Tribal wisdom

benefits TB science

DR PHINDILE GINA

Academic Fellowship Award

University of Cape Town

Pulmonology

A Kwa-Zulu Natal tribal leader's wisdom in establishing a clinic alongside his family kraal and erecting a school nearby, could have indirectly led to his granddaughter today potentially helping control, or even end, the global TB epidemic.

Dr Phindile Gina, a final year PhD student at the University of Cape Town, is currently pioneering a highly promising immunotherapy approach for treating TB and drug resistant TB. If she succeeds, she could help slow, or even halt, an inexorably spreading epidemic that has reached near-crisis proportions in South Africa.

Explaining her initial interest in medicine, she says, "I wanted to do medicine at a very young age. We were from the rural Jozini district in northern Kwa-Zulu Natal and my grandfather Johannes "Masongwevu" Gina, was an Induna who initiated several community projects. So, as children we had early exposure to missionary doctors who worked in the clinic alongside our home. My mother was a teacher at the local primary school and my dad was in the Department of Public Works. They played a huge role in our lives, always emphasising education. It was never a question – all five of us kids knew we would study."

Awards tumble her way

In 2016, her MMed thesis on early morning urine sampling improving the diagnostic sensitivity for the LAM test in HIV/TB co-infected people, won her the Best MMed project prize. Two years later, her research team leader, Professor Keertan Dheda, won a global Scientific Leadership prize for a four-country study that demonstrated urine LAM-guided treatment strategy reduced mortality in hospitalised patients with advanced HIV by almost 20% (Lancet, 2016). Phindile was also part of this study. Today the World Health Organization (WHO) is rolling out and scaling up this strategy across Africa.

Then, in 2018 Phindile won the UCT Department of Medicine's Basic Science project prize for her PhD research project where she is using human lung cells to test if some of the FDA-approved drugs can kill TB bacteria by stimulating the body's immune system.

She's working whatever hours it takes to advance her laboratory experiments aimed at eventually conducting human clinical trials in a hope to get life-saving medicine to market – and changing the face of TB/HIV medicine.

"I usually work 14 to 20 hours a day. Sometimes I get home at two in the morning and I am back at the lab at six in the morning. Everything is time-critical in lab bench work. Seeing whether the compounds elicit any immune response requires constant monitoring. There is a tendency for it to degrade and dissolve. You cannot just put it in the fridge and look at it tomorrow. Once you've started an experiment, you have to finish it," she laughs.

A radical new treatment approach

Phindile is adopting an entirely new approach to TB drug therapy, one that will affect the front end of the ordinary TB epidemic and the extraordinary multiple drug resistant and extreme-dug resistant strains that threaten thousands more lives every day.

Her Discovery Academic Fellowship Award gives her the financial ability to conduct pure research without worrying about earning an income. She's investigating the role of autophagy in tuberculosis, using human lung cells.

She explains, "Currently the drug treatment targets the mycobacterium tuberculosis. There's evidence that our immune cells should be able to kill any infection including TB – but somehow the TB bacteria is capable of producing toxins, which render our immune cells incapable of doing what they're created for. As a result TB can live inside the cells that are meant to kill it. I'm testing compounds that can unlock that system or activate our immune system such that our body is able to fight back this deadly infection. I am looking at the ways to manipulate the immune system by inducing autophagy for host-directed TB therapies."

Not short on ambition, Phindile, says that adding to the global TB medicine collection will help meet the WHO target of a 95% reduction of TB by 2035. The main vision is a world free of TB, zero deaths, disease and suffering due to TB.

"With the current medicine for extreme-and multi-drug resistant TB, I doubt we'll be able to meet those targets," she says.

She plans to take her project into clinical trials soon, emphasising that worldwide, the WHO estimated that about 558 000 people suffered from drug-resistant TB in 2017, posing a significant threat to populations.

"Everyone's at risk. Some people don't even know they have it. Because it is air-borne and so many of our people crowd together for whatever reason, this is a public health emergency. In South Africa, an estimated 14 000 people fell ill with drug-resistant TB in 2017. That may look relatively small in terms of numbers, but they're increasing instead of coming down," she stresses.

Her most optimistic outlook? "I might be biased," she chuckles, "but right now there's too much work being done on diagnosing and counselling patients. We have to look for new medicines. We have a limited window to treat this TB crisis. We can't continue down the same route."

Asked what she does to relax, Phindile laughs, "I sometimes get a weekend in a month. I'm an outdoor person, so I love hiking and running and doing half-marathons whenever I can." Her work might just see her breaking the global TB research marathon tape before anyone else.

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Tactical research to benefit patients

Immunotherapy has been transforming cancer treatment in recent years and Phindile is using the same concept for discovery of possible compounds to treat TB. She has chosen two FDA-approved medicines, which seem to be working, to turbo-boost the speed at which they might reach patients. Among the advantages of the host-directed therapy, is that it's not susceptible to resistance. It rehabilitates the body's immune cells wherever TB infection occurs (mainly in the lung), and reduces inflammation and fibrosis, thus limiting lung-tissue damage. Phindile explains that secondary complications from TB-damaged lungs are a major problem, even among cured patients.

"If we can shorten the duration of TB therapy (currently up to six months), we can vastly improve adherence and thus begin to address the prevalence of extreme and multi-drug resistant TB," she adds.