

Insights from the Network

No disease is too rare for treatment and therapy discovery: A CF perspective

By Dr. Amy Wong

Scientist, Developmental & Stem Cell Biology, Hospital for Sick Children

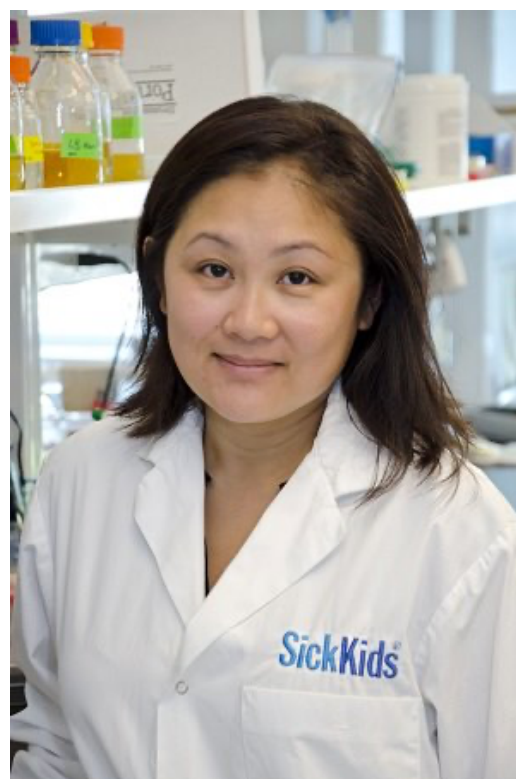
Assistant Professor, Department of Laboratory Medicine & Pathology, University of Toronto

For most people, \$300,000 is a life-changing amount of money. But for a small portion of the population with a rare genetic disease called cystic fibrosis (CF), \$300,000 is the cost of a year's supply of a life-saving drug. These drugs, called CFTR modulators, were approved in Canada in 2020 and are intended to treat CF in over 90% of those diagnosed with the genetic defect. Patients prescribed the drug are expected to take it regularly, but access to the drug remains a barrier for many.

With the high cost, coverage through private insurance is limited, and government plans, like OHIP and the Trillium Drug Program in Ontario, are only intended to cover those without private insurance.

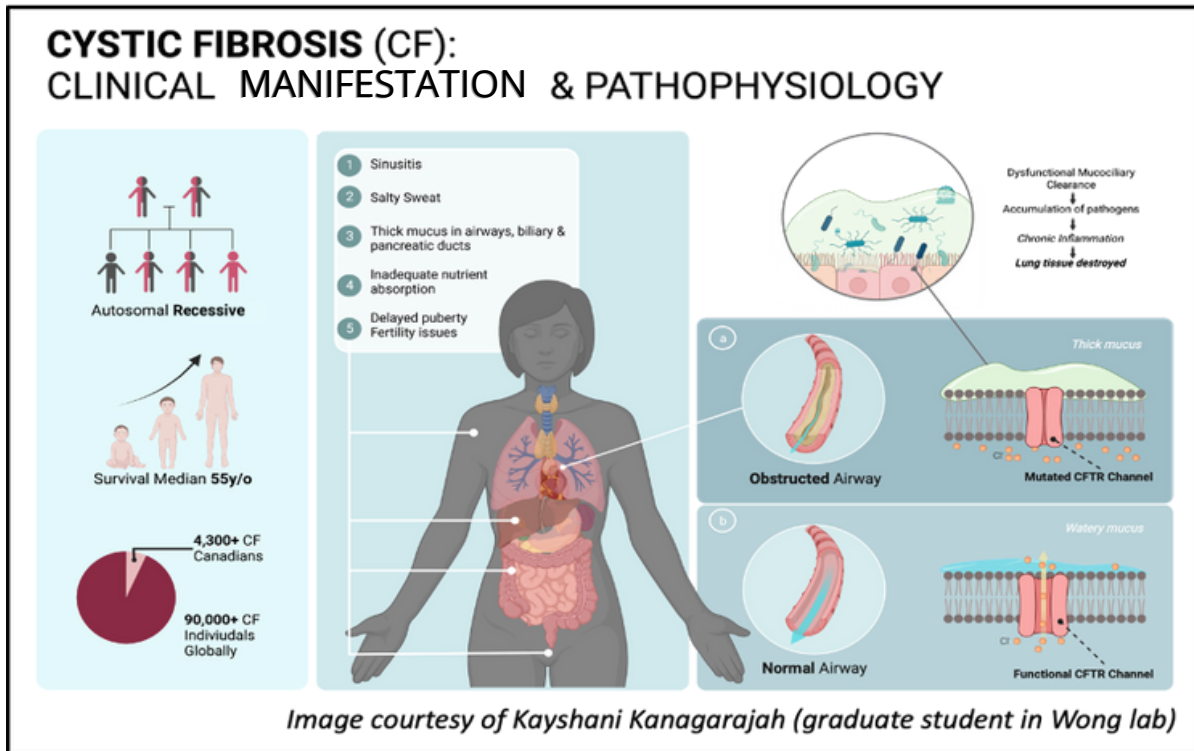
In March 2023, the [Government of Canada announced](#) a pivotal investment of up to \$1.5 billion over the course of three years to support the first-ever National Strategy for Drugs for Rare Diseases with the goal to increase access to promising drugs and improve the health of patients across Canada.

As part of this announcement, \$32 million over five years will be invested by the federal government in Canadian Institutes for Health Research (CIHR) to advance research in rare diseases and include a focus on developing better diagnostic tools. This is a long-awaited and welcoming announcement for people with rare diseases like CF and is a giant step towards providing potentially life-altering and life-saving therapies to many Canadians who need them.



Dr. Amy Wong
Hospital for Sick Children,
University of Toronto

The CF gene was discovered in 1989 by a team of scientists at the Toronto Hospital for Sick Children. Globally, there are over 90,000 people with CF (pwCF). Approximately 4,500 of them reside in Canada. More than 90% of pwCF have a common mutation affecting the protein processing of the CFTR channel called F508del in at least one allele. Naturally, identifying a drug that targets this common mutation would not only save lives but improve the quality of life for the majority of pwCF. However, finding that “one drug fits all” approach has proven to be difficult as current modulators have been shown to have varied effects.



CF disease manifestations are observed shortly after birth when structural changes in the airways and impaired lung functions are identified in prenatal scans. Postnatal insults and chronic airway infections further exacerbate lung disease leading to irreversible damage. Through Stem Cell Network funding, our team has identified a role for CFTR in the formation of airways and discovered novel cell types in the developing human fetal lung that express high levels of CFTR.

Using our CF iPSC-derived models of fetal lung, we show that treatment with CFTR modulators can rescue cellular differentiation and improve chloride transport in mature airway cells. This supports earlier work in which in utero pre-treatment of a ferret model of CF with a modulator drug showed significant improvement in CF-related disease such as improved pancreatic function and reduced mucus accumulation and bacterial infections in the lung. Our work lends support for early interventions with these drugs to treat CF disease before it is too late and too costly.



In June 2021, a transformative triple combination drug called Trikafta was approved by Health Canada for pwCF 12 years and over with at least one F508del mutation. By April 2022, the drug was also approved for children 6-11 years. However, in Canada the youngest population with CF (under six years) is not yet eligible even though early intervention can have a significant impact on disease progression and lung function. On April 26th, the FDA approved Trikafta for children 2-6 years old with at least one copy of the F508del mutation. We are hoping Health Canada will follow suit and thereby provide these drugs to the younger population. Importantly, as powerful and transformative as Trikafta may be for the majority of pwCF, there is still no cure for CF. More research is needed to find effective therapies for rare CF for which no current modulators are expected to work.

Efforts led by Canadian scientists including our team at SickKids are developing cell-based models to predict patient-specific responses to current and new CF drugs. The goal is to find therapies for the remaining CF population. We expect to see a greater push for Health Canada to approve the use of therapeutic drugs evaluated on these cell-based predictive models. The potential to predict patient-specific responses could be a game changer in lessening the economic burden for the patient and our healthcare system.

