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PRESENTATION TITLE: Molecular Phenomics Approaches to Understanding the Natural History of COVID-19 and Post-Acute COVID-19 Syndrome

ABSTRACT: The COVID-19 pandemic has posed a unique set of intertwined medical and economic problems that have impacted on the lives of hundreds of millions of people and will continue to do so for many years. SARS COV-2 also continues to evolve with the regular emergence of new sub-variants with different biological and infective properties. As with other β-coronaviruses, SARS COV-2 may cause life threatening respiratory disease, but notably this is accompanied by major multi-organ effects that cause a range of systemic pathologies with a variety of emergent sub-phenotypes. The systemic effects are not directly coupled to the respiratory effects as much as they are to the immunological effects of the disease. Long-term disease persistence, Long-COVID, or post-acute COVID-19 Syndrome (PACS) is common, and now affects millions of people worldwide.

Phenomics is the systematic study of the continuum of gene-environment interactions throughout life and the measurement of the emergent physical and chemical properties that result from these interactions and define individual and population phenotypes in health and disease. In *molecular phenomics* we are concerned with the chemical and biochemical signatures (metabolites, proteins, transcripts etc.) of cells and biofluids and how these change in characteristic ways during the onset, development, and recovery from disease. We and others have shown that molecular phenomic approaches reveal much of the complexity of the multi-organ impacts and the systemic biochemical perturbations caused by COVID-19 and provide new quantitative metrics for assessing the functional recovery and systemic long-term risks from the disease. Many of the effects of COVID-19 mimic multi-organ drug toxicity with a multitude of embedded pathway perturbations. The use of standardized exploratory and targeted metabolic phenotyping linked to immunology has proved to be a powerful approach for exploring the journey from the “normal” population physiological state through the acute phase of the disease and into the “Long COVID” and “recovery” states from the disease. In particular, the immuno-metabolic drivers of Long COVID are still poorly understood and require new diagnostic, prognostic and predictive tool development. There is also much debate on the possible impacts of COVID-19 on children and potential lifetime impacts of early exposures and these too can be considered from a phenomic perspective, and our work reveals that the biochemistry of COVID-19 in children is like that in adults even in the absence of severe lung symptoms.

In this lecture I will illustrate the integrative use of multiple phenomic technologies for studying the COVID-19 patient journey using collections of samples from multiple populations around the world and demonstrate

a translational strategy for population level monitoring and assessment of PACS and functional biochemical recovery from the disease.

BIOGRAPHY: Professor Nicholson obtained his PhD from St Thomas's Hospital Medical School, King's College, University of London in 1980. After a series of academic appointments in Pharmacology and Chemistry at Birkbeck and University College London, he made full Professor of Biological Chemistry in 1992. He was subsequently appointed as Professor and Head of Biological Chemistry at Imperial College London in 1998 and Head the Department of Surgery and Cancer from 2009 to 2018, Director for the Centre for Gut and Digestive Health, and Director of the MRC-NIHR National Phenome Centre (2012-2018). Since 2018 he has been Emeritus Professor at Imperial College, London. He became the Pro-Vice Chancellor for Health Sciences at Murdoch University and Director of the Australian National Phenome Centre in Perth, Western Australia in 2019. One of the pioneers of biological NMR spectroscopy, metabolic phenotyping and systems medicine, his major research focus is on the development of diagnostic and prognostic molecular phenotyping analytical technologies as applied to personalised healthcare, metabolic disease, and population phenotyping. For the last 3 years he has been leading an international group working on the metabolic sequelae of and long-term complications of COVID-19. He is a "Highly-Cited" Researcher in Pharmacology and Toxicology and Cross-Field Science between 2013 and 2022 (Clarivate H index = 137, Google H = 161, 110K citations) and has received various research prizes including: The Royal Society of Chemistry (RSC) Silver (1992) and Gold (1997) Medals for Analytical Science and Analytical Chemistry respectively; The UK Chromatographic Society Jubilee Silver Medal (1994); Pfizer International Prize for Chemical and Medicinal Technology (2002); RSC medal for Chemical Biology (2003); RSC Interdisciplinary Prize (2008); Pfizer Global Research Prize for Chemistry (2006) and the Semmelweis-Budapest International Prize for Biomedicine (2010). He holds multiple visiting, and Honorary Professorships including Fudan University, Shanghai, Nanyang Technological University, Singapore, The Mayo Clinic, University of New South Wales, Shanghai Jiao Tong University, Zhejiang University, University of Western Australia, Chinese Academy of Sciences, Wuhan, and Dalian. He was elected, Fellow of The UK Academy of Medical Sciences (2010); Honorary Lifetime Fellow of the International Metabolomics Society (2012); Honorary Lifetime Member of the US Society of Toxicology (2013); Albert Einstein Honorary Professor of the Chinese Academy of Sciences (2014); Elected Honorary Fellow of the Royal College of Physicians (London) (2018); Honorary Doctor of Science, *Honoris Causa* (Hong Kong Baptist University), in 2020.