MRC funds large-scale human genetic database…

A substantial part of the MRC's plans for its increased funding comes under the umbrella of the "post-genome challenge." According to this scheme, the MRC is to support large-scale, systematic approaches to revealing gene function, which will capitalize on the mass of sequence information generated by the Human Genome Project. To do this, it is focusing on four programs—two that target training in bioinformatics and related disciplines to bolster the scientific base and two that promote genetic studies in mice and humans.

David Porteous

Under the latter program, £12 million ($20 million) has been set aside to 'kickstart' the creation of a national genetic database. The aim is to collect a representative sample of around 100,000 individuals that, using high-throughput technologies, will be systematically studied to discover genes that contribute to many common diseases and allow identification of factors that affect responsiveness to drugs—pharmacogenomics. This venture will most likely be undertaken in collaboration with various medical charities and the National Health Service.

David Porteous of the MRC's Human Genetics Unit in Edinburgh, who has been instrumental in setting up the program, says that the money will be used to conduct studies on 60,000 existing tissue samples beginning next year, and thereafter to promote the collection of new samples and to establish technical centers that can undertake the type of industrial-scale analysis that is the project's aim.

As with other DNA database projects, however, there are many ethical issues that await resolution before the MRC can proceed. Patient confidentiality and informed consent are critical and of immediate importance, as the project will begin with genetic analysis of samples from existing patient cohorts. Although some of these patients have consented to broad-based genetic analysis of their samples, in other cases retrospective agreements will have to be reached.

Even murkier is the issue of what procedures should be followed once results of studies are obtained. Is it appropriate, for instance, to inform supposedly anonymous sample donors that they have a disease susceptibility? This may be acceptable if adequate prevention and treatment options are available, but the appropriate action is unclear regarding conditions for which there is no effective therapy.

The most controversial issue is the question of ownership, both of biological material and access to data, and the role of the pharmaceutical industry. Iceland is currently grappling with the same questions, and debate continues over a parliamentary bill which will allow one Icelandic biotechnology company (deCODE) exclusive rights to the health records of every citizen for its own genetic studies or for licensing to third parties.

Porteous envisages a somewhat different situation for the UK, based primarily on a relationship between academia and the NHS, which he insists "will in no way compromise patient confidentiality or incur any of the not unreasonable concerns about ownership of information and proprietary rights over particular patient sample sets." From this basis non-exclusive licenses for broad and general use by the pharmaceutical industry may be granted.

"If we don't have these [industrial] collaborations we will have failed. We must ensure that the best treatments come through the pharmaceutical industry, it is very much a partnership," Porteous told *Nature Medicine*. Within the context of such collaborations, he added, "maybe government agencies and charities can play a stronger role in setting the agenda rather than [have it shaped primarily by the pharmaceutical industry]."

REBECCA CURRIE, EDINBURGH

…and enhances mouse genetics programs

A new, coordinated mutagenesis program and an ongoing genome sequencing effort will also receive priority funding from the MRC's "post-genome challenge" investment in mouse genetics. The expansive mutation screening project will pre-empt a similar effort by the US National Institutes of Health, which has also now made mouse genetics a high priority. The moves reflect general scientific thinking that mouse studies will be in the vanguard of approaches for functionally interpreting the human genome sequence.

The level of funding for both projects is yet to be determined, but the Sanger Centre in Cambridge is likely to get the largest share to enhance its mouse genome sequencing program. Most of the funds available for the mutation screening program will be directed to the MRC's Mammalian Genetics Unit in Harwell, Oxfordshire. According to Nick Hastie, Director the MRC Human Genetics Unit in Edinburgh, the MRC is inviting applications from members of the research community who wish to add further mutation screening rationales. "40,000 mice are to be screened for a wide range of disorders so any new test that can be added will make it a more efficient screen," he commented, adding that the MRC's own tests will be in the areas of cancer, heart disease, diabetes and a range of neurological and psychiatric disorders.

Nick Hastie

The project has already garnered commercial interest from SmithKline Beecham (SB), which is contributing over £1 million to a pilot neurological/behavioral screen in return for first rights on any interesting mutations. Although Hastie says that screens for academic researchers will be largely separate to those for companies such as SB, he concedes that "whether there will be some overlap between the two is not clear." Such overlap may create tension if competing claims for the same mutant mice compromise either academic access or company exclusivity deals. This is an issue that the MRC will be eager to clarify, given speculation that it is considering a commercial spin-off for mouse genetics.

Commenting separately on the MRC's commitment to also support bioinformatics training, Hastie notes that this area has been identified as a potential bottleneck for post-genomic future research, as there are not enough people trained in this area coming through the academic system (*Nature Med*. **4**, 1214; 1998). As evidence of this he indicates that the Ph.D. studentships offered by the MRC in bioinformatics have been difficult to fill. One of the main problems he cites is competition from industry that can pay higher salaries.

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