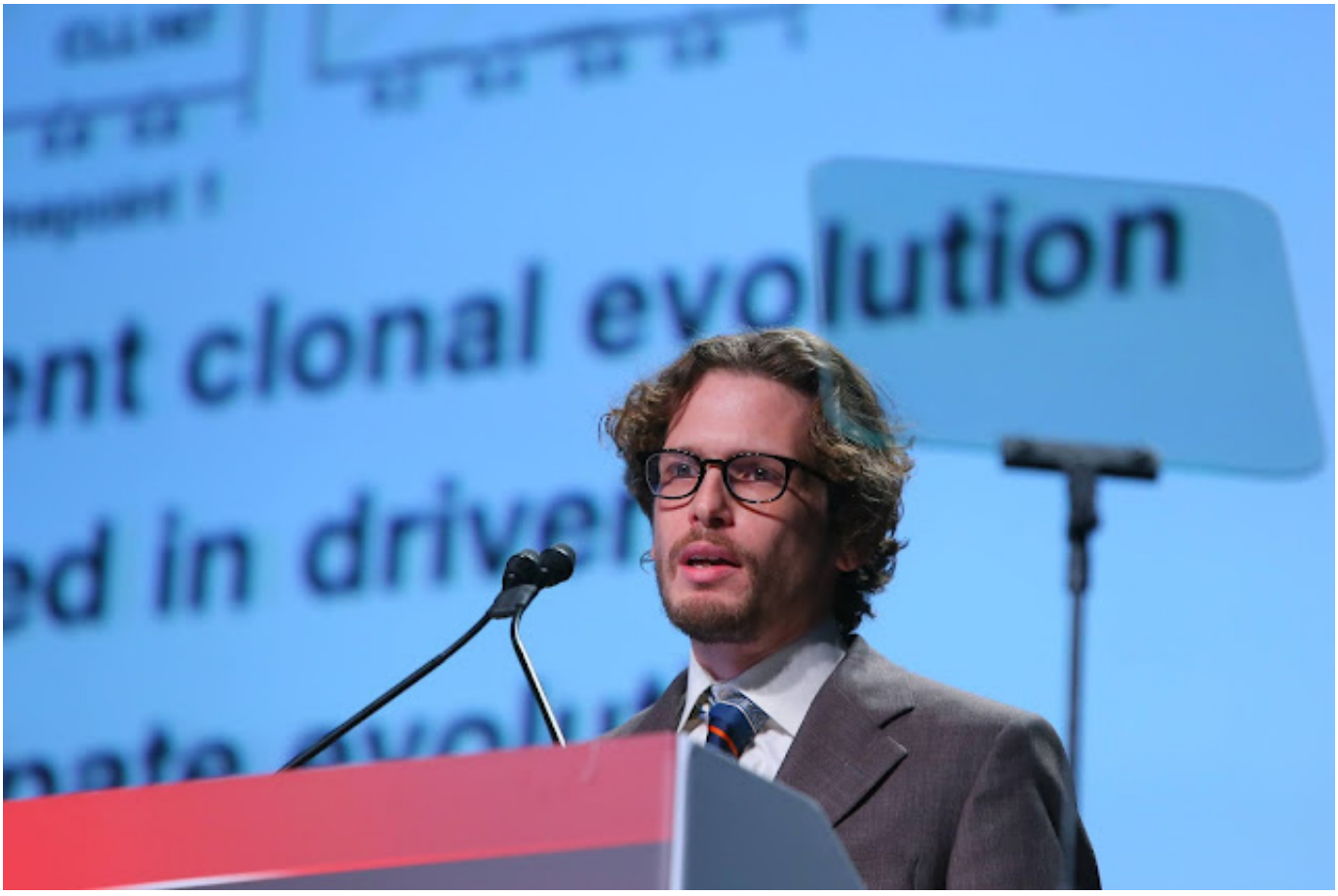
simply blood
Deconstructing Blood Cell Research
Building the Hematology Community

2021 Interview Spotlight Series: Part I

- June 07, 2021

This week on Simply Blood we are kicking off our 2021 Interview Spotlight Series. In Part I we are featuring the ISEH 2021 New Investigator's Invitee: Dan Landau, M.D, Ph.D. Here, Dr. Landau answers questions about his scientific passions, unusual but highly successful career path, mentorship and more. Interested in hearing more about Dr. Landau's fascinating work? Don't miss his session at this year's ISEH Virtual Scientific Meeting!



1. What is your key scientific question? What do you consider as your major contribution to the field over the past 5 years?

The lab's key scientific question is exploring the fundamental principles of human somatic evolution. We are fascinated by the realization that the trillions of cells in our body continuously evolve throughout life, with significant implication to human health and disease. Cancer represents an extreme case of human somatic evolution where in a "runaway process" cells evolve more rapidly at the expense of the multi-cellular host. Our goal is to generate a comprehensive 'information theory' of somatic evolution, tackling a fundamental gap in evolutionary biology at the intersection between multicellular and unicellular life. Beyond the basic science aspects, as a physician-scientist and an oncologist I seek to harness this knowledge to design the next generation of therapeutic algorithms, anchored in data science principles, and directly addressing somatic evolution.

Over the past 5 years since I have started my independent group in New York, we strived to radically expand our understanding of somatic evolution. We developed new ways to predict and track cancer evolution using genome wide screens and the application of machine learning to ctDNA (Bolan et al, Cell Systems, 2019; Zviran et al, Nature Medicine, 2020). We have shown that cells diversify not only genetically but also epigenetically throughout the process of somatic evolution (Pastore et al, Nat Communications, 2019; Pan et al, Cancer Discovery, 2021). This realization motivated us to pioneer novel multi-omics sequencing technologies to discover how somatic mutation interact with epigenetic and transcriptional identity at the level of the single-cell – the atomic unit of the evolutionary process (Nam et al, Nature, 2019; Gaiti et al, Nature, 2019; Chaligne et al, Nature Genetics, in press). Finally, we are particularly excited to expand this perspective beyond cancer to clonal mosaicism in normal tissues, as a window to the earliest phases of the neoplastic process (Izzo et al, Nature Genetics, 2020; Nam et al, Nature Review Genetics, 2021).

2. What were the main stages of your career path and what have you learnt from each of them?

I had a somewhat unorthodox path. I first trained as an MD in Israel, and then served as a physician in the air force for four years. The feeling of attending in the hospital at the height of COVID crisis in NYC this past year, reminded me a bit of this period, in the sense of treating patients despite a sense of personal risk.

I then went on to complete clinical training at Yale in medicine and in hematology and oncology on the physician scientist track. I was fortunate to work and train with exceptional humans and physicians, like Thom Duffy and Peter Marks. I have learned so much about clinical medicine as an art, and even more importantly I learned what true dedication to patient care should look like. I also learned to see the work of an oncologist as a privilege. To be able to help patients, even if ever so modestly, to shoulder this unimaginable burden. As oncologist you witness the full spectrum of human emotion, the good and the bad, all heightened due to the proximity of death. Being able to help, even if only with a kind word, or a hand on a shoulder is an incredible privilege.

After completing the clinical part of my training, I was looking for a lab to train as a scientist. I interviewed in some amazing labs but didn't quite find what I was searching for. Although I am not sure at the time I was able to put it in words, I think what I was missing was the "systems" perspective. I then heard (by chance) a talk by Nir Hacohen from the Broad about an siRNA screen and was blown away by the ability to interrogate a biological phenomenon systematically. I decided to pursue science training at the Broad institute and DFCI, which was a tricky path for a person in a Yale training program. Although there was naturally quite a bit of opposition, at the end of the day, I had strong advocates in both institutions that saw their mission as supporting trainees in pursuing their passion, to the best degree possible.

This was followed by an amazing period of learning and growth at the Broad. I truly felt like a kid in a candy store. Despite a general call to reason not to spread too thin, I was continuously swept up by curiosity and recruited more mentors to my mentorship family. Starting with Catherine Wu, my primary mentor in cancer biology, then learning the ins and outs of cancer genomics with Gaddy Getz, epigenomics with Alexander Meissner and mathematical modelling with Martin Nowak. Without consciously aiming for it, I came out with a unique inter-disciplinary training that allowed me to formulate a vision to develop work on somatic evolution. There were many others who contributed incredibly generously of their time to help cultivate ideas and hone professional growth (Brad Bernstein, Levi Garraway, Tod Golub, Jesse Boehm, David Weinstock and Jay Bradner are just a few names that come to mind out of a much longer list). Even more so, I was patiently mentored by my peers, who were kind and generous as I took baby steps throughout this learning process (Scott Carter, Mike Lawrence, Michael Ziller, Ivana Bozic to name but a few). When I look back, I am struck by the sense of intellectual freedom and generous collaboration, where a trainee's spontaneous knock on the door and a crazy idea are always welcomed.

In 2016, I started my own research group at Weill Cornell Medicine and NYGC. It was a bit intimidating to start a group in a completely different environment. Lots of self-doubt. I knew that we would need to reinvent ourselves to a large degree, rather than go on to pursue the next obvious steps of my post-doctoral work.

What have I learned from these different stages? I am struck by how limited my knowledge was at each step (much more limited than students starting out in my lab), and how much serendipity and chance actively shaped the path. But nonetheless, there were certain principles or foundations that were there as trusted (often unconscious) guides and friends. Let curiosity and passion sweep you forward, even in directions that are not always the simplest to follow. At the fork in the road, always choose the road that is rising. The one that challenges you most, where the learning curve is steepest. Find good people along the way, ones that share your basic values and motivations, ones that are generous with their time and creativity, and trust that these connections will lead you to the right paths (even if you can't always see these clearly ahead). Challenge yourself to make sure that your work is unique at every step of the way. Are you truly bringing a new perspective to a problem you care deeply about?

3. What is the recipe for building such a successful research program in such a short timeframe? What advice would you give to early career researchers trying to set up their own laboratory?

Thank you Alba and Dawn for the kind words. In many ways, our research program exceeded my own hopes when starting out, and there is still much more to do, much more to learn. I would love to claim some magical recipe, but honestly, there is so much that is owed to pure good luck and so much that is owed to others. Fantastic trainees that were willing to take a bet on a new lab with all of the risks involved. An environment with never ending willingness to support and collaborate. And just a lot that is owed to how the ecosystem supports new labs. Whether it is funders and review panels willing to take risks on new ideas, or whether it is the scientific community at large that embraced our work and helped move it forward.

If I had to single out some features that helped, I would start by saying that investing in recruiting talented and driven individuals is key. Once you do, give them the independence and support to shine, so that the sum will be far greater than its parts. Another key is to challenge ourselves to pursue projects where we can offer something that is orthogonal to the field. Innovation, whether it is in technology development, novel computational perspectives, conceptual biological innovation, or ideally all three mixed together make for great (and fun) projects. Lastly, embrace the risk that comes with bold ideas. Especially for a new lab, it is better to take risks and fail than to not take risks. Ido Amit once told me early on, that if you don't get "burned" by failure it may mean that you didn't take enough risk. A new lab is a lot like a start-up company, and the start-up funding is a clear mandate to innovate.

Finally, I would pass on advice that I received from Eric Lander just before starting out. To focus on building the right lab culture. Lab culture is the single most important feature that needs to be set early on, and one that is hard to change later. Of all of our achievements, I am proudest of our culture. A culture which values collaboration, rigor, passion and creativity.

4. How do you integrate your various scientific commitments (academic-based research, technology development, start-up company, clinical duties), and how do each of them contribute to your vision?

Great question… I am still trying to figure this out myself!

I find that I need to be able to focus and dive deeply into the subject matter to really be able to contribute and learn. This also means giving up on opportunities and knowing to say no – in order to cultivate what is really at the core of the work. In the lab, I strive to be very upfront about engagement, and safeguard myself, as well as trainees, from over spreading. We want to pursue ambitious goals and pursue them to

the highest level. This requires focus. Of course, none of this can really work without a team of exceptional scientists in the lab who are independent thinkers and incredibly self-driven. We constantly help each other and learn from one another.

On the start-up front, I am really excited to be able to take our work and build towards concrete clinical impact. As someone who is often immersed in basic and conceptual work, the ability to leverage our work for clinical benefit is an extraordinary privilege. Fortunately, the team, led by Asaf Zviran who pioneered this work in the lab, is truly extraordinary.

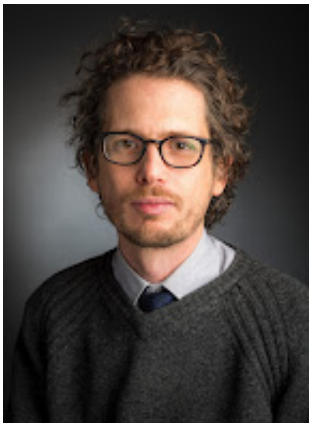
Clinically, my contributions are limited to inpatient blocks on the transplant service. I really value this time with patients, but also made the difficult decision not to have an outpatient clinic. I knew that patients will always come first and that it would limit the ability to realize our vision on the lab front. My clinical engagement is made possible by a team of dedicated, capable and knowledgeable professionals that are always around to troubleshoot and consult. I could not have done this without this incredible support.

5. What is the key to manage such an interdisciplinary team with researchers from very different backgrounds?

A common thread in the lab is that the projects we pursue always take us out of our comfort zone, always push us towards new learning and growth. We have yet to pursue a project that was an obvious next step. I think those projects have a ton of value for really deep science and hope that we can do more in the future, but for a new lab, the priorities were different. This also meant that we need to have people bring in different expertise and work collaboratively. Even more importantly, to actually lead collaboratively. This is hard to do and a testimony to the unique make-up of the scientists in the lab, who always put science first. This allowed us to build a unique portfolio of research that deeply integrates wet lab tech development, deep biological insight and cutting-edge computational work, with lots of input and guidance from great collaborators in the community.

6. What do you value the most in a student or member of your team?

In the spirit of the previous question, I value different things in different people and often think of my role as figuring out how to create the right environment to allow everyone to succeed and grow as scientists. Generally speaking, creativity, collaboration, independent thinking, attention to detail, and scientific curiosity are aspects I value most. I have been fortunate to work with people who embody these values to the highest level and know how to work together to bring them to life in our work.



Dan A. Landau, MD, PhD
Associate Professor of Medicine, Division of Hematology and Medical Oncology,
Associate Professor of Physiology and Biophysics,
Weill Cornell Medical College.
Core Member,
New York Genome Center.
landaulab.org

Interviewed by Alba Rodriguez-Meira of the ISEH Publications Committee & Dawn Lin of the ISEH New Investigators Committee

Annual Meeting | Career Development | ISEH | Life as Scientist | New Investigators | Research | Technology

Enter Comment

Popular posts from this blog

ISEH 2025 Society Award Winners

- *March 11, 2025*

On behalf of the Awards Committee, ISEH would like to congratulate the recipients of the 2025 ISEH Society Awards which will be presented at the ISEH 54th Annual Scientific Meeting . Donald Metcalf Award Winner - Constanze Bonifer The recipient of the 2025 Donald Metcalf Award is Dr. Constanze ⋯

READ MORE

Message from the President: 2021 Society Updates

- *March 25, 2021*

Dear Friends and Colleagues, I write this message reflecting upon what was an unprecedented time for hematology and hematology researchers. Looking back on last year, I am truly amazed by how our Society reacted to our member's experiences with lab shutdowns, socioeconomic upheaval in reaction ⋯

READ MORE

Lab Spotlight: Vanuytsel Lab

- *November 14, 2024*

Each month, Simply Blood spotlights a lab contributing to the fields of hematology, immunology, stem cell research, cell and gene therapies, and more. Get to know groups doing cutting edge research from around the world! This month, we are featuring the Vanuytsel Lab which is based out of the Center for ⋯

READ MORE