SPRING 2020

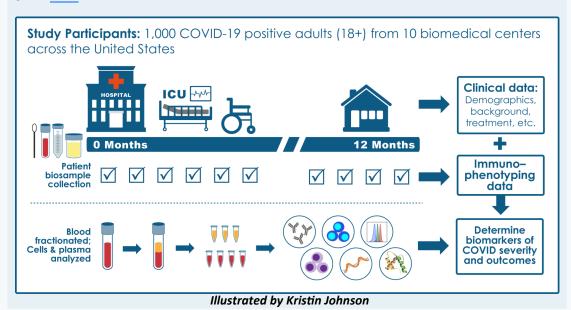
IMPACC

We know that the consequences of COVID-19 disease start by infection from a virus. But how does the body react to that viral invasion? To answer that question, the *Precision Vaccines Program* (PVP) at Boston Children's Hospital will play key roles in an NIH-funded nationwide study designed to learn how the immune systems of people hospitalized with COVID-19 respond to the disease over time. Called IMmunoPhenotyping Assessment in a COVID-19 Cohort (IMPACC), the study will include up to 2,000 patients from 10 to 12 medical centers across the country. The information collected could guide new strategies for diagnosing and treating COVID-19 and possibly identify new targets for drug treatment.



"This effort involves trying to understand how the virus interacts with the body, to find biomarkers that predict outcome from disease, and see how the virus affects people even after they recover," says PVP Director Ofer Levy, MD, PhD, who will serve as principal investigator for the IMPACC site at Boston Children's. "It will hopefully provide crucial clues to developing new diagnostics, therapeutics, and vaccines for COVID-19."

Click here for more information.





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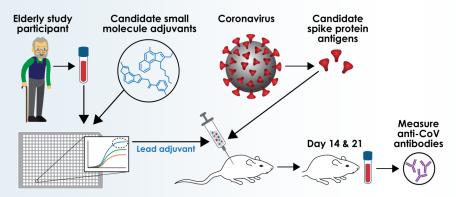
ADJUVANT DISCOVERY PROGRAM

Adjuvant Discovery & Development Laboratory

An individual's response to a vaccine may vary based on a range of factors age, sex, pre-existing conditions. Funded by NIH/NIAIDs Adjuvant Discovery and development Program contracts, the Precision Vaccines Program's Adjuvant Discovery & Development Laboratory (ADDL) led by David J Dowling, PhD focuses on identifying small molecule adjuvants the ADDL works to identify novel small molecule adjuvants to boost immunity in vulnerable populations such as the young and elderly to enable next generation vaccines against pathogens such as pertussis (whooping cough) and influenza.

Development of an Adjuvanted SARS-CoV-2 Vaccine Optimized for the Elderly

Vaccine development is often slow and inefficient in part due to failure to consider species and age-specificity in preclinical studies. The coronavirus pandemic highlights the need to accelerate and de-risk targeted vaccine development. In this context, the ADDL is taking a fresh approach to discovery and develop a novel adjuvanted SARS-COV-2 vaccine optimized to protect those at greatest risk of severe COVID- i.e., the elderly. The ADDL is screening a large pipeline of adjuvants including those from commercial sources, collaborating institutions, as well as "home grown" Precision Vaccines Program (PVP) molecules, for those that are most active towards human elderly leukocytes. Leads are being formulated with SARS-COV-2 spike antigen and being tested for immunogenicity both human in vitro models and in adult and elderly mice.



Development of an Adjuvanted Vaccine for the Treatment of Opioid Use Disorder

Opioid Use Disorder (**OUD**) is a public health crisis resulting in nearly 100 deaths a day in the U.S. with adolescents and young adults especially vulnerable. Development of an opioid vaccine could prevent overdose deaths but responses to candidate vaccines demonstrate rapidly waning antibody levels. Moreover,

opioids have immunomodulatory effects such that adjuvant responses of youth with OUD may be distinct. Accordingly, the ADDL has been awarded an NIH/NIAID contract to develop an adjuvanted opioid vaccine tailored to those with OUD. In collaboration with Dr. Sharon Levy of the Adolescent Substance Use & Addiction Program at BCH, the ADDL is studying the distinct immune system of those with OUD to inform selection of optimal adjuvant for this effort whose goal it is to advance an adjuvanted opioid vaccine to clinical trial at BCH.



Dr. David Dowling

ADDL Position available

Skilled Research Fellows or Technologists interested in joining the ADDL's efforts should directly contact Dr. David Dowling: david.dowling@childrens.harvard.edu

BCG Vaccines

Bacille Calmette-Guérin (BCG), the live attenuated Mycobacterium bovis vaccine against tuberculosis (TB), was once again in the spotlight during the Optimmunize Meeting organized in February 2020 by Dr. Christine Benn and colleagues. Several groups presented data from observational studies, clinical trials and basic science studies supporting BCG's beneficial off-target effects, such as decreasing neonatal mortality, protecting children against malaria and inducing innate immune memory in the elderly. BCG immunomodulatory properties have also sparked interest in its potential use to prevent or alleviate autoimmune and inflammatory diseases, including type 1 diabetes mellitus and multiple sclerosis.

Recent epidemiological studies investigating the effects of national BCG immunization programs or lack

thereof on COVID-19-related cases and deaths, show negative correlations between universal BCG vaccination policies and disease incidence. Multicenter trials of BCG to reduce COVID susceptibility and/or severity are currently underway in Australia, led by Dr. Nigel Curtis, and The Netherlands



Dr. Nigel Curtis

with additional studies being considered in Europe and the United States.

Studies at the *Precision Vaccines Program* have shown that licensed BCG formulations vary widely in viability and innate immune activating properties. Much remains to be learned regarding the relative protective efficacy of different licensed BCG formulations and it is important to ensure that BCG vaccines selected for use in large-scale immunization schemes maintain the stability of their characteristics. Future studies should directly compare licensed BCG formulations, including their optimal timing of administration, and measure both heterologous and specific protection in high mortality populations.

PVP IN THE NEWS



Dr. Ofer Levy's interview with Brianna Keilar @ CNN

Recent Publications From PVN Members

Paolo Palma et al. "The HIV-1 Antibody Response: A Footprint of the Viral Reservoir in Children Vertically Infected With HIV" **7-May-20** https://www.thelancet.com/journals/lanhiv/article/PIIS2352-3018(20)30100-4/fulltext

Byron Brook et al. "BCG vaccination–induced emergency granulopoiesis provides rapid protection from neonatal sepsis" **6-Mar-20** https://stm.sciencemag.org/content/12/542/eaax4517

Asimenia Angelidou et al. "Licensed Bacille Calmette-Guérin (BCG) formulations differ markedly in bacterial viability, RNA content and innate immune activation" 24-Feb-20

https://www.sciencedirect.com/science/article/pii/S0264410X19316147?via%3Dihub

Pankaj Sharma et al. "The TLR5 Agonist Flagellin Shapes Phenotypical and Functional Activation of Lung Mucosal Antigen Presenting Cells in Neonatal Mice" 18-Feb-20

https://www.frontiersin.org/articles/10.3389/fimmu.2020.00171/full

Etsuro Nanishi et al. "Toward precision adjuvants: Optimizing science and safety" **1-Feb-20**

https://journals.lww.com/co-pediatrics/FullText/2020/02000/ Toward precision adjuvants optimizing science and.18.aspx

Membership

We are pleased to highlight an enhanced membership structure. Under the banner of the *Precision Vaccines Network* (PVN), we encourage you to join our Network to be kept abreast of recent developments, opportunities, initiatives, and conferences.

You can receive our quarterly newsletter by simply emailing us.

Positions Available

The *Precision Vaccines Program* is seeking skilled and motivated individuals to serve in key roles such as Program Manager and Lab Manager.

Please <u>contact us</u> to obtain more information including a job description.

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Precision Vaccines Network

by the numbers

>380 Members
17 Countries
5 Continents
2 International Conferences

>745 Twitter followers
>210 Facebook followers
>150 LinkedIn followers









