

NIH gearing up to tackle the human genome

- New office to be created
- Prospects for 50 new fellows

Washington

THE National Institutes of Health (NIH) have left the sidelines and entered the fray in the effort to map and sequence the human genome. Director James Wyngaarden last week revealed NIH's plans following a two-day meeting of an *ad hoc* committee on complex genomes that he brought together to advise him on how NIH should proceed. The meeting marked a change in course for NIH and the human genome project. The recommendations did not consider whether the project should proceed, but how.

Wyngaarden says budget commitments from Congress and the Reagan administration have now made it possible for NIH to formulate long-range plans. Congress appropriated \$17.3 million to NIH specifically earmarked for genome activities in 1988, and the president's 1989 budget requests \$28 million for the project.

The first step will be to form a new genome office in the office of the NIH director, headed by an associate director. Although money will still be doled out by the individual institutes (primarily the National Institute of General Medical Sciences) the new associate director will coordinate the grant-making process, guided by a programme advisory committee.

NIH's plans fall largely along the lines recommended by the National Research Council (NRC) in a report released last month (see *Nature* 331, 467; 1988) with total spending set ultimately to reach approximately \$200 million per year. An immediate goal is a genetic linkage map with a resolution of one centimorgan. A working group of the *ad hoc* committee recommended that such a map, constructed with generally available probes, should be completed "as rapidly as possible". The working group estimated the cost for completing a linkage map in the next 3-5 years at \$50-70 million.

A key aspect of the NIH efforts will be graduate and postgraduate training. It is recommended that NIH should support 50 new post- and pre-doctoral fellows to ensure a steady supply of researchers needed to complete the project.

The basis for making grants will be projects that are intended to improve the scale of current activities between five- and tenfold. This idea of using improvements in scale as a basis for making grants is found frequently throughout the NRC report. It is intended to keep a rein on the project, making investigators provide

specific targets for improvements. Maynard Olson of Washington University and a member of the *ad hoc* committee says that loose definitions make it difficult to judge a project's success or failure.

Olson, who played an instrumental role in developing yeast artificial chromosomes that hold the promise of creating DNA clone libraries of 1 million base fragments, says the scale concept is crucial to make sure the project does not get out of hand. Olson says that although there is some fear that a large mapping and sequencing effort would rob other projects of funding, another concern is that the project would be propelled for political rather than scientific reasons.

As one of the few researchers involved in projects aimed at physical mapping of entire genomes, Olson worries that others have underestimated the difficulties of making such a map of the human genome. The largest genome to have a high-resolution physical map is *E. coli*, but that is only 4.7 million bases, compared to 3,000 million for the human genome.

Completion of the project does not consist solely of establishing a sequence for the human genome. Wyngaarden has made it clear that analysis of the genomes of other species will be an integral part of the project. Wyngaarden also says that NIH will continue to support individual investigations designed to make sense of sequence information as it is amassed.

Reaction to NIH's plans has been mostly enthusiastic. James Watson, director of the Cold Spring Harbor Laboratory, says he is extremely pleased that NIH have taken the bit in pursuing the genome project. David Smith, who heads the Department of Energy's efforts in this area says now that NIH have staked out a position it will be easier to establish momentum for the project.

George Cahill, of the Howard Hughes Medical Institute, also a participant in the *ad hoc* meeting, says that Hughes' efforts will focus on data handling. Work on merging genetic databases will begin immediately while NIH are putting their plans into practice. Congressional interest in the genome project will also be a factor in how far NIH can go with it. Congress may be reluctant to put NIH in charge of what will certainly be a technology development programme in its early stages. That role may belong with the Energy Department and the National Science Foundation.

Joseph Palca

Congress keen to top NIH's requests

Washington

"By far the best budget proposal from any administration in a decade" is how NIH director James Wyngaarden described the 5.4 per cent budget increase proposed by the administration for 1989. But Wyngaarden, testifying before the House Appropriations Subcommittee in his role as spokesman for the administration, did not deter his traditional supporters. The subcommittee appears ready once again to give more than NIH is officially asking for.

Wyngaarden's testimony focused on the achievements of the NIH and contained no hint of a hard-luck story. But he did voice worries, shared by members of the committee, that NIH are losing good people to universities and teaching hospitals because of large pay differences. "It's not yet a haemorrhage but remedial action is needed", he claimed.

In cross-questioning by the committee, the adequacy of the budget came under close scrutiny. For in spite of the "magnificent increase" heralded by Wyngaarden, NIH's budget formulation office estimates that a further \$500 million is necessary to maintain NIH's current levels for 1989.

For grant applicants, the biggest worry is that there will be 800 fewer grants next year. The level of funding per grant is also at issue. Although rising since 1982, the level of 1974 has only recently been regained. And the discrepancy between the awards recommended by the study section reviewers and the amounts actually awarded (downward negotiation) will reach a record 13.3 per cent in 1989. Meeting the targets for numbers of grants means less to spend on each.

Committee members pressed Wyngaarden to identify projects and opportunities that would be short-changed or excluded under the proposed budget. This yielded few specific answers apart from the clinical trials programme where funds for new trials are severely limited. Wyngaarden promised to submit details of what had been cut from a much larger, provisional request prepared in an earlier phase of the budget negotiations.

Subcommittee chairman William Natcher (Democrat, Kentucky) seemed confident that Congress could outdo the administration.

This will be a "People's Appropriation Bill" he claimed, arguing that money for such a good cause would not be refused. Some of his staff are less sanguine. The Bipartisan Budget Agreement, which limits the overall increase on non-defence spending to 4.8 per cent, has placed a ceiling on everyone's expectations.

Penelope Austin