

## MEDIA RELEASE

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### **INTERNATIONAL RESEARCH COLLABORATION IDENTIFIES A GLOBALLY ACCESSIBLE TREATMENT STRATEGY FOR COVID-19**

*Research shows it may be possible to treat lethal COVID-19 inflammation with a widely available and inexpensive chemo drug*

Singapore — An international research collaboration involving researchers from the National University Cancer Institute, Singapore (NCIS) and the Icahn School of Medicine at Mount Sinai in the United States of America has found that a widely available and inexpensive drug used for cancer treatment could potentially be used in the treatment of COVID-19. In pre-clinical tests, the team reported that the chemotherapeutic drug, Topotecan, reduces the morbidity and mortality of SARS-CoV-2 infection by inhibiting the expression of inflammatory genes in the lungs of laboratory models of COVID-19. The findings from the study, published online in the scientific journal *Cell* on 30 March 2021, have potential implications for COVID-19 treatment in humans.

Co-author of the study, Dr Anand Jeyasekharan, Consultant and Assistant Director of Research (Medical Oncology) at the Department of Haematology-Oncology, NCIS, said: “A key finding from this study is that the suppression of SARS-CoV-2 induced inflammation by the Topoisomerase 1 inhibitor (Topotecan) occurs at doses lower than that typically used in cancer treatment. Topotecan has been used in oncology for over 25 years, with a well understood safety profile in humans, and importantly is both inexpensive and globally available. This research is therefore timely given the lack of universal access to vaccines”.

The safety and efficacy of this treatment strategy in humans will soon be evaluated at clinical sites around the world. Dr Jeyasekharan and the NCIS team in Singapore have already secured a research grant to conduct a Phase 1 clinical trial of Topotecan in COVID-19 patients. This research is supported by the Singapore Ministry of Health’s National Medical Research Council and the National Research Foundation under the COVID-19 Research Fund (NMRC Project No. MOH-000444). “The aim of the Phase 1 study is to establish the lowest dose of Topotecan that can safely reduce COVID-19 inflammatory markers in patients. Continuing our theme of globally applicable research, we have established a collaboration with the department of medical oncology at the Christian Medical College in Vellore (India) to take this trial forward,” Dr Jeyasekharan shared.

The pathophysiology of SARS-CoV-2 infection has been the subject of intense study over the last year. Scientists have observed that the virus triggers excess production of cytokines and chemokines – chemicals that are normally secreted by cells of the immune system to help fight infection. In some patients, an exaggerated immune system response, which characteristically occurs in the lungs, can flood the infected area with white blood cells, resulting in severe inflammation, tissue damage and often death. Reduction of the inflammatory state in such patients could therefore improve their clinical outcomes.

Associate Professor Ivan Marazzi of the Microbiology Department at the Icahn School of Medicine at Mount Sinai who led the study said: “So far, in pre-clinical models of COVID-19, there are no therapies – either antiviral, antibody, or plasma – shown to reduce SARS-CoV-2 inflammation when administered after more than one day post-infection. This is a huge problem because people who have moderate or severe COVID-19 often do not present to

hospitals until many days after infection. We took a different approach, and sought to find a potential therapy that can be used during later stages of the disease. We found that topoisomerase 1 (TOPO1) inhibitors given can limit the “hyper-inflammation” in the lungs of infected animals even days after the infection”.

The current study, which also has contributions from partners in Hong Kong, the United Kingdom, and other global sites, expands on that earlier work by the Mount Sinai team. In a 2016 research paper published in the journal *Science*, Dr Marazzi’s team found that inhibiting the activation of inflammatory genes by TOPO1 inhibitors could help prevent animal deaths from viral and bacterial infections, and suggested this could be a potent strategy against future pandemics.

Dr Jessica Sook Yuin Ho, a Singaporean postdoctoral researcher at the Icahn School of Medicine and lead author of the *Cell* paper, explained: “The fact is, a multitude of inflammatory genes and signaling pathways are dysregulated during a SARS-CoV-2 infection. We demonstrated that TOPO1 inhibitors broadly dampen inflammatory gene expression in laboratory models of COVID-19, regardless of specific gene or activation pathway. It is possible that other anti-inflammatory agents are less effective in the late stages against COVID-19 because they target single inflammatory mediators or specific gene expression programs.”

Dr Jeyasekharan added: “Repurposing of existing drugs represents a valuable global strategy for treating COVID-19. However, only a few that show pre-clinical promise have gone on to be efficacious in patients. Topotecan is an attractive candidate given that it is safe and inexpensive with generic formulations existing throughout the world. Clinical trials such as the one we have set up with NMRC funding are a critical step in the process of assessing the potential of drugs for such use, with the possibility that they would eventually be proven helpful for use by patients in need across the world.”

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Chinese Glossary

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## **About National University Cancer Institute, Singapore**

The National University Cancer Institute, Singapore (NCIS) offers a broad spectrum of cancer care and management covering both paediatric and adult cancers, with expertise in prevention, screening, diagnosis, treatment, rehabilitation and palliative care. The Institute's strength lies in the multi-disciplinary approach taken to develop a comprehensive and personalised plan for each cancer patient and his or her family. Our award-winning clinician-scientists and clinician-investigators conduct translational research and clinical trials, providing patients with access to evidence-based cancer diagnostics, technology and therapies. For more information about NCIS, please visit [www.ncis.com.sg](http://www.ncis.com.sg).