

| BONGANI MAYOSI |

TOP THREE AWARDS

- Order of Mapungubwe, Silver (Medicine), 2009
- South African Medical Research Council's Platinum Award, 2016
- National Research Foundation A-rating in recognition of world-leading research on poverty-related heart disease, 2016

DEFINING MOMENT

Sitting in the back of my father's Land Rover, driving to see patients in his district in the Eastern Cape. I always wanted to be a doctor like him; it wasn't even a decision I had to make.

WHAT PEOPLE DO NOT KNOW

My wife and I used to be competitive ballroom dancers. We danced for Wolfson College at Oxford University, and in 1999, we were part of the dance team that won the Oxford Cup.



KING OF HEARTS

The son of a district surgeon and a nurse, Bongani Mayosi was always going to study medicine. His father, George, had been in the early group of doctors to graduate from the University of Natal's 'black' medical school in Durban, which opened in 1947. George specialised in obstetrics after working as a district surgeon for the small hamlet of Ngqamakwe in the Eastern Cape. This is where Bongani grew up, surrounded by the rolling hills of the Transkei.

Bouncing along the potholed roads in the back of his father's Land Rover, Mayosi had an early introduction to the routine life of a doctor. His father would pull up outside a shop in a nearby village and set up a makeshift clinic. As for his education, his parents saw to that – and to that of the rest of the children in Ngqamakwe. When the Mayosis arrived, the closest school was a long walk away in a nearby village of Ngculu. But Mayosi's mother had trained as a teacher before re-schooling as a nurse, and with the help of other parents in the village they set up a school in the hamlet. The school took in every child able to walk in the village in order to make up numbers. Different grades were taught in one large church hall. It was an excellent environment for learning, Mayosi recalls. His whole generation graduated in their mid-teens, earlier than they would have at a more formal school.

Once out of school, Bongani followed in his father's footsteps and went to study medicine at the University of Natal. Competitive by nature, he wanted to exceed his father's accomplishments. He discovered that the school made provision for students to earn a research degree after their third year of medicine. Few people used it – after all, it meant losing a year's earnings as a qualified physician. But Mayosi was able to convince two of his professors to take him on as a student: one a professor of anatomy, the other a pharmacology professor. That was when the joy of discovery seized hold of Mayosi.

"I spent a year studying the small navicular bone in the human foot. Seeing my work published, and defending it, was a wonderful experience," he says.

After graduating with distinction from the Bachelor of Medical Science degree in 1986, Mayosi went back to finish his medical degree, also with distinction. He left medical school in 1989 and went for a residency in Port Elizabeth. It was meant to be a temporary move away from Durban, which had become home. At PE's Livingstone Hospital he met a group of people hailing from Groote Schuur and the University of Cape Town (UCT).

"They kept going on about the place, and I wanted to come see what it was all about before returning to Durban," he says. He and his wife both held the Cape dear, having spent their honeymoon there some years before. "We'd already fallen in love with the geography," he says. And the medical research community seemed to brim with opportunities for the ambitious couple, so they decided to move there.

DECODING SUDDEN HEART FAILURE

Mayosi started off in Groote Schuur's Division of Neurology. But during his rotations at the hospital he fell in love with cardiology. It was a discipline of some renown in the hospital, which was the setting of the world's first human heart transplant in 1967 under the deft scalpel of Christiaan Barnard.

One of the first clinical problems to tickle his mind was that of unexplained heart failure. That is where a young person comes to the clinic very sick with shortness of breath, a swollen body and enlarged heart. The phenomenon was not understood at all, but Mayosi had a hunch there could be a heritable factor at play. And so he started assembling samples from families where several members were affected.

In 1998, six years after joining UCT, Mayosi boarded a plane bound for the UK to take up a doctoral post at the University of Oxford. His luggage held eight samples from a family affected by sudden unexpected death due to an unexplained form of heart muscle disease called arrhythmogenic right ventricular cardiomyopathy (ARVC). Initially, he hoped that his PhD could identify the genetic variant that caused the illness in this family. But the technology of the time, even at Oxford, was not sufficient to draw good

conclusions from so few samples. When he returned from South Africa five years later, the family samples returned with him, unstudied.

Instead, Mayosi spent his time at Oxford studying conditions where genetics may be one of many factors causing disease. For instance, a thick heart is more likely to develop cardiac arrhythmias. High blood pressure is one of the known reasons why the heart thickens. But there are other factors, such as genetics.

“What I had to work out in my PhD was the proportion of the variability of heart muscle thickness that is influenced by genes. It was a wonderful project, and intellectually more stimulating than the one I came to Oxford wanting to do,” he says.

It took another 15 years for Mayosi and his colleagues to crack the conundrum of his patients with ARVC. When he returned from Oxford he recruited his first postdoc to work on the problem at UCT. A wrong turn in the genetic analysis led the team to study the wrong part of the chromosome for seven years. Then the advent of exome sequencing allowed for improved analysis, and in March 2017, the team finally published a paper identifying the culprit: A mutation on a gene called *CDH2* (N-cadherin), which increases the risk of heart muscle disease and cardiac arrest.

The discovery was “probably the biggest breakthrough in South African cardiology since Dr Chris Barnard’s first heart transplant,” Mayosi told the media at the time. In addition to being a first on South African soil, the gene codes for a protein that has not been linked to heart disease previously. The next step is to understand how, biologically, the mutation causes the condition. Once that is understood, it could lead to completely new treatments for heart muscle disease and sudden death. Mayosi relishes the challenge that lies ahead. “We’re at base camp. Now we have to ascend Mount Everest.”

A FAMILY AFFAIR

In 2016, Mayosi received an A-rating by the National Research Foundation, identifying him as a world leader in research on heart diseases related to poverty. He studies pericardial tuberculosis (TB), caused by *Mycobacteri-*

um tuberculosis, the bug that causes TB. Pericardial tuberculosis is the most common form of pericarditis – inflammation of the heart sac – in Africa and other places where TB rates are high, especially as a result of widespread HIV infections. The condition causes chest pain, can disturb the heart rhythm and even cause death.

Mayosi’s team have defined how pericardial TB presents in the HIV era, how to diagnose it and how to treat it. “That work has redefined the field of pericardial TB in the world.” He has also worked on the prevention of rheumatic heart valve disease by setting up the first multinational studies with colleagues from all over the world.

Another breakthrough came from working with his wife, a dermatologist and fellow UCT professor. Together they have studied a family with a rare condition that mottles and scars the skin of its sufferers. So far, they have identified the gene that causes the condition, something that could be interesting for a range of other illnesses, Mayosi says. Scarring is a common complication of diseases like TB, heart disease and liver disease. TB scars the lungs, heart attacks scar the heart and cirrhosis scars the liver. This scarring can lead to problems down the line. Mayosi hopes that by understanding the genetic cause of the rare skin disease studied with his wife, they can shed light on ways to prevent scarring in general.

But life is not just about battling disease. Mayosi’s pride and joy are – literally – his two daughters, Vuyi and Gugu. “Vuyi means joy and Gugu means pride,” he explains with a smile. Vuyi, the eldest, has finished medical school and is a first-year intern in Johannesburg. She is a third-generation doctor. Gugu is at UCT studying occupational therapy in her fourth year.

A BRIGHT FUTURE

Mayosi became head of the UCT Department of Medicine in 2006. He’s a member of numerous national and international learned societies, including the Royal College of Physicians of London and the American College of Cardiology.

He has also bagged several prestigious research grants for UCT and his department, earning over 100 million rand in total since 2010. In 2016, he won

a 15 million Rand grant focusing on non-communicable diseases from the Newton project, a collaborative funding programme between the governments of the UK and South Africa to strengthen research links between the two countries. In 2013, he led a team that received a whopping 34 million Rand over 42 months from the H3Africa programme, an initiative to build genomic research capacity in sub-Saharan Africa. That same year he obtained a 23 million Rand grant from the South African Technology Innovation Agency, the National Research Foundation and other funders to buy a whole-body magnetic resonance imaging scanner for use in research.

Given that he only turned 50 in 2017, his achievements so far are impressive. So what is left?

Apart from continuing to chip away at his research projects, he wants to feel when he hangs up his lab coat in a decade or two's time a sense of 'completeness'. "I want to pursue a total academic career. I want to play a role in leadership and administration, in research, and also in national and international life." Most importantly, he wants to continue to be useful and to break new ground in global medical knowledge.

"My career has been a little unusual. I've tended to go for research niches that are under-occupied, where my group might even be alone in the world to study a particular question." That means he can take his time compared with colleagues in more popular fields, where regular publications are vital to keep up with the competition.

"From that point of view our work on the heart muscle disease gene could be considered a failure!" he says. After all, the team only produced two papers in the course of 20 years. But the quality of the papers, and the insights they present, are what matter – not their frequency, he points out.

This is something he encourages young researchers to keep in mind when carving out their own careers: "In our team we spend time thinking and experimenting, and we publish when we have something significant to say. That only works if you identify areas that are locally important, but also globally applicable. I study the exceptions to learn about things that are common."



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Academy of Science of South Africa (ASSAf), (2017). Legends of South African Science.

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