



A biomarker assay to risk-stratify patients with symptoms of respiratory tract infection

Shahid Husain^{1,2,3}, Andrew T. Sage^{2,3}, Lorenzo del Sorbo^{2,3,4}, Marcelo Cypel^{2,3,5,6}, Tereza Martinu^{2,3,5,7}, Stephen C. Juvet ^(a)^{2,3,5,7}, Andrea Mariscal^{2,3}, Julie Wright⁸, Bonnie T. Chao², Alaa A. Shamandy ^(b)^{9,10}, S. Hossein Mousavi², Jin Ma¹¹, Bo Wang^{9,10,12,13}, Jerome Valero^{2,3}, Mingyao Liu^{2,3,5}, Megan Landes^{14,15}, Sharaniyaa Balachandran^{2,3}, Kimberley Hudson^{2,3}, Michelle Ngai⁸, Marialessia Capuano¹⁶, Maria Gelardi¹⁶, Enrico Lupia¹⁶, Daniel R. Marinowic¹⁷, Frederico O. Friedrich¹⁷, Carine R.R. Schmitz¹⁸, Leticya S.M. dos Santos¹⁹, Florencia M. Barbe-Tuana¹⁹, Marcus H. Jones¹⁷, Kevin C. Kain⁸, Tony Mazzulli²⁰, Sam Sabbah^{14,21} and Shaf Keshavjee ^(b)^{2,3,5,6}

¹Division of Infectious Diseases, Toronto General Hospital, University Health Network, University of Toronto, Toronto, ON, Canada. ²Toronto Lung Transplant Program and Latner Thoracic Research Laboratories, Toronto General Hospital Research Institute, University Health Network, University of Toronto, Toronto, ON, Canada. ³Ajmera Transplant Centre, University Health Network, University of Toronto, Toronto, ON, Canada. ⁴Interdepartmental Division of Critical Care Medicine, Medical and Surgical Intensive Care Unit, University Health Network, University of Toronto, Toronto, ON, Canada. ⁵Institute of Medical Science, University of Toronto, Toronto, ON, Canada. ⁶Division of Thoracic Surgery, Department of Surgery, University of Toronto, Toronto, ON, Canada. ⁷Division of Respirology, Department of Medicine, University of Toronto, Toronto, ON, Canada. ⁸Tropical Disease Unit, Department of Medicine, University of Toronto, Sandra Rotman Centre for Global Health, University Health Network, Toronto General Hospital, Toronto, ON, Canada. ⁹Department of Computer Science, University of Toronto, Toronto, ON, Canada. ¹⁰Peter Munk Cardiac Centre, University Health Network, Toronto, ON, Canada. ¹¹Biostatistics Research Unit, University Health Network, Toronto, ON, Canada. ¹²Department of Laboratory Medicine and Pathobiology, University of Toronto, Toronto, ON, Canada. ¹³Vector Institute, Toronto, ON, Canada. ¹⁴Department of Emergency Medicine, University Health Network, Toronto, ON, Canada. ¹⁵Division of Emergency Medicine, Department of Family and Community Medicine, University of Toronto, Toronto, ON, Canada. ¹⁶Division of Emergency Medicine and High Dependency Unit, Cittá della Salute e della Scienza di Torino Hospital-Molinette Site, Department of Medical Sciences, University of Turin, Turin, Italy. ¹⁷School of Medicine, Pontifical Catholic University of Rio Grande do Sul, Porto Alegre, Brazil. ¹⁸Biochemistry, Federal University of Rio Grande do Sul, Porto Alegre, Brazil. ¹⁹School of Health, Sciences and Life, Pontifical Catholic University of Rio Grande do Sul, Porto Alegre, Brazil. ²⁰Department of Microbiology, Mount Sinai Hospital, Toronto, ON, Canada. ²¹Division of Emergency Medicine, Department of Medicine, University of Toronto, Toronto, ON, Canada.

Corresponding author: Shaf Keshavjee (shaf.keshavjee@uhn.ca)



https://doi.org/10.1183/ 13993003.01808-2022

Received: 8 March 2022 Accepted: 25 July 2022



Results RALI-Dx biomarkers were significantly elevated in patients who required hospitalisation across all three sites. A machine learning algorithm that was applied to predict hospitalisation using RALI-Dx biomarkers had a mean±sD area under the receiver operating characteristic curve of 76±6% (Canada), 84±4% (Italy) and 86±3% (Brazil). Model performance was 82±3% for COVID-19 patients and 87±7% for patients with a confirmed pneumonia diagnosis.

Conclusions The rapid diagnostic biomarker panel accurately identified the need for inpatient care in patients presenting with respiratory symptoms, including COVID-19. The RALI-Dx test is broadly and easily applicable across many jurisdictions, and represents an important diagnostic adjunct to advance ED decision-making protocols.