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OBITUARY

E Donnall Thomas (1920–2012)

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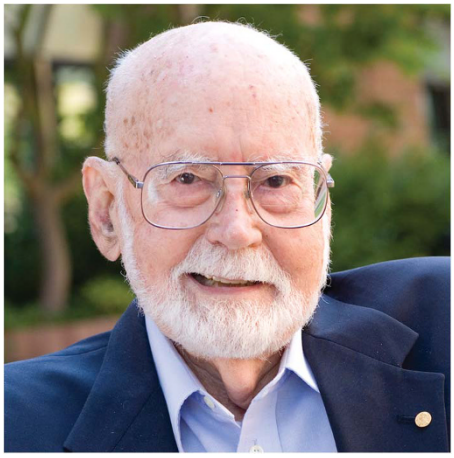

Professor E Donnall Thomas, the 1990 Nobel laureate in Physiology or Medicine and a towering figure in bone marrow transplantation, died in Seattle on 20 October, 2012. He shared his Nobel Prize with Professor Joseph E Murray who pioneered kidney transplants.

Don Thomas' path to the Nobel started in Boston (naturally) where he studied the release of stimulatory factors by irradiated yeast, a pathway that eventually led to the molecular cloning of diverse hematopoietic hormones such as erythropoietin (EPO) and granulocyte colony-stimulating factor, drugs given to hundreds of transplant recipients daily. Interestingly, he also participated in the care of the first children treated for leukemia with aminopterin, a predecessor of methotrexate.

However, Don was drawn into the transplant world by another series of extraordinary events. In 1945, parallel with the Manhattan project's target to develop the atomic bombs, the US Government recruited scientists at the National Institutes of Health to determine ways to counter the effects of radiation on humans (President Franklin D Roosevelt had been advised by Einstein that the Germans were on a similar, fortunately, unsuccessful path). It was soon noted that spleen shielding could prevent death from an otherwise lethal whole-body radiation dose. This led to the mistaken notion that the spleen secreted something that favored bone marrow recovery, leading ultimately to the discovery of EPO. However, it was soon shown that an infusion of bone marrow cells from an unirradiated mouse could also protect against radiation-induced bone marrow failure. Don seized on this observation and spent the rest of his life perfecting this approach, first in dogs (he wisely chose an outbred species to get closer to the human situation) and later in young persons with advanced leukemia.

His was not an easy road. The human leukocyte antigen (HLA) system was not yet identified and many recipients rejected their grafts or developed graft-versus-host disease. Control of infections was far less developed than today and there were not reliable diagnostic or therapeutic interventions for virus infections, especially, cytomegalovirus. And there were many critics who labeled his early clinical trials 'unethical'. But Don carefully and patiently worked out the fundamental problems, first in dogs and then in humans. A key element was that he believed in what he was doing. He knew that bone marrow transplants could work, and he was determined to make this happen in humans.

I recall a conference on bone marrow transplants in Santa Barbara in the early 1970s when fewer than 100 transplants, most unsuccessful, had been done worldwide. There were six participants among them: Don, George Santos, George Mathe' and Bob Graw. Because I was a PhD student with John Fahey at nearby UCLA, I was privileged to serve coffee and listen in. George Mathe' went off to other topics. Bob Graw (wisely?) decided to drop out of what seemed an uphill battle and practice pediatrics. George Santos stuck with it, but it was Don, with his extraordinary team of laboratory and clinical colleagues, that brought bone marrow transplants to fruition.

Today, 65 000–70 000 people receive bone marrow transplants every year. About one-half of these are allotransplants, and the remainder are autotransplants. More than one million have been done worldwide, and countless people owe their lives to Don Thomas' dedication to getting transplants to work.

Many things (always best realized in retrospect) accounted for Don's success where others failed or gave up. I find three most important: (1) Don had a sound scientific and experimental basis for his belief that he could make transplants work in humans, (2) Don was stubborn. He pursued his beliefs despite substantial criticism from many quarters. As Jaques Barzan noted: 'The intellectuals' chief cause of anguish are one another's works.' and (3) His secret weapon, Dottie Thomas, his life-long collaborator and a fierce competitor in her own right. Although none of us will be able to have the Dottie Thomas, we can take a valuable lesson from the first two traits in our scientific pursuits.

The late astrophysicist Carl Sagan (who paradoxically received a bone marrow transplant for myelodysplastic syndrome from Don's team) said: 'Extraordinary claims require extraordinary evidence.' Don Thomas had that evidence and the will to see it through.

Robert Peter Gale
Department of Medicine, Imperial College, London, UK
E-mail: rgale@celgene.com