "Hormone replacement therapy are the three most controversial words in clinical medicine today," commented Michelle Warren and Sari Halpert from Columbia University in New York, NY, USA (Warren & Halpert, 2004).