CENTRE FOR GENOMICS ENHANCED MEDICINE

Patient Impact Story

The Gift of Getting Answers

Marsha has always been interested in science, so when her mother and several people in her family were diagnosed with stomach cancer, she wanted to do all she could to find out if it was hereditary.

Marsha volunteered for genetic testing which prompted 32 additional family members to also volunteer their DNA and join her quest to find out why this disease was so prevalent.

Researchers initially looked for mutations in the CDH1 gene that is linked to an aggressive stomach cancer called hereditary diffuse gastric cancer." There is no way to screen for diffuse gastric cancer because it starts as microscopic spots in the stomach wall and doesn't form a visible tumor," says Dr. Lynette Penney, a top-level medical geneticist and researcher with the Center for Genomics Enhanced Medicine (CGEM). For people with a mutation in this gene the risk of cancer coupled with the lack of good screening options prompts doctors to often recommend preventative gastrectomy – surgery to remove the stomach.

Upon getting her family's genetic test results, Marsha said she was "extremely relieved." None of her family members with gastric cancer had a mutation in the CDH1 gene. Dr. Penney explains, "About 40 per cent of the time when we see diffuse gastric cancer that runs in families, it's related to a CDH1 gene mutation, but if you flip that around, it means that 60 per cent of cases aren't related to the CDH1 gene so there must be other causative factors."

Looking at the flip side of this coin is what allowed the geneticists to make an exciting discovery. They compared the genomes of Marsha's family; those affected with gastric cancer against those unaffected, and found a change in the MAP3K6 gene in four family members with cancer. The MAP3K6 gene is suspected to be a tumor suppressor in the digestive tract.

In collaboration with the BC Cancer Agency, the research team then broadened their reach, screening 115 more people with diffuse gastric cancer but without a CDH1 mutation. They discovered a Portuguese family had the same genetic change in the MAP3K6 gene, as well as four other people with different mutations in the MAP3K6 gene.

> *"We were first to identify and flag changes within the MAP3K6 gene and are excited to be pushing gastric cancer research further ahead," continues Dr. Penney.*

Through the collaborative efforts at CGEM, researchers are now looking to determine whether this gene, if it is not working properly, may cause hereditary gastric cancer. While more evidence is needed to see if there are other factors involved, Dr. Penney envisions a future where clinical testing could be offered to detect MAP3K6 alterations and diagnose this disease in its earliest stages. "Understanding the genetic drivers that give a person an increased risk of gastric cancer also helps us understand how best to treat that person's cancer," she says.

Marsha, who still goes for cancer screening every three years, reflects on the impact this research will on generations to come, "It's empowering because if you know you have the genetic mutation for stomach cancer then you can prepare in advance to get screened more often, lower your risk with diet and lifestyle changes, and find alternatives to avoid taking the drastic measure of having your stomach removed."

Photo Credit: Nick Dollimount

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