The genetic lottery
By Katie Cincotta

How four letters changed my mother's life.

When it comes to winning and losing in life – having good luck or bad luck – most of us think about the lottery: about what winning a few million could do to change our life. Cruises through Europe, designer fashion, a beach house with a view.
Not many of us think about the genetic lottery we are born with – whether or not that exclusive DNA code will keep us alive and kicking long enough to enjoy a retirement in the sun, and see our grandchildren grow up.
At the moment of conception, we are all thrown a dice. We inherit the genetic code from both our mother and father: 23 chromosomes from the mother's egg and 23 chromosomes from the father's sperm, which together will determine what we will look like, how smart we are, and what might be in store for our body.
For my mother Josephine Cincotta, it came as a huge shock to be told at the age of 64 that she was the carrier of a rare genetic disorder – X-ALD. X-linked Adrenoleukodystrophy – that this strange sounding disease – one of over 60 known Leukodystrophies – could cause serious neurological symptoms, including numbness in her hands and feet, stiffness, loss of balance, bladder incontinence – that she was facing a degenerating nervous system that in the most severe cases could impair mobility enough to warrant a wheelchair.
After three and half years of testing, of countless appointments, of scans with specialists, she finally had an answer for why she had been getting tightness in her legs, her arms and back, numbness and tingling in her fingers and toes, and a persistent rash on her legs.
I remember sitting alongside my mother when she received the diagnosis from her neurologist Dr Mark Faragher. It was in January 2015 after extensive genetic testing that they found the ABCD1 gene that would explain her muscle spasms, her stiffening gait, her fatigue.
We asked many questions that day. What will happen? Is there a cure? Is anyone else in the family at risk? The neurologist said he simply didn't have the answers. In more than 20 years of practice, he'd only seen two cases of Adrenoleukodystrophy. We would have to seek out expert opinion from a genetic neurologist at the Alfred Hospital, Professor Elsdon Storey. The session with Professor Storey was incredibly valuable and revealed that my grandmother was a carrier of the mutated gene, even though she never had any symptoms in her 86 years.
In the months that passed we Googled frantically, worried, Googled some more, and remained baffled by what this neurological disease would mean for our mother's future.
X-ALD brought confusion and unease, not just to my mother but our entire family. We had no known affected male relatives in our family history, so came to this disease without warning.
As children of a female carrier, we had to decide whether or not to get tested, to find out whether we too would come up in the random roll of the ALD dice.
My sister and I and our brother, who are all in our 40s, have no symptoms and have decided not to be tested.
My mother is one of those unlucky few that has developed symptoms from X-ALD. They began most noticeably when she turned 60, and possibly decades before with ongoing bladder infections and incontinence which she thought was an after-effect of childbirth.
Her mornings are slow. Hot showers help. Her walk is often unsteady. She has fallen several times, when her leg doesn't get the signal from her brain to move.
But she is doing what she can to find relief and keep her body moving: a weekly hydrotherapy session at the pool with her girlfriends (which often turns into a gossip session about their husbands), physiotherapy, rehab, exercise classes, medication to control the muscle spasms and help ease the pain.
Still, my mother felt disheartened, afraid and alone. It was Neurogenetics Professor Michael Fahey who suggested making contact with the ALD support group to help mum cope with the mental strain of this disease. That connection has been life changing.
As an ALD sufferer herself, Sister Julie Thomas founded The Australian Leukodystrophy Support Group (now known as Leukodystrophy Australia), and without this incredible network many of those afflicted would be facing this disease alone.
As my mother says: "I felt isolated with a disease nobody knows anything about. Since I've spoken to my support group ladies, it has lightened my pain. The simple act of talking, listening and sharing our stories makes us feel less alone, less forgotten, better able to face the daily struggles. Just a simple phone call to each other – to check in and see how we're going, it makes such a difference. A voice

on the other end of the phone who is willing to listen, that's a precious thing that makes this organisation so valuable."

What none of these health issues can take from my mother is her fighting spirit, her stubborn fortitude is something we all admire. Where she finds peace and purpose is in the garden. She seems to move more easily there, her mind content with the task at hand. Even pulling weeds gives her joy.

My father recently found a group in London called Raremark who bring people with rare diseases together to share information, and consider clinical drug trials.

Their motto is a powerful one: "In rare disease, you are not alone."

Finding out about the latest research and connecting with people who know something about this rare and debilitating disease gives my mother comfort and hope.

She admits there's a sense of frustration with an illness that is so obscure. For cancer, mental health and more mainstream neurological diseases like MS and Motor Neuron Disease, there is awareness and funding. For diseases on the fringe like ALD, which is only relatively new to the medical community, it's harder to get answers and research dollars.

My mother's form of the neurodegenerative disease is slow progressing, and not nearly as debilitating as what young children with ALD face.

With the push for newborn testing of Adrenoleukodystrophy, there's hope we can screen for childhood cerebral ALD – the most severe form of the disease.

Local researchers such as Associate Professors Rick Leventer and Michael Fahey, in association with several overseas researchers, are paving the way forward for an end to neurological diseases.

Right now, they are trying to work out the neural pathways and understand how the damage is being caused. Stem cell transplants and gene therapy are two treatments being investigated.

Oral drugs such as MIN-102 and VK0214 are moving through trial phases in America and Europe, with promising results from preclinical testing.

Raremark reports that "Research into gene therapy for ALD is ongoing and, if development of the treatment is successful, it will provide individuals with ALD with a potentially one-time treatment that targets the genetic cause of a disease, not just the symptoms."

Progress might be slow, but it is being made. After the success of the fundraising efforts of the 'ice bucket challenge', Motor Neuron Disease researchers in Australia found that a compound – Copper-ATSM – could protect motor neurons in the spinal cord of mice, alleviating symptoms and extending life span, with human trials now under way.

Until that elusive cure is found, our calling is to increase awareness, to offer our stories, to embrace the medical arsenal of therapy and support services at our disposal to manage symptoms. There is power in numbers – not just for scientists trying to find a cure, but for the peace of mind of sufferers who have been dealt this hand and are struggling to accept the loss of control and freedom that goes with a broken nervous system.

Despite the misfortune of landing one wonky gene in the genetic lottery – my mother is happy to have a loving family, a tight-knit circle of friends, and a determined mind-set that she will continue to live an active and fulfilling life despite the constraints on her body.

The Covid19 pandemic has made that more of a challenge. With lockdowns shutting off the group exercise classes and hydrotherapy pool that help alleviate her symptoms, she's had to find new ways to keep her body moving.

"Because there is no cure, you have to help yourself. I do my exercises in the shower and I try to go to physio once a fortnight. If I let my muscles tighten, I tend to lose my balance and that's when I stumble."

A pain management specialist has also helped her treat the muscle spasms with drugs such as Baclofen, while her rheumatologist assists with cortisone injections in the shoulders.

The family's little dog Poppy – a Cavalier Papillon cross – also offers a boost both mentally and physically, trailing mum in the garden and snuggling on the couch, which has been especially comforting during the lockdowns of the last year.

Mum says the combination of those efforts – exercise, drugs, pet therapy and a positive mindset – work together to reduce the debilitating impact of her damaged nervous system.

She hopes sharing her story will encourage other people to share theirs. When you tell others about the long and confusing road to being diagnosed, how difficult it is to process that you have inherited a rare genetic disease that was only classified in the 1990s, what it is like to live with pain and mobility issues – it's a way of moving forward with confidence, a way of feeling less alienated, a way of accepting that you are a part of this strange family called Adrenoleukodystrophy, despite never having a choice in the matter. Maybe together, we can bear that burden, better than we can alone.