

ASK AN EXPERT

COVID-19 Trials with Dr. Michael Grant

BY DR. MICHAEL GRANT

Michael Grant received his PhD in Molecular Virology and Immunology from McMaster University. He is a professor of Immunology and Infectious Diseases at Memorial University of Newfoundland. His main interest is the immunology of viral infection with a focus on human immunodeficiency virus, hepatitis C virus, cytomegalovirus and most recently, SARS-CoV-2, the cause of COVID-19.

Your current project includes investigating antibodies of participants who think they may have contracted the virus. Could you briefly describe this project? What about these antibodies in particular interests you?

Our research involves investigating humoral immunity (antibodies) against SARS-CoV-2 in persons who recovered from COVID-19 with illness severity ranging from asymptomatic to requiring hospitalization. We also recruited close contacts of confirmed cases and people who believed they may have contracted SARS-CoV-2 but never tested positive. Features of the antibody response against SARS-CoV-2 directly relate to the role of immunity in protection from infection or from illness. The first question we posed is how does the antibody response against

SARS-CoV-2 relate to illness severity? The consensus from previous studies, corroborated by our data, is that persons with more severe cases of COVID-19 make stronger antibody responses against SARS-CoV-2(1-3).

Of concern is whether weaker antibody responses associated with mild illness leave persons at risk for re-infection with the possibility of more severe illness. The second question we are addressing is how stable is the antibody response against SARS-CoV-2? Previous studies were contradictory with some reporting rapid decay of antibody levels and others reporting stability(1-6). In our study, confirmed cases infected in March and April 2020 had high levels of antibodies when first tested in November 2020, and these levels were stable over the following three months. Stability of the response is also a key issue with vaccinees for gauging the duration of protection following vaccination. We are now enrolling vaccinees into our study to compare the strength and stability of their



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responses to those of recovered persons. So far, we have observed responses similar to those of persons recovered from severe cases of COVID-19. In parallel, we are studying functional features of anti-SARS-CoV-2 antibodies such as virus neutralization, antibody dependent cell-mediated cytotoxicity and antibody dependent enhancement of infection. These features relate to the strength, fine specificity and protective efficacy of the antibody response.

As Newfoundland has had remarkably low COVID-19 infections compared to other provinces, are you concerned about participation numbers? How has the response from the public been since your call for participants late last year?

While Newfoundland was fortunate to have relatively few

cases during the first wave of COVID-19, persons with confirmed infection enthusiastically joined the study to learn what sort of immune response they had made. We also identified 15 cases of recovery from COVID-19 where people were in close contact with a confirmed case, but were negative for SARS-CoV-2 RNA at time of testing by public health.

“Many people volunteered for the study because they believed they may have had COVID-19 and wanted confirmation”

Almost all turned out negative for antibodies against SARS-CoV-2, but testing them now provides us with pre-vaccination baseline samples for our expanded study of vaccinees. This part of the study is growing rapidly with the ongoing vaccine rollout and the second wave of COVID-19 hitting Newfoundland relatively hard in February 2021. More recovered persons and others who think they were exposed are volunteering for the study, and virtually exclusive infection with the B.1.1.7 variant in St. John’s during the second wave offers a unique opportunity to compare immunogenicity and study cross-neutralization of the different strains.

Are there similar projects in other parts of Canada? How are you collaborating with other teams at the Canada’s COVID-19 Immunity Task Force?

Research groups across Canada linked through the Canadian Immunity Task Force were funded to study different aspects of immunity against SARS-CoV-2 follow-

ing infection. We share protocols, data and perspectives regularly and will employ consensus protocols in future studies of the vaccine response against SARS-CoV-2. While a standardized format to study antibody responses can be readily agreed on by multiple labs, best methods for addressing complex aspects of cellular

immunity against SARS-CoV-2 following infection or vaccination remain a work in progress. There is nothing comparable to an antibody neutralization assay that applies to cellular immunity against SARS-CoV-2. Thus, discussions are ongoing regarding the optimal application of flow cytometry, enzyme-linked immune absorbent spot (ELISPOT) and other platforms to study cytokine production, cytotoxicity, proliferation and memory formation by SARS-Cov-2-specific T cells.

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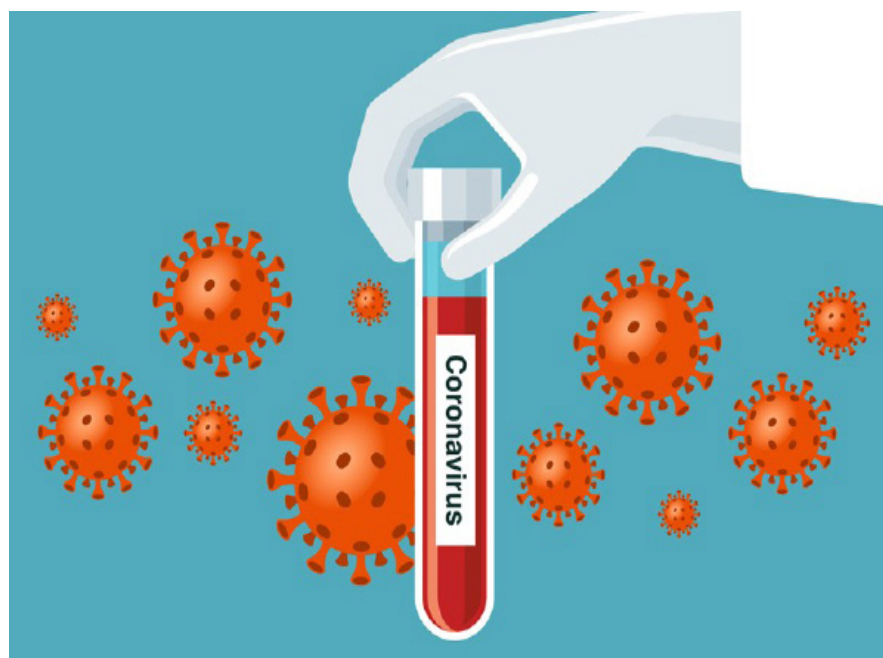


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