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We have several goals for our Cystic fibrosis (CF) research work. We are using high-precision instrumentation (including fluorescence and electrophysiology) to understand how the normal Cystic fibrosis transmembrane conductance regulator (CFTR) protein works as a molecular machine to mediate chloride flux and hence salt and water across the cell surface of airway cells - the major tissue affected in CF disease.

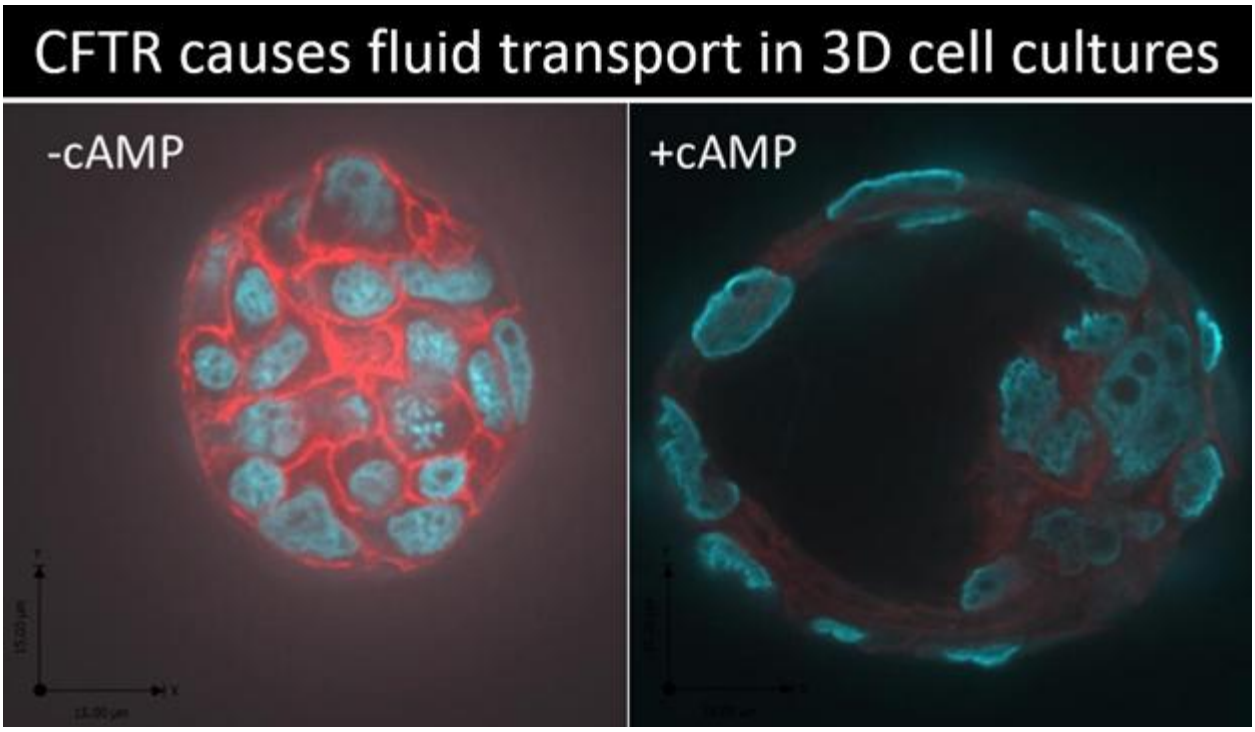
Detailed, mechanistic studies of mutant CFTR proteins reveal how mutations (such as deltaF508 and G551D) cause the CFTR protein to malfunction and also provide insights into potential "repair" strategies.

Such strategies include the discovery of small molecules that bind the mutant CFTR protein to induce it to work more like the normal CFTR protein. Such small molecules are called mutant CFTR "modulators". Our goal is to identify "CFTR modulators" that have the potential to become cost-effective drugs that will enhance the quality of life of patients with CF.

Large scale genomics studies emphasize the variability in lung and intestinal disease amongst CF patients, even amongst patients with the identical CFTR mutations. We are working with geneticists and clinical researchers to determine what other non-CFTR genes account for such patient-to-patient variability and explain why one patient may exhibit "milder" disease than another. Identifying the role of such "modifying genes" will inform the development of new therapies that could work like a "modifier gene" to lessen disease severity. Such therapies are being tested in cell cultures models and in mice.

Finally, we are working with stem cell biologists such as James Ellis and Janet Rossant to develop patient-specific lung cell culture system from small skin cell samples. We anticipate that such lung cell cultures will allow us and other researchers to determine which drug or drug combination will be most effective for each patient.

Our progress in identifying "repair" strategies for mutant CFTR led to a new avenue for CFTR drug discovery - an avenue that is being pursued in collaboration with the large pharmaceutical company: GlaxoSmithKline. Further, we are assisting additional pharmaceutical companies to test the efficacy of their new potential therapies using our expertise in studying "repair" mechanisms for the major CF causing mutant (delta-F508) in cell cultures and in mice with the major mutation.



Epithelial cells form organ-like structures in special cell culture conditions. These microscopic images show tiny structures (one hundredth to one tenth of a millimetre), decorated with colourful, fluorescent labels to enhance visibility. Cell nuclei are coloured blue and the cytoskeleton rich cell peripheries are coloured red. When CFTR is stimulated (+cAMP), it causes fluid transport into the cavity of the structure- modeling fluid secretion in tissues where normal CFTR is working. These types of studies help us to understand the normal function of CFTR in the body. Disease-causing mutations in the CF gene prevent this function but certain investigational drugs can partially restore cavity swelling. So- this cell culture system is helpful for testing therapeutic interventions for mutant CFTR. Experiments performed by Saumel Ahmadi, PhD candidate in the Bear Lab.

My training in science focused on understanding how human cells regulate their size, shape and contents by regulating transport across their membrane surface. I arrived at SickKids for my first job as an independent scientist at the same time as the discovery of the CF gene. When I learned that the CFTR protein resides in the surface membrane of airway and intestinal cells –I was excited to find out how it worked and how disease-causing msutations in CFTR affected the membrane transport by these cells. My group contributed to our current knowledge that the normal CFTR protein regulates membrane transport of salt and water. In my group - we now use our knowledge about the mutant CFTR protein to develop strategies to repair its defects pharmacologically. Finally - we think that pharmacological repair of mutant CFTR and the restoration of normal salt and water transport across airway cells will improve the health of CF patients and this belief motivates our research.

Click here for a complete list of Dr. Christine Bear's publications at NCBI PubMed.

I am committed to exposing young people (including high school students) to the scientific process, the excitement surrounding scientific discovery and the importance of informing the community about the promise of our work for helping people with disease. Right now there are three undergraduate university students, four graduate level university students and a postdoctoral fellow working hard to solve scientific problems relevant to understanding the basis for cystic fibrosis and providing insights into therapeutic strategies. In addition, there are four highly qualified professional scientists with special expertise in the laboratory and involved in training the next generation of scientists in basic scientific discovery as well as testing new strategies for therapy development.

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