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The Red Blood Cell Man

by André Picard

Thomas Chang is the Jules Verne of artificial blood research. Going where no man has gone before, Chang's steadfast commitment to basic research has given life to artificial blood

In 1956, Thomas Ming Swi Chang, an undergraduate student in physiology, wanted to impress upon his professors that he was serious about science. The 23-year-old decided he would build artificial blood cells, a notion considered as fanciful as impossible. "I thought if artificial organs could be built-- why not the the basic unit, the cells? I was naive."

Yet, by transforming his Douglas Hall residence room into a makeshift laboratory, Chang soon achieved his goal. Equipped only with a cheap perfume atomiser, some collodion (a cellulose nitrate solution that, at the time, was used to coat wounds) and haemoglobin borrowed from a lab, and blessed with room-

mates who were indulgent about the nasty smell, the science student managed to build one-millimitre round thin plastic cells that contained haemoglobin, the compound in red blood cells that carries oxygen and whisks away carbon dioxide.

Forty years later, Dr. Chang, BSc'57, MD'61, PhD'65, has earned his academic stripes many times over, as a tenured professor of physiology, medicine, biomedical engineering, and an associate professor of chemistry and chemical engineering. And as director of the Artificial Cells & Organs Research Centre, he is still toiling away in a McGill laboratory that has the air of a residence room, trying to expand and perfect his youthful invention, one that has already …… set the stage for revolutionary developments in genetic engineering……..

The tainted blood tragedy, which saw more than 60,000 people in the Western world infected with the AIDS virus (more than 1,200 of them in Canada), has given urgency to the search for safe substitutes. It has also pushed the self-effacing Dr. Chang into the limelight and brought him long-overdue recognition, including an Order of Canada. He has published more than 400 scientific papers and 21 books. An international symposium on blood substitutes he hosted at McGill in August drew an overflow crowd of 350. " I looked around and realized most people there owed their jobs to Dr. Chang." said one scientist.

..... Dr. Chang stays focused on whole cell research. "I'm a red cell man," he declares. Artificial red cells, for example, would be a god-send in the emergency room because they would allow doctors to infuse blood without worrying about allergic reactions to the wrong blood type. Artificial blood can be stored for six months or more, while blood components have a limited shelf life, from a few days for platelets to 42 days for red cells. These storage limitations make it difficult to ensure an adequate supply, particularly in extreme conditions like war. ……. A steady drop in donations, another result of the tainted blood tragedy, means there is a perpetual blood shortage.

Until recently, the cost of substitutes has been high. But safety concerns have driven up the cost of donor blood; even in Canada, where blood is donated voluntarily and provided "free" to hospitals, the cost of collecting and testing a unit of blood is about $225 -- the Red Cross does at least seven tests on each unit -- and that is without factoring in the costs of lawsuits by those who received tainted blood.

More than 100 million units of blood are transfused worldwide each year, translating into a huge potential market for artificial blood. Dr. Chang, however, has never been that interested in the commercial aspects of his discoveries. "To me as a scientist what is most important is what is most useful to the patient, not what is good for your reputation or what pays the most money. The sick patient should be the most important stimulus for our work."

In the late 1960s, Dr. Chang made the kind of breakthrough that could make him both famous and rich -- the discovery that enzymes carried in artificial cells could be used to correct inborn errors of metabolism, the beginnings of an exciting field that, eventually, should see genetic diseases treated with a pill. He was nominated for a Nobel Prize for that work but, in 1970, put it aside to pursue ……artificial cells containing activated charcoal to treat drug poisoning. The technique, haemoperfusion, has become the standard treatment in poisoning cases, and saved thousands of lives…….. use about 200 grams of artificial cells in a fist-sized column, and a blood pump mimicks the purification job performed by a healthy organ by filtering the patient's blood through the charcoal-filled cells. Although a simple concept, the trick was building membranes that allow toxic molecules, but not the precious red blood cells, to be extracted. Together with a French company (in Montreal), he developed the organ and the operation was bought out by American company. That artificial organ cost only about $35, compared to more than $5,000 for a dialysis machine (in the early 1970s) as a result, however it did not catch on with biotechnology companies.

"I think of research as something you do in the basement in your spare time. It's like a full-time hobby and I'm just lucky to be paid," Dr. Chang says, letting out one of the laughs that always punctuate his conversation. Over the years he has been wooed by many universities and the highly-competitive biotechnology industry, but .....

Dr. Chang turned his back on money long ago when he chose a career in medicine. His grandfather, a native of Swatow, had built one of the biggest industrial empires in the city, but his family moved as refugees to Hong Kong in 1950, and left this all behind. "In China in those days, a physician was a very low-level position. My choice was a kind of insult to the family. So we made an agreement: I would go to the best school in the world, and do something to make the family proud."

Today, Dr. Chang is taking another unconvential stand, staying put in Quebec, despite the political turmoil. "I'm not a political person, but I want to say that I have been well-supported by the Quebec and Canadian governments over the years. I don't want to chip and run for better money just because things are getting a little bit difficult," he says. (Dr. Chang has had grants from the Medical Research Council of Canada since 1965, and from the Quebec Ministry of Science and Education since 1985.) Besides, he wants to remain close to his four children, all of whom live in Montreal and Ottawa. Harvey, MD'83, is on staff at the Jewish General Hospital; Victor, BEng'86, is an engineer with the Canadian Space Agency; Christine, P&OT'86, is a physiotherapist and Sandra, BEd'91, is a teacher. His wife of 38 years, Lancy, is a dialysis nurse at the Montreal General Hospital.

At a time when he should be planning for retirement, the 63-year-old scientist is busier than ever. If AIDS had not come along, Chang might be pursuing his

research in obscurity…… Most researchers have embraced Dr. Chang's notion of having artificial cells carry modified haemoglobin to the body. The biotechnology companies are …….. looking for new sources of haemoglobin. While Dr. Chang derives the oxygen-carrying material from human blood donations, others are deriving it from cow's blood and genetically-engineered E. coli bacteria…….. .

Developments are just as exciting in his other field, using artificial cells to "transplant" living cells into people with genetic deficiencies. For example, artificial cells carrying insulin-secreting cells from animals could free millions of people from the hassle of daily injections. With Chang's encouragement, Connaught Laboratories of Toronto, where insulin was first discovered, has been working on this concept for almost 20 years, and it is moving from the realm of science fiction to reality. Chang is also working on artificial cells containing genetically engineered cells which may one day replace the need for dialysis. Artifical cells could help treat phenylketonuria (PKU), a common genetic disease which causes mental retardation, by loading the missing enzymes into an artificial cell and feeding them into the gastro-intestinal tract, allowing the body to process the amino acid that does the damage……..

In fact, the potential for artificial cells is almost limitless, at least in theory. There is talk today of building artificial cells that would transport miniaturized surgical robots to the nether regions of the body, and of synthetic cells that could transform the body wastes of astronauts into useful proteins -- none of it any more fanciful than the idea of constructing an artificial cell was in 1956.

Yet Dr. Chang remains philosophical and humble, saying that, after 40 years of work with artificial cells, he is becoming more aware of the limitations of science and more like his great-grandfather, a Protestant preacher.

"You can become very religious when you do research with artificial cells. We all think we are so advanced as scientists, that we are so good and brilliant. But if you look at it objectively, no matter how smart we are, we will never be able to copy what has been made by God, not even a simple red blood cell. We can only hope to make a simple substitute, and right now we are still taking our first steps."

André Picard is the author of The Gift of Death: Confronting Canada's Tainted Blood Tragedy. *(HarperCollins Canada Ltd.)*

AN INTERVIEW WITH PROFESSOR CHANG CAN BE VIEWED AT:
www.artcell.mcgill.ca/bloodTV.wmv Requires high speed internet or Lan and takes a few minutes to download