BULLETIN

CANADIAN GENETIC DISEASES NETWORK

SCIENTISTS PINPOINT REGION FOR CYSTIC FIBROSIS MODIFIER GENE

Toronto - June 1, 1999: An international team of researchers, led by Canadian Genetic Diseases Network researcher, Dr. Lap-Chee Tsui of The Hospital for Sick Children and the University of Toronto, has identified a region on chromosome 19 that contains a gene which modifies the severity of cystic fibrosis (CF). While such a modifier gene has been found in mice with cystic fibrosis, this is the first time a similar gene has been shown to exist in humans. The results are published in the June issue of the scientific journal *Nature Genetics.*

Cystic fibrosis is the most common single gene disorder in the world, affecting one in every 2,000 children. In patients with CF, the secreting glands fail to function properly. Many body organs are affected, including the lungs, pancreas, liver, sweat and salivary glands, gastrointestinal tract and the male reproductive tract. The majority of patients with CF succumb to severe lung infections before age 30.

"The area we have pinpointed contains a gene that is involved in modifying the severity of a common intestinal obstruction in patients with cystic fibrosis", explains Dr. Julian Zielenski, the paper's lead author "Up to 20 percent of CF patients have this obstruction, called meconium ileus, but we've never been able to find a connection between a mutation in the CF

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gene and the development of the obstruction. Now we know that the obstruction is not caused by a specific mutation in the CF gene itself, but by the activity of a modifying gene." The data generated by previous HSC research in mice led directly to this most recent discovery.

The cystic fibrosis gene, identified in 1989 by Dr. Tsui and colleagues at HSC and the University of Michigan, has more than 800 different mutations, all causing variations in the disease. However, not all clinical variations in cystic fibrosis can be attributed to mutations in the gene. As a result, scientists have suspected that other factors are involved, such as the activity of other genes which have a modifying effect on the disease or various environmental conditions. However, modifier genes have never been found in humans.

The identification of modifier genes in CF will allow scientists to gain a better understanding of the different clinical presentations of the disease which, it is anticipated, will lead to insights into prognosis and management of cystic fibrosis, as well as development of novel therapies.

The Canadian Genetic Diseases Network is a not-for-profit nation-wide centre of research excellence under the federal Networks of Centres of Excellence Program. CGDN creates strategic partnerships to commercialize discoveries for the benefit of health care in Canada and worldwide. Fifty scientists and their teams, based in 18 universities, hospitals, and research centres across Canada, focus on the molecular and cellular causes of inherited disease. In 1997, CGDN was awarded a further seven years' core funding by the Networks of Centres of Excellence Program via the Medical Research Council of Canada, to conduct an expanded research program "From Genes to Therapies."

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