Mount Sinai

Marc and Jennifer Lipschultz Precision Immunology Institute

NEWSLETTER | SPRING 2022

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Location, Location, Location: Perturb-map adds spatial awareness to functional genomics.

Over the past decade, there has been an explosion of technologies to discover the functions of the more than 20,000 protein-coding genes in our bodies. Deleting a gene in a cell to determine its function can be done in a matter of days: a disruptive sequence can be synthesized and shipped to the lab overnight. Pooled genetic screens dramatically revolutionized our ability to determine gene function, but phenotyping single cells after such gene disruption in large scale screens was difficult.

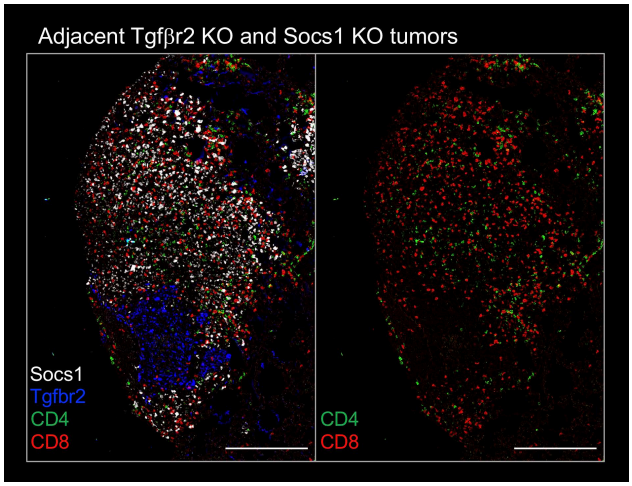

Figure 1

Perturb-map analysis enabled the team to look at how genetically distinct subclones might influence each other. Quite remarkably, the answer was very little, at least in the case of Socs1 and Tgfbr2 knockout tumors. As seen in the image, even when Socs1 and Tgfbr2 KO tumors were adjacent, the immune composition of the tumors, hot for Socs1 and cold for Tgfbr2, remained spatially distinct. Therefore, the cancer cells were controlling their microenvironment at micron scale distances.

In 2018, Aleksandra Wroblewska and Maxime Dhainaut in Brian Brown's lab designed a high throughput technology for phenotypic screens with single cell resolution using protein barcodes, known as "Pro-Codes"[1]. Pro-Codes are designed for tracking individual vectors once they are introduced to cells via pools of vector libraries packaged in virus for transduction. The individual vectors can contain different CRISPR guideRNAs or other transgenes, alongside a unique Pro-Code for identification of the specific cells that received it. As proof-of-concept, they designed Pro-Codes with CRISPR guide RNAs targeting genes involved in the interferon-signaling pathway to identify which genes regulate antigen-dependent T cell killing. Several labs in PrIISM are now using the technology, and it has enabled faster, easier interrogation of genes involved in multiple disease models.

Pro-Codes are a powerful tool, but were limited to the study of phenotypic changes after processing of tissue in vitro using single cell methods like CITE-seq and flow cytometry. But spatial context in vivo can be critical to gene function. This is especially true in tumors, and for the coordination of the immune response to the cancer cells. Tumors are a heterogenous mixture of different cell types, and mutations in various genes in distinct cells may influence the surrounding microenvironment. You can easily knock-out one gene in one cell in a culture dish, but may not see any phenotype if the surrounding cells can compensate. Moreover, perturbation of certain genes, such as cytokines, may not elicit any useful information since they act in a paracrine fashion on many different cell types that may not be present. Therefore, investigating gene function in vivo is critically important for understanding the functions of gene products that are outside of the cell in which they are expressed, dysregulated or disrupted. For example, the activity of genes that modulate T cell activation checkpoints, such as PD1, can only be defined if their ligand is present on the right cell type that activated this checkpoint, and there may be other cells involved in influencing the outcome of the T cell checkpoint. Only in vivo will all these complex factors be present, therefore, spatial functional genomic assays are needed to tease apart how they work.

1 Wroblewska, Dhainaut, *Cell*, November 2018.
2 Dhainaut, Rose, *Cell*, March 2022.

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Brian's lab wanted to see what was happening in tumor tissue and how the activities of different genes affect the tumor microenvironment, but the tools to do this did not exist. To solve this problem, they combined their Pro-Code system with several methods for visualizing individual cell phenotypes within the context of intact tissue, including spatial transcriptomics and a multiplex imaging technique called MICSSS, which was developed by other PrIISM scientists, Sacha Gjnatic and Miriam Merad. The result was a powerful spatial functional genomics platform they dubbed "Perturb-map", which can uncover the in vivo context-specific functions of many different genes at once, in healthy tissue and in different disease models. Their work is reported in a paper in the April 2022 issue of Cell[2].

Maxime designed libraries of up to 120 Pro-Codes, transduced the libraries into a mouse breast cancer and lung cancer cell line, and performed multiplex imaging to assess the clonality of the tumors. The first result from these images was striking: all of the seeded lung tumors in the mouse were clonal, encoding only one Pro-Code, whereas the breast tumors were a mixture of multiple different Pro-Code expressing cells. Samuel Rose, a computational scientist, implemented imaging de-barcoding algorithms and statistical analyses to translate the images, so the group could 'see' things that weren't immediately apparent on first look. Sam translated Maxime's images into a digital readout and developed a pipeline to characterize different tumor lesions in an unbiased manner and study them at scale in different tissues.

Maxime then designed a Pro-Code library with CRISPR guideRNAs targeting 35 different genes involved in cytokine signaling that were thought to regulate tumor immunity. Two of the genes, Tgfbr2 and Socs1, revealed contrasting yet extremely intriguing phenotypes. The group stained lung tumor lesions for various immune markers, such as CD4, CD8, F4/80, and CD11b, and found that lesions lacking Socs1 showed high T cell infiltration, in stark contrast to Tgfbr2 knockout lesions, which were completely immune excluded (Figure 1). But even more interesting, and one of the most profound biological findings of the paper Brian argues, is that when Socs1 and Tgfbr1 knockout tumor lesions were adjacent to one another, each of their immune phenotypes stayed the same: the immune cells infiltrating the Socs1 knockout tumor remained tightly within that lesion, leaving a gaping space of immune desert within the Tgfbr1 knockout lesion.

The Pro-Code system and its extension into Perturb-Map are just two of several innovative technologies that have emerged from the Brown lab. Brian notes that oftentimes these technologies arise from informal conversations amongst collaborators and colleagues about a specific biomedical problem that cause them to think, "Why can't we solve it in a different way?" The Pro-Code project was prompted by CRISPR screens that required deep sequencing to deconvolute the specific genes disrupted. This indicated if gene knockout led to 'enrichment' or 'de-enrichment' in a particular context but "we wanted to know more," Brian said. "That's how we got to thinking that we want to be able to use CyTOF or imaging so that we can perform complex phenotyping to understand better the functions of a gene…" One of the rationales for Perturb-map began with a project aimed at finding new immune checkpoint molecules like PD1 that they could target for cancer immunotherapy. The Brown lab began generating CRISPRs to target approximately one thousand human receptors that could be potential checkpoints. However, when looking at the list, Brian realized that half of the ligands for these receptors are probably not present in vitro and many of the genes being targeted are also not present, or were unlikely to function in the same manner as they would in vivo. "The screens we were planning, and many labs were doing, were not capturing the large class of genes operating extracellularly," said Brian.

The Perturb-map project brought many intriguing biological findings and was an exciting project for all involved. **"There were a lot of times where we had the temptation to go off track because there were so many interesting findings that we wanted to pursue," says Maxime.** In addition to the biology, the innovation and design was extremely rewarding for all the investigators. For Sam, one of the best parts was "when we started seeing the de-barcoded imaging and had the inkling that this was working." At this point, Sam made a larger commitment to continue working on this project as he transitioned to a post-doctoral position in Dana Pe'er's lab at Memorial Sloan Kettering Cancer Center, who shared Sam's enthusiasm for the project.

New technology development is exciting because **"you get to look at things that not many people have seen because you made the system to view it from a different angle… It can transform the way you understand the biology," says Maxime**. For Brian, seeing that the technology worked, and its potential, was also fulfilling. But the most exciting part, and an aspect that is somewhat underappreciated about technology innovation in general, is that the group introduced "a concept of what has been limited and missing" that researchers may not have been aware of before the technology was invented. This is because the group as technology inventors understood the problem before others did.

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MESSAGE FROM THE DIRECTOR MIRIAM MERAD, MD PhD

The last two years of pandemic have been a crazy and extraordinary time. From the start, when we were still not sure how infectious SARS-CoV-2 was, immunologists knew they had the knowledge to understand the disease and they stepped up to try to help and that was quite beautiful. I have to highlight several initiatives PrIISM contributed to the pandemic response.

First, Nicolas Vabret launched the Immunology Preprint Review Club, with students and postdocs from PrIISM reviewing the flurry of COVID-related preprints in collaboration with faculty to parse the noise from the real interesting biology, so students could help with the pandemic response while their own research was put on hold. A partnership was then formed between PrIISM and *Nature Reviews Immunology*, and expanded to include Oxford University, and it's a beautiful story continuing beyond COVID. The Preprint Club is one of the first organized community initiatives to challenge the traditional model of peer review before publication. It gives trainees an authentic experience in learning to evaluate papers with their reviews having an impact in the world outside of traditional journal clubs, and encourages broader reading of the literature. I know it was very helpful to the community. You can read more about the preprint journal club from Nicolas on page 6.

In the second effort, the Immunology Institute coordinated by the Human Immune Monitoring Center, started to collect samples from hospitalized patients. In fact, we built the largest single center collection in the world with 800 COVID patients sampled at different times during the disease course. Most hospitals were mobilizing resources for doctors to take care of patients, of course, but it still moves me to remember how supportive Dean Charney was of the critical need to mobilize resources for research. He said the sky is the limit: just tell me what you need to explore why patients are dying.

This COVID BioBank collection enabled us to understand what type of inflammatory signature occurred in severe disease[1], and the nature of the COVID multisystem inflammatory syndrome in children[2]. The COVID BioBank has facilitated many fantastic studies that have explored the role of tissue resident macrophages in severe COVID[3], identified a severe form of MIS-C in children with Down syndrome[4], and how antigen persistence in the gut is required for the maintenance of antibody responses to SARS-CoV-2[5]. The efforts of many within the Institute and the trainees really helped with this collection.

1 Del Valle, *Nature Medicine*, August 2020.
2 Gruber, *Cell*, November 2020.
3 Chen, *BioRxiv*, January 2022.
4 Malle, *JCI*, October 2021.
5 Gaebler, *Nature*, January 2021.

We've been back full force for over a year in terms of research efficiency, with many people returning to their pre-COVID projects, faster than most institutions across the US. I am excited to hear about these projects at our work-in-progress seminars, and looking forward to these being in-person, as I love sharing coffee and cookies together at WIP.

2022 got off to an amazing start, with Marc and Jennifer Lipschultz presenting a milestone gift that will transform PrIISM and the institute is now named the 'Marc and Jennifer Lipschultz Precision Immunology Institute' in their honor. Their visionary support has helped us recruit new faculty that allow us to expand into newer research areas for PrIISM, such as immunometabolism with the recruitment of Dan Puleston, and neuroimmunology with the recruitment of Brian Kim.

Everyone will be able to meet new PrIISM faculty and trainees at our upcoming PrIISM retreat, which will be the first time we've gathered in two years and I am looking forward to seeing all of you. This year, we have asked some faculty to talk about a high-level view of their research programs, and we hope to have lively discussions about what new areas of immunology we should engage.

I'm very excited that we will all be meeting and seeing everyone again in one room, and I look forward to a fantastic day of science and friendship!

ALICE KAMPHORST: MOVING CD8+ T CELLS PAST EXHAUSTION

Alice Kamphorst joined PrIISM in 2018 as an Assistant Professor of Oncological Sciences and a member of the Cancer Immunology Research Program at the Tisch Cancer Institute. Alice started out as a scientist in Brazil, investigating mechanisms of oral tolerance for her Master's project with Dr. Ana Maria Caetano de Faria. She then trained as a graduate student with Michel Nussenzweig at The Rockefeller University in New York, before joining Rafi Ahmed's lab in Atlanta for a postdoc.

She has explored how dendritic cells present antigen, and how exhausted CD8+ T cells can be reinvigorated by PD1 immunotherapy. Her group now investigates how costimulatory molecules, chemokines and cytokines, and CD4+ T helper cells control the differentiation and function of CD8+ T cells in conditions of chronic antigen stimulation due to infection and cancer. Here, Alice tells us more about her personal and scientific journey to PrIISM.

How did you become interested in science originally and why immunology specifically?

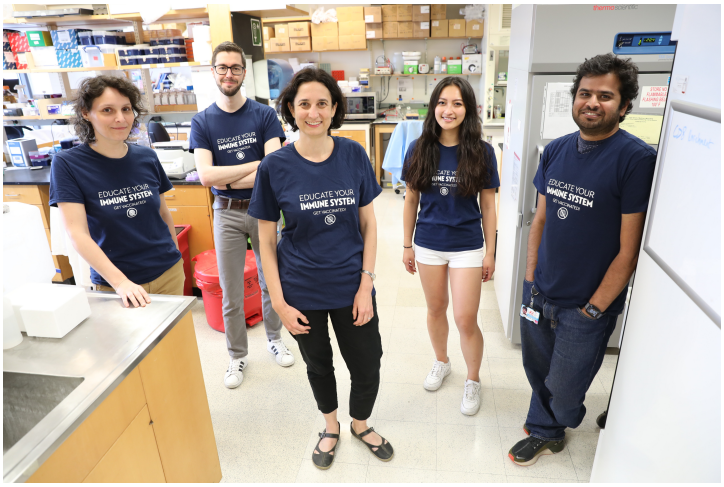
My family tells me that they knew I would become a biologist because I had snails as pets as a kid. Also, my grandfather was an optical engineer and he made lenses for telescopes and microscopes. Apparently, I asked him for a microscope when I was very young and I really loved that microscope. My mom is a mathematician and my dad is a physicist, so science and research were always present in my life. I thought I was going be a mathematician when I was younger, as I really liked math. But then when I had biology classes, I really fell in love with biology. My interest in immunology came from seeing the public health crises and reading about research on HIV and Ebola, so I went to college wanting to do immunology.

Is immunology a popular topic to study in Brazil?

Most people in Brazil in immunology study parasitic diseases. But I went to the only lab that didn't study tropical diseases in my university and I worked on mucosal immunology and oral tolerance. I wanted to understand what is the immune system doing when you are not sick. But the science of parasitology is very interesting to me nowadays and I enjoy it so much. It's fascinating how your body responds to a specific pathogen and you can learn so much from it.

What inspired your move to study for a PhD in the US?

I was very fortunate. I had the experience of living in Switzerland for four years and Boston for one year while my parents did their PhDs and sabbaticals, and I always wanted to do my PhD abroad. It was also very common in Brazil, as the Brazilian government were keen to have people do their PhD abroad and come back to train their own scientists. By the time it was my turn, fellowships to do



left to right: Verena van der Heide, Etienne Humblin, Alice Kamphorst, Ashley Lu, Abishek Vaidya.

a full PhD abroad were not really available anymore as they had enough people in Brazil to train the next generation. It was more common for people to spend one year abroad training before their PhD defense in Brazil. But I really wanted to have the full experience. At that time, I was completely in love with dendritic cells and my master degree advisor in Brazil put me in contact with Michel Nussenzweig. I came to New York for a conference and scheduled to meet Michel. I guess he liked my enthusiasm for science and he was very supportive and encouraged me to apply for the PhD program at The Rockefeller University.

Why are you interested in chronic antigen stimulation, which seems harder to study than short term responses?

I know! These projects that we do, you know, are kind of crazy. We have to wait seven weeks to get chronic infection, and now that I'm studying how these different T cells are maintained, we have to wait seven more weeks. So, it's really not the ideal project for a new PI to start a lab on. But compared to acute infection and priming for vaccines, we know much less about chronic stimulation, and it is so common. It's so important in cancer, chronic infection and other diseases, such as transplant and autoimmunity. It's harder to model, but I think it's fascinating.

Some people are being advised to get a fourth COVID shot. Are there valid concerns about repeated vaccine shots leading to tolerance or T cell exhaustion?

There is evidence that people that waited longer between doses had a better immune response, but you have to have a balance. We were in a public health crisis and I'm not sure if we are out of that yet. So, it was a balancing act between getting as many people protected fast at a certain level that would prevent death, and not so much focus on long term responses. I do think public health decisions are different then scientific decisions and we need to be careful.

Most vaccines provide protection through B cell activation and antibodies. But if we consider CD8 T cells, they need to rest to mature into really good memory T-cells. People are saying the germinal centers from vaccines against COVID can persist for months, it's really impressive! We definitely need to study these sustained responses. There are more studies of T cells in chronic situations than B cell responses.

Your lab started March 2018, so the pandemic came at a critical time. How did you and your lab adapt?

I had a small group of people when the pandemic hit, and I had not received an NIH grant yet. So, it was a very stressful time for me. And I have two kids. One of them was in kindergarten, the other one was in third grade. While my third grader dealt pretty well with the shift to remote schooling, it was a nightmare for the kindergartener. They need a parent all the time there with them reading questions and helping. And it was very difficult.

My husband works for Health and Human Services and he was analyzing data from nursing homes – a very relevant topic at the time, so he was also very busy in his work. Luckily his work was remote and they gave him a lot of flexibility, but basically, we were working shifts. He was starting to work at 4:00am to be done at 11.00, while I would stay with the kids. Then I would start working in the afternoon and he would take over. And that's how our life was for more than a year. So, it was really tough.

I had to drastically reduce our mouse colony because there weren't going to be enough people to change the cages during the lockdown. And my research relied heavily on mice, so that was a big thing for me and definitely delayed my research programs a lot. Mount Sinai was great and it was amazing that we were back working in June 2020, which was very soon compared to other places.

Kamphorst rambling with her husband and two children.

We've been allowed to slowly ramp back up. But it had a huge impact because our work relies on different mouse strains and we need a lot of mice. I think it took until December 2020 when we actually came back to the right numbers of cages.

In summer 2020, my husband and I drove to his mom's house in Atlanta. After one week, I flew back to work on my R01 grant and my family stayed. We spent four weeks apart, and I guess it was worth it because I was able to get my R01 funded. I feel very proud of it because I was able to get it done despite a really tough year, with massive obstacles.

How should academic institutes balance more fundamental scientific research and clinical discovery?

One of the reasons I went to Rafi's lab for my post-doc, was his research in mice, non-human primates and people. I started my research there working in mouse models with chronic infection but I wanted to have a research project with human samples as well. I was working on the PD1 pathway and then the clinical trials with PD-1 blockade started in cancer patients. So it was a huge opportunity and we were able to find great clinical collaborators. If you have nice findings in mouse models but then can show that it happens in people as well, it's really much stronger evidence that you're asking an important question.

The reason I joined Mount Sinai specifically was because they were very supportive of a young PI that wanted to do both models and human work. We still do a lot of basic mechanistic studies in immunology in PrIISM, but because of Miriam's leadership, medical background and her vision for the Institute, at the end of the day, we are addressing the big questions of disease in humans.

ALL THE IMMUNOLOGY THAT'S FIT TO (PRE)PRINT

The preprint club turned 1 this year.

COVID-19 proved the importance of preprints and how they complement peer-reviewed journals, but also highlighted their limitations. PrIISM students, postdocs and faculty were the first to work together as a community to critically evaluate many SARS-CoV-2 preprints with the aim of accelerating the succinct communication of sound scientific findings. Now, we have joined forces with other universities to create the first global immunology preprint journal club to assess up-and-coming trends in the field of immunology.

Early career immunologists from Oxford University in the UK, the Karolinska Institute in Sweden, and PrIISM meet once a week for the preprint journal club. We present two recent preprints, collectively score them on Novelty, Significance and Scientific Demonstration, write corresponding reviews that are posted online, and publish monthly highlights of the best preprints in *Nature Reviews Immunology*. We want to test alternatives to current peer review approaches and make good use of all the brainpower invested in journal clubs around the world. What we've achieved so far: 50 preprint reviews posted on www.preprintclub.com; 18 publications highlighted in *Nature Reviews Immunology* and now listed in a specific Preprint Watch section; the creation of a new Community Review section on BioRxiv that directly links to our website.

Where do we go from here? We expand! The Karolinska Institute recently joined the project. Now another journal, *Nature Reviews Cell and Molecular Biology*, is looking for new early career groups to start a clone of our initiative, but focused on cellular and molecular biology. Spread the word!

Location, Location, Location.

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For example, when the windshield wiper was made, people probably understood the need for a method of clearing windows while driving in the rain. But when the rear window wiper came about, people perhaps didn't realize they needed it until it was invented. Similarly, with certain technologies, only when it is invented do others see how it fills a critical gap in the technology space and that they can now use it to make many new discoveries. In addition to the innovative technology and novel findings, both Maxime and Sam agree that witnessing how a group of people can come together to implement such a project was one their favorite parts of working on it. **"No one can do it alone," says Maxime. Each person's contribution was essential to the success of the project, he says. Each and every author had a unique contribution, and no matter how small, what "they did, only they could've done."**

So what is next for Perturb-Map? Brian intends to use the technology to unravel more biological phenomena, such as identifying and understanding the immune regulators of tumor composition and heterogeneity.

The Perturb-map technology comes on the heels of the 32-year quest to read the complete human genome sequence. Though we now have the ability to read the entire human genome, we really only know how to interpret some of the story. Some sentences within the book are in their own unique language, and fundamental research in biology is key to understanding it all. Technologies such as Perturb-map will accelerate our progress towards understanding the human genome. In the tumor immunology space, Perturb-map will propel the development of targeted therapies for cancer, and further our understanding of the causes of other diseases.

Recent PrIISM Publications

Single cell atlas of human lung cancer patients reveals immune cell activation module associated with responses to immunotherapy

***Cancer Cell,* December 2021**

With advances in sequencing technology, scientists can now rapidly profile the genomes of human tumors. Yet most centers sequence only a few thousand cells from a small cohort of patients, limiting the discovery of new therapeutic targets.

By leveraging the tight collaborative relationship between PrIISM and surgeons in the lung cancer screening program at Mount Sinai Hospital, Dr. Miriam Merad's group performed single cell CITE-seq of thousands of immune cells from thirty-five lung cancer patients. The "depth of cellular profile built a great and strong database," says Dr. Merad, "This is a textbook that we have, and we all have to look at it". The results are published in the Dec. 2021 issue of *Cancer Cell*.

Using this rich dataset, PrIISM MD-PhD student Andrew Leader defined a lung cancer activation module (LCAM) in the specific immune cells infiltrating tumors that render them more responsive to immunotherapy. When he dove deeper into the data, Andrew found two distinct macrophage groups: one resembled monocyte-derived macrophages (MDMs), the circulating "inflammatory macrophages" that make their home in tissues at the time of injury. The other was tissue resident macrophages (TRMs), the alveolar macrophages seeded in the lung during embryonic development. TRMs were on the tumor's side: they were close to tumor cells and facilitated tumor growth by causing the cancer cells to become invasive, and the TRMs harkened regulatory T cells to help tumor cells evade killing by cytotoxic T cells. MDMs were more prominent in late tumors, which suggests that TRMs are the major players promoting tumorigenesis.

Macrophage-targeting therapies are gaining traction in cancer, and this study pushes the idea for targeting tissue-resident macrophages with the LCAM profile. "These databases are so important. We should continue to expand, and profile and share. It is an example of how much more you can learn," says Dr. Merad. The authors plan to extend to other cancers, and the large hepatocellular carcinoma and colorectal cancer programs at Mount Sinai are conducive to a similar large-scale study. The overall model is to deeply profile the tumor microenvironment, then probe it functionally in mouse models, and identify therapeutic targets. Initiating clinical trials to translate the findings andsave patients' lives is the ultimate driver of this research strategy. **"When you are driven by the impact in patients, you will build elegant models and want to prove to yourself that you are on right path. I think we should do science that way, always." says Dr. Merad.**

Loss of anti-viral protein identified as cause of autoinflammatory disease leading to new treatment

***Cell*, August 2021**

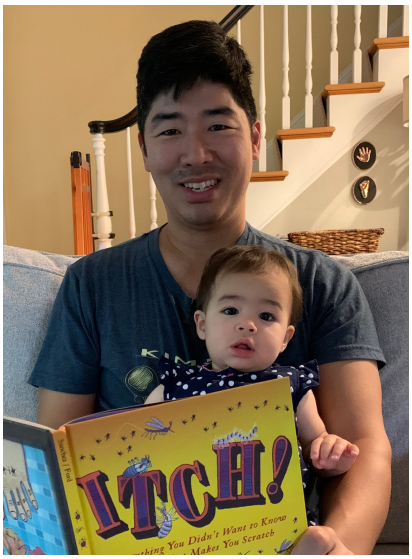
Mice lacking functional TANK binding kinase 1 (TBK1), a protein critical for defense against viruses, die in utero. A recent study published by Justin Taft, a PrIISM PhD student in Dusan Bogunovic's lab, identifies biallelic loss of the TBK1 gene in humans with an unusual autoinflammatory syndrome.

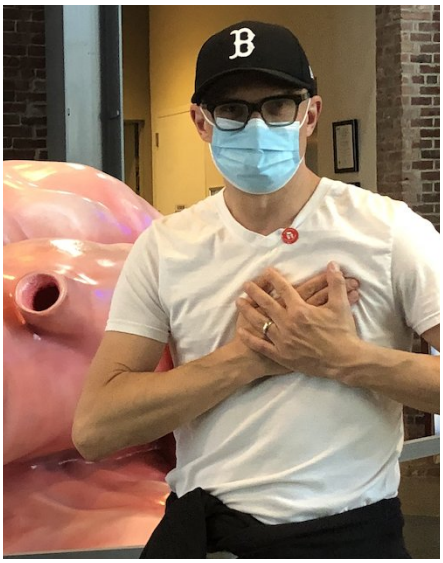
Dr. Iris Hollink of Erasmus University Medical Center in the Netherlands initiated this study by contacting Dr. Bogunovic and describing two patients experiencing symptoms similar to that of type-I interferonopathies but with no interferon signature. Type-I interferonopathies are due to the overactive ringing of the cellular alarms intended to recognize viral intruders, which leads to autoinflammation. Steroid treatments were not doing a good job of keeping the patients' symptoms in check, so their physicians were in search of the underlying cause to find a more permanent solution. By whole exome sequencing and subsequent variant analysis of the patients' genomes, the group had identified genetic changes in TBK1 that were equivalent to complete absence of the gene. So how could loss of a supposedly key kinase for interferon responses result in an autoinflammatory disease that looked like overactivation of the interferon pathway?

Justin found that the patients were not susceptible to viral infection because the related kinase IKKε compensated for TBK1 loss to allow for IFN-I signaling. Moreover, the cause of their autoinflammation was increased RIPK1-mediated cell death by necroptosis, a type of cell death that is messy, sending cellular debris everywhere that alerts the immune system for a clean-up. Necroptosis is triggered by TNF signaling, but is regulated by TBK1, so goes unchecked in these patients. The team informed the physicians that the patient's phenotype was due to the TNF-related function of TBK1, and that they should try an anti-TNF drug already on the market. Shortly after starting the drug, the first patient had a miraculous remission of her symptoms. **"I remember when we got the email that she was doing better," Justin recalls. "That was really gratifying."**

This study was a unique way to uncover the contrasting roles of a gene; often mouse models are needed to further characterize a gene's function, which can be complex and time consuming, but "when we have people," namely patients with monogenic diseases, "we don't need to make a mouse," says Justin. Now that these mutations have been profiled, and with the widespread use of genetic sequencing in the clinic, more patients can be identified. "The more you look, the more you find," says Justin.

WELCOMING NEW PrIISM FACULTY MEMBERS





Brian Kim, MD PhD

Scratching the surface of neuro-immunology

Prof. Kim joined ISMMS as Director of the new Mark Lebwohl Center for Neuroinflammation and Sensation, established January 2022.

Prof. Kim is a world leader in the new field of neuro-immunology and neuro-inflammation, which is revealing how the peripheral nervous system that controls our senses and ability to perceive the outside world is intimately intertwined with the immune system. He is interested in how this can be targeted to alleviate human suffering from diseases such as itch and dermatitis.

Fil Swirski, PhD

Getting to the heart of immunology

Prof. Swirski joined ISMSS in July 2021 as the inaugural Director of the new Cardiovascular Institute, launched in summer 2021.

Prof. Swirski has published many ground-breaking studies that show how inflammation and macrophages drive atherosclerosis. The Swirski lab now explore how lifestyle factors and life experiences, and how we respond to them, influence cardiovascular health and disease via the complex communication pathways between the brain and the peripheral immune system.

Diego Chowell, PhD

Math counts in immunology

Dr. Chowell joined ISMMS as a new assistant professor in the Department of Oncological Sciences, in April 2021.

Dr. Chowell uses computational approaches like machine learning to predict how patients with cancer will respond to immunotherapies. The Chowell lab is also harnessing the tools of computational biology and experimentation to decipher the molecular determinants of immune recognition and dissect the reciprocal interactions between evolving tumor genomes and their host immune ecosystems.

Articles contributed by Miriam Saffern, Nicolas Vabret and Marie Anne O'Donnell.

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