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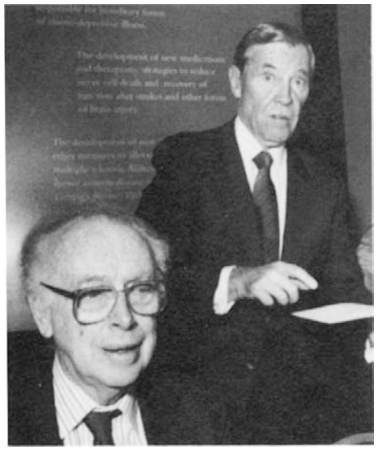
Pushing the brain initiative

In few areas of biomedical research is the impact of the revolution in genetics as great as neuroscience. Even so, it would have been surprising if the dozens of eminent neuroscientists who were invited by James Watson to Cold Spring Harbor six months ago to ponder the state of neuroscience could have foreseen the rapid identification of the genes for Huntington's disease (HD), amyotrophic lateral sclerosis (ALS) and adrenoleukodystrophy, let alone a host of other notable advances in genetic analysis. But, as this is the 'Decade of the Brain', many in the United States are becoming concerned that neuroscience research is not faring as well as it should among the lawmakers who decide the priorities in biomedical funding.

Chief among those concerned is David Mahoney, 70, a retired businessman who was chief executive of Norton Simon before the company was bought out, leaving him unemployed (albeit some $40 million better off). Long a supporter of neuroscience, Mahoney subsequently directed his considerable energies into supporting neuroscience institutes at Harvard and the University of Pennsylvania and in being chairman of the Dana Foundation, which aims to promote the understanding and treatment of the broad spectrum of neurological disorders. This culminated recently in the launch of the Dana Alliance for Brain Initiatives, an organization comprising more than 50 distinguished neuroscientists devoted to advancing brain research and public awareness. A recent opinion poll on behalf of the Dana Foundation provides much food for thought: nine out of ten Americans surveyed know someone who has suffered from a neurological condition (hereditary or otherwise), but, surprisingly, only one out of four associates such illnesses with brain disorders.



Mahoney (standing) and Watson promoting the Dana Alliance.

The problem posed by brain disorders is immense. In the United States alone, 50 million people are affected by neurological disorders, costing the taxpayer more than $300 billion a year. The Dana initiative therefore intends to promote ten research objectives formulated at the Cold Spring Harbor meeting that are thought to be achievable by the end of the decade (see box). Two of the objectives have essentially been reached already, thanks to the cloning of the genes for ALS and HD (discussed in this issue[1]), and the rapid progress in mapping familial Alzheimer's disease. But these achievements mark just the beginning of the many contributions of genetics to this vital field. All four known disorders caused by triplet repeat expansions are neurological conditions, and the efforts being made to find similar genes will probably explain a great many more. Despite large gaps in our understanding of fragile X syndrome, the most common hereditary form of mental retardation, a series of papers in this issue sheds light on the behaviour of these repeat sequences[2,3] and a means of detecting similar stretches in the genome[4]. Genetics is also providing valuable insights in other branches of neuroscience, such as the mapping of genes for

Dana Alliance top 10 objectives in neuroscience by the year 2000

1. Identification of the genes that are defective in familial Alzheimer's and Huntington's diseases.
2. Identification of the genes responsible for hereditary forms of manic-depressive illness.
3. Development of new medications the therapeutic strategies to reduce nerve cell death and enhance recovery of function after strokes and other forms of brain injury.
4. Development of new drugs and other measures to alleviate the effects of multiple sclerosis, Alzheimer's disease, motor neuron disease, Parkinson's disease and epilepsy.
5. Identification of new treatments to promote nerve regeneration following spinal cord and peripheral nerve injury.
6. Development of effective treatments for manic-depressive illness, anxiety disorders, and forms of schizophrenia.
7. Discovery, testing and application of agents that will block the action of cocaine and other addictive substances.
8. Development of new treatments for pain associated with cancer, arthritis, migraine headaches and other debilitating illnesses.
9. Identification of the genes that cause hereditary deafness and blindness.
10. Elucidation of the neuronal mechanisms involved in learning and memory.

hereditary deafness (in a large kindred from Costa Rica)[5], epilepsy[6] and stroke[7], and the association of mutations in the thyroid receptor gene with cases of attention-deficit hyperactivity disorder[8]. A new cause of hereditary blindness is also described in this issue[9]. Many other important, if less well recognized, neurological disorders are succumbing to linkage mapping. This issue of *Nature Genetics* contains a report of the linkage of familial dysautonomia[10] to chromosome 9, and next month's issue will include articles on the mapping of genes for a form of spinocerebellar ataxia[11] and Machado-Joseph disease[12]. The initiative will, of course, encompass many other neurological conditions including the treatment of substance abuse, spinal injuries and depression, areas in which encouraging advances are being made. But, as Watson says, gene identification offers not only the quickest route to effective therapies but also the possibility of ridding society of some diseases.

Mahoney and others realize that communicating these exciting developments to the general public and politicians is essential if recent gains are to be fully exploited. To this end, the Dana Alliance is promising a campaign to educate the public, including electronic town hall meetings and an "800" toll-free telephone number for journalists with scientific queries. More pressing is the need to convince members of Congress, but despite the notable support of congressmen such as Senator Bill Bradley (Democrat, New Jersey), there are many other worthy causes vying for research dollars. Indeed, the latest funding proposals give little grounds for optimism. The proposed 1994 budget sent by President Bill Clinton to the congress contained healthy increases for AIDS, breast cancer and the National Genome Center, but virtually all other divisions of the National Institutes of Health (NIH) suffered by comparison. Both the National Institute for Mental Health and the National Institute of Neurological Disorders and Stroke - two of the ten largest branches of the NIH in terms of funding, with a combined annual budget well in excess of a billion dollars - will suffer cuts of more than one per cent (before inflation). Of course, no-one in the neuroscience community suggests that AIDS and breast cancer are not eminently worthy causes, but like investigators in many other fields, they believe that more money is needed.

Recent history shows that a grass roots campaign to lobby politicians can be extremely effective in stimulating increased funding. Women's groups outraged by the toll of breast cancer learned from the AIDS activists, with the result that for the past two years the NIH has received a substantial increase in funding earmarked for breast cancer, in addition to the $210 million allotted last year to the US Army for this purpose. Groups representing the growing elderly community in the United States have also been vocal in demanding more money, and with some success. The neuroscience community will probably have to wait another year for the sort of increases it is hoping for, but the momentum being generated by genetic discoveries should help to make an utterly convincing case. □

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