Vaccine and Immunotherapy Center
Massachusetts General Hospital
2020 Holiday Newsletter

Message from the Director

Dr. Mark C. Poznansky

Dear Friends of VIC – 2020 has been an extraordinarily challenging year for all of us that I hardly need to detail. We know that the COVID-19 pandemic has deeply affected our families, our peace of mind, our spiritual and intellectual lives. It turned out that the VIC team was in the right place at the right time to address these new scientific and clinical challenges and our friends and family, collaborating companies, research foundations and US Government organizations stood up to help us get our work done. As a result of this support we have been able to commence and accelerate development of a novel T cell-based vaccine for COVID-19 along with our partner Voltron Therapeutics. We are working with an eminent lab at the Dana Farber Cancer Institute on a novel therapeutic for the infection. With tremendous support from Analog Devices we have initiated collaborations with Multerra and Pinpoint technologies to develop novel and rapid tests of the virus and its impact on the human immune system. I must stress that the VIC team continued working, either in the laboratory or virtually, at 100% operational speed throughout this time to develop new cell-based therapies for type 1 diabetes and ALS. We continued to explore new high dimensional immunology platforms for guiding the diagnosis and treatment of diabetic foot ulcers and prostate cancer. All this achieved with the tremendous help of the core senior scientific team including Drs. Reeves, Chen, Alagpulinsa, Gelfand and Sîrbulescu and our amazing Associate Director, Dr. Ann Sluder and Project and Administrative Manager, Phoebe Ingram. These individual stories of research success are detailed below, and I hope that you will find time to read them.

VIC Pivots to COVID-19 Vaccine Development

One of the key elements of VIC's ethos is that we study how the immune system is involved in disease, rather than the disease itself. This makes our findings relevant to a range of otherwise unrelated diseases and means we can apply our technologies wherever the unmet need is greatest. The spread of a previously unknown virus at the beginning of this year showed the value of this approach. We were able to rapidly reapply our vaccine platform which we were developing - and continue to develop - as a personalized treatment for ovarian cancer to address the COVID-19 pandemic. We quickly set up an agreement with a subsidiary of Voltron Therapeutics to fund this new venture. Throughout the lockdown, Dr. Patrick Reeves marshalled an amazingly dedicated team of undergraduates and graduate students over Zoom from their bedrooms and kitchen tables to identify the best portions of SARS-CoV-2 to include in a vaccine. These have gone into two candidate vaccines which we are testing for the ability to induce an immune response in mice and protect hamsters from COVID. Everyone hopes to see the first vaccines made widely available by large companies before ours is ready, but those first generation vaccines are mostly designed to produce antibody responses to just one viral protein – Spike. While initial indications are that this approach works well - at least in the short term - there are widespread doubts about the durability of antibodies to coronaviruses. VIC's vaccine is designed to induce a strong T cell response - the evidence so far shows that this is more likely to give longer lasting protection.

COVID-19 and the Immune System

While much of Massachusetts was locking down in March, the team at VIC were swinging into action to respond to the new challenge. The generosity of VIC donors allowed us to respond rapidly and get completely new research programs up and running within a couple of weeks. A band of intrepid students, including two who had just arrived from Europe but decided to stay and help rather than return to the familiarity of home, turned our biohazard containment facility into a site where samples from COVID-19 patients could be safely processed and studied. Resources like this are an essential basis for any scientific study. Faced with the nationwide shortage of PPE, VIC donors stepped in to help with a shipment of face shields and supply of protective equipment. Friends at VIC connected us to a group at Cell Signaling Technologies in Danvers, MA, a leading developer of antibody-based research tools, and together we developed a powerful new tool that profiles the antibody repertoires in patients in profound detail.

We teamed up with MGH colleagues to collect blood, saliva, and epidemiological information from nearly 400 people in Chelsea, one of the hardest hit cities in Massachusetts. Contacts in rural Georgia enable us to compare an unrelated population with contrasting demographics. VIC's high-level data science team are using the results from these people to open a unique view of how the virus affects people differently, and how antibody and cellular immune responses contribute to the different physiological profiles seen, from completely asymptomatic infection to life-threatening illness. This picture will guide us and many others as we develop vaccines and refine therapeutic approaches to guide the immune system to eliminate the virus without damaging the body.

Rescuing and Restoring Insulin Production from the Pancreas in Type 1 Diabetes

Type 1 diabetes is caused by the invasion of the pancreas by autoimmune cells that destroy the insulin-producing beta cells. To date, a treatment to prevent or reverse type 1 diabetes has been a challenge. With support of a Tosteson Fund for Medical Discovery Fellowship and a Physician-Scientist Development Award from the MGH Executive Committee on Research, Dr. David Alagpulinsa and his team have developed a novel approach to "push" and "pull" stem and immune regulatory cells, respectively, into the pancreas, to stop autoimmune cells from destroying beta cells. We have demonstrated that treatment of mice that develop type 1 diabetes with drugs that cause stem cells and regulatory T cells to come into the blood circulation (pushing) together with expressing a chemokine that attracts these cells in the pancreas (pulling) prevents the disease from occurring in these mice. The treated mice did not have autoimmune cells in their pancreas and their beta cells remained intact. In contrast, untreated mice developed type 1 diabetes with their pancreas invaded by autoimmune cells and their beta cells destroyed. This is an exciting and encouraging outcome.

Advancing a Novel B Cell Immunoregulatory Therapy for Patients with ALS

Last year and in early 2020, VIC achieved a major step forward that led to the first ever in-human administration of B cells from the blood in a patient with a devastating neurodegenerative condition. The patient received consecutive infusions of B cells with minimal to no adverse reaction, indicating the potential of this therapy in humans. This breakthrough was built upon the innovative work of Dr. Ruxandra Sîrbulescu, who discovered at VIC that B cells could both protect and enhance the regeneration of tissues, including central nervous system tissue. This work and findings are now part of VIC protected intellectual property. Dr. Sîrbulescu has led a series of preclinical studies that confirmed the safety and efficacy of this novel cell-based immunotherapy in animal models. This resulted in the rapid approval from the FDA for us to conduct a first human study of safety in under a year. Implementing this complex project involved tremendous teamwork managed at VIC and involving scientists, physicians and nurses at the MGH and DFCI. None of this work, from bench to bedside could have been completed without generous philanthropic support particularly from the Ward Family Foundation. Currently, Dr. Sîrbulescu's group is actively working to understand and modulate the mechanisms through which B cell therapy acts, in order to further improve its efficacy for subsequent clinical administration in patients.

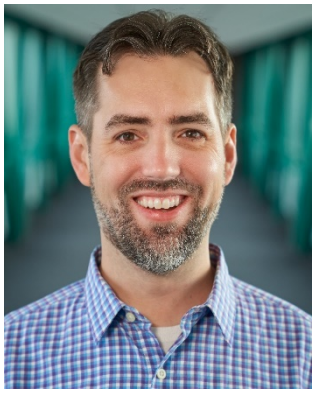
And Finally

Our invited Prof. Dulcie Coleman lecturer this year was Prof. Lisa Morici, from Tulane University School of Medicine, who gave an outstanding talk on 'Warp speed ahead: vaccination in the 21st century'. The Dr. Melvyn Field Award was presented to Dr. Alagpulinsa for his innovative research in the field of type 1 diabetes and the Will Tankard Junior Scientist award to Augustin Vannier for his dedicated work developing a new assay for detecting the breadth of the immune response to COVID-19. We would like to thank all family and friends of VIC, old and new, including Analog Devices, UniFirst and New England Biolabs who made donations this year and made the impossible possible. You all helped bring VIC successfully and impactfully through this very challenging year. We are grateful for your continued support into 2021.

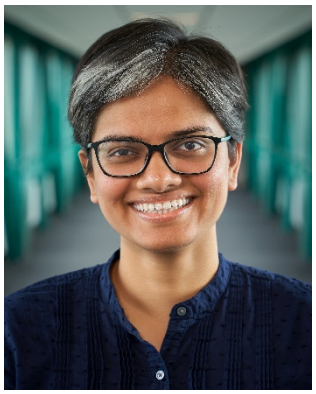
A Very Happy Thanksgiving to All

http://advancingcures.org/donate/

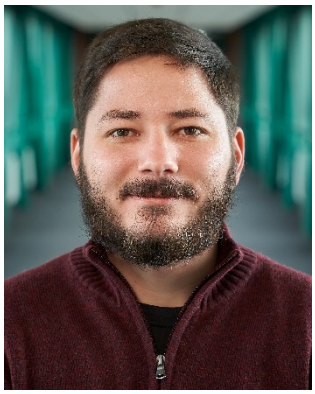
VIC Pandemic Response Heroes – 2020



Dr. Patrick Reeves
Developed and designed a new COVID-19 vaccine

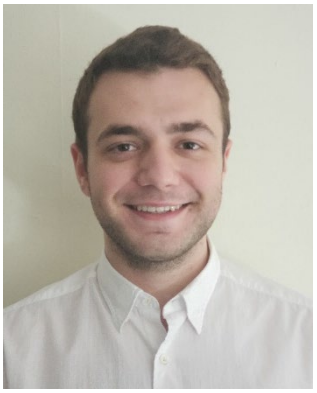


Dr. Susan Raju Paul
Developed novel immune assays for cancer and ALS



Michael Chapin
Maintained VIC Lab operations throughout the pandemic

Morgan Friesen
Supported COVID-19 vaccine and therapeutic development



Augustin Vannier
Developed a novel assay for assessing anti-COVID-19 immunity

Thank you for your sterling contributions to VIC during the pandemic