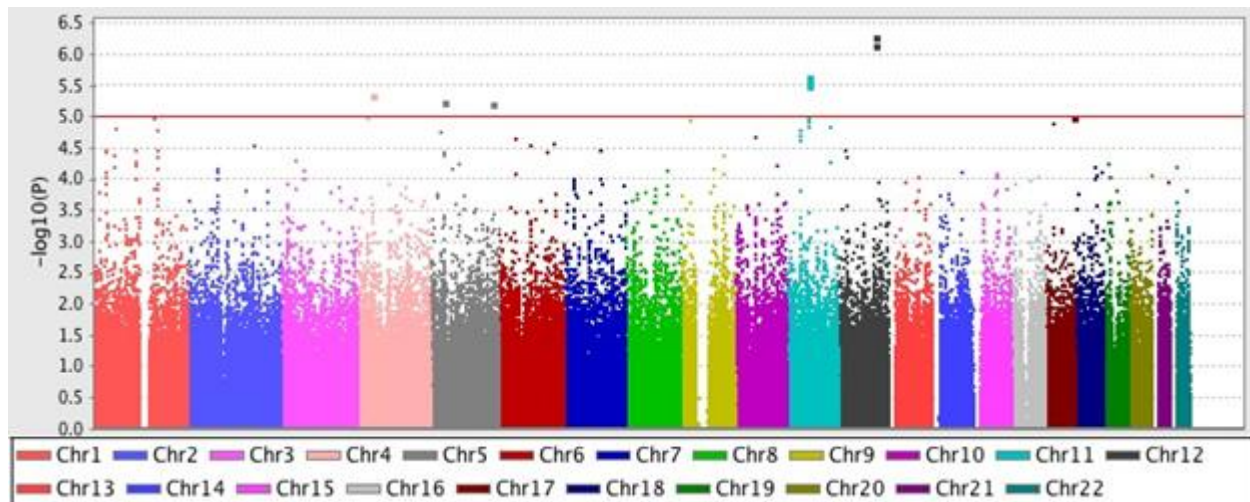


Lisa Strug, PhD

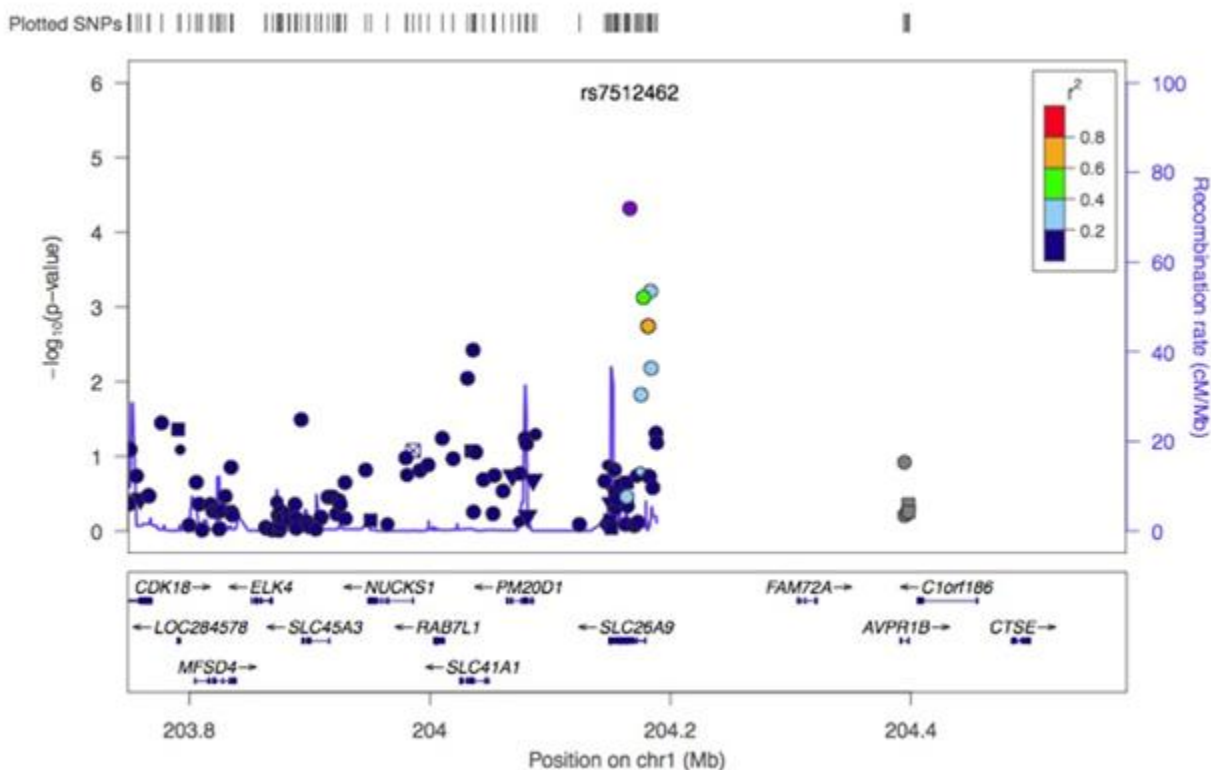
- Research Institute, Child Health Evaluative Sciences, Scientist
- University of Toronto, Dalla Lana School of Public Health, Assistant Professor

The focus of our research program is to understand why two individuals with the same Cystic fibrosis (CF) causing CF transmembrane conductance regulator (*CFTR*) genotype have different disease severity. Individuals with the same *CFTR* mutations have different degrees of lung, intestinal and pancreatic disease. A significant amount of that variability can be explained by other genes besides *CFTR* that are referred to as modifier genes, because they modify the course of the CF disease. To identify these modifier genes we work with patients, physicians and CF nurses to collect DNA and detailed clinical information to see, across all individuals, which genes correlate with different measures of disease severity. The figure below provides an example of the degree of correlation (y axis) across all the genes in the genome (x-axis). The higher points suggest involvement in CF severity by that gene.



Manhattan Plot for Lung Function

We have already identified modifier genes that contribute to severity in the CF lungs, intestine and pancreas. All of these modifiers reside alongside *CFTR* on the apical plasma membrane of the cell. This observation suggests that these modifiers may compensate for lack of *CFTR* function, making the disease more or less severe; therefore augmenting function in these genes may provide an alternative therapeutic target. We can also, ultimately, use these modifiers to personalize treatment: if we know at birth that an individual has greater risk for acquiring early, more severe, lung disease we can interfere by offering more aggressive treatment earlier in the course of their CF disease, even before standard lung function measurements may be reliably taken.



$$P_g \left\{ \left(\frac{cl(\hat{\theta}_{c\psi})}{cl(\hat{\theta}_{c\psi_g})} \right)^{a/b} \geq k \right\} \rightarrow \Phi \left(-\frac{c^*}{2} - \frac{\log k}{c^*} \right)$$

Mathematical modeling to identify genes in large pedigrees.

I have always loved mathematics, but it was not until I interned in a hospital that I realized all of the interesting careers in biomedical sciences that mathematics could contribute to. I was exposed and interested in medical research at an early age, when my parents would leave magazines about public health lying around the house. These magazines highlighted the importance of medical research and often provided colourful conversation pieces at our family dinner table.

Two people were fundamental in directing me towards a career in CF research: Robbie Thompson and Dr. Mary Corey. Growing up, I watched my close friend Robbie Thompson live with CF and go on to die from the disease in his 20s. Watching this process was devastating. I met my scientific mentor, Dr. Mary Corey, while I was a graduate student in biostatistics. Dr. Corey showed me how I could use my statistical training to make a difference in the lives of children living with CF, and that quickly turned into my life goal.

[Click here for a sample of Dr. Lisa Strug’s publications at NCBI PubMed.](#)

Trainees:

Melissa Miller (post-doctoral fellow) – Miller is trying to identify modifier genes that contribute to CF disease in newborns, such as weight and height at birth, or the degree of prenatal pancreatic damage. For pancreatic damage, Miller uses Trypsinogen, a biomarker of pancreatic damage, and the newborn screening measure for CF. In addition to identifying modifier genes, Miller is looking at whether disease severity outcomes in CF can be predicted using modifiers and early measures of disease.

Weili Li (PhD student) – Li is working on developing new statistical methods to determine whether the specific modifiers we are identifying play a role in altering CF disease severity in multiple affected organs.

David Soave (PhD student) – Soave is developing and implementing methodology to use longitudinal measurements of pancreatic disease from birth over time, to see if we can create models to predict later onset of diabetes. These predictive models could be used in the clinic to help personalize approaches to individual's CF care.

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