A Puzzle to Solve

"Yeah, it's true we're all dealt a set of cards.

But it's also true that it's up to us to figure out how to play the hand."

— Francis S. Collins

A few weeks had gone by since I started treatment for cancer that April of 2004 and blood work showed that my platelets and white blood cells were dropping drastically. Nevertheless, I hoped to see someone to help me figure out my fate. I found a psychic in Granville Island, about a half-hour walk from the cancer clinic. I do not recall what she said but I suddenly remembered that I had an appointment for more blood work and I jogged back to the clinic.

Staff noticed I was sweating and when I told them that I ran to get there on time, they were not impressed. Intense activity during issues with the blood was highly not recommended. Indeed the results were not good. I had what they called grade 4 toxicity which can be fatal. I urgently needed transfusions and ended up staying four nights on the 5th floor of the BC Cancer Agency, taking a small break from the radiation.

On one day I had lunch with my mom outside on the patio and commented how the food was so much better than at Vancouver General Hospital where I had had the brain biopsy in March, a week after a grand mal seizure. It was nice being outside in the fresh air. I couldn't imagine what she was going through; her 29 year old son with a form of cancer that had a very poor prognosis. She had her own experiences at the BC Cancer Agency as a patient a number of

years before. Twice. Being with my mom that day helped to lessen the discomfort of the line sticking out my arm for the transfusions.

Later, in the evening quietness, as I sat in my chair getting another transfusion, I felt the urge to get up, walk with the pole that my platelet bag was attached to, and go to my desk on the 3rd floor. Or perhaps I should wait until the morning and surprise my colleagues, walking with my gown on, showing off my butt, saying hi with a big smile.

As much as I missed my job though, I had more important things to worry about. We needed to get rid of this darn tumour in my head. I knew this cancer would be a harder puzzle to solve than the one I helped solve the year before.

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The sample had arrived from Winnipeg ready for DNA sequencing. At the time, the GSC (Genome Sciences Centre) on the 3rd floor of the BC Cancer Agency in Vancouver was the only major genome sequencing centre in Canada. Back then, many were depending on our facility to produce the complete sequence of the SARS coronavirus (SARS-CoV), and urgently. People were dying. We were aware that the CDC (Center for Disease Control) in Atlanta was doing the same and we hoped to report our findings before them. I had been at the GSC for 3 years by that point in bioinformatics and was very excited to be involved.

During the week of April 7th, 2003, others had worked late in the lab to extract the coronavirus' DNA and put them through the DNA sequence machines. Sequencing was done using what is now an older method called Sanger is sequencing. Each piece of DNA sequence from the lab was about 600-700 base pairs long. These are called "reads." It was known that the SARS coronavirus genome would be about 30K bases long. So to put it simply, we had to

overlap reads, align them, to put together the full genome sequence of the coronavirus using various software packages and the code we development.

On Friday, April 11, 2003, data from the lab started to become available and our team in bioinformatics worked all day to analyze it. With each batch that became available, I transferred the data immediately to my computer for analysis. A couple of other brilliant colleagues who reported to me, Obi and Anca, designed a data pipeline for putting together the puzzle—the complete sequence of the SARS coronavirus genome.

No one had asked us to work late, but it was an exciting time and it was hard to go home for the weekend knowing we could to be the first in the world to put together the genome. DNA sequence was continuing to come in from the lab that evening. Around ten o'clock, a few from the lab joined others in bioinformatics to go out to eat. I remained at my desk with no interest in taking a break. Some came back after to check on things and then left. Soon I was the only one at the genome centre.

Other than my heart beating faster than normal, the only other sound was the humming of my computer and at 2:25 am, the complete genome appeared on my screen. I jumped up in excitement before sitting back down to scroll through the genome sequence and verify that what I saw was indeed complete. So this is what the world is waiting to see I thought to myself. And I was the first to see it. I was in awe that this was what was causing such a scare. Little did I know that 17 years later, there would be a rush to analyze another coronavirus—Covid-19 (SARS-CoV-2).

I typed out a quick email. "Mom, we did it!"

I then sent a short message to inform staff of where we were at in the analysis. I wanted to be absolutely sure I had the full sequence though; I spent the next hour and a half scrolling on

my screen. Thousands of letters; As, Ts, Gs, and Cs denoting the 4 bases of DNA. For the first time, reads were overlapping with no gaps from the start of the virus's genome to the end. I sent an image to the laser printer—a complete picture of DNA coverage for the full SARS coronavirus genome. It was 4 am and I danced around my desk holding the paper in the air as if it was the Stanley Cup. I had just scored the winning goal but there was no one around cheering. I emailed the image I printed and I decided that it was time to head home and catch a few hours of sleep. No doubt my email would cause a flurry of interest. I was the first in the world to hold the full genome sequence of the coronavirus in my hands.

I made my way out from the 3rd floor into the dark that was transitioning to light. As I walked up the quiet street to my apartment about 10 minutes away, I sensed a bitter-sweetness in the fresh air. There was no one to share my excitement with other than the moon above me. I would have liked to have arrived home, crawled into bed, and whispered to my girlfriend that we did it. Alas, it was not to be as we had split the previous year. I wondered who would be the first to see my email.

My eyes opened slowly and I saw that it was 10 am. I was aiming to head back to work much earlier and so I rushed out. For sure there will be some activity I thought, assuming my supervisors saw my email. I walked into the office that Saturday morning like it was a normal workday and immediately sensed the excitement. Anca and Obi were at their desks along with my supervisors Marco and Steve. The lab was busy and more sequence was to be coming in which we would use to further analyze the genome and confirm the quality of the DNA.

The more reads, "puzzle pieces," that overlapped and connected at a certain location, the more confident we were with the quality and accuracy of the final result. We continued to work throughout the day as more and more data became available knowing the full genome sequence could potentially allow researchers throughout the world to come up with effective forms of treatment. Someone brought in donuts from Tim Horton's along with Egg McMuffins and a full selection of Safeway orange juice—pulp, no pulp, and low acid. The local media showed up and were at my desk while Marco and I examined the sequence. Later that day we held a press conference.

After reviewing and confirming the results in Marco's office later that Saturday night, April 12, 2003, we felt we were ready to report our findings. Steve would be uploading the complete sequence to a known public database and informing the media that we had made the sequence public. I decided to take Obi and Anca out for a late celebratory bite to eat at the Cactus Club. On Sunday, we made the second page of the local newspaper.

"Scientists at the BC Cancer Agency have made a major breakthrough in solving the puzzle of the killer virus known as SARS. The Vancouver scientists are the first to crack the genetic code of the Severe Acute Respiratory Syndrome virus—which will speed the diagnosing of victims of the often-fatal disease and help with the work of finding a vaccine. The group, working out of the Michael Smith Genome Sciences Centre, made the discovery at 4 am yesterday"

— *The Province,* April 13, 2003

We announced our findings before the CDC which I think made many Canadians proud. Our work unexpectedly traveled quickly not just in Vancouver but throughout the world from

articles in the NY Times to cover stories in a few other magazines such as Newsweek and BC Business. I was not able to make out what the Japanese magazine wrote but at least Anca, Obi, and I looked good in one of the photos. We got all kinds of feedback including someone who was angry that we released the DNA sequence with the claim that someone could recreate the virus.

The next task was to put together and submit a research paper to a top journal. We ended up publishing in Science back to back with the CDC's publication in May. I was proud of our accomplishment and knew that we would do many more great things at the genome centre; I looked forward to contributing and advancing my career.

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Well, the next major discovery after I collapsed in 2004 was of my brain cancer. Glioblastoma. With a prognosis of 15-18 months, the deadly cancer sadly hit Gord Downie 11 years later. Would I have the courage to handle everything with grace the way he did? I learned that there may have been cancer cells in my brain while I was dancing with SARS that night two floors below me.

I couldn't fall sleep one night at the clinic and was up until 4 am again. As before, it was quiet, allowing me to read the sequence of my thoughts. My third week of treatment and I could not even complete the chemotherapy. How could we deal with the cancer without treatment? I was still getting radiation although they had put that on pause for a couple days.

I imagined being back at my desk on the 3rd floor, analyzing my tumour genome sequence with a coffee and a bowl of Timbits beside me. What did the DNA of my tumour look like, any interesting mutations, and could we discover something that would lead us to the best

way to treat it? I wondered if I should have had surgery even though they thought the tumour was too deep. Was the dosage of the chemotherapy too high for my body to handle? Was this a sign that I was extremely sensitive to the drug, and hence it was working? What did the psychic say? Should I just ignore the prognosis? Only time would tell.