

*My mother first became ill when I was just a child, around seven. At that young of an age I didn't have the capacity to grasp what was happening. I just knew the word; I knew what it was called, what she was sick with. But by the time the cancer came back for a second, and then a third time, I had grown accustomed to the progression of the treatment, but I never stopped to ask myself, "Why is this happening to my mother?" I've had time to distance myself, and I'm now here to find out what was actually happening. Not only the science behind the transition from normal tissue cells to cancerous ones—how cancerous tumors actually form—but also looking into the repercussions of this on my family: what this disease did within my mother as well as what it caused consequentially. I'm trying to understand, to make some sense out of what happened.*

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“Everybody dies eventually, but mommy’s not going to die from this.” I exhaled. That was the cue for my seven-year-old self to go outside and play. All I heard was “mom’s not going to die.” I didn’t care about the logistics of the cancer, or what the treatment was. I was seven, and the scariest part was seeing my mother bald. I didn’t know what was going on and I couldn’t tell you what cancer was if you had asked. I just knew that my mother had it, but that it was going to be okay. *Daddy said so.*

The cancer cells didn’t care about this. They didn’t care about the promise that I thought I heard from my parents, and they kept growing. They weren’t supposed to. They didn’t know that the doctor said that she wasn’t going to die from this. *She wasn’t going to die from this.* But cancer cells can’t hear. They aren’t like the others. These cells were just as persistent as my mother’s resistance, but they had the upper hand. They knew what they were doing: how to evade death, how to live where they were not supposed to, and how to leave their place in the body without being noticed. These cells were dangerous, but the peril of this disease had always been downplayed to me; *she was going to fight this.* But how does a person fight something that is inside of her, something that has taken control of the structure of her body, invaded the tissue, and leached into her bloodstream? How can a person fight something that sometimes cannot even be found? How does this even happen to someone? And where does it all start?

2001

“It was 2001 and mom woke up with a lump on her neck that looked like a half of a golf ball” (Jess). That was where it started for me. Jess, my father, took my mother to the doctor to have it checked out. They aspirated the mass to check the cells and reassured my mother that it was just a swollen lymph gland. But the tests didn’t show what they had hoped they would, so they had to biopsy the mass and she came home afterwards with gauze covering her neck—it was the first visible evidence of her sickness (Ede). It was through this initial test that my parents found out my mother had cancer.

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Before telling my sisters and me, all of us below the age of twelve, my parents flew to Stanford to get another opinion on what she had, what the prognosis was and what the possible treatments were. The doctor at Stanford was very reassuring, saying that her cancer was very aggressive, which at first seems more frightening, but actually it reacts well to chemotherapy, comforting them by having a course of treatment in mind when they didn't know where to start. My parents were new to this, we were all new to this, and none of us knew what to do. They didn't know how to tell us or even what to tell us or when, but the doctors reassured them on what to do. "The doctors said that when we say that mommy has cancer, the first thing you're going to say is 'is mommy going to die?' and they said to say that everyone dies but mommy's not going to die from this" (Jess). So that was what they told us. Being only seven, that statement alone assured me. I was still going to have a mother. I didn't need to think much further about what was happening to her, what the treatment was going to be or how lousy she might feel; all I had to think about was that I was going to still have my mother with me. I got to see her everyday because she was doing outpatient chemotherapy at St. John's Hospital and radiation at St. Joseph's Hospital. I was never away from my mother and to me very few things appeared to be different. Everyone told me that she was going to get through it, which blinded me to the fact that I had no idea of what went on inside of her body to cause this and what it was capable of doing.

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Normal cells are taken for granted: cells that know when to stop growing, cells that know when to self destruct, cells that know their place in the body. This is what we're accustomed to, but when cancer takes over, all of these characteristics go out the window. "[Cancer's] two main characteristics are uncontrolled growth of the cells in the human body and the ability of these cells to migrate from the original site and spread to distant sites" (thefreedictionary.com). These cells evade the defense mechanisms found in all healthy tissue cells- they've found a way to grow past their necessitated size, they live far past their typical life span, and they've found ways to detach themselves and move throughout the entire body. It's amazing how frequent this disease is considering how difficult it is to have all of the different cellular changes working simultaneously. It's difficult to comprehend that these miniscule changes, which happen without the affected cell even realizing anything is occurring, can cause one out of every four deaths in America (ibid).

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My mother got through the first treatment, and ended up spending the next four years in remission. It wasn't until the summer of 2006 that the cancer metastasized and came back again. She woke up one morning and knew that something was wrong. We were back East, so the first doctor she saw was in Rochester, New York and they diagnosed her with fibroid tumors—something very common—and according to them it was nothing to worry about. But my mother knew better, which was why she and my father flew back home to Los Angeles to visit the doctor from the first treatment. But this doctor was in agreement with the one from Rochester and still said that it was nothing. It was at this point that my father called his friend, who had recently fought cancer himself, to recommend another doctor to see. He set my parents up with a surgeon from Cedar-Sinai who finally diagnosed my mother with non-Hodgkin's lymphoma, which had metastasized all throughout her uterus and ovaries.

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Once a cancer has metastasized, it becomes much more complicated and difficult to treat, not to mention the severity of the disease increases as well. In fact, ninety percent of cancer deaths are caused by metastasized tumors. But what does it mean for a cancerous tumor to have metastasized? In the simplest explanation, “a tumor has metastasized when it has spread to other parts of the body, grown, and invaded and destroyed healthy tissues” (medicalnewstoday.com). This becomes much more difficult to treat because the cancer is in multiple parts of the body, and a treatment for one place may not work for another. Once it has spread from its original site, it becomes very likely that the cancer has spread to places where it goes undetected, leading to parts of the disease going untreated. Once the cancer has begun to spread, there is no saying where else it could be, making it much more dangerous and potentially fatal (ibid).

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For this second round of treatment there was no more outpatient treatment, which was why this was the time when I started to feel comfortable around a hospital. The second treatment began with a surgery to remove the mass, and once that healed she moved to City of Hope for further care. I saw this treatment take more out of my mother. She looked weaker and was cold and shaking and I had to wear gloves, a mask, and a gown in order to be in the hospital room with her on my birthday. She had to fight harder this time, push further, and endure more. This time the cancer wasn't a small lump in her neck that was very contained; the cells had spread and taken up a much larger portion of her body mass, ending up to be about the size of a grapefruit in her abdomen. According to my father “she saw the best things in life but was also mean as shit” and that combination of things helped her fight the cancer (Jess). It gave her a reason to fight and the persistence to get through it.

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But how exactly do the cancer cells spread throughout the body? Part of it is due to the cancer cells' ability to dislodge themselves from the extracellular matrix, the "scaffolding" that helps cells form a three-dimensional structure in tissue. On the surface of every cell there are proteins called integrins that attach to the extracellular matrix. These proteins are keeping every cell in its place—the integrins tether the cells to the matrix but "when the cancer cells are ready to metastasize the integrins let go" (Paddock). When cancer cells become more metastatic, "there is a loss of adhesion to normal tissue structures" and they become "unstuck" which allows them to move freely throughout the entire body (ibid). This control over the integrins is also advantageous when the cancer cells want to reattach themselves at a new site: "as they become more aggressive, they gain the ability to stick to and grow on molecules" (ibid). To metastasize, cancer cells need this control over integrins not only to dislodge from the original tumor site but also to attach themselves to the new metastasized site.

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The first step of the second treatment was to remove the mass as best they could. This called for a complete hysterectomy—the surgical removal of the uterus, cervix, ovaries and fallopian tubes. Then, after a week or so of recovery time she went out to City of Hope for chemotherapy and a stem cell transplant. This meant that they took out over 5,000,000 of her stem cells and stored them in a safe place. She was then given numerous massive doses of chemotherapy, completely knocking out her immune system. After the chemotherapy, they in essence "rebooted" her immune system by reintroducing her own stem cells into her body to rebuild her immune system again. This type of treatment makes it possible to give large amounts of chemotherapy, which in the absence of the ability to reintroduce her own stem cells would prove fatal. If they didn't take out her stem cells before the chemotherapy, it would have been impossible to regain any semblance of an immune system (Jess, Ede, Zoe).

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But how were the cancer cells even able to invade healthy tissue? What makes it possible for cancer cells to do that? A cancer cell's ability to do this is partly due to a lack of CIL, or contact inhibition of locomotion: "the process by which cells *in vitro* change their direction of migration upon contact with another cell" (Mayor). CIL is needed to restrict the cells to remain at the right place within an organism and this restriction comes from neighboring cells. When a cell touches its neighbor it knows to stop growing and to stay put. But when this is absent it allows those liberated cells to migrate and live in parts of the body where they weren't intended (ibid). Because diminished CIL behavior allows cancer cells to move throughout the body, it leads to them settling elsewhere and invading the healthy tissue that is present there.

Cancer cells utilize CIL not only to help with invading and settling, but also with their migration to other parts of the body; this is because there are two types of CIL, and

cancer cells utilize them differently. Homotypic CIL is when two cells of the same type encounter each other and exhibit CIL, and heterotypic CIL is when two different cell types encounter each other and display CIL. Malignant cancer cells “have lost heterotypic CIL but maintain homotypic CIL between cancer cells, which aids in collective migration and dispersion of the tumor” (ibid). Heterotypic CIL is absent in cancer cells and this allows those cells to move from their original site and to travel throughout the entire body. It also makes it possible for the cancer cells to “invade territories populated by other cells” (ibid). But they maintain homotypic CIL, so when a cancer cell comes into contact with another cancer cell they know to stop moving and to attach to each other, eventually forming another tumor.

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## 2011

When my mother got sick for the third time, her body was weaker and the treatment took even more out of her than before. It was five years later and my mother was living in a house by herself after deciding to move out of our house. We all started noticing that she was acting ‘loopy’ and ‘out of it’, but everyone just attributed it to stress from living on her own (Jess, Zoe, Ede). Every year on Mother’s Day, my mother had standing plans to go to a spa for a week with her friends, but that year she came home early. Her friends called my father and expressed their concerns, saying that my mom was repeating herself and was speaking incoherently all morning. She drove herself home and the next day my parents went to the doctors to get a work up and a brain scan. “[They] were at mom’s house baking for [my sister’s boyfriend’s] graduation when the doctor called with the news. Breaking that news to her was the hardest thing I had ever done or thought I would ever have to do. However, watching mommy’s intellectual capacity diminish over the next year due to the drugs, the surgery and the cancer was the hardest thing” (Jess).

The doctor said that there was a mass in her head and that they had to do further tests. It was a brain tumor. When my parents first heard the news, they “talked about the fact that this was much more serious than the first two. First, it was in her brain and second, it was her third time through this and she was older and a number of drugs obviously weren’t working” (Jess). There was no time to digest the news: we had to act fast and start treatment immediately.

A few days after getting the results from the MRI, my parents went back out to City of Hope for consultations. They saw the same doctor from the second treatment and two days later, on May 18<sup>th</sup>, they were already doing pre-op for her brain surgery to remove as much of the mass as they could. From the date of her surgery until the end of September, she was going back and forth to City of Hope for the first attack of chemotherapy. Throughout this entire treatment I could see her getting weaker and her admissions into the hospital started to last longer and longer. At the end of October she started the second round of chemotherapy, which was followed up with radiation. But even with all of the treatment, she was still getting worse. She was constantly being readmitted to the hospital, whether it was from her counts being too low or her running a

fever, making her prone to infection. We kept trying, and pushing further, and thinking of new things to try, but nothing seemed to work. They did another brain scan and it showed that another mass was forming in her brain; the cancer was still growing, and dividing, and moving throughout her body.

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As my mother was getting weaker, the cancer cells were growing stronger than ever, most notably due to their ability to avoid apoptosis, genetically programmed cell death. More specifically, apoptosis is “an organized, genetically programmed cell death process by which multi-cellular organisms specifically destroy, dismantle, and dispose of cells” (Bignold). But apoptosis is different than a normal cell coming to the end of its life cycle—it is triggered by a cell being damaged and unable to repair its DNA or by a cell being in a diseased state (Argyle).

Cancer cells have found a loophole, and they “don’t experience programmatic death, but instead continue to grow and multiply” (medicalnewstoday.com). Apoptosis “provides a controlled mechanism for eliminating cells that are irreversibly damaged” which is why suppressing this gene is essential for the growth of cancer—because it not only allows them to “survive beyond their normal life span” and avoid death (Bignold), but it makes it possible for them to reproduce and to pass down their damaged DNA in the process (Argyle). So as other cells are dying and going through the natural phases of a cell’s life, cancer cells continue living, and reproducing, and invading and destroying healthy tissue cells, and metastasizing.

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At this point the doctors started to become less hopeful and more realistic- she definitely wasn’t getting better. Between December and March, she kept going back and forth between our house and the hospital, and even when she was at home we had to give her medicine every day. By March her eyesight started to deteriorate, and on March 21<sup>st</sup>, she went to get pet scans of her eyes. That day in the hospital she was incoherent, “slurring her speech” for the few minutes that she could stay awake, and half of her face began to “droop”—that was when my father made the decision to get all of my family back home (Jess, Zoe, Ede). I got a call in the middle of class on a Wednesday afternoon and my father told me to leave school and drive out to City of Hope. When I got there she didn’t look like herself, she was so “frail and little” and could hardly speak, and when she could it was barely audible (Jess).

We drove her back home and even getting to the car became a struggle because “her motor skills were deteriorating” (Jess). We got home and got her into bed and my father arranged for a hospice nurse to stay at the house for the next week. “There was no more medicine left to try” and any medicine would have been futile because her body couldn’t take it- she couldn’t fight the cancer and she didn’t have to anymore (Jess).

This was the first time throughout all of the rounds of treatment that I began to lose hope. “She was lying in bed all the time, was sleeping for most of the day and would

wake up for only a few minutes at a time.” It was clear that the cancer had taken over. For the last two treatments we had always been hopeful, the doctors had always been optimistic and given good prognoses so I didn’t know what to think at this point. But my father had talked to my mother about what they would do if that outcome were to happen and she was very clear with her wishes: she didn’t want to die in a hospital and she didn’t want us to be sad. Instead, she wanted to be at home with all of us around her and she didn’t want to be in any pain. The hospice nurse gave her morphine patches to deal with the pain and we sat with her every single day. A few days after we brought my mother home, the doctor visited and told us that keeping her hydrated and fed would only prolong the inescapable so we stopped the fluids and the food, only providing her with morphine in the last days to manage her pain and to make her comfortable. That’s what everyone kept saying: *make her comfortable*. Near the end she slipped into a coma (Jess). She was comfortable.

Early in the morning on March 29<sup>th</sup>, my mother passed away. We had tried everything we could—stem cell transplants, surgeries, multiple chemotherapies, radiation—but the cancer kept coming back. Throughout the treatment she lost what made her; by the end there was nothing left but her frail body. She was gone.

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Cancer cells are smart. The healthy cells in our bodies have defense mechanisms built in to defend against diseases and invasions, but cancer has found all of the loopholes. When the diseased genomes take over, they know exactly what to change in order to survive. They know how to evade the cell’s programmatic death, making it able to pass on its contaminated DNA and to live far longer than a cell should. These cells know how to dislodge themselves from their appropriate place, making them able to search the entire body for another place to pillage. They know how to avoid interaction with normal tissue cells- how to avoid their signals and keep on their programmed path of destruction while somehow keeping their ability to bond with other diseased cells intact. This disease knows how to survive, how to live inside a living body, but through its survival it weakens the host.

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So now I know. Now I understand what caused my mother’s pain and what made her shrivel into a frail skeleton of who she was. Now I know what caused all the medicine and the IV drips and the trips to the hospital. Now I know what caused all of the tubes and needles and cringes on my mothers face. What caused the surgeries and the hospital gowns and the sponges for her dry mouth. So now I know. Now I know.

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