New testing will allow researchers to determine the effectiveness of drugs on individual patients. Contributed

THE NEXT BREAKTHROUGH

SickKids leads the way in cystic fibrosis research

Christine Bear was at the Hospital for Sick Children when SickKids' researcher Dr. Lap-Chee Sui discovered the gene responsible for cystic fibrosis. Identifying the defective gene was not only a major breakthrough in human genetics; the 1989 discovery increased the life expectancy for children with the disease.

While there is still no cure for CF, SickKids continues to lead medical advances that allow children and adults living with the disease to lead longer and fuller lives.

Today, Bear heads up a team of SickKids researchers at the Bear Lab, who are working to find a way to repair the defects caused by the mutation in the CFTR (cystic fibrosis transmembrane conductance regulator) gene.

CF is a rare disease, says Bear, but as a genetic disease, it's one of the most common. It is also a disease that, in severe cases, affects multiple body systems, including the lungs, the intestines, and the pancreas, requiring patients to undergo a heavy course of daily therapies.

"Although the mean lifespan has increased dramatically over the past few decades from teenage years — up to 50 years of age is the average life span now — many patients still will die in their 20s and 30s. It's a life-shortening disease," says Bear, one with "an onerous treatment burden throughout their lives.

"Our major focus now is therapy development," says the researcher. "That's a fundamental aspect of our work, but then we're also very aware that all patients will probably not respond similarly to the same drugs."

So the Bear Lab is exploring a more individualized approach to CF therapy.

"We need to find ways to study how a patient's own lung cells or pancreas cells will respond to new interventions," says Bear. "This involves collaboration with the clinician and the patient, of course.

Dr. Christine Bear Contributed

They're all part of this, they're very interested in finding the best medications for themselves or their children.

"The new technology of stem cell biology is at the forefront of where we're going," she says. "This involves collaboration with stem cell biologist Janet Rossant, who is the head of our research institute."

Dr. Rossant found that skin taken from a patient can be turned into stem cells and then turned into any of the different tissues that could be affected by CF. "Then you've got that person's lung tissues, and then you can ask 'does this new intervention work on this patient,'" says Bear.

"We can use their own stem cells," she adds. "They're a renewable resource of tissue, so you don't have to keep taking tissue from the same patient.

"We're not there yet, but that's where we want to go."

The technology could make a difference for CF patients like Madi Vanstone. The 13-year-old made headlines last year after successfully lobbying the provincial government to help her family pay for a new drug, Kalydeco. The drug works well targeting Vanstone's particular mutation — a rare one that affects only 3 per cent of CF patients in Canada — but comes with a high price tag.

"We think that with some of our methods for testing … we'll find that a new emerging drug might work even better on her (Vanstone's) mutation," Bear says. "This kind of comparison will enable new drugs to come into the market and maybe drive down prices of drugs that are too expensive."

Bear notes that a new combination drug called Orkambi — which received recommendation for approval by an FDA advisory committee in the U.S. earlier this month — could be used to treat approximately 40 per cent of Canadian patients diagnosed with delta-F508, the most common mutation known to cause CF.

But 30 per cent of delta-F508 patients are not responding to Orkambi, according to Bear. "With our new platform for personalized drug testing, we're going to be able to identify those people before they go on the drug and then try some even more novel combos to see if they work better than Orkambi.

"Our research is really dependent on grant funding," adds Bear.

"National agencies tend to be a little bit risk averse. Philanthropy has been essential to kick start new ideas," says Bear, adding that philanthropic funds for some new ideas have filtered through to SickKids Cystic Fibrosis Centre, where she is co-director alongside Dr. Felix Ratjen, division chief of Paediatric Respiratory Medicine at the hospital.

"We really don't want anybody left behind because a particular new combo of drugs doesn't work on them," Bear adds. "We want to find something for everybody."

By the numbers

- About 1 in every 25 Canadians carries the gene responsible for CF.
- Approximately 1 in 3,600 Canadian babies is born with cystic fibrosis.
- There are approximately 1,997 mutations of the CF gene.
- Approximately 4,000 Canadians live with cystic fibrosis.
- The annual cost of the CF drug Kalydeco, which was approved by Health Canada in late 2012, is $300,000.

Source: Dr. Bear, SickKids