7. RESEARCH

Molecular genetics provides new tools to investigate the processes of health and disease.[159] In addition to the potential for health care applications, these technologies could foster the development of a world-class Canadian biotechnology sector. The research required to realize these benefits will be a major focus of national and international activity for a long time to come.

Considerable research is needed to realize the potential health care and commercial opportunities of genetic knowledge.

There are numerous areas in which Canadian researchers can contribute, including:

- development of better methods for cloning and sequencing DNA and better computer capability for handling sequence data;
- contribution to the international effort to map and sequence the human and other genomes;
- identification of the physiological role of particular human genes and of the significance of the silent stretches of DNA between genes;
- correlation of genes and their expression;
- clarification of the biological processes underlying health and disease;
- investigation of the degree and origin of genetic variation in Canadian populations and of clustering of genes in certain populations;
- development of diagnostic and treatment technologies for specific genetic diseases and mutations;
- research on identification and control of mutagens.

There are many priority areas for research, including investigation of mutations that are specific to Canadian populations.

There are several specific reasons for Canadians to be involved in genetic research. As a consequence of immigration and settlement patterns, some diseases and mutations occur with higher than average frequency in certain regions of the country or subgroups of the population. Research is needed to identify these mutations and to develop solutions to health problems of particular concern to Canadians.

In addition, Canada could benefit from the health, biotechnology, and commercial opportunities that will arise nationally and internationally from the genetic technologies.

"Big" versus "Small" Science

Development of human gene maps and genome sequences is "big science" and requires international cooperation and extensive effort, time, and money. As the rate of mapping and sequencing accelerates, the critical chore of accessing current information will become more difficult. However, several countries are now in the process of forming the Human Genome Organization (HUGO), an international body for coordinating human genome mapping and information. HUGO will aid international efforts by, for example:

Gene mapping and sequencing involve international cooperation.

- providing common systems to facilitate international transfer of data;
- developing consistent reporting formats; and
- assisting in the collection, storage, and distribution of DNA clones and human cell lines.

The organization and funding of genome mapping and sequencing have sparked vigorous debate in the United States, Japan, England, and France.[160] Despite the importance of the information generated, there is concern that the funding of such "big science" projects will siphon money away from

independent "small science" research. New approaches, such as sequence-tagged-sites mapping, provide "small" and "big" players with equal opportunity to participate in the mapping project.

Canadian Participation

Canada has made significant contributions to genetics research.

Canada has been a major contributor to genetic research, primarily in identifying the role of specific genes and gene-disease relationships, and in developing effective screening and treatment technologies for genetic diseases. Most of the genome mapping work is being done in the United States, Japan, and Europe, but Canadian scientists have played and are continuing to play an important part in this international effort. Our contributions are based not on large mapping and sequencing programs, but rather on investigating those portions of DNA where mutations are found with high frequency in Canadian populations. Canadian studies of families with certain genetic diseases have provided valuable information. Canada has world-class research teams and research centres, and exceptional competence in data storage and analysis. Canadian researchers are currently at the forefront in the investigation of such important diseases as Duchenne muscular dystrophy, cystic fibrosis, hypercholesterolaemia and Huntington disease.[161]

A network on genetics of human diseases has been established in the National Centres of Excellence Program.

The Canadian government recently acknowledged the importance of human genetics research in Canada by establishing a network called "Genetic Basis of Human Disease: Innovations for Health Care" in the National Networks of Centres of Excellence Program.[162]

Underfunding

Despite the infusion of new research funds in the National Centres of Excellence Program — including $17 million over four years for genetics research — medical research in Canada is chronically underfunded.[163] Whether expressed in absolute dollars, or as a percentage of gross national product or per capita contribution, Canadian allocations to medical research fall significantly below expenditures in other developed countries.[164] Underfunding has a particularly negative impact on new areas of research, on individuals early in their research careers, and on research that requires sophisticated equipment or technology. Molecular genetics research is vulnerable on all three counts. These resource limitations hamper our progress in resolving important health problems.

Underfunding is hampering progress in solving important health problems.

In 1988-89, an estimated $400 million was allocated to health sciences research in Canada.[165] This total includes funds from federal and provincial governments and from voluntary agencies and foundations. The relevant private sector allocations are not known but may constitute an additional 10 per cent. The Medical Research Council (MRC) is the single largest source of medical research funding in Canada, providing $190 million, or 48 per cent of the total, in 1988-89.

The proportion of medical research funds spent on genetic research in Canada is small.

The proportion of medical research funds spent on genetic research in Canada is small, but the precise amount is difficult to determine. In the case of the MRC, this is because much of the relevant funding is allocated through MRC granting committees other than the genetics or molecular biology and

biochemistry committees. In 1988-89, the genetics review committee approved grants of $3.8 million (3.5 per cent of all research grants) and the molecular biology and biochemistry committee approved grants of $16.2 million (12.5 per cent of total grants). Over the past five years funding levels for molecular biology and genetic research have increased slightly.[166]

The MRC awards funds to applicants on the basis of excellence of the research proposal and past performance of the researcher. It rarely targets specific research topics. It is important to maintain basic research, which has accounted for some of the major advances in medicine, but there is also a legitimate need for targeted research; and there are areas in genetics-related research that warrant targeting.

Both basic and targeted research are necessary.

Finally, innovative approaches, including group and program grants and research networks, foster the establishment of research teams and provide opportunities for coordinated research that is multidisciplinary and multitechnological in nature.

Private Sector Biotechnology Research

In 1986, 52 biotechnology companies — 30 per cent of all Canadian firms involved in biotechnology — undertook research and development in the area of health care.[167]

As a consequence of Bill C-22, investment in one relevant area — drug-related research and development in Canada — is growing. In 1988, 57 patented drug firms reported a total R&D expenditure of $164.5 million.[168] Much of the research involved participation of universities, medical schools, research teams, and networks. A Pharmaceutical Manufacturers Association of Canada survey of 47 of its members indicated that investment in R&D increased from 4.9 per cent of sales in 1987 to 6.4 per cent in 1988; the industry goal is 8 per cent by 1991, and 10 per cent by 1996.[169]

However, among the 30 biotechnology companies that responded to a 1989 Science Council survey, fewer than 10 were active in development of specific diagnostic or therapeutic products for genetic diseases.[170] Those firms that were active focused on the more common single-gene and multifactorial disorders, including cystic fibrosis, thalassaemias, muscular dystrophy, haemophilia, dwarfism, dementias, cancers, and cardiovascular disease. Most of the research on the relevant drugs is undertaken by large multinational firms. This is a reflection of the time (9-12 years) and investment (an estimated $200 million) required to bring a new drug to market.[171]

Few private sector firms are involved in developing specific diagnostic or therapeutic products for genetic diseases.

Firms cited various reasons for the relatively low rate of private sector research activity in gene-disease diagnostics and therapeutics, including:

- a lack of available funding, particularly venture capital funding;
- the fledgling state of scientific knowledge on gene-disease relationships;
- inadequate patent protection;
- uncertainty regarding possible regulatory changes affecting diagnostic and therapeutic products;
- uncertain market demand; and
- potential public concerns over ethical issues related to genetic technologies.

There are several reasons for the low rate of private sector research.

Various mechanisms could enhance the level of private sector research.

The biotechnology firms identified mechanisms that they believed would enhance the level of private sector research. Chief among these were tax credits for investors, tax credits for firms, increased direct funding, and better patent protection. Part of the solution would involve more business and entrepreneurial training for university science students. In addition, more assistance in the areas of marketing, financing, and management should be available to scientists and small firms at the start-up level.

More publicly funded research would better delineate gene-disease links and pave the way for private sector involvement. There is also a need for some fundamental market development work, specifically to raise the awareness of governments, physicians, and individuals of the potential benefits of genetic diagnostics and therapeutics. If a market exists and the basic scientific knowledge is available, the private sector will develop appropriate products.

Research Guidelines

There is a need for wider awareness, discussion, and adoption of guidelines and review procedures to ensure that proposed research projects incorporate safety and ethical considerations and do not pose a risk to the human participants or the environment. In addition to the existing national guidelines for use of recombinant DNA technology, there are MRC guidelines dealing with human experimentation and somatic cell gene therapy research.[172] Only MRC-funded researchers must follow the MRC guidelines, although other research funding organizations such as the Natural Sciences and Engineering Research Council and some hospital research and ethics committees have chosen to adopt them. It would be desirable if all researchers in these fields did so.

Research guidelines should be widely distributed and adopted.

The existing guidelines indicate respect for the potential hazard to humans associated with genetic research. Researchers and policy makers alike recognize that the continued development of guidelines, and if necessary regulations, will be essential as human genetic research evolves. The recently established National Council on Biomedical Ethics will assist in ensuring that effective review procedures and appropriate guidelines and protocols are in place to cover medical research in Canada.