

‘Who do you think you are?’

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I grew up in Bramhall, Cheshire, in the 1950s. In 1953, my family and neighbors all watched the coronation of Queen Elizabeth II on the small black and white TV in our living room. I was 6 years old. Little did I imagine that my mother and I would visit the Queen at Buckingham Palace 50 years later when I would be given my OBE for services to International Breast Cancer Research.

My father and his three brothers were all born in Bramhall but educated traditionally away from their parents – with prep school in North Wales and the Leys School, Cambridge. By contrast, my mother’s family has ancient roots dating back a 1000 years in Mottram St Andrew near Prestbury, Cheshire. They are Mottrams and three are recorded to be present at the Battle of Poitiers in 1356. They were elite horse archers as part of the Black Prince’s personal bodyguard. My maternal grandfather had been an officer in the Cheshire Regiment in two world wars and his house in Wilmslow was an ‘Aladdin’s cave’ of uniforms, war trophies, and weapons displayed or secreted everywhere. This was my family who gave me a strong sense of right and wrong and stressed the value of service to others and the nation. Nothing in this early upbringing would predict any path to progress in breast cancer research. My interests were Roman history, a passion for chemistry, training, organizing, leading, and teaching other children in our neighborhood. I was not interested in schoolwork at Moseley Hall Grammar School for boys in Cheadle; but my chemistry teacher Mr Anderson captured my imagination as did Mr Charles Bescoby, my biology teacher. We will meet Mr Bescoby later.

My father had bought me a chemistry set and an air rifle when I was 10 years old. By the time I was 12 years old, my mother had allowed me to turn my bedroom into a chemistry laboratory. Experiments would often get out of hand, so a fuming brew would be hurled out of the window onto the lawn below leaving the curtains ablaze. Naturally the lawn died but on one occasion I convinced

my mother that I could use chemistry to grow it back. Yes, I was successful but the grass regrew an interesting shade of blue! Now for the air rifle.

I discovered I could knock down all the lupins with my air rifle, fired from my bedroom window. I remember overhearing a conversation between my mother and father as they inspected the damaged flowers, ‘Look’ my mother exclaimed ‘some large insect has taken a chunk out of each stem and it has fallen over’. I was an excellent shot, just like my grandfather who was the musketry training officer for the Cheshire Regiment.

I had no significant career objectives at that time, but at 15 years of age I am not sure anyone has. Perhaps join the Army or perhaps become a chemistry technician at the nearby ICI Pharmaceuticals Division, Alderley Park. But then failure enters your life. I only got three ‘O’ levels; five were required to stay in school and get into the sixth form, so I was about to be turned out to get a job in the real world. But failure at a young age is good I believe, in retrospect (but definitely not at the time) as it sets, in some, resolve. It was my mother’s unshakable support that created the resolve.

During the summer in 1963, I secured a technician’s job in organic synthesis at ICI, Alderley Park, but they suggested I should stay in school. My mother and I visited Mr Armishaw, the headmaster at Moseley Hall to plead my case. He did not have a chance! She promised I would comply with the law and would quickly get two further O levels and would take A-level Chemistry, Zoology, and O-level physics as ‘he already had a job offer from ICI to be a technician’. I was in the sixth form and I started the Zoology Club. I also chose to teach other boys university-level biochemistry and Mr Bescoby gave me a laboratory. Unexpectedly, Mr Bescoby suggested to my parents I should apply for university. I was, however, making plans to do something else – I was the drummer in a rock band! Late one night, it was the final straw for my mother

'Decide: Drummer or University'. I often wondered what happened to the other band members in the Hollies (or was it Freddie and the Dreamers?).

Mr Bescoby was now to teach me a lesson in commitment to the lives of others that I never forgot. I practice his philosophy every day. I was offered one interview at one University; the University of Leeds, Department of Pharmacology. In those days, everyone had a face-to-face interview, and I was greeted by Dr Ronnie Kaye and Dr Ted Clark of the Pharmacology Department. Dr Clark asked about a certain organic chemical reaction and I was off 'Very interesting as this is the topic of my biochemistry talk next week at the Zoology Club'. They could not shut me up. These two men were to 'give me my one chance' because of the letter my Headmaster (actually Mr Bescoby) had written supporting my application. Years later, Dr Kaye was to tell me that it stated 'Craig Jordan is an unusual young man (then repeated in capitals) a VERY UNUSUAL YOUNG MAN'. 'We had to see for ourselves what this meant' he continued. I stress in my mentoring that every 'chance' is the opportunity to win the gold medal in the Olympic finals (Fig. 1).

Back at Moseley Hall, Mr Bescoby chose to enter me for the scholarship (S-Level) zoology examinations. DNA was the hot topic since Watson and Crick's publications in the 1950s. Now they had won the Nobel Prize in 1963 so it was certain this would be an exam question. Mr Bescoby gave me a book on DNA and tutored me for an hour twice a week. I passed the S-level zoology examination and got the A-level grades necessary to go to Leeds. I won the school prize in zoology but bought a chemistry book.



Figure 1

The occasion before me being awarded the first honorary degree in medicine at Leeds University for humanitarian research 2001. I was delighted that Dr Ted Clark (I), my PhD supervisor, and Dr Ronnie Kaye could both be present at the degree ceremony. Both of these faculty members in the Pharmacology Department at Leeds University interviewed me in 1964 and subsequently offered me a place to go to the university.

Years later, I dedicated my first molecular biology paper to Mr Bescoby. We were the first to stably transfect the estrogen receptor (ER) into an ER-negative breast cancer cell (Jiang SY & Jordan VC 1992 Growth regulation of estrogen receptor negative breast cancer cells transfected with cDNA's for estrogen receptor. *Journal of the National Cancer Institute* **84** 580–591). A couple of years after publication, his daughter located me to tell me of her father's death, but the pride he had at my scientific success. Apparently, he used me as his example of an 'ugly duckling that turned into a swan' to subsequent generations of boys at Moseley Hall. Recently, Prof. Richard Vaughan-Jones at Oxford, another former pupil at Moseley Hall, told me this. Mr Bescoby's daughter enclosed his obituary and I discovered that he was the leader of the Manchester Branch of the Communist Party. In his case, he wanted to rebuild a better world after the Second World War, but never once did he choose to persuade me, or even discuss his political views. An honest man and dedicated teacher. He changed my life and perhaps built a future for women's health.

Dr Kaye, as head of Special Studies Pharmacy, would be my supporter and tutor at Leeds. I took the challenge of Leeds University very seriously. I was learning to survive academically in the spring of 1966, but I was concerned that the special studies Pharmacy course in the Pharmacology Department would not equip me for a career in cancer therapeutics. I thought a change should occur to better position me for a career in drug discovery.

Dr Kaye agreed to arrange a meeting with Dr Mogeey, the admissions tutor in Pharmacology. We three met in Dr Mogeey's office. He was a scary Scots Irishman who frowned at me over his half-moon glasses 'Well, I have reviewed your record, but I don't think your good enough to transfer.' After a pause, that seemed forever following this hammer blow, I rose to my feet and announced 'I will come top in the class of 120 in 3rd year Organic Chemistry, I will get a first in biochemistry and I will pass my mandatory advanced level physics course.' I turned and narrowly avoided smashing his glass door as I exited. I did as I said but now chose to decline the offer to transfer. However, I was wrong about Dr Mogeey.

Years later, I discovered that Dr Mogeey wrote one of my confidential letters of recommendation to be his colleague and faculty member in Pharmacology. The letter went something like this 'I have known Craig Jordan express strong emotional opinions in response to personal criticism. He has now learned to channel his energy for achieving success'. The following year (1966), I was to receive an Ackroyd Scholarship from Leeds University.

It transpired that Dr Mogey had nominated and supported me for this honor. An honest gentleman. I later discovered that Prof. Sir George Porter, President of the Royal Institution was a chemistry student at Leeds. He stated how proud he was to be an Ackroyd Scholar as it gave him confidence to succeed. This is why today I support the Jordan Prize in Medicinal Chemistry at Leeds University and the Jordan Prize and Trophy for the best Cadet annually in Leeds University Officer Training Corps (LUOTC). I have supported both since 1996 but why the OTC? Remember grandfather?

Growing up in the early 1960s, I learned to respect the commitment and tradition of service exemplified by the British Army. But my grandfather would say 'have nothing to do with the Army. I know, I have been in two world wars' but then he would say 'but when war comes, as it surely will, you had better be ready'. Well there was a challenge! My first stop on going to Leeds University in October 1965 was the OTC to sign on. But all was not what it seemed in my life.

I was born in New Braunfels, Texas, on July 25, 1947. My mother, a fire service officer, had met and subsequently married an American officer from Dallas in 1944 and they went back to Texas after the war. They divorced in 1950 with my mother and I returning to Cheshire. I never met or had any first-hand knowledge of my 'DNA Dad'. My stepfather had adopted me as his legal son, so I became a British citizen. In October 1965, I joined the LUOTC and started to learn to be an officer. But in spring 1966, just in the same week that Dr Mogey interviewed me for transfer to Pharmacology, the officer commanding the OTC called me to his office and stated 'You were born in America, so you cannot be an officer in the Army. I am sorry but there it is'. A terrible week for me at Leeds, but you fold or fight. It is a test of resolve. I thought about the roadblock in my future plans for 6 months and then acted. I secretly visited our family solicitor who eagerly agreed to challenge the Ministry of Defense *pro bono* by getting a ruling from the Home Office. The Home Office letter declared that the Ministry of Defense could not deny me access to a commission. My commission occurred following my interview with the commissioning board in the summer of 1969. I had a first-class honors degree and the last Medical Research Council (MRC) scholarship to support me crystallizing the ER with an estrogen or an antiestrogen to discover how 'failed contraceptives' worked. However, as I sat waiting outside for my name to be called, I overheard someone on the board state 'Well, I suppose we better interview him anyway!'. That did not sound too positive. It was time to

prepare for the Olympic final against the board! After introductions, it was clear I was sinking fast. Then came the question 'Why do you want to be commissioned as an officer in the British Army'. Without hesitation I replied 'I have a first class honors degree and a MRC scholarship to do a doctorate. Should I be worthy of a commission I request to be sent on Regular Army courses so I can use my knowledge to the full'. I was awarded a commission in the infantry and was immediately sent to the Regular Army operations training course in Nuclear, Biological, and Chemical (NBC) Warfare Defense; today's 'weapons of mass destruction'. This was just as I was learning to ovariectomize mice with my new PhD supervisor Dr Ted Clark, the man who had interviewed me to be admitted to Leeds back in 1964. He was not thrilled!

This initiative, in 1970, started a chain of events over the next 30 years. High points were: talent spotted for recruitment into the Intelligence Corps, on the Staff of the Deputy Chief Scientist (Army), attached to US Army, training as a narcotics officer in America, Sandhurst, Foreign Armies study, talent spotted by the SAS, Regular Army Reserve Officer, SAS, a personal recommendation by General Sir Michael Rose (of Iranian Embassy Siege fame 1980) to join the SAS Regimental Association, and finally, a presentation from General Sir Richard Dannatt, Chief of the General Staff in recognition of my commitment to the training of future officers. At the start of this odyssey to enter my alternate universe, following top secret security clearance by MI5, I recall thinking 'here I am guarding the Holy Grail, when 4 years ago I was declared an *enemy of the state*'. But back to the real world?

I started my love affair with 'triphenylethylenes' in 1969. The story of how a 'failed contraceptive' ICI 46 474 was reinvented as tamoxifen is told in the accompanying article (Tamoxifen as the First Targeted Long-Term Adjuvant Therapy for Breast Cancer). The critical interdependent role of the individuals involved (Mike Baratt, Arthur Walpole, Mike Harper, Dora Richardson, Roy Cotton, Lois Trench) is important as each was committed to the success of tamoxifen and actively support my career development. But one individual, Dr Eliahu Caspi at the Worcester Foundation, gave me the best advice. In 1974, at the end of my Been to America (BTA) experience, when I was about to return to Leeds, I was called into Dr Caspi's office. His task was to evaluate my CV and decide whether to offer me a job. He stated abruptly 'But you don't have any publications. You are collaborating with lots of people but you have nothing on paper to evaluate!' After a stunned silence during my replay of my 'Mogey moment' in 1966, I replied 'but I haven't discovered anything yet'.

His advice was perfect: 'Tell them the story so far. Write papers that are connected so you become known for a theme and body of work'. My 2-year BTA subsequently resulted in more than a dozen publications and a career was begun. Years later, I was invited to be the inaugural Eliahu Caspi Memorial lecturer at the Worcester Foundation. His accomplished family told me of their father, a Polish Jew, being captured and held in a Russian Prisoner of War camp (the Germans invaded from the West, the Russians from the east). He survived and escaped to the Middle East where he witnessed the birth of Israel as a member of the Hagana (early Israeli Defense Force) and then found his way to America. Following a PhD in Chemistry at Clark University, Worcester, he spent a distinguished career in steroid metabolism at the Worcester Foundation in Shrewsbury.

I found my way back to America in 1980 and the circle of my life started to close as the career opportunities opened. My father and grandfather both died in 1972 and my mother encouraged me to advance my career wherever that would be. By 1980, I accepted a job with Paul Carbone to go to the Wisconsin Clinical Cancer Centre. My mother decided to find my DNA relative 'Luther Trammel and his wife Lorraine in Houston who had helped us in 1950 following my mother's divorce from my 'DNA Dad'. She wrote to the library in Houston for addresses and candidates were offered. Luther and Lorraine replied. Luther was the son of one of the Hamilton sisters and I was the grandson of the other, through my 'DNA Dad'. In 1983, I drove my family to Houston to be greeted with the cry 'He has the Hamilton teeth'. Genetics in action!

At breakfast on the first morning in Houston, I was presented with a silver christening cup by Lorraine with the words 'I always knew you would sit around this table one day. I give this back to its rightful owner as it was given to me by your mother in 1950 as she left. It was the only thing she had of value and she wanted us to remember you'. This was now 33 years later! The cup is engraved Virgil Craig and was sent by my grandfather to commemorate my birth. Then Lorraine handed me an envelope containing short stories. To me short stories meant children's stories so I did not give this much thought until years later. This story unfolds after hearing tales about 'the War' and my 'DNA Dad'. My mother met 'DNA Dad' before D-Day June 6, 1944. He returned from the momentous landing 4 months later and they married. He returned to his unit and was present at the Battle of the Bulge, even today America's largest battle. When I read the short stories I went cold. The notepaper was from a company Air Land International with offices in

Washington (Silver Spring, MD), Ankara, Bangkok, Yemen, Jeddah, etc. (you have got the picture!). Clearly, he was working with some strange arm of the US government (enough said). All the stories were about fighting in Thailand's civil war and drug smuggling in the Golden Triangle (northern Thailand) – Special Forces and Narcotic, i.e. my two areas of expertise in law enforcement in the US/UK and NATO. I, myself, could have written any of these stories.

All my life I had believed it was the influence of my grandfather's DNA and my mother's nurture but it was natural selection by my mother for my 'DNA Dad' too. He died in 1992.

I feel the key to success in my career has been my ability to build and lead small independent teams. This was true in my unconventional 'alternate universe' and in my science career. My Tamoxifen Teams were created in half a dozen places around the world over 4 decades. We always started with an empty suite of laboratories, then hired and trained staff to forge a Team. The successive Tamoxifen Teams quickly turned ideas into lives saved and I am privileged to have aided the career development of the members. I have always tried to put back what I myself received from my honest mentors. When asked later Dr Kaye would reply – 'I was only doing my job' Good words to live by. In 2013, the Tamoxifen Team was recognized on the Wall of Honour at the Royal Society of Medicine in London. This is my gift of respect for their excellent research accomplishments.

I am honored by the generosity of my academic colleagues on both sides of the Atlantic to be recognized by elections to prestigious professional societies. In the United Kingdom: fellowship of the Academy of Medical Sciences and honorary Fellowship of the Royal Society of Medicine. In the United States: member of the National Academy of Sciences, Fellow of the AACR Academy (<http://www.aacr.org/home/scientists/aacr-academy/inaugural-class/v-craig-jordan.aspx>), and ASCO's '50 Oncology Luminaries' (<http://cancerprogress.net/node/2086>).

The Tamoxifen Teams contributed a succession of new ideas that all translated from the laboratory to clinical practice: to use tamoxifen in the clinic with long-term adjuvant therapy, chemoprevention with tamoxifen, the selective ER modulators, the warning about an association between tamoxifen and endometrial cancer, raloxifene to prevent osteoporosis and prevent breast cancer at the same time, the evolution of acquired resistance to tamoxifen, and the new biology of estrogen-induced apoptosis.

These ideas all come out of simple and straightforward laboratory experiments dependent on the changing

environment of the Tamoxifen Teams. Nevertheless, the ideas matured over time through resolve and persistence and especially through a supportive environment from academia, industry, and comprehensive cancer centers. Jules Verne wrote 'whatever one man is capable of conceiving (in my case SERMs), other men are capable of achieving.' That is multidisciplinary translational research; a.k.a. pharmacology. Much has changed since the barbaric days of breast cancer therapy in the 1960s. The story of the Tamoxifen Teams illustrates that progress is about people and passion. People make discoveries, people become advocates for change, and people change healthcare. An investment to provide opportunities for people works. Who are they? It is any young person willing to train themselves for that chance at the Olympic gold medal final and be self selected.

Declaration of interest

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