Publications of the Week

Bacterially Derived Synthetic Mimetics of Mammalian Oligomannose Prime Antibody Responses That Neutralize HIV Infectivity

Pantophlet, R. and Kosma, P., et al. | Nature Communications | December 4, 2017

Read the Publication

This week we profile a recent publication in Nature Communications from ***Dr. Ralph Pantophlet*** *(middle) at Simon Fraser University.*

My lab is part of a growing group of researchers at SFU with a focus on infectious diseases and immunology (Infectious Diseases and Immunology Group). The core of this group, consists of myself and Drs. Mark Brockman, Zabrina Brumme, Jamie Scott, Felix Breden, Rob Holt and Jonathan Choy. Drs. Brockman, Brumme, Scott and myself are also part of SIRCH, the SFU Interdisciplinary Research Centre for HIV, which is headed currently by Dr. Bob Hogg. Research in my lab is currently focused on vaccine design and vaccine immunology pertaining to two agents in particular: HIV-1 and influenza. The overall objective of our work is to develop novel strategies and approaches for the design of a vaccine component that elicits virus-neutralizing antibodies (nAbs), with emphasis on those capable of targeting conserved sites on the outer spikes that decorate the surface of these viruses. Because of the conserved nature of the target sites, such nAbs are expected to exhibit broad anti-viral activity and thus, in principle, would help to provide broad immunity against infection in vaccinees. In the case of flu, this could mean better protection against potential pandemic viruses or not needing annual vaccination for at least certain individuals. In the case of HIV, this would mean protection against perhaps a majority of virus strains that a vaccinee may be exposed to.

What is the significance of the findings in this publication?

There are many scientific challenges to the design of a broadly effective HIV vaccine. One of the longstanding challenges has been the design of a component that can elicit broadly reactive nAbs. One of the target sites on the HIV spike that have been identified through past research are so-called oligomannose sugar molecules that largely coat the virus spike. It has proven challenging to elicit antibodies that can target these sugar molecules. The exact reason(s) is (are) not fully understood. However, one likely reason is that the sugar molecules are the same as those found on some mammalian proteins; meaning that mammalian immune systems –such as ours– are not easily triggered into producing antibodies to such sugar molecules. (This phenomenon is termed self tolerance; the inability of our own immune system to produce antibodies to 'self' molecules).

Our Nat Commun paper, along with another that recently appeared, reports on the chemical design of analogs of these sugar molecules, based on a bacterial sugar molecule, and their potential for 'tricking' the mammalian immune system into the production of antibodies that can cross-react with the sugar molecules on the HIV spike. As a surrogate for antibody responses in humans, we used small animals (rats) transgenic for human antibody genes; i.e., these animals make human-like antibodies upon immunization. As noted in the paper, further studies are needed to expand on this first report, including optimization of the formulation to stimulate more robust antibody production and assessment of whether the elicited antibodies recognize 'self' proteins. Nevertheless, the work presents a promising new avenue to overcome one of the many challenges to the development of an effective HIV vaccine.

In 2016, my lab secured a CIHR Operating Grant dedicated to innovative HIV research that helped us finalize some of the work published in the Nat Commun paper. Recently, we were able to secure a 4-yr investigator-initiated grant from the NIH to continue this work. Among the first steps is to develop derivative molecules that better represent what could be used in the clinic in the future. Specifically, we need to conjugate our analogs to a carrier protein that is clinically acceptable; in the paper we used BSA (albumin), which is easily obtained, cheap and easy to manipulate but that would not be transferable to the clinic. Second, we need to probe formulations that will evoke more robust responses. Specifically, we will be exploring various adjuvants (immune-stimulating agents) to identify at least one that works will with our particular molecules. Another area of interest will be to isolate antibodies from immunized animals and study these in molecular detail to better understand how, at the molecule level, they recognize the sugar molecules, thus helping to inform how the immune system is being 'tricked' into cross-recognition.

This research was funded by:

Research published in the Nat Commun article was supported by funding from CIHR (CHR-126629 and IBC-150408), a sub-award from the Canadian HIV Vaccine Initiative (THA-118628), the Austrian Science Fund (P26919-N28), the NIH (R01 AI084817 and UM1 AI100663) and a Collaboration for AIDS Vaccine Discovery grant. I am supported also by a salary award from the Michael Smith Foundation for Health Research (no. 5268).

Read the Publication

Upcoming Events in Vancouver

March 26, 2019

The SBN Biotech Expo & Conference

@ UBC Robson Square

March 28, 2019

SFU Postdoc Research Day

@ SFU Burnaby

March 28, 2019

D.R.I.N.K.S

2019 Norman Bethune Symposium
@ UBC Robson Square

April 3, 2019

UBC Medicine Career Day
@ BC Children's Hospital Research Institute

View All Events

Recent Jobs

Product Manager, Epithelial
STEMCELL Technologies

Scientist, Pulmonary
STEMCELL Technologies

Research Associate
BC Centre for Disease Control

Postdoctoral Fellow
BC Cancer

Patent Agent
Zymeworks

View All Jobs