File No. CI 20-01-29284

THE QUEEN'S BENCH
Winnipeg Centre

APPLICATION UNDER: *The Constitutional Questions Act*, C.C.S.M., c. 180

AND UNDER: The Court of Queen's Bench Rules, M.R. 553-88

IN THE MATTER OF: *The Public Health Act*, C.C.S.M. c. P210

B E T W E E N:

GATEWAY BIBLE BAPTIST CHURCH, PEMBINA VALLEY BAPTIST CHURCH, REDEEMING GRACE BIBLE CHURCH, THOMAS REMPEL, GRACE COVENANT CHURCH, SLAVIC BAPTIST CHURCH, CHRISTIAN CHURCH OF MORDEN, BIBLE BAPTIST CHURCH, TOBIAS TISSEN, ROSS MACKAY,

Applicants,

- and -

HER MAJESTY THE QUEEN IN RIGHT OF THE PROVINCE OF MANITOBA and DR. BRENT ROUSSIN in his capacity as CHIEF PUBLIC HEALTH OFFICER OF MANITOBA, and DR. JAZZ ATWAL in his capacity as ACTING DEPUTY CHIEF OFFICER OF HEALTH OF MANITOBA

Respondents.

AFFIDAVIT OF JASON KINDRACHUK
AFFIRMED: MARCH 2, 2021

DEPARTMENT OF JUSTICE
Constitutional Law Branch
1205 - 405 Broadway
Winnipeg, Manitoba
R3C 3L6

Per: Heather Leonoff

Telephone No. (204) 945-0679
Facsimile No. (204) 945-0053

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HER MAJESTY THE QUEEN IN RIGHT OF THE PROVINCE OF MANITOBA and DR. BRENT ROUSSIN in his capacity as CHIEF PUBLIC HEALTH OFFICER OF MANITOBA, and DR. JAZZ ATWAL in his capacity as ACTING DEPUTY CHIEF OFFICER OF HEALTH OF MANITOBA

Respondents.

AFFIDAVIT OF JASON KINDRACHUK

I, JASON KINDRACHUK, of the City of Saskatoon, in the Province of Saskatchewan, **AFFIRM AS FOLLOWS:**

1. I have personal knowledge of the facts and matters hereinafter deposed to by me, except where same are stated to be based upon information and belief, and those I believe to be true.

2. I have a PhD in biochemistry, obtained in 2007, from the Univeristy of Saskatchewan. I am currently an Assistant Professor and Canada Research Chair in emerging viruses in the Department of Medical Microbiology & Infectious Diseases, University of Manitoba. My field of expertise is the investigation of emerging viruses, the infections they cause and their impact on global health. I am presently seconded as part of a 12-month research partnership agreement at the Vaccine and Infectious Disease Organization, University of Saskatchewan, Canada, where I am helping lead and facilitate national COVID-19 research response efforts. I have been engaged in research regarding coronavirus since 2013 following the emergence of Middle East respiratory syndrome coronavirus. My curriculum vitae is attached as Exhibit A.

3. At the request of Manitoba Justice, I have provided a report detailing my understanding of some of the important issues regarding the virus SARS-CoV- 2 and the disease it causes, namely COVID-19. I acknowledge that in preparing this report and providing expert evidence, legal counsel for the Government explained that my role is to assist the court to determine the matters in issue. I further acknowledge that it is my duty to provide evidence that is fair, objective and non-partisan and to opine only on matters that are within my area of expertise. This duty prevails over any obligation that I may owe to any party on whose behalf I am engaged. Attached as Exhibit B is a copy of my report.

4. I make this affidavit bona fide.

AFFIRMED before me in the City of Winnipeg, in the Province of Manitoba, through use of video conferencing as permitted by order under *The Emergency Measures Act*, this 2 day of March, 2021.

Heather Leyl
A Barrister-at-law entitled to practice in and for the Province of Manitoba

JASON KINDRACHUK

This is Exhibit " A " referred to
in the Affidavit of Jason Kindrachuk
Affirmed before me this second
day of March A.D. 2021

A Barrister-at-Law entitled to practice
in and for the Province of Manitoba

Jason Kindrachuk, PhD

Laboratory of Emerging and Re-emerging Viruses
Department of Medical Microbiology & Infectious Diseases
University of Manitoba
Winnipeg, MB, Canada
Tel: (204) 789-3807
Email: Jason.Kindrachuk@umanitoba.ca

EDUCATION

2002-2007 **Ph.D., Department of Biochemistry**
University of Saskatchewan, Saskatoon, SK, Canada
Supervisor: Dr. Scott Napper
Thesis Title: *Host and Pathogen Sensory Systems as Targets for Therapeutic Intervention*

1996-2001 **B.Sc. (Honors), Department of Biochemistry**
University of Saskatchewan, Saskatoon, SK, Canada

PROFESSIONAL EXPERIENCE

2017-present **Assistant Professor**
Canada Research Chair
Laboratory of Emerging and Re-Emerging Viruses
Department of Medical Microbiology and Infectious Diseases
University of Manitoba
Winnipeg, MB

Associate Professor
Department of Biochemistry
College of Medicine and Allied Health Sciences
University of Sierra Leone
Freetown, Sierra Leone

2014-2016 **Staff Scientist**
Critical Care Medicine Department
Clinical Center
National Institutes of Health, Bethesda, MD, USA

Sept 2014 **Scientific Lead – Field Diagnostics**
Ebola Virus Disease Outbreak Response Efforts
Centers for Disease Control/Department of Defense Joint Operations
Monrovia, Liberia

2013-2014 **Principal Research Scientist**
Battelle Memorial Institute
Integrated Research Facility
National Institutes of Allergy and Infectious Diseases

National Institutes of Health, Frederick, MD, USA

2009-2013 **Visiting Fellow**
Emerging Viral Pathogens Section
National Institutes of Allergy and Infectious Diseases
National Institutes of Health, Bethesda, MD, USA

2007-2009 **Postdoctoral Fellow**
Centre for Microbial Diseases and Immunity Research
Department of Microbiology and Immunology
University of British Columbia, Vancouver, BC, Canada

SCIENTIFIC AFFILIATIONS & COMMITTEE ACTIVITIES

Affiliations

2020-present **Visiting Scientist** – Vaccine and Infectious Disease Organization-International Vaccine Centre

2020-present **Science Contributor** – Forbes Media, LLC

2020-present **Volunteer, Regional Leader** – COVID-19 Resources Canada

2020-present **Volunteer, Infection Control Lead** – Heart to Heart International COVID-19 Preparedness and Response Efforts

2019-present **Visiting Researcher** – The International Center for Medical Research in Franceville, Gabon (CIRMF)

2018-present **Visiting Scientist** – Public Health Agency of Canada, Special Pathogens Section

2018-present **Visiting Scientist** – Canadian Food Inspection Agency, Special Pathogens Unit

2017-present **Investigator** – Children's Health Research Institute of Manitoba

Committees and Review Panels

2020 **Panel Member** – CIHR Institute of Infection and Immunity Consultation on Variant Strains of SARS-CoV-2

2020 **Member** – World Health Organization COVID-19 Solidarity Serology Study Group

2020 **Member** – World Health Organization Ad Hoc Committee on COVID-19 Animal Models

2020 **Session chair** – Tuberculosis and other Infectious Diseases, University of Nairobi HIV/AIDS Collaborative Conference

2019-present **Member** – Community for Emerging and Zoonotic Diseases, Canadian Network for Public Health Intelligence (CNPHI)

2019 **Member** – CIHR Strategic Planning Meeting

2019 **Review Panel Member** – New Frontiers in Research Fund Exploration Grant

2018-present **Director** – Canadian Society for Virology Executive Council

2018-present **Associate Member** – CIHR College of Reviewers

2018 **Co-Chair** – Emerging Viral Diseases and Global Preparedness Symposium

2018 **Organizing Committee Member** – Canada's Role in Global Public Health Conference

2017-present **Review Panel** – American Association for the Advancement of Science (AAAS) Research Competitiveness Program

2017-present **Reviewer** – Manitoba Poster Competition of the Canadian Student Health Research Forum

2017-present **Review Panel** – Research Manitoba PhD Scholarship Competition

2016 **External Reviewer** – National Science Centre, Poland (Narodowe Centrum Nauki – NCN) PRELUDIUM Funding scheme

2014 **Reviewer** – Alberta Livestock and Meat Agency (ALMA)

2012-2013 **Scientific Advisor** – World Health Organization Advisory Committee on Variola Virus Research (ACVVR): Provided updates and participated in critical discussions regarding ongoing variola virus research as a member of the US delegation

AWARDS & HONOURS

2018 Department of Medical Microbiology Faculty Educator Award

2018 National Institutes of Allergy and Infectious Diseases Merit Award

2017 Tier 2 Canada Research Chair Award

2015 National Institutes of Health Director's Award

2015 National Institutes of Health Clinical Center Summer Internship Program Best Mentor Award

2013 University of Maryland Integrated Life Sciences Honors College Mentor Award

2010-2013 National Institutes of Health Visiting Fellow Intramural Research Training Award

SCIENTIFIC JOURNAL ADVISORY BOARDS

2019-present **Guest Editor** – Viruses (Pathogenesis of Emerging Viruses Special Issue)

2019-present **Associate Editor** – Viruses

2019-present **Associate Editor** – Frontiers in Microbiology

2016-present **Associate Editor** – BMC Infectious Diseases

2014-present **Associated Review Editor** – Frontiers in Veterinary Science

PROFESSIONAL ASSOCIATIONS & MEMBERSHIPS

2019-present **Member** – Infectious Diseases Society of America

2017-present **Member** – Canadian Society for Virology

2017-present **Member** – Canadian Society of Microbiologists

2014-present **Member** – American Society for Microbiology

2014-present **Member** – American Society for Virology

PUBLICATIONS

1. Escandón, K., **Kindrachuk, J.**, Lee, R.S. and Rasmussen, A.L. (2020) Face masks, SARS-CoV-2 inoculum, COVID-19 severity, and immunity: is there any evidence to support a link? *Ann Intern Med*. [In Submission]
2. Webb, A.L., Schindell, B., Soule, G., Siddik, A.B., Abrenica, B., Memon, H., Su, R., Safronetz, D. and **Kindrachuk, J.** (2020) Sertoli cells remain viable and inhibit viral replication during Ebola virus infection. *Sci Rep*. [In Submission]
3. Francis, M.E., Richardson, B., McNeil, M., Rioux, M., Foley, M.K., Ge, A., Pechous, R.D., **Kindrachuk, J.**, Cameron, C.M., Richardson, C., Lew, J., Cameron, M.J., Gerdts, V., Falzarano, D. and Kelvin, A.A. Male sex and age biases viral burden, viral shedding, and type 1 and 2 interferon responses during SARS-CoV-2 infection in ferrets. *Sci Trans Med.* [In Submission]
4. Escandón, K., Rasmussen, A.L., Bogoch, I.I., Murray, E.J., Escandón, K. and **Kindrachuk, J.** (2020) COVID-19 and false dichotomies — a nuanced review of the evidence regarding public health, COVID-19 symptomatology, SARS-CoV-2 transmission, masks, and reinfection. *BMC Infect Dis.* [In Submission]
5. Forbes, K.M., Anzala, O., Carlson, C.J., Kelvin, A.A., Kuppalli, K., Leroy, E.M., Maganga, G.D., Masika, M.M., Mombo, I.M., Mwaengo, D.M., Niama, R.F., Nziza, J., Ogola, J., Pickering, B.S., Rasmussen, A.L., Sironen, T., Vapalahti, O., Webala, P.W., and **Kindrachuk, J.** (2020) Towards a coordinated strategy for intercepting human disease emergence in Africa. *Lancet Microbe*. [Accepted]
6. Schindell, B.*, Allardice, M.*, Lockman, S. and **Kindrachuk, J**. (2020) Drug Identification and Repurposing During a Novel Viral Pandemic (Invited Perspective). *ACS Infect Dis*. [Accepted]
7. Nickol, M.E., Lyle, S.M., Dennehy, B. and **Kindrachuk, J.** (2020) Dysregulated Host Responses Underlie 2009 Pandemic Influenza-Methicillin Resistant Staphylococcus aureus Coinfection Pathogenesis at the Alveolar-Capillary Barrier. *Cells*. 9: 2472
8. Connelly, M., Swerczek, J., **Kindrachuk, J.**, Vannella, K., Ramos-Benitez, M., Sun, J., Dougherty, E., Danner, R., Moore, I., Herbert, R. and Chertow, D.S. (2020) A Model of Prolonged Human Intensive Care and Recovery in Rhesus Macaques. *Sci Rep*. [Accepted]
9. Pascoe, C.D., Jha, A., Ryu, M.H., Ragheb, M., Basu, S., Stelmack, G., **Kindrachuk, J.**, Gaurveau, G.M., O'Byrne, P.M., Ravandi, A., Carlsten, C. and Halayko, A.J. (2020) Oxidized phosphatidylcholine are produced in response to allergen inhalation and promote inflammation. *Eur Respir J.* 3: 2000839
10. Cevik, M., Kuppalli, K., **Kindrachuk, J.** and Peris, M. (2020) Transmission and risk factors for severe acute respiratory syndrome coronavirus 2. *BMJ*. 371: m3862
11. Rashid, M, Zahedi-Amiri, A., Glover, K.K.M., Ang, G., Nickol, M.E., **Kindrachuk, J.**, Wilkins, J.A. and Coombs, K.M. (2020) Zika virus dysregulates human sertoli cell proteins involved in spermatogenesis with little effect on blood-testes tight junctions. *PLoS Negl Trop Dis*. 14: e0008335
12. Vanella, K.M., Stein, S., Connelly, M., Swerczek, J., Amaro-Carambot, E., Coyle, E.M., Babyak, A., Winkler, C.W., Saturday, G., Gai, N.D., Hammoud, D.A., **Kindrachuk, J.**, Peterson, K.E., Brenchley, J.M., Whitehead, S.S., Khurana, S., Herbert, R. and Chertow,

D.S. (2020) Nonhuman primates exposed to Zika virus *in utero* are not protected against viral re-challenge over one year postpartum. *Sci Trans Med*. 12: eaaz4997

13. Khurana, S., Ravichandran, S., Hahn, M., Coyle, E.M., Stonier, S.W., Zak, S.E., **Kindrachuk, J.**, Davey Jr., R.T., Dye, J.M. and Chertow, D.S. (2020) Longitudinal human antibody repertoire against complete viral proteome following acute Ebola virus infection reveals protective sites for vaccine design. *Cell Host Microbe*. 27: 262-276.e4
14. Ralph, R., Lew, J., Zeng, T., Francis, M., Bei, X., Roux, M., Toloue, M. Rubino, S., Daw, N., Al-Ahdal, M.N., Kelvin, D.J., Richardson, C., **Kindrachuk, J.**, Falzarano, D., and Kelvin, A.A. (2020) 2019-nCoV (Wuhan virus), A Novel Coronavirus, linked to Chinese Pneumonia Cases: Human-to-Human Transmission, Travel-Related Cases and Vaccine Readiness. *J Infect Dev Ctries*. 14: 3-17
15. Willman, M., Kobasa, D. and **Kindrachuk J¶**. (2019) A comparative analysis of factors influencing two outbreaks of Middle Eastern respiratory syndrome (MERS) in Saudi Arabia and South Korea. *Viruses*. 11: 1119.
16. Nickol, M.E., Ciric, J., Falcinelli, S.D., Chertow, D.S. and **Kindrachuk, J¶.** (2019) Characterization of Host and Bacterial Contributions to Lung Barrier Dysfunction Following 2009 Pandemic Influenza-Methicillin Resistant Staphylococcus aureus Co-infection. *Viruses*. 11: 116.
17. Schindell, B.G., Webb, A.L. and **Kindrachuk, J¶.** (2019) Persistence and Sexual Transmission of Filoviruses. *Viruses*. 10: 683.
**article highlighted in NBC News article "Ebola is back in the Congo — and America's Africa policies aren't helping contain its spread"*
18. Nickol, M.E. and **Kindrachuk, J¶.** (2019) A Year of Terror and a Century of Reflection: Perspectives on the Great Influenza Pandemic of 1918-1919. *BMC Inf Dis*. 19: 117.
19. Kashem, M.A., Li, H., Toledo, N., Omange, R.W., Liang, B., Liu, L.R., Yuan, X., **Kindrachuk, J.**, Plummer, F.A. and Luo, M. (2019) Toll-like Interleukin 1 Receptor Regulator is an important modulator of inflammation responsive genes. *Front Immunol*. 10: 272.
20. Dyall, J., Gross, R., **Kindrachuk, J.**, Johnson, R.F., Olinger, G.G., Hensley, L.E., Frieman, M.B., and Jahrling, P.B. (2017) Middle East respiratory syndrome and severe acute respiratory syndrome: current therapeutic options and potential targets for novel therapies and vaccines. *Drugs*. 77: 1935-1966.
21. **Kindrachuk, J¶.** (2017) Invited Editorial: Selective Inhibition of Host Cell Signaling for Rotavirus Antivirals: PI3K/Akt/mTOR-Mediated Rotavirus Pathogenesis. *Virulence*. 9: 5-8.
22. Barnes, K.G.*, **Kindrachuk, J.***, Lin, A.E.*, Wohl, S., Qu, J., Tostenson, S.D., Dorman, W.R., Busby, M., Siddle, K.J., Matranga, C.B., Davey, R.T., Sabeti, P.C, and Chertow, D.S. (2017) Evidence for replication and high concentration of ebola virus in semen of a patient recovering from severe disease. *Clin Infect Dis.* 65: 1400-1403.
*Authors contributed equally to this work
23. Kash, J.C.*, Walters, K.A.*, **Kindrachuk, J.**, Baxter, D., Scherler, K., Janosko, K.B., Adams, R.D., Herbert, A.S., James, R.M., Stonier, S.W., Memoli, M.J., Dye, J.M., Davey, R.T., Chertow, D.S., and Taubenberger, J.K. (2017) Peripheral blood transcriptional analysis of a severe ebola virus disease patient reveals dramatic transitions during critical illness and recovery. *Sci Transl Med.* 9: eaai9321.
*Authors contributed equally to this work

24. Falcinelli, S.D., Chertow, D.S., and **Kindrachuk, J¶.** (2016) Integration of Global Analyses of Host Molecular Responses with Clinical Data to Evaluate Pathogenesis and Advance Therapies for Emerging and Re-Emerging Viral Infections. *ACS Infect Dis.* 2: 787-799.

25. Davis, S.A.*, Chertow, D.S.*, **Kindrachuk, J.**, Schwartzman, L.M., Suzich, J., Alsaaty, S., Logun, C., Shelhamer, J.H., and Taubenberger, J.K. (2016) 1918 Influenza Receptor Binding Domain Variants Bind and Replicate in Primary Human Airway Cells Regardless of Receptor Specificity. *Virology*. 493: 283-246.
*Authors contributed equally to this work

26. Chertow, D.S., **Kindrachuk, J.**, Sheng, Z.M., Pujanauski, L., Cooper, K., Nogee, D., St. Claire, M., Solomon, J., Perry, D., Sayre, P., Janosko, K.B., Lackemeyer, M.G., Bohannon, J.K., Hensley, L.E., Kash, J.C., Jahrling, P.B. and Taubenberger, J.K. (2016) An experimental model of lung injury in rhesus macaques following influenza and bacterial co-infection. *Antiviral Res.* 129: 120-9.

27. Walters, K.A., D'Agnillo, F., Sheng, Z.M., **Kindrachuk, J.**, Schwartzman, L.M., Keustner, R.E., Chertow, D.S., Golding, B., Taubenberger, J.K. and Kash, J.C. (2016) 1918 pandemic influenza virus and Streptococcus pneumoniae coinfection results in activation of coagulation and widespread pulmonary microvascular thrombosis in mice and humans. *J Pathol*. 238: 85-97.

28. Falcinelli, S., Gowen, B., Trost, B., Napper, S., Kusalik, A., Safronetz, D., Prescott, J., Johnson, R.F., Wahl-Jensen, V. Jahrling, P.B. and **Kindrachuk, J¶**. (2015) Characterization of the functional host response to Pichinde virus infection in the Syrian golden hamster. *Mol Cell Proteomics*. 14: 646-57.

29. **Kindrachuk, J.¶**, Ork, B., Hart, B., Holbrook, M., Frieman, M., Johnson, R.F., Dyall, J., Olinger, G.G., Hensley, L.E., Jahrling, P.B. (2015) Temporal kinome analysis demonstrates that MERS-CoV selectively modulates ERK/MAPK and PI3K/AKT/mTOR signaling. *Antimicrob Agents Chemother*. 59: 1088-99.

30. Kuhn, J.H., Andersen, K.G., Bào, Y., Bavari, S., Becker, S., Bennett, R.S., Bergman, N.H., Blinkova, O., Bradfute, S., Brister, J.R., Bukreyev, A., Chandran, K., Chepurnov, A.A., Davey, R.A., Dietzgen, R.G., Doggett, N.A., Dolnik, O., Dye, J.M., Enterlein, S., Fenimore, P.W., Formenty, P., Freiberg, A.N., Garry, R.F., Garza, N.L., Gire, S.K., Gonzalez, J.P., Griffiths, A., Happi, C.T., Hensley, L.E., Herbert, A.S., Hevey, M.C., Hoenen, T., Honko, A.N., Ignatyev, G.M., Jahrling, P.B., Johnson, J.C., Johnson, K.M., **Kindrachuk, J.**, et al. (2014) Filovirus RefSeq entries: evaluation and selection of filovirus type variants, type sequences, and names. *Viruses*. 6: 3663-82.

31. **Kindrachuk, J.*¶**, Wahl-Jensen, V.*, Safronetz, D., Arsenault, R., Hoenen, T., Traynor, D., Postnikova, E., Napper, S., Blaney, J.E., and Jahrling, P.B. (2014) Temporal systems kinomics demonstrates that Ebola virus infection selectively modulates transforming growth factor β signaling in hepatocytes. *J Virol.* 88: 9877-92.
*Authors contributed equally

32. Dyall, J., Coleman, C., Hart, B., Venkataraman, T., Holbrook, M., **Kindrachuk, J.**, Johnson, R.F., Olinger, G.G., Jahrling, P.B., Laidlaw, M., Johnson, L., Glass, P., Hensley, L.E., and Frieman, M. (2014) Discovery of FDA-approved inhibitors of Middle East respiratory syndrome coronavirus infection. *Antimicrob Agents Chemother.* 58: 4885-93.

33. Jahrling, P.B., Lauren, K., St. Claire, M., Johnson, R., Bollinger, L., Lackemeyer, M., Hensley, L., **Kindrachuk, J.**, and Kuhn, J.H. (2014) Medical management and imaging of animals infected with risk group 4 pathogens at the NIAID Integrated Research Facility at

Fort Detrick, Maryland. *Pathog Dis.* 71: 213-9.

34. **Kindrachuk, J.¶**, Falcinelli, S., Wada, J., Kuhn, J.H., Hensley, L.E., and Jahrling, P.B. (2014) Systems kinomics: a new paradigm for characterizing host responses to high consequence pathogens at the NIH/NIAID Integrated Research Facility at Frederick, MD. *Pathog Dis.* 71: 190-98.

35. Lackemeyer, M.G., de Kok-Mercado, F., Wada, J., **Kindrachuk, J.**, Wahl-Jensen, V., Kuhn, J.H., and Jahrling, P.B. (2014) ABSL-4 aerobiology biosafety and technology at the NIH/NIAID Integrated Research Facility at Fort Detrick. *Viruses*. 6: 137-50.

36. Hart, B.J., Dyall, J., Postnikova, E., Zhou, H., **Kindrachuk, J.**, Johnson, R.F., Olinger, G.G., Jahrling, P.B. and Hensley, L. (2014) Interferon-beta and mycophenolic acid are potent inhibitors of MERS-CoV in cell-based assays. *J Gen Virol.* 95: 571-7.

37. Trost, B., **Kindrachuk, J.,** Maattanen, P., Napper, S., and Kusalik, A. (2013) PIIKA 2: novel tools for the analysis of kinome microarray data. *PLoS ONE*. 8: e80837.

38. Trost, B., **Kindrachuk, J.**, Scruten, E., Griebel, P., Kusalik, A. and Napper, S. (2013) Personalized profiles of cellular kinase activity: the kinotype. *BMC Genomics* 14: 854.

39. **Kindrachuk, J.**, Jenssen, H., Elliott, M., Nijnik, A., Fang, Y., Pistolic, J., Pasupuleti, M., Thorson, L., Ma, S., Easton, D., Bains, M., Arnusch, C.J., Finlay, B., Sahl, H.G., Breukink, E. and Hancock, R.E.W. (2013) Manipulation of innate immunity by a bacterial secreted peptide; the lantibiotic nisin Z is selectively immunomodulatory. *Innate Immun*. 19: 315-27.

40. Achtman, A.H., Pilat, S., Law, C.W., Lynn, D.J., Janot, L., Ma, S., **Kindrachuk, J.**, Finlay, B.B., Brinkman, F.S.L., Smyth, G.K., Hancock, R.E.W., and Schofield, L. (2012) Effective adjunctive therapy by an innate defense regulatory peptide in a preclinical model of severe malaria. *Sci Transl Med.* 4: 135ra64.

41. Steinstraesser, L., Hirsch, T., Schulte, M., Kueckelhaus, M., Jacobsen, F., Mersch, E., Al-Benna, S., Stricker, I., Afacan, N., Jenssen, H., Hancock, R.E. and **Kindrachuk, J.** (2012) Innate defense regulator peptide 1018 in wound healing and wound infection. *PLoS One.* 7: e39373.

42. **Kindrachuk, J¶.**, Arsenault, R., Kusalik, T., Kindrachuk, K.N., Trost, B., Napper, S., Jahrling, P.B. and Blaney, J.E. (2012) Systems kinomics demonstrates Congo Basin Monkeypox virus infection selectively modulates host cell signaling responses as compared to West African Monkeypox virus. *Mol Cell Proteomics.*11: M.111.015701.

43. Gao, G.*, Cheng, J.T.*, **Kindrachuk, J.**, Hancock, R.E.W., Straus, S.K. and Kizhakkedathu, J. (2012) Biomembrane interactions reveal the mechanism of action of surface-immobilized host defense IDR-1010 peptide. *Chem Bio.* 19: 199-209.
*Authors contributed equally to this work

44. Gao, G., Yu, K., **Kindrachuk, J.**, Brooks, D.E., Hancock, R.E.W., and Kizhakkedathu, J.N. (2011) Antibacterial surfaces based on polymer brushes: Investigation on the influence of brush properties on antimicrobial peptide immobilization and antimicrobial activity. *Biomacromolecules*. 32: 3899-909.

45. Wahl-Jensen, V.*, Kurz, S.*, Buehler, L.K., **Kindrachuk, J.**, DeFilippis, V., da Silva, J., Fruh, K., Kuhn, J.H., Burton, D.R. and Feldmann, H. (2011) Ebola virion binding to and entry into human macrophages profoundly effects cellular gene expression prior to expression of virus proteins. *PLoS Negl Trop Dis.*5: e1359.
*Authors contributed equally to this work

46. Garlapati, S.*, Eng, N.F.*, Kiros, T., **Kindrachuk, J.**, Mutwiri, G.K., Hancock, R.E., Babiuk,

L.A. and Gerdts, V. (2011) Immunization with PCEP microparticles containing pertussis toxoid, CpG ODN and a synthetic innate defense regulator peptide induces protective immunity against pertussis. *Vaccine.* 29: 6540-8.
*Authors contributed equally to this work

47. McAndrew Lynn, M.A., **Kindrachuk, J.**, Jenssen, H., Pante, N., Elliott, M., Napper, S., Hancock, R.E.W., and McMaster, R. (2011) Effect of BMAP-28 antimicrobial peptides on Leishmania major promastigote and amastigote growth: role of leishmanolysin in parasite survival. *PLoS Negl Trop Dis.* 5: e1141.

48. Gao, G.*, Lange, D.*, Hilpert, K., **Kindrachuk, J.**, Zou, Y., Cheng, J.T., Kazemzadeh, M., Yu, K., Wang, R., Straus, S.K., Brooks, D.E., Chew, B.H., Hancock, R.E. and Kizhakkedathu, J.N. (2011) The biocompatibility and biofilm resistance of implant coatings based on hydrophilic polymer brushes conjugated with antimicrobial peptides. *Biomaterials*. 32: 3899-909.
*Authors contributed equally to this work

49. **Kindrachuk, J.**, Scruten, E., Attah-Poku, S., Bell, K., Potter, A., Babiuk, L.A., Griebel, P.J., and Napper, S. (2011) Stability, toxicity and biological activity of host defense peptide BMAP28 and its inversed and retro-inversed isomers. *Biopolymers*. 96: 14-24.

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*Authors contributed equally to this work

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BOOK CHAPTERS

1. Chertow, D.S. and **Kindrachuk, J.** (2019) Respiratory Viruses: Influenza, Measles, SARS, MERS, and Smallpox. In: Highly Infectious Diseases in Critical Care: A Comprehensive Clinical Guide. Springer New York.
2. Falcinelli, S.D., Ciric, J., **Kindrachuk, J.** (2018) Variola Virus: Clinical, Molecular and Bioterrorism Perspectives. In: Defense Against Biological Attacks. Springer New York.

3. Jahrling, P.B., Goff, A.J., Johnston, S.C., **Kindrachuk, J.**, Lin, K.L., Huggins, J.W., Ibrahim, S., Lawler, J.V., Martin, J.W. (2016) Chapter 11: Smallpox and Related Orthopoxviruses. In: Textbooks of Military Medicine: Medical Aspects of Biological Warfare.
4. **Kindrachuk, J.**, Kuhn, J.H. and Jahrling, P.B. (2015) The role of viral protein phosphorylation during filovirus infection. In: Global Virology. Springer New York.
5. **Kindrachuk, J.** and Napper, S. (2013) Sample Preparation and Profiling: Probing the kinome for biomarkers and therapeutic targets: peptide arrays for global phosphorylation-mediated signal transduction. In: Comprehensive Biomarker Discover and Validation for Clinical Application. Royal Society of Chemistry.
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NON-PEER REVIEWED PUBLICATIONS

1. Why Early Wins Over Covid-19 Do Not Mean Victory: Canada's Cautionary Tale. *Forbes.* https://www.forbes.com/sites/coronavirusfrontlines/2020/11/04/why-early-wins-over-covid-19-do-not-mean-victory-canadas-cautionary-tale/?sh=740b94722041
2. The Realities of Biomedical Research During a Pandemic. *Forbes.* https://www.forbes.com/sites/coronavirusfrontlines/2020/09/17/a-virologist-explains-the-realities-of-biomedical-research-during-a-pandemic/#62d6a66111a2
3. A Virologist Explains Why It Is Unlikely COVID-19 Escaped from A Lab. *Forbes*. https://www.forbes.com/sites/coronavirusfrontlines/2020/04/17/a-virologist-explains-why-it-is-unlikely-covid-19-escaped-from-a-lab/#58bd5fb63042
4. How The Coronavirus Pandemic Has Impacted International Research Programs: A Personal Perspective. *Forbes.* https://www.forbes.com/sites/coronavirusfrontlines/2020/06/06/how-the-coronavirus-pandemic-has-impacted-international-research-programs-a-personal-perspective/#b10049750bbf
5. Repurposing Drugs Is Key to Fighting the Coronavirus Pandemic, This Virologist Explains. *Forbes*. https://www.forbes.com/sites/coronavirusfrontlines/2020/05/08/repurposing-drugs-is-key-to-fighting-the-coronavirus-pandemic-this-virologist-explains/#5c9efd1217ce
6. No Mercy for the Coronas. *La Liberté*. https://www.lalibertesciencesmagjunior.ca/
7. The Value of Social Media Now. *New York Times*. https://www.nytimes.com/2020/03/27/opinion/letters/iran-sanctions.html
8. How social media is changing research and reactions to coronavirus outbreak. *The Conversation*. http://theconversation.com/how-social-media-is-changing-research-and-reactions-to-coronavirus-outbreak-130748
9. Ebola survivors can pass on the virus: we're trying to understand what role sex plays. *The*

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REPORTS

1. CIHR-PHAC-CADTH – Best Brains Exchange – Transmission Routes for COVID-19: Implications for Public Health. Canadian Institutes of Health Research (CIHR); 2020 October. https://cihr-irsc.gc.ca/e/52238.html
2. Heating, Ventilation and Air Conditioning Systems in Public Spaces. Ottawa: Canadian Agency for Drugs and Technologies in Health (CADTH); 2020 June. (CADTH technology review).
3. Public statement for collaboration on COVID-19 vaccine development. World Health Organization. 13 April 2020. https://www.who.int/news-room/detail/13-04-2020-public-statement-for-collaboration-on-covid-19-vaccine-development
4. WHO Advisory Committee on Variola Virus Research, 15th Meeting. Report of the Fourteenth Meeting, Geneva, Switzerland, 24-24 September 2013. WHO/HSE/PED/CED/2013.2
5. WHO Advisory Committee on Variola Virus Research, 14th Meeting. Report of the Fourteenth Meeting, Geneva, Switzerland, 16-17 October 2012. WHO/HSE/PED/CED/2013.1

FUNDING

1. Tier 2 Canada Research Chair in the molecular pathogenesis of emerging and re-emerging viruses
   Funding Sources:
   2017-2022 Canada Research Chairs Program
   Total Funding – 500,000 (Canadian dollar)
   Principal Investigator
2. Identification of the molecular determinants underlying asymptomatic Ebola virus testicular infections and long-term effects on reproductive health
   Funding Sources:
   2020-2025 Canadian Institutes of Health Research Project Grant
   Total Funding – 950,000 (Canadian dollar)
   Principal Investigator
3. Animal models for SARS-CoV-2: vaccines and immune enhancement
   Funding Sources:
   2020-2022 Canadian Institutes of Health 2019 Novel Coronavirus (COVID-19) Rapid Research Funding
   Total Funding – 999,793 (Canadian dollar)
   Co-Applicant
4. Scalable, Customizable, Digital Health Communication Materials to Help Canada Address the COVID19 Pandemic
   Funding Sources:
   Canadian Institutes of Health COVID-19 Rapid Research - Social Policy and Public Health Responses
   Total Funding – 311,296 (Canadian dollar)

Co-Applicant

5. Broad Spectrum CoV Therapeutic; rhACE2 Immunoadhesin to treat COVID19
   Funding Sources:
   MITACS Accelerate
   Total Funding – 90,000 (Canadian dollar)
   Principal Applicant
6. Prairie Infectious Immunology Network 2020
   Funding Sources:
   2020-2021 Canadian Institutes of Health Research Planning and Dissemination Grant
   Total Funding – 10,000 (Canadian dollar)
   Co-Principal Investigator
7. Characterization of the molecular pathogenesis of severe influenza and influenza-bacterial infections at the alveolar-capillary barrier
   Funding Sources:
   2018-2020 Research Manitoba New Investigator Operating Grant
   Total Funding – 130,000 (Canadian dollar)
   Principal Investigator
8. Investigation of kinase-mediated cell signaling pathway modulation at the vector pathogen-livestock interface in vector-borne livestock diseases
   Funding Sources:
   2018/4 - 2023/3 Natural Sciences and Engineering Research Council of Canada (NSERC) Discovery Grant
   Total Funding - 165,000 (Canadian dollar)
   Principal Investigator
9. Establishment of a high-throughput molecular dynamics facility
   Co-applicant: Denice Bay
   Funding Sources:
   2017/11 - 2022/11 Canada Foundation for Innovation (CFI) John R. Evans Leaders Fund
   Total Funding - 609,191 (Canadian dollar)
   Principal Investigator
10. Deciphering the bat kinome by immunometabolic peptide kinome arrays: critical insights for emerging viral diseases
    Funding Sources:
    2018/7 - 2019/6 University of Manitoba Dr. Paul H. T. Thorlakson Foundation Fund
    Total Funding - 30,000 (Canadian dollar)
    Principal Investigator
11. Characterizing the molecular mechanisms of Ebola virus persistence at the blood-testis barrier
    Funding Sources:
    2018/8 - 2019/4 University of Manitoba Tri-Agency Bridge Funding
    Total Funding - 60,000 (Canadian dollar)
    Principal Investigator
12. Characterizing the molecular mechanisms of Ebola virus persistence in a 3D co-culture model of the blood-testis barrier
    Funding Sources:
    2018/3 - 2019/3 Manitoba Medical Service Foundation (MMSF) Operating Grant
    Total Funding - 19,219 (Canadian dollar)

Principal Investigator

13. Capacity Building Projects in an Institution of Higher Learning in the Developing World
Funding Sources:
2018/1 - 2019/10 University of Manitoba International Program and Partnership Seed
Total Funding – 5,000 (Canadian dollar)
Principal Investigator

INVITED PRESENTATIONS

1. Covid-19: Current state of knowledge. **Wastewater Epidemiology Group**. Public Health Agency of Canada. Virtual. 2021
2. Covid-19: Current state of knowledge. **Covid-19 Genome Sequencing Group**. Public Health Agency of Canada. Virtual. 2021
3. Vaccines & Therapeutics for COVID-19. **Café Scientifique**. Virtual. 2021
4. Balancing science and disinformation during Covid-19. Stem Skills for the 21st Century. **Bioscience Association of Manitoba**. Virtual. 2021
5. Eleven Covid months equals one decade - Emerging virus research during a pandemic. **Quebec Centre for Advanced Materials (QCAM)**. Virtual. 2020
6. Emerging Virus Research in the Time of Covid. Global Health Seminar Series. **Tel Aviv University**. Virtual. 2020
7. COVID-19 Transmission: Current state of virology knowledge. **Community-based aerosol transmission of Covid-19 and HVAC systems**. Canadian Agency for Drugs and Technologies in Health (CADTH). Virtual. 2020
8. Transmission Routes for COVID-19: Implications for Public Health. **CIHR-PHAC-CADTH – Best Brains Exchange**. Canadian Institutes of Health Research (CIHR). Virtual. 2020
9. Heating, Ventilation and Air Conditioning Systems in Public Spaces. Ottawa: **Canadian Agency for Drugs and Technologies in Health (CADTH)**. Virtual. 2020
10. 2020 Fall Member Forum: What's Next? The Aftermath of the COVID-19 Crisis. **Western Transportation Advisory Council (WESTAC)**. Virtual. 2020
11. Basic, Translational and Public Health Research During a Novel Pandemic. **School of Public Health, University of Saskatchewan**. Virtual. 2020
12. Characterizing tissue-barrier specific pathogenesis of epidemic and pandemic emerging viruses. **Infectious Disease, Microbiome, and Public Health Conference**. Virtual. 2020
13. COVID-19: Early Assessments of the First Coronavirus Pandemic. **Value Partners Annual General Meeting**. Virtual. 2020
14. COVID-19 and infection, prevention and control. **Canadian Dental Association**. Virtual. 2020
15. COVID-19: The Emergence and Spread of a Pandemic in the Age of Social Media. **UM Learning for Life Program**. University of Manitoba. Virtual. 2020
16. COVID-19: Monitoring the Emergence and Pandemic Spread of SARS-CoV-2 in Real Time. **International Life Sciences Institute – North America**. Virtual. 2020

17. Characterizing Emerging Virus Circulation and Spillovers in West and Central Africa. **Society of Clinical Research Associates**. Winnipeg, Canada. 2020
18. The Real Hot Zone: Studying Emerging Virus Circulation and Spillover in the Lab and the Field. **Department of Microbiology, Immunology & Infectious Diseases, University of Calgary**. 2020
19. COVID-19: An Emerging Public Health and Economic Crisis. **Manitoba Young Presidents Organization**. Winnipeg, Canada. 2020
20. Characterizing emerging virus circulation and spillovers in West and Central Africa. **Annual University of Nairobi HIV/AIDS Collaborative Conference**. Nairobi, Kenya. 2020
21. Identifying the molecular determinants underlying Ebola virus persistence in incidental and reservoir hosts. **KAVI Institute for Clinical Research**. University of Nairobi, Nairobi, Kenya. 2020
22. Characterizing the molecular determinants underlying severe Ebola virus disease and post-recovery persistence. **International Infection, Immunity and Inflammation Conference (I4C)**, Vancouver, Canada. 2019
23. Investigating the molecular pathogenesis of emerging and re-emerging viruses at the interface of basic and clinical research. **Manitoba Chemistry Symposium**, Winnipeg, Canada. 2018
24. Navigating the Storm: merging basic research with clinical information for (re)emerging infectious diseases. **Canadian Society of Microbiologists Annual Meeting**, Winnipeg, Canada. 2018
25. Are We Ready for the Next Pandemic? Reflections from the laboratory and the field**. CPD Medicine Program: Trends & Challenges in Virology**, Winnipeg, Canada. 2017
26. Investigating Interactions between the Host and High-Consequence Pathogens with Systems Kinomics. **University of Delaware Graduate Student Seminar Series**. University of Delaware, DE. 2015.
27. Characterizing High-Consequence Pathogens through Systems Kinome Analysis. **NICBR Exploring Careers in a Scientific Environment Symposium (NECSES)**. Fort Detrick, Frederick, MD, 2014.
28. Species-Specific Kinome Analysis for the Investigation of the Molecular Pathogenesis of High-Consequence Pathogen and Identification of Novel Therapeutic Targets. **American Society of Virology**. Fort Collins, CO, 2014.
29. Temporal kinome analysis demonstrates Ebola virus selectively modulates transforming growth factor β signaling. **6th International Symposium on Filoviruses**. Galveston, TX, 2014.
30. Use of live variola virus in systems kinomics for identification of host targets for therapeutic intervention. **15th Meeting of the WHO Advisory Committee on Variola Virus Research.** Geneva, Switzerland, 2013.
31. Systems kinome analysis of differential host responses to variola virus and monkeypox virus. **US Delegation to WHO.** Eisenhower Office Building, Washington, DC, 2013.
32. Ebola virus selectively modulates transforming growth factor-β signaling as demonstrated by temporal kinome analysis. **American Society of Virology.** Pennsylvania State University, PA, 2013.

33. Investigating high-consequence viral pathogenesis under (negative) pressure. **Vaccine and Infectious Disease Organization (VIDO).** Saskatoon, SK, 2012.
34. Use of live variola virus in systems kinomics for identification of host targets for therapeutic intervention. **14th Meeting of the WHO Advisory Committee on Variola Virus Research.** Geneva, Switzerland, 2012.
35. Temporal kinome analysis of Ebola virus molecular pathogenesis. **Centers for Disease Control (CDC): Special Pathogens Branch.** Atlanta, GA, 2012.
36. Temporal systems kinomics analysis of host cell responses to Ebola virus. **Keystone Symposium: Cell Biology of Virus Entry, Replication and Pathogenesis (X7).** Whistler, BC, 2012.
37. Kinome analysis reveals differential host cell responses to west african and congo basin monkeypox virus. **Gordon Research Conference – Chemical and Biological Terrorism Defense.** Ventura, CA, 2011.

CONSULTING

1. Covid-19 infection prevention and control procedures – Winnipeg Blue Bombers
2. Covid-19 expert advice – Young Presidents Organization (Winnipeg Chapter)
3. Covid-19 transmission – Manitoba Government

PATENT SUBMISSIONS

1. Small Cationic Anti-biofilm and IDR Peptides.
   United States. PCT/US2014/052993. 2014/08/27.
   Patent Status: Pending
2. Combination adjuvant formulation.
   United States. US9408908 B2. 2013/02/15.
   Patent Status: Granted/Issued
   Year Issued: 2016
3. Immunomodulatory compositions and methods for treating disease with modified host defense peptides.
   United States. US9102754 B2. 2008/06/27.
   Patent Status: Granted/Issued
   Year Issued: 2015

This is Exhibit " B " referred to
in the Affidavit of Jason Kindrachuk
Affirmed before me this second
day of March A.D. 2021

A Barrister-at-Law entitled to practice
in and for the Province of Manitoba

REPORT PREPARED FOR MANITOBA JUSTICE ON

SARS-COV- 2 AND COVID – 19

Jason Kindrachuk, PhD
Laboratory of Emerging and Re-emerging Viruses
Department of Medical Microbiology and Infectious Diseases
University of Manitoba
Winnipeg, Manitoba, Canada

February 26, 2021

1. Background

I am an Assistant Professor and Canada Research Chair in emerging viruses in the Department of Medical Microbiology & Infectious Diseases, University of Manitoba. My field of expertise is the investigation of emerging viruses, the infections they cause and their impact on global health. I am engaged in multiple international scientific outreach activities with regional partners across Africa including Sierra Leone, Gabon and Kenya. I am currently seconded as part of a 12-month research partnership agreement at the Vaccine and Infectious Disease Organization, University of Saskatchewan, Canada, where I am helping lead and facilitate national COVID-19 research response efforts. I also serve as an Associate Professor in the College of Medicine and Allied Health Sciences at the University of Sierra Leone and as a Visiting Scientist at the Centre International de Recherches Medicales de Franceville in Gabon, one of two biosafety level 4 facilities in Africa. I have also served in a volunteer capacity as an infection prevention and control expert for Heart to Heart International, an international disaster response agency, throughout the Covid-19 pandemic. Heart to Heart International, founded in 1992, has shipped more than $1.7 billion in humanitarian aid across more than 130 countries. It is a global humanitarian organization that focuses on improving public health and responding to the victims of disaster worldwide.

My education is as follows. I completed my undergraduate and graduate training at the University of Saskatchewan and completed my PhD in 2007 in the Department of Biochemistry. Following this, I participated in and led several projects as a postdoctoral fellow in Dr. Robert E.W. Hancock's laboratory, Centre for Microbial Diseases and Immunity Research, University of British Columbia. Here, my work focused on the design and development of novel anti-infective therapeutics and vaccine adjuvants, which are substances that are added to vaccine formulations to help amplify the immune response to the vaccine, for emerging pathogens. During this fellowship, the focus of my research was the investigation of emerging and re-emerging pathogens of importance to global public health, notably antibiotic resistant bacteria. These investigations fostered my commitment to both basic scientific research approaches and application of this research to public health in developed and developing nations. In 2009, I joined the National Institutes of Health (NIH) in Bethesda, MD, USA, as a Visiting Fellow to expand my expertise in the molecular mechanisms that underlie severe infections focusing on emerging and re-emerging viruses. Following this fellowship, I served in multiple senior scientific and leadership capacities, including Principal Research Scientist (NIH Integrated Research Facility-Frederick) and Staff Scientist (Critical Care Medicine Department, NIH). I also volunteered as a Scientific Lead in diagnostic support for the Centers for Disease Control/Department of Defense joint operations in Monrovia, Liberia during the 2014 Ebola virus disease outbreak.

Research History

My research has contributed to our understanding of the complex mechanisms underlying emerging viruses, their transmission and the infections they cause. Research in my laboratory focuses on the circulation, transmission and clinical aspects of emerging viruses that pose the greatest threat to global human and animal health. My current Covid-19 research includes:

1) Characterization of how SARS-CoV-2 manipulates human immune responses to cause severe disease in high-risk patient populations

2) Investigation of repurposed drugs as SARS-CoV-2 therapeutics through kinome analysis

3) Characterization of neurological and reproductive health complications in animal models of SARS-CoV-2 infections. Further, the animal models we are developing will allow us to inform how neurological manifestations associated with Covid-19 occur in humans.

Prior to my work on SARS-CoV-2 and Covid-19, my research focused on viruses that pose the greatest threat to global human and animal health. These included Ebola virus, Middle East respiratory syndrome coronavirus (MERS-CoV) and influenza viruses. A summary of these research activities follows below.

1) Ebola virus research (basic and clinical) & support efforts.

I have conducted extensive research into Ebola (Wahl-Jensen, Kurz et al. 2011, Kindrachuk, Wahl-Jensen et al. 2014, Falcinelli, Chertow et al. 2016, Barnes, Kindrachuk et al. 2017, Kash, Walters et al. 2017, Schindell, Webb et al. 2018, Khurana, Ravichandran et al. 2020) and received a 2018 National Institute of Allergy and Infectious Diseases (NIAID, NIH, Bethesda, MD, USA) Merit Award for my work. In 2014, I served as Scientific Diagnostics Lead in Liberia during the Ebola virus disease epidemic in West Africa. I provided daily situation reports and recommendations to local and international officials. I received a National Institutes of Health Director's Award in 2014 for these efforts. I have also recently received a five-year project grant from the Canadian Institutes for Health Research for my work on Ebola virus persistence, sexual transmission and long-term reproductive health impacts in Ebola virus disease survivors.

2) MERS-CoV efforts.

My work on coronaviruses began in 2013 following the emergence of Middle East respiratory syndrome coronavirus. This work culminated in multiple peer reviewed publications on therapeutic screening and identification as well as characterization of molecular pathogenesis (Dyall, Coleman et al. 2014, Hart, Dyall et al. 2014, Kindrachuk, Ork et al. 2015, Falcinelli, Chertow et al. 2016, Dyall, Gross et al. 2017, Willman, Kobasa et al. 2019).

3) Variola virus and monkeypox virus pathogenesis.

I developed and led collaborations with the US Centers for Disease Control and Prevention to investigate variola virus pathogenesis, the etiologic agent of human smallpox. This

work demonstrated that kinome analysis could be used as a predictive drug repurposing tool for orthopoxviruses. Based on this, I was invited to serve as a member of the US delegation at the World Health Organization Advisory Committee of Variola Virus Research. Meeting reports, including overviews of my work, are publicly available (WHO 2012, WHO 2013). My work on monkeypox virus was the first to identify how the West African and Congo Basin virus behave differently at the cellular level and may explain the differences in case fatality rates between the two clades (Kindrachuk, Arsenault et al. 2012).

4) Influenza viruses.

I have investigated influenza virus pathogenesis extensively with a focus on influenza-bacterial co-infections (Chertow, Kindrachuk et al. 2016, Davis, Chertow et al. 2016, Walters, D'Agnillo et al. 2016). This included pandemic and seasonal strains, including 1918 H1N1 virus. My work provided increased clarity regarding the mechanisms employed by pandemic and seasonal influenza viruses to infect cells as well as assessing the role of aerosol infection in acute respiratory distress during influenza virus infection in Rhesus macaques, with or without bacterial co-infection. Recently, my group published findings on 2009 pandemic H1N1-*Staphylococcus aureus* co-infections and provided perspectives on the 1918-1919 influenza pandemic (Nickol, Ciric et al. 2019, Nickol and Kindrachuk 2019).

I have been actively engaged in emerging infectious disease research and response efforts throughout my research career. In 2014, I was as a Scientific Lead in diagnostic support for the Centers for Disease Control/Department of Defense joint operations in Monrovia, Liberia, during the West African Ebola virus disease outbreak. I continue to work with local communities and perform research on the African continent. I have an active research program in Sierra Leone where I am leading investigations that focus on the long-term reproductive health impacts found in Ebola virus disease survivors. Here, we are working with local survivor advocacy groups to identify complications that are faced by survivors through anonymous surveys. My research group is also collaborating with similar advocacy groups and researchers in Liberia on this work. I have also co-founded the Consortium for Intercepting Emerging Diseases in Africa (CIEDA) with Dr. Kris Forbes (University of Arkansas) which brings together partners from North America, Europe and Africa to increase surveillance and identification of emerging infectious diseases that could impact global human and animal health. This work began through my research partnership with the Interdisciplinary Centre of Medical Research of Franceville, Gabon, where I am a Visiting Scientist. I also have emerging infectious disease collaborations at the University of Nairobi Institute for Tropical Infectious Diseases, Kenya, where I have led emerging virus training programs for trainees and staff.

Covid-19 and SARS-CoV-2 Grants, Reports and Committee Appointments

My research group is currently examining the effects of respiratory virus co-infection on disease outcome during SARS-CoV-2 infection in hamsters. I was a co-applicant on a grant funded by the Canadian Institutes for Health Research (CIHR) entitled "Animal models for SARS-CoV-2: vaccines and immune enhancement" in Spring, 2020. I have also received funding as a co- or lead-applicant for two additional grants: i) Scalable, Customizable, Digital Health Communication Materials to Help Canada Address the COVID19 Pandemic (CIHR); and ii) Broad Spectrum CoV Therapeutic; rhACE2 Immunoadhesin to treat COVID19 (MITACS Accelerate).

My work on SARS-CoV-2 began in early January of 2020 following the identification of the emergent virus in Wuhan, China, as a novel coronavirus. Following the emergence of SARS-CoV-2, I have been involved in various research investigations that have included development of animal models of infection, characterization of biological variables on disease severity, novel drug development and behavioral assessments of Covid-19 infection prevention and control messaging. In addition, I am currently investigating the differences in molecular pathogenesis in respiratory cells from patients with no underlying respiratory complications and those with chronic obstructive pulmonary disorder. My work on SARS-CoV-2 began in early January of 2020 when I co-authored a publication with other Canadian emerging virus experts on the emergence of a new virus (then called 2019-nCoV).

I have published two peer reviewed manuscripts on SARS-CoV-2, including as a co-author on a peer-reviewed clinical review of Covid-19 for *The BMJ* (Cevik, Kuppalli et al. 2020, Ralph, Lew et al. 2020), and three additional manuscripts that are currently in submission or revision. I have subsequently been involved in three additional manuscripts on Covid-19 that are currently in submission or in revision, two of which are available as pre-prints (Escandon K 2020, Francis, Richardson et al. 2021). I have also been involved in two publicly available reports from national committees on Covid-19 transmission as well as multiple national and international Covid-19 committees. These are outlined below.

Published Reports on Covid-19 Transmission:

i. CIHR-PHAC-CADTH – Best Brains Exchange – Transmission Routes for COVID-19: Implications for Public Health. Canadian Institutes of Health Research (CIHR); 2020 October. https://cihr-irsc.gc.ca/e/52238.html

ii. Heating, Ventilation and Air Conditioning Systems in Public Spaces. Ottawa: Canadian Agency for Drugs and Technologies in Health (CADTH); 2020 June. (CADTH technology review). Heating, Ventilation, and Air Conditioning Systems in Public Spaces (cadth.ca)

National and International Covid-19 Committees:

i. Panel Member – CIHR Institute of Infection and Immunity Consultation on Variant Strains of SARS-CoV-2
ii. Panel Member – CIHR-PHAC-CADTH – Best Brains Exchange – Transmission Routes for COVID-19: Implications for Public Health. Canadian Institutes of Health Research (CIHR); 2020 October. https://cihr-irsc.gc.ca/e/52238.html
iii. Panel Member – Heating, Ventilation and Air Conditioning Systems in Public Spaces. Ottawa: Canadian Agency for Drugs and Technologies in Health (CADTH); 2020 June. (CADTH technology review). Heating, Ventilation, and Air Conditioning Systems in Public Spaces (cadth.ca)
iv. Member – World Health Organization COVID-19 Solidarity Serology Study Group
v. Member – World Health Organization Ad Hoc Committee on COVID-19 Animal Models

2. Current Knowledge of Covid-19 Severity and SARS-CoV-2 Transmission

There has been extensive investigation into the relation between biological risk factors and Covid-19 disease severity. Severe disease, including intensive care unit admission and fatal disease, are associated with older age, race/ethnicity, gender and socioeconomic status. The US Centers for Disease Control and Prevention outlined and ranked the risks for severe Covid-19 based on supportive published evidence including case series, cohort studies, cross-sectional studies, meta-analyses and systematic reviews (CDC 2021). While older age is convincingly linked to severe Covid-19, the outlined risks were not limited to those in high age groups. Factors strongly linked to severe disease in adults include cancer, chronic kidney disease, COPD, cardiovascular disease, obesity, pregnancy, sickle cell disease, smoking, organ transplantation and type 2 diabetes. In Manitoba, Covid-19 case numbers were highest in the 20-29 age group with nearly equal proportions of males and females based on the province's updated data as of 19 February 2021 from their publicly available data (Manitoba 2021). This was followed by the 40-49, 50-59 and 10-19 age groups, respectively. As of 19 February 2021, total hospitalizations, intensive care unit admissions and deaths were 2,177, 405 and 879, respectively. Province-wide, the greatest proportion of hospitalizations have been found in the 65-79 age group. However, hospital admitted cases including the 35-49 and 50-64 age groups were greater than those in the 65-79 age group. Cases admitted to the intensive care unit were similar between the 65-79 and 50-64 age groups (Figure 6 Age Distribution of Severe COVID-19 Cases Compared to All Cases, Manitoba, 2020 – 2021; (Manitoba 2021)). The Manitoba numbers have similar trends with those in other jurisdictions, including the US, and demonstrate that younger age groups are susceptible to moderate or severe illness and at risk for hospitalization and intensive care unit admission.

There has been considerable insight regarding SARS-CoV-2 and Covid-19 over the past 14 months. Notably, this has included identification of the pathogen as a novel coronavirus, the likely origin of the virus, mechanisms of human-to-human transmission, the susceptibility of

additional animal species as incidental hosts for SARS-CoV-2 (including cats, dogs and mink), characterization of clinical disease and supportive care management (including high-risk groups), therapeutic management for clinical disease, and the design, development and licensure of multiple vaccines as well as dozens currently in various phases of clinical trials.

Of particular concern to public health officials and governments is the current state of knowledge regarding SARS-CoV-2 transmission. Early assessments for SARS-CoV-2 transmission identified respiratory droplets, aerosols and fomites (inanimate objects such as surfaces that can harbor infectious virus) as primary drivers of virus transmission. This was based largely on prior analysis of respiratory viruses, including the original SARS-CoV in 2002-2004, as there was a need to identify appropriate non-pharmaceutical interventions to reduce transmission and community spread. Prior observations from SARS- and MERS-CoV had showed limited community transmission with virus being spread primarily in healthcare settings through close contacts. Scientific evidence strongly supports that SARS-CoV-2 transmission is primarily driven by respiratory droplets and aerosols. While fomites are still considered as a potential route of infection, they are not considered as a driver of transmission in the pandemic. Respiratory droplets (>5–10 μm in diameter) remain suspended for short periods of time and are transmitted over short distances though this can be dependent on airflow. Small-particle aerosols (<5 μm) can disperse quickly and remain airborne while traveling longer distances. Current research has largely focused on the role of small-particle aerosol transmission in SARS-CoV-2 infections. Epidemiological data suggests that close contact, defined as anyone who has shared an indoor space with a case for a cumulative total of 15 minutes over a 24 hour period (Canada 2020), or enclosed settings is a major driver for SARS-CoV-2 transmission (Leclerc, Fuller et al. 2020, Qian, Miao et al. 2020). Recent animal model investigations (Chan, Yuan et al. 2020, Kim, Kim et al. 2020, Richard, Kok et al. 2020, Sia, Yan et al. 2020) and epidemiological studies (Cai, Sun et al. 2020, Jang, Han et al. 2020, Lu and Yang 2020, Park, Kim et al. 2020) suggest that small-particle aerosol transmission can occur during prolonged exposure in enclosed settings with reduced ventilation.

There has been considerable scientific investigation into the role of pre-symptomatic (prior to onset of symptoms) and asymptomatic (no symptom development though infected) transmission for Covid-19. Of central focus has been characterizing how the viral load (amount of virus) within the respiratory tract of an infected individual changes throughout the course of infection, both prior to symptom onset and following symptom resolution. The presence (viral load) and duration (kinetics) of virus within the respiratory tract are important determinants for the duration of infectiousness and thus transmission. Cevik and colleagues recently published a systematic review that incorporated data from 5,340 individuals across 79 studies (Cevik, Tate et al. 2021). Prior assessments of viral loads in the respiratory tract through repeated sampling suggests that peak viral loads occurred either just prior to (pre-symptomatic phase), or coincident with, symptom onset (Kim, Chin et al. 2020, Wolfel, Corman et al. 2020, Zou, Ruan et al. 2020). In the systematic review by Cevik et al., the authors identified 12 reports that provided temporal viral load data for individuals with asymptomatic infections. Viral loads in the reports were

found to be similar to (four reports) or lower than (two reports) those from symptomatic patients. However, viral clearance appeared faster in asymptomatic patients based on observations from six reports. This review provided temporal evidence for viral accumulation and clearance in asymptomatic patients. These observations are in good agreement with prior contact tracing studies where the highest risk of transmission fell from a few days prior to symptom onset to five days post-onset.

The contributions of asymptomatic and pre-symptomatic infections to SARS-CoV-2 transmission have been broadly investigated. An early study in April 2020 by Kimball and colleagues investigated an outbreak of Covid-19 in a long-term care facility in King County, Washington, US (Kimball, Hatfield et al. 2020). Following the initial identification of a Covid-19 case in the facility, broad testing was employed 16 days later and demonstrated rapid spread of the virus had occurred with positive tests found in 30.3% of residents. Early adoption of infection prevention and control measures had been instituted following the identification of the first case. Nearly half of the residents that had positive test results were not symptomatic at the time of testing and the authors concluded that the evidence suggested transmission from asymptomatic and pre-symptomatic residents may have contributed to spread. Wang and colleagues performed a retrospective cohort study of 335 people in 124 families and with at least one laboratory confirmed Covid-19 case and provide strong evidence for the importance of the pre-symptomatic transmission of SARS-CoV-2 (Wang, Tian et al. 2020). Further, they found that face mask use by the primary case and family contacts prior to symptom onset in the primary case was 79% effective in reducing transmission. In a prospective study, Cheng and colleagues demonstrated that secondary transmission was higher among individuals with initial exposures to index cases within 5 days of symptom onset as compared to day 6 or later (Cheng, Jian et al. 2020). This study also found that transmission was similar whether contacts only had pre-symptomatic or post-symptomatic exposure to index cases. In the four clusters for which the date of exposure could be determined, pre-symptomatic transmission occurred 1-3 days before symptom onset in the pre-symptomatic source case. Clinical and epidemiological assessment of 243 Covid-19 cases, between January 23, 2020 - March 26, 2020, were reviewed to identify potential cases of pre-symptomatic transmission of SARS-CoV-2. Out of 243 cases, 157 were locally acquired (Wei, Li et al. 2020). The authors found seven epidemiologic clusters where pre-symptomatic transmission likely occurred and ten of the cases within these clusters were attributed to pre-symptomatic transmission, accounting for 6.4% of the 157 locally acquired cases.

There have been a growing number of investigations that have focused on delineating true asymptomatic and pre-symptomatic infections to help provide additional context regarding transmission potentials across the clinical disease spectrum and infectious period. Johansson and colleagues employed a decision analytical model to examine virus transmission from pre-symptomatic, symptomatic and asymptomatic individuals (Johansson, Quandelacy et al. 2021). Model assumptions were that peak viral transmission occurred at the median of symptom onset,

30% of infected individuals were true asymptomatic infections and were 75% as infectious as symptomatic individuals. The model suggested that 59% of all infections occurred from those without symptoms of disease where 35% were patients that were in the pre-symptomatic stage of disease and 24% had asymptomatic infections. Buitrago-Garcia and colleagues recently examined asymptomatic and pre-symptomatic SARS-CoV-2 infections and transmission through a systematic review (Buitrago-Garcia, Egli-Gany et al. 2020). Using data from 94 studies, the authors calculated the overall estimate of true asymptomatic infection was 20% with the balance of 80% being those with pre-symptomatic infections. However, the authors also stated that most studies included in the review were not designed to estimate asymptomatic infection proportions and thus combination non-pharmaceutical interventions will continue to be needed to help curb virus transmission. These sentiments were also echoed by Byambasuren and colleagues in their recent systematic review of asymptomatic Covid-19 (Byambasuren O 2020). The authors reviewed 13 studies and the asymptomatic proportion of described cases ranged from 4-41% with a corresponding overall proportion of asymptomatic infections as 17% exclusive of pre-symptomatic infections based on their meta-analysis. The authors stated that this remained sufficient to warrant policy attention. A recent systematic review and meta-analysis by Buitrago-Garcia and colleagues assessed 79 studies found that 20% of infected individuals remained asymptomatic throughout the course of infection (Buitrago-Garcia, Egli-Gany et al. 2020). In seven of the studies with defined populations, asymptomatic infections rose to 31%. The secondary attack rate, and thus indication of transmission potential, was lower for asymptomatic infection as compared to symptomatic infection with a relative risk ratio of 0.35, suggesting that there is greater risk for transmission from those with symptomatic disease; however, risk of transmission remains from those with asymptomatic infections. Interestingly, the authors also found that the relative risk ratio of pre-symptomatic transmission as compared to symptomatic transmission was 0.63, further demonstrating that transmission in the absence of symptoms presents a risk. Moreover, the authors state that based on the contributions of asymptomatic and symptomatic infections in virus transmission, “combination prevention measures, with enhanced hand hygiene, masks, testing tracing, and isolation strategies and social distancing, will continue to be needed”. A recent investigation by Li et al assessed household transmission rates in Wuhan through a retrospective observational study (Li, Li et al. 2021). The authors assessed 29,578 primary cases, 27,101 households and 57,581 household contacts in their analysis. The odds ratio for infection from asymptomatic individuals was lower than from symptomatic cases (0.21), similar to those reported by Liu et al (Liu, Chu et al. 2020). Importantly, the odds ratio for infection from pre-symptomatic cases was higher than from post-symptom onset cases (1.42). Thus, while true asymptomatic transmission may occur less frequently than during symptomatic transmission, there was a greater likelihood of transmission before symptom onset (pre-symptomatic) than post-symptom onset. The authors concluded that pre-symptomatic cases were more infectious than symptomatic cases and individuals with asymptomatic infection less infectious than their symptomatic counterparts. Qiu and colleagues recently conducted a critical assessment of available secondary attack rate data from individuals with asymptomatic, pre-

symptomatic and symptomatic SARS-CoV-2 infection. Eighty studies were included for their analysis and in agreement with other investigations, secondary attack rates (defined as the probability that an infected individual will transmit the disease to a susceptible individual) from asymptomatic cases were found to be lower than symptomatic cases (Qiu, Nergiz et al. 2021). Importantly, their analysis demonstrated that secondary attack rates were similar between pre-symptomatic and symptomatic cases. The authors did not include a review from Madewell et al. (Madewell, Yang et al. 2020) as the study included only household contacts and data up to July 29, 2020. Overall, while SARS-CoV-2 transmission is likely lower from individuals with asymptomatic infections as compared to symptomatic cases, those in the pre-symptomatic phase of disease appear to be able to transmit the virus similarly to symptomatic individuals.

There have been numerous investigations on the relation between viral load, transmission and biological characteristics including age, sex and disease severity. A recent systematic review by Koopmans et al. reviewed data from 26 studies to determine the relation between viral load dynamics and Covid-19 severity, age and sex (Chen PZ 2021). Higher viral loads were found in those with severe disease as compared to those with non-severe infections. Interestingly, viral load within those with symptomatic infections was not altered by age or sex as children had similar viral loads following symptom onset as their non-severe adult counterparts. While severe Covid-19 has largely been linked to age and underlying health comorbidities, there is growing appreciation that children can be infected and transmit SARS-CoV-2. Recent reports have suggested that transmission is efficient in children ≥10 years old (Park, Choe et al. 2020, Szablewski, Chang et al. 2020). In the conclusion of the analysis of SARS-CoV-2 transmission at the summer camp in Georgia (Szablewski, Chang et al. 2020), Szablewski et al suggested that asymptomatic infection was common amongst the cases and could have contributed to undetected transmission as suggested in additional studies (Dong, Mo et al. 2020, Gotzinger, Santiago-Garcia et al. 2020, Huang, Zhang et al. 2020, Team 2020). More recently, a case report from Lopez and colleagues investigated Covid-19 outbreaks at childcare facilities in Utah (Lopez, Hill et al. 2020). Twelve children (mean age 7 years; range 0.2-16 years) were found to have acquired SARS-CoV-2 in the facilities and transmitted the virus to 12 of 46 non-facility contacts that were assessed. Importantly, three of 12 children had asymptomatic infection (25%) and two transmitted the virus.

Taken together, there is strong scientific evidence for SARS-CoV-2 transmission to primarily occur from a few days prior to symptom onset up to ~5 days post-onset. Direct assessments of viral loads and the kinetics of viral shedding, when virus is released from infected cells in the respiratory tract, are in agreement with this and contact tracing studies in household cohort studies provide direct evidence for asymptomatic and pre-symptomatic transmission of SARS-CoV-2. Further, additional epidemiological studies of SARS-CoV-2 suggest that similar patterns of asymptomatic and pre-symptomatic transmission likely occur within children as with adults.

3. Exposure time and virus particle transmission

Exposure risk guidance is primarily based on the relation between exposure time and SARS-CoV-2 infection. By Health Canada guidelines, a high risk exposure (close contact) includes anyone that has shared an indoor space with a positive Covid-19 case for a prolonged period (a period of 15 cumulative minutes over 24 hours) without adhering to appropriate mitigation measures (Canada 2020). This also includes anyone with a close-range contact with a positive Covid-19 case or anyone that has been in settings where that person engaged in singing, shouting or heavy breathing (including exercise). Given the role of aerosol exposure in transmission, the accumulation of virus-laden aerosol particles in the air of an enclosed setting could result in continued exposure of individuals to virus over a prolonged period.

There have been multiple super-spreader events during the Covid-19 pandemic that have been linked to close contacts in enclosed settings, including faith-based settings or places of worship. Most notably, infection of 53 of 61 attendees (33 confirmed and 20 probable cases) from a single symptomatic individual occurred during a 2.5-hour choir practice in Skagit County, Washington, USA (Hamner, Dubbel et al. 2020). Three of those infected during the practice were hospitalized and two succumbed to infection. A similar super-spreader event occurred in Arkansas where 35 of 92 church attendees were infected, three fatally, during a five-day period (March 6-11) (James, Eagle et al. 2020). Additionally, contact tracing found at least 26 additional Covid-19 cases among community members that had reported contacts with church attendees and had likely been infected during those contacts, including a fatal disease case. The index cases, a husband (pastor at the church) and his spouse, were likely infected during a two-day period (March 6-8) with potential pre-symptomatic transmission from the pastor to others during a group event on March 11. Of the 61 total identified cases (35 church attendees and 26 contacts), eight were hospitalized and four had fatal infections. These observations have not been limited to North America. A super-spreading event linked to a service at Shinchunji Church of Jesus, Daegu, South Korea is postulated to have resulted in >3,900 secondary Covid-19 cases (Shim, Tariq et al. 2020) and choir-related outbreaks have been reported in Berlin and Amsterdam (Bahl, de Silva et al. 2020).

Alsved et al. recently examined exhaled respiratory particle generation during breathing, talking and singing (Alsved M 2020). The generation of aerosol particles, as determined by particle number emission rates, were highest from those singing loudly with exaggerated diction followed by loud singing alone, normal singing, loud talking, normal talking and breathing. Addition of a face mask to those singing loudly reduced particle emission rates to levels found during normal talking. The authors examined SARS-CoV-2 release from those with confirmed Covid-19 during singing and talking. While virus was not detected, the authors identified several limitations in the study including variations in patient viral loads, test positivity versus infectious virus presence in the respiratory tract, and dilution steps in the sample preparation method.

These observations are in line with prior studies looking at respiratory viruses and aerosol particle emission. Previously, Lindsley and colleagues examined the release of influenza virus in aerosol particles during coughing and exhalation (Lindsley, Blachere et al. 2016). The authors collected aerosol particles produced during coughing or exhalation from 61 patients with influenza-like illness. Aerosol particles with infectious virus were collected from 28 (53%) patients while coughing and 22 (42%) patients from exhalation. These results demonstrated that normal exhalation can generate virus-laden infectious particles which could potentially lead to virus accumulation over extended periods of exposure in an enclosed setting.

Previous investigations have also assessed droplet and aerosol emission during common vocal activities. An investigation by Bahl et al. examined the spread of droplet and aerosol generation during singing (Bahl, de Silva et al. 2020). This was done using a detailed flow visualization of aerosols and droplets emitted during singing of a major scale using an image-based flow diagnostic system. The authors found that droplets generated by singing did not settle rapidly suggesting high aerosol generation which could saturate the indoor environment in the absence of adequate ventilation. Further, the direction of the generated droplets suggested that they could pose a potential infectious risk for other members arranged in multiple adjacent and distant rows. Recommendations from the authors to reduce droplet and aerosol exposure included reduction in group numbers, greater physical distancing between members, softer singing and shorter duration, and the implementation of face masks. Of interest, prior investigations of particle emission patterns during normal speech by Asadi and colleagues demonstrated that particle emission during normal speech is correlated with the loudness of vocalization, is highly heterogeneous and could amplify respiratory pathogen transmission (Asadi, Wexler et al. 2019). A similar study from Mürbe and colleagues assessed the release of aerosol emissions from adolescents: four boys and four girls aged 13-15 (Murbe, Kriegel et al. 2021). Overall, while the emission spectrum reflected that found in adults (highest during shouting followed by singing and speaking) the emission of aerosol particles was lower during singing than adults. However, particle emission was within the same order of magnitude between the two groups during speaking.

Taken together, there is accumulating evidence and historical data demonstrating that SARS-CoV-2 emission from infected individuals is likely positively correlated with vocal activities and increases with the volume and exaggeration of vocalizations. Importantly, the emission of aerosol particles is of particular importance given that they can accumulate in the air of enclosed spaces over time based on their physical characteristics and increasing the potential for infection beyond proximal contacts (at 2 m or less in distance away). This highlights the importance of reducing emissions through non-pharmaceutical interventions including masking and social distancing.

4. Infection Prevention Measures

The use of face masks as an additive preventative measure against Covid-19 has been widely discussed and debated since early 2020. Evidence for the use of masks as an infection prevention and control measure must account for setting, population, mask type and design. Medical masks and filtering facepiece respirators have been demonstrated to reduce respiratory viral infections in healthcare settings (Jefferson, Del Mar et al. 2011, MacIntyre and Chughtai 2015, Offeddu, Yung et al. 2017, Chou, Dana et al. 2020, Garcia Godoy, Jones et al. 2020, MacIntyre and Chughtai 2020). Medical masks have also been demonstrated to have an infection prevention benefit within the community including in households, educational settings and pilgrimages; however, there is less evidence for the use of cloth masks to prevent transmission or contracting infection (Chughtai AA 2013, MacIntyre and Chughtai 2015, Barasheed, Alfelali et al. 2016). A single randomized control trial cautioned against the use of cloth masks compared to medical masks for healthcare workers (MacIntyre, Seale et al. 2015). However, it should be appreciated that exposure to high viral loads and extended exposure times are more common within healthcare settings. Among cloth masks, hybrid and cotton-made multi-layer masks seem to perform best in terms of both filtration efficacy and wearing comfort. The efficacy of medical masks in reducing influenza virus and common cold coronaviruses for limiting respiratory emissions from symptomatic individuals, as well as for the wearer, has been demonstrated through mechanistic studies (Johnson, Druce et al. 2009, Makison Booth, Clayton et al. 2013, Milton, Fabian et al. 2013, Leung, Chu et al. 2020). Observational studies on the use of masks for reducing SARS-CoV-2 transmission have demonstrated a benefit in community settings (Chen, He et al. 2020, Hendrix, Walde et al. 2020, Hong, Lin et al. 2020, Nir-Paz, Grotto et al. 2020, Payne, Smith-Jeffcoat et al. 2020, Wang, Tian et al. 2020). A recent randomized control trial from Bundgaard et al. examined masks and SARS-CoV-2 infection (Bundgaard, Bundgaard et al. 2020). The primary findings from the authors were that mask use did not reduce the SARS-CoV-2 infection rate among wearers by more than 50% in a community with modest infection rates, some degree of social distancing, and uncommon general mask use. However, the authors also state that their findings were inconclusive based on their large confidence intervals. In addition, this analysis was performed in a setting where mask mandates were not in effect and thus only provide potential assessments on the degree of protection mask wearers might encounter in a setting where others were not wearing masks. The authors also stated that the findings should not be used to conclude that a recommendation for everyone to wear masks in the community would not be effective in reducing SARS-CoV-2 infections, because the trial did not test the role of masks in source control of infection.

Ueki et al. recently employed aerosol simulation to assess masking and demonstrated that cotton, surgical and N95 masks all provided a protective effect against SARS-CoV-2 transmission and their simulations suggested that protection was most efficient when masks were worn by an infected individual (virus spreader vs receiver). Use of a mask during exposure to virus resulted in decreased uptake of virus by the receiver across all mask types. A cotton mask reduced virus uptake by 20-40% compared to the use of no mask. Addition of a mask (cloth or

surgical) to the virus spreader reduced transmission by >50%. At high concentrations of released virus from a non-masked spreader (10^8 pfu), beneficial reductions in transmitted virus were lost with use of a cloth mask on the receiver. These results provide support for the use of masks across populations whether infected or not.

More recently, Brooks and colleagues assessed cloth and surgical mask fit for reducing SARS-CoV-2 transmission (Brooks, Beezhold et al. 2021). Their results demonstrated that the use of unknotted surgical masks or cloth masks alone blocked 56.1% and 51.4% of particles from a simulated cough, respectively. The authors highlighted that these results used only a single style of cloth masks and may not be generalizable to all cloth or surgical masks. However, these results compliment other investigations of mask use as a preventative measure for SARS-CoV-2 transmission. Importantly, the authors also suggested that masking is beneficial for reducing SARS-CoV-2 transmission in addition to other non-pharmaceutical interventions, including distancing, avoidance of groups in poorly ventilated enclosed spaces and hygiene. In January 2021, Rader and colleagues assessed the effects of masks, and mask mandates, as well as physical distancing on SARS-CoV-2 transmission in the US (Rader, White et al. 2021). More than 350,000 individuals aged 13 years or older responded to the authors' random survey from June-July 2020. Multivariate logistic regression modeling demonstrated that communities with high incidence of mask wearing and distancing had the highest predicted probability of SARS-CoV-2 transmission control. Conversely, the authors found an inverse relationship between the percentage of reported mask wearers and R_t, the effective reproduction number, which describes average number of secondary cases per primary case at a particular time. This effect was sustained with adjustment for demographic variables, distancing and peak transmissibility during the first Covid-19 wave. Further, the recommendation for mask use was echoed in late 2020 by Howard and colleagues which suggested that mask wearing by infectious people in addition to mask wearing by susceptible people would have benefits at the population level during the pandemic (Howard, Huang et al. 2021). Thus, the accumulating evidence regarding face masks as a non-pharmaceutical intervention for SARS-CoV-2 transmission provides strong support for the usefulness of masks in this regard while it is also dependent on mask factors such as quality and proper fit.

While the benefits of face masks as a non-pharmaceutical intervention have been well described it must be appreciated that these interventions are not standalone fail safes but rather a multi-faceted approach that includes multiple synergistic infection prevention and control measures. Haug and colleagues recently examined the implementation of non-pharmaceutical interventions across the globe and ranked these based on reported effectiveness (Haug, Geyrhofer et al. 2020). The study utilized a comprehensive, hierarchically-coded dataset of >6,000 non-pharmaceutical interventions across 79 territories from March-April 2020. The least effective interventions were found to be government actions to provide or receive international help, measures to enhance testing capacity or improve case detection strategy, tracing and tracking measures, land border and airport health checks and environmental cleaning. Overall, the authors found that no single non-pharmaceutical intervention would act as a single failsafe

measure to reduce SARS-CoV-2 transmission. Perhaps unsurprisingly, curfews, lockdowns and closing/restriction of congregation areas for small or large groups were the most effective strategies to reduce R_t. Restriction of individual movement also ranked high though the adverse social consequences of such measures were recognized by the authors. These results argue for a combination of approaches that implement multiple non-pharmaceutical interventions at the level of both individuals as well as populations. A recent review by Perra posited that modeling of non-pharmaceutical interventions overwhelmingly demonstrated the importance of interventions to curb SARS-CoV-2 transmission and that the success of these interventions in controlling transmission was related to their early implementation (Perra 2021). Further, the author also concluded that many investigations demonstrated that face mask implementation was beneficial.

5. Issues Requiring Continued Research

The roles of virological and biophysical factors (including the minimum infectious dose, virus concentrations and viability in indoor and outdoor settings) in SARS-CoV-2 transmission remain elusive. Detailed investigations of the relative contribution of these factors to transmission are needed though will likely extend beyond the current public health emergency. Thus, adherence to established non-pharmaceutical interventions should remain the focus of the global response pending further research.

Long-term complications in Covid-19 recoverees

There is a growing appreciation that Covid-19 can result in extended health complications and abnormalities, independent of disease severity and age (Rubin 2020). These include extended fatigue, shortness of breath, joint and chest pain, and neurological complications. A recent study from Italy suggested that 44% of recovered patients reported a worsened quality of life post-Covid-19 (Carfì, Bernabei et al. 2020). A US study by Tenforde et al. reported that 35% of surveyed patients had not returned to their normal state of health two to three weeks following a positive Covid-19 test result with 20% of those surveyed being 18-34 years of age with no underlying chronic medical conditions at the time of survey (Tenforde, Kim et al. 2020).

Reproductive health concerns

Recent data has suggested that severe Covid-19 can result in reproductive tissue damage in males. An investigation by Ma et al. assessed pathology in the testes from males with fatal disease and found strong signs of germ cell damage and may indicate the potential for reproductive health impairment in severe disease (Ma, Guan et al. 2021). Yang and colleagues had similar observations for reproductive tissue damage in deceased male Covid-19 patients including seminiferous tubular injury, reduced Leydig cell populations and mild lymphocytic inflammation (Yang, Chen et al. 2020). There have also been recent insights regarding the potential for Covid-19-related complications during pregnancy. Yang et al. provide evidence that

SARS-CoV-2 infection during late pregnancy is associated with increased risks of adverse birth outcomes (Yang, Mei et al. 2020). Kotlyar et al. also recently provided evidence for vertical transmission of SARS-CoV-2 in the third trimester (Kotlyar, Grechukhina et al. 2021). These data suggest that SARS-CoV-2 infections may have impacts on both reproductive health and pregnancy that could have detrimental impacts on younger populations.

Variants of concern

The recent emergence of SARS-CoV-2 variants of concern, which includes B.1.1.7 (first identified in the UK), B.1.351 (first identified in South Africa) and P.1 (first identified in Brazil), has resulted in new concerns regarding the global burden of Covid-19. Concerningly, B.1.1.7 has increased transmissibility ranging from 30-70% over circulating non-variants of concern and has been associated with increased risk of severe and fatal disease in hospitalized patients (Horby P 2021). While less is known regarding B.1.351 and P.1, shared mutations within the spike protein have been related to immune evasion and enhanced transmission. The selective pressures that mitigate these changes have yet to be determined. The emergence of B.1.1.7 in the UK resulted in the overtaking of circulating SARS-CoV-2 strains within a few months, a trend echoed in additional countries including Ireland and Denmark. The enhanced transmissibility associated with this variant have resulted in renewed public messaging regarding the importance of infection prevention and control measures, including mask use and social distancing, to curb community transmission of these variants of concern and others that may emerge. There have also been concerns regarding the potential for re-infections with B.1.351 and P.1 due to their adoption of mutations associated with immune evasion and decreased ability for antibodies from convalescent Covid-19 patients or vaccinees to neutralize these variants. Thus, decreased community transmission will reduce the potential for additional emergence of variants of concern that could have better immune escape mechanisms that could have detrimental impacts on global vaccination programs.

Herd Immunity

There have been rampant discussions regarding the potential of natural herd immunity, dictated by broad infections in the community, as a mechanism to curb global transmission of SARS-CoV-2. While focused protection has been raised as a mechanism to protect those at highest risk for severe disease while allowing the virus to transmit in the absence of broad employment of non-pharmaceutical interventions, there are serious concerns regarding the public health outcome of such a strategy. In particular, the resurgence of Covid-19 in Manaus, Brazil, provides a cautionary tale for a natural infection-based herd immunity-style approach. Manaus was devastated by the first wave of the pandemic with 4.5-fold excess mortality (Orellana, Cunha et al. 2020). A serological assessment of antibodies in Manaus suggested that between 44-66% of the population was infected with SARS-CoV-2 by July 2020, which followed the epidemic peak (Buss, Prete et al. 2021). This rate rose to 76% by October 2020, surpassing the theoretical herd immunity threshold for Covid-19 of 67%. However, virus transmission

continued with a devastating second surge of SARS-CoV-2 infections by mid-January 2021 (Sabino, Buss et al. 2021). The authors provided four potential explanations for their observations. First, attack rates could have been overestimated during the first wave. However, as the authors suggest, even with an upwards bias there should have still been a larger effect of population immunity given the breadth of the first wave in 2020. Second, the authors raised concerns regarding the potential impacts of waning immunity in those that were previously infected. Could decreasing protective immunity in individuals infected during the first wave have resulted in a resurgence of Covid-19 due to reinfections in this population? Such a phenomenon would be devastating for an infection-based herd immunity strategy as the threshold for sustained herd immunity to curb virus transmission would be impeded. Third, the emergence of virus variants that might evade immunity generated from prior SARS-CoV-2 infection. Two virus variants, P.1 and P.2, have been identified in Brazil that possess a mutation in the spike protein that has been associated with immune evasion. Reinfections have been identified in Brazil for both P.1 and P.2 (Naveca F 2021, Resende PC 2021, Vasques Nonaka 2021). And fourth, new SARS-CoV-2 variants circulating in Manaus may have higher transmissibility than currently circulating strains. While the emergence and spread of the B.1.1.7 variant of concern has been associated with increased transmissibility (Horby P 2021) there is no current data for other variants of concern to suggest that they have a competitive transmission advantage over circulating strains in their regions of emergence. Indeed, the recent emergence of the variants of concern (B.1.1.7, B.1.351 and P.1) serve as a reminder that continued transmission of the virus results in mutations within the viral genome that could lead to increased rates of infection.

Overall, the current data from Brazil provides supportive evidence that a herd immunity approach through natural infections could have devastating impacts on public health. The recent resurgence of infections in January 2021 with a seropositivity that surpassed the proposed threshold for herd immunity highlights the dangers of such a strategy. Further, the recent emergence of variants of concern with mutations associated with immune evasion mechanisms, and the reduced ability of antibodies from convalescent patients to neutralize these variants, adds questions regarding the potential for reinfections in those with natural immunity leading to further sustained community transmission.

6. Conclusion

In conclusion, the current data overwhelmingly suggests that both asymptomatic transmission and pre-symptomatic transmission contribute to SARS-CoV-2 transmission with increasing reports suggesting that pre-symptomatic transmission in particular plays an important role in these events. Given this, there is an inherent need to utilize non-pharmaceutical interventions including, but not limited to face masks, to reduce transmission events from those in our communities that are unaware that they are infected and contagious. Primary points of consideration include:

- **Morbidity and mortality**: while much of the pandemic has centered around the increasing fatalities nationally and globally, there has been less discussion regarding the effects of Covid-19 associated morbidity. Hospitalization data demonstrates that this disease can have health impacts on individuals across multiple age groups and adds significant stress on national healthcare systems and capacity.
- **SARS-CoV-2 transmission routes**: there is growing appreciation for the role of aerosols in SARS-CoV-2 transmission in addition to respiratory droplets. Aerosols have the potential for broader transmission within enclosed settings in the absence of multiple non-pharmaceutical interventions (including face masks, distancing, ventilation) and data demonstrates that aerosols may be an important factor in pre-symptomatic transmission of the virus.
- **Non-pharmaceutical interventions**: while there is strong evidence that face masks provide a benefit for reducing SARS-CoV-2 transmission they are not a single failsafe intervention measure. This requires a multi-faceted approach that includes multiple interventions due the synergistic effects these measures.
- **Virus variants and herd immunity**: the recent emergence of SARS-CoV-2 variants of concern that have increased transmissibility and the immune evasion characteristics supports the need to curb transmission in the global community quickly prior to further variant emergence. The emergence of P.1 in Brazil has suggested that new variants may be able to circulate even in populations that have exceeded the proposed herd immunity threshold with potentially devastating public health consequences. Thus, approaches that combine non-pharmaceutical interventions in addition to expanding vaccination campaigns will have the greatest opportunity to curb community transmission of the virus expediently.

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