Lab Spotlight: Ott Laboratory

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Simply Blood Lab Spotlight

Each month, Simply Blood spotlights a lab focused on the research of basic hematology, immunology, stem cell research, cell and gene therapy, and other related aspects. Get to know these different labs around the world! This month, we are featuring the **Ott Lab at Massachusetts General Hospital**.

How long have you had your lab?

We opened the lab here at the MGH Cancer Center in September, 2017.

How many members make up your lab? Students/postdocs?

Currently the lab is staffed with a lab manager and two research technicians - one in charge of running high-throughput small molecule screening assays and another in charge of functional genetic assays using the CRISPR/Cas9 gene editing technology. We also have a computational analyst in our group who is responsible for processing and analyzing genome-

wide transcriptomic and epigenomic datasets. Currently we are in the process of recruiting several postdoctoral fellows, including a synthetic organic chemist and a molecular biologist to lead several new projects in the lab.

What is the major research theme of your lab?
Our major goal is to discover gene expression control factors that are uniquely essential for malignant lymphoid cell growth and survival, and to develop methods to target these factors pharmacologically. Recently there has been a convergence of technological and pharmaceutical innovations that have revealed chromatin/epigenetic modulators and transcription factors as 'druggable' with synthetic small molecules, and many of them are currently being deployed clinically for the treatment of lymphoid malignancies (e.g. lenalidomide in myeloma, targeting the TFs IKZF1 and IKZF3; inhibitors of the histone methyltransferase EZH2 that are being evaluated in EZH2-mutant lymphomas; BET bromodomain inhibitors currently under clinical study in lymphoma, leukemia, and myeloma). We believe that these medicines are just the tip of the iceberg, and so our lab aims to expand the 'menu' of early-stage chemical tool compounds for use in pre-clinical target interrogation and validation studies. We employ high-throughput screening, structure-based medicinal chemistry, and systems-oriented approaches (genome-wide transcriptomics, chromatin state measurements, proteomics) in order to understand the mechanism of action of new compounds we synthesize, nominate potential response biomarkers, and anticipate the clinical contexts in which our tool molecules may be developed as therapeutics.

What is the most exciting project in your lab right now?
We have begun a number of really exciting projects over the last several months. One project we are very excited about is using genome-wide chromatin accessibility measurements of primary myeloma cells to construct transcription factor networks that define the disease. We're coupling these measurements with CRISPR-based editing of myeloma-specific enhancers to identify both the transcription factors and individual genomic regions that are essential for myeloma cell survival. We have already identified a number of candidate factors, and are exploring some new tool compounds that may selectively perturb their activity in myeloma disease models.

What facilities or equipment does your lab absolutely depend on?
As a multidisciplinary lab, we depend on a lot of infrastructure here at MGH. When the lab started we immediately set up our tissue culture facilities, our own node on the MGH computational cluster, chemistry fume hoods, and high-throughput flow cytometry. As the lab matures, we will begin some in vivo work using mouse models of lymphoma and myeloma and so will utilize the fantastic animal facilities here at MGH.

What advice do you have for new investigators just opening their lab?
First, there are a lot of different ways to find success as the head of a laboratory - and there certainly is no one piece of advice that I can give that will be the single key. In this job, to be successful, you'll have to be good at a lot of different things. But one thing that I have found

very useful as we have launched the lab is to deliberately schedule writing time. There is a lot to do in the lab to get projects and experiments up and running (getting equipment ordered and functioning, troubleshooting protocols, hiring the right personnel, meeting your new faculty colleagues), and all of those things do need to be priorities. But I make sure to schedule several hours of uninterrupted writing time each day - whether I'm writing a grant application, a draft for a paper, or even just a new project plan for myself - the focused act of committing compelling ideas to text on paper is an absolutely essential skill and is one of the most important things an investigator will have to do throughout his or her career. So I wanted to make sure to build these habits early.

What was the most exciting part about starting your new lab?
Starting new projects! It is an incredibly satisfying experience to hire a new scientist, suggest a new project or idea, and then follow her early progress as she begins to work independently. It really is a joy to watch your scientific ideas come to life.

Does your lab attend the ISEH annual meeting?
We have heard so much about the incredible ISEH community. While we have not attended ISEH yet, we aim to become a part of and contribute to this community in the very near future.

How do members of your lab celebrate accomplishments?
We are lucky that our laboratory is located in a vibrant neighborhood right on the Boston Harbor. When we celebrate, we'll go to a restaurant on the pier or to a local brewery. We're also planning a lab ski trip, perhaps when we start publishing our first manuscripts.

Does your lab have any fun traditions?
Annually we will participate in the MGH Cancer Center retreat, an ongoing tradition where new science from across the Center is presented at a venue outside of Boston (like Cape Cod, or up in the New Hampshire mountains). Also, once every few months the group will go out to dinner together after a day of work in the lab. We don't do this for any specific special occasion, but I think it is important for us to regularly spend some relaxed time together beyond our scientific group meetings - we'll talk a little science, review some recent literature, but also catch up on life outside the lab.

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http://www.massgeneral.org/research/researchlab.aspx?id=1768