Communication and Marketing Department
Isebe loThungelwano neNtengiso
Kommunikasie- en Bemarkingsdepartement
Private Bag X3, Rondebosch, 7701, South Africa
Tel: +27 (0) 21 650 5427/5428/5674
www.uct.ac.za | www.news.uct.ac.za

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UCT-led international study uncovers gene clues to severe COVID-19 in children

Researchers from the University of Cape Town (UCT) and the University of Southampton, together with international partners, have identified patterns of gene expression associated with severe COVID-19 in children that are shared with other serious respiratory infections, as well as patterns that distinguish these illnesses.

The findings, published in *BMC Infectious Diseases*, offer early clues about how the immune system responds to severe lower respiratory tract infection, identify which children are at higher risk and may offer potential targets for treatment.

Lower respiratory tract infections (LRTIs) - including COVID-19, respiratory syncytial virus (RSV) and pulmonary tuberculosis (PTB) - are major causes of childhood illness and death, particularly in low- and middle-income countries.

The researchers analysed gene expression in blood samples from 333 children from South Africia. They also compared samples from children hospitalised with severe COVID-19, with those from children with RSV lower respiratory tract infection or PTB. In addition, a healthy group of children were compared including children with only mild or asymptomatic SARS-CoV2, the cause of COVID-19, and a control group of healthy children.

They identified more than 5 000 genes expressed differently in children with severe infections. They also discovered 10 groups of genes which were expressed in a similar pattern across the different lower respiratory tract infections. These were linked to immune responses, cell regulation and other biological processes involved in infection.

The researchers also identified 82 genes that helped distinguish mild or asymptomatic SARS-CoV2 infection from severe COVID-19, suggesting that gene-expression patterns could be used as an indicator of disease severity.

Professor Heather Zar, principal investigator of this study, and of the Drakenstein Child Health Study – a birth cohort study from which many of the children were included – and Chair of UCT's Department of Paediatrics & Child Health, said: "There's been limited research examining biological responses to these infections in African children. There's also been few studies on host gene expression in infants and children with COVID-19 as well as other LRTIs globally, so this study helps to close an important evidence gap."

Dr Negusse Kitaba, senior research fellow at the University of Southampton and lead researcher, expressed similar sentiment, highlighting how the findings address the gaps by identifying differences in gene activity associated with disease severity.

"These findings provide new insights into the biological pathways involved in disease severity and highlight genes for further investigation as potential biomarkers and therapeutic targets," said Dr Kitaba.

The study also points to the value of bringing together expertise and data from different research settings, according to Professor John Holloway, Professor of Allergy and Respiratory Genetics from the University of Southampton. He said: "This study highlights the value of international collaboration in understanding childhood respiratory disease and provides a foundation for future research into why some children develop severe infection."

According to the study, further research with larger groups of children will be needed to determine whether these promising gene signature discoveries can be developed for clinical use.

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Issued by: UCT Communication and Marketing Department

Ridovhona Mbulaheni
Media Liaison and Monitoring Officer
Communication and Marketing Department
University of Cape Town
Rondebosch
Tel: (021) 650 2333
Cell: (064) 905 3807
Email: ridovhona.mbulaheni@uct.ac.za
Website: www.uct.ac.za