A unique intellect

JULIE McCROSSIN talks to an unsung hero who is quietly working to help millions with gene-related diseases

Researcher and inventor Professor Richard Cotton, 65, director of the Genomics Disorders Research Centre at Melbourne's St Vincent's Hospital, is a man on a global crusade. If he's successful, he could improve the lives of millions of people all over the world by helping doctors to treat or prevent diseases with a genetic component.

Richard Cotton's dream is to catalogue all the human gene variations that cause disease and make this information available to clinicians, patients and researchers, free of charge, on a database curated by the leading expert on each gene. He is the driving force behind this global initiative, which received international support at a meeting he hosted in Melbourne in June this year.

His work has the potential to fundamentally improve the way we deal with cancer, heart disease and schizophrenia, as well as myriad less-well-known conditions with a genetic component, such as cystic fibrosis and sickle-cell anaemia. If he achieves his goal, he could even help to uncover the causes of common diseases such as breast cancer and asthma.

"The heart of it is that 60 per cent of all humans are affected directly or indirectly in their lifetime by faulty genes," Prof

Richard Cotton on his Wangaratta farm in 1963.

Richard Cotton says the consistent themes of his life are an 'inquiring mind' and a belief that 'there must be a better way'. 'I always try to live the problem and be amongst the problem,' he says.

Richard Cotton grew up on a 40-hectare orange farm in South Wangaratta, which his parents bought in 1938. His father Graham, who died when Richard was three, studied at the Hawkesbury Agricultural College and managed a citrus farm at Swan Hill before buying the Wangaratta property Cotton still owns and runs today.

Cotton says he doesn't remember his dad. However, when he was eight he discovered a copy of *The Washington Post*, which his father loved to read, still lying around the house.

"I think it says he was interested in things beyond farming and I suspect he was bright."

His mother Esther, who was dux of her school and active in the Country Women's Association, was a very important person his life. "I was an only child and it was she and I together since the age of three," he explains. He is especially grateful for her decision to send him to board at Melbourne Grammar School, where he remembers the joy of living with "60 brothers" and how he "adored physics" and "thinking about problems and working out why things happened".

When he told the headmaster, Brian Hone, that he intended to do a diploma of agriculture like his father, Hone encouraged him to think about going to university.

"It was a turning point," Cotton now believes. He decided to study agriculture at Melbourne University. He describes it as "the most stunning, stunning course because you did everything from geology through to economics, social studies, bacteriology and animal husbandry". It was at Melbourne University that he discovered he "adored" microbiology.

After completing a doctorate, he was accepted by the University of Cambridge Medical Research Council to work in the Laboratory of Molecular Biology, which had produced five Nobel Prize winners. He asked and answered fundamental research questions, laying the foundations that led to a Nobel Prize for the laboratory.

Back in Australia, he became interested in the biochemical genetics of humans and, during a period at Melbourne's Royal Children's Hospital, he met "these poor families who had these tragic cases of inherited disease" and he asked himself, "What can be done for them?"

Cotton went on to develop a series of technologies to detect the gene mutations that underlie birth defects and cause disease.

He says the consistent themes of his life are "an inquiring mind" and "a belief that there must be a better way". He believes he was "born with an inquisitive mind" because "I can't stop asking the next question and I like to think deeply about things. I always try to live the problem and be amongst the problem."

In June this year, a meeting including members of the World Health Organization and the American College of Medical Genetics as well as the European Commission, the United Nations Educational, Scientific and Cultural Organization (UNESCO), the Organisation for Economic Co-operation and Development (OECD), the US Center for Disease Control, Google and genetic experts from Africa, Asia, South America, Europe and the Arab world agreed to support Richard Cotton's vision for a global database and to call it the Human Variome Project.

Just as the Human Genome Project details the complete set of genes in a human being, so this Human Variome Project will set out to document all the available information on the faults in genes that influence disease.

It's a massive undertaking that will build on an earlier project instigated by

Cotton explains at his modest research laboratory in St Vincent's Hospital, near the green parks of central Melbourne.

"The international meeting in Melbourne has given us a mandate to collect these variations or faults in genes, together with what effects they have on human health, and to set up a system for making it available free of charge."

Prof Cotton became aware of the need for such a database in 1991 when he established the journal *Human Mutation*. "I was absolutely horrified to discover that no one was responsible for collecting all the faults in genes that make people sick," he says.

"At the moment, if a clinician has a patient and they get back a laboratory result that indicates a fault in a gene, they need to know if that particular fault is a problem for the patient, if it has been seen before and what effect it may have on the patient. At the moment, tracking this stuff down can take a lot of time for a highly busy clinical geneticist. The information is not in the public domain. It is not complete. It is not accessible in one place."

MAIN PHOTOGRAPH BY JULIE RENOUF.

Cotton's dream is to catalogue all the human gene variations that cause disease and make this information available to clinicians, patients and researchers, free of charge, on a database curated by the leading expert on each gene. It has the potential to help millions.

Cotton known as the Mutation Database Initiative, co-ordinated by the Human Genome Organisation. This consortium of database curators involved 600 members in 34 countries and led to the creation of the Human Genome Variation Society. Cotton was a central figure in all these developments.

It seems the mapping and sequencing of the human genome have led to a massive increase in the rate of discovery of variations or mutations in genes. The discoveries are recorded in the private files of scientists, laboratories and clinicians, and then are published in a range of journals or on websites. There are some commercial databases that give access to the most up-to-date research in return for a subscription of several thousand dollars.

If Richard Cotton is successful in gaining the initial government funding for co-ordination from Melbourne, he hopes it will be a very different situation in just five years. "We propose to have a series of international editors who are responsible for each gene. I'd like to attract a major, internationally known scientist back to Australia to run the project. This database will be a global public good, providing free, high-quality information for the benefit of humanity."

Cotton is confident he will be able to attract the many millions of dollars needed to complete this massive, multi-year project from international sources, including US foundations such as The March of Dimes and the one set up by Google. Both sent people to the Melbourne meeting in June. "It would be unthinkable if they could find a reason not to fund it, because we had the world's top geneticists, top health organisations and top funding bodies, all saying this needs to be done," Cotton explains.

Cotton and his wife Elizabeth, a paediatrician, have three children, who have also inherited the "inquisitive mind". Caroline, 32, is a teacher at Scotch College, James, 30, runs an international software firm and Michael, 27, works as a consultant.

Cotton's love for his family and his pride in their work shines from his eyes as he repeatedly acknowledges the valuable support of his wife and children. He also emphasises the essential contribution to the Human Variome Project of his executive officer, Heather Howard, herself the mother of a child with a genetic disorder.

As I walk away from Richard Cotton's laboratory, I feel I've been in the presence of a man blessed with a unique intellect and the talents necessary to fulfil a history-making project of great significance for the whole human race. ∎