Filip Swirski

Understanding How Inflammation Both Heals and Hurts the Heart

Jaclyn M. Jansen

Atherosclerosis is the most common cause of heart disease, but the condition is largely misunderstood. When the average person thinks of atherosclerosis, they imagine blood vessels narrowed by the buildup of thick, sticky fats, much like a clogged kitchen drain. In reality, that's only half the story. The immune system also plays a part: in trying to heal the lesions, it reacts to plaques with inflammation, which further hardens and narrows blood vessels. This deeper understanding of how atherosclerosis arises offers new avenues for both treatment and prevention of heart disease, the leading cause of death worldwide.

Filip Swirski, Research Scholar and Principal Investigator at Massachusetts General Hospital and Associate Professor of Radiology at Harvard Medical School, is a leader in studying the role of the immune system in cardiovascular disease. Trained as an immunologist at McMaster University, he is now applying his knowledge of innate immunity and inflammation to the study of atherosclerosis and, more recently, other diseases, as varied as sleep disorders, sepsis, Alzheimer, and colitis.

As a postdoctoral researcher, he began to explore the role of leukocytosis, and monocytosis in particular, in atherosclerosis. Monocytes are part of our innate immunity, the body's ancient surveillance system that flags dangers, pathogens, and injuries. Swirski's work demonstrated that these inflammatory cells are recruited to growing atherosclerotic lesions. He found that monocytes accumulate continuously as the lesions progress.[1] His work was among the first in a growing field that has defined the essential role of monocytes and systemic inflammation in atherosclerosis.

Filip Swirski

Monocytes usually mature into immune cells known as macrophages. These scavenger cells are responsible for devouring invaders and other dangers. But in the case of atherosclerosis, this protective mechanism backfires. Macrophages devour lipid plaques in the blood vessel wall, spurring inflammation, and narrowing the lumen. Swirski identified a distinct subpopulation of monocytes that develops into these macrophages, a key component of the inflammatory response.[2,3]

Swirski went on to further examine how these distinct subpopulations of monocytes arise. The majority of monocytes develop in the bone marrow, but Swirski identified a pool of these cells that are generated in the spleen as an additional source and infiltrate atherosclerotic lesions.[4,5] He also uncovered 2 monocyte populations that are required for healing, in collaboration with Matthias Nahrendorf.[6] Taken together, his work offers broad insights into the production, recruitment, and mobilization of inflammatory cells to atherosclerotic lesions and the infarcting myocardium. Beyond these cardiovascular disease studies, however, Swirski also identified new mechanisms in sepsis and a pathway by which the body recycles iron.[7–9]

In a recent conversation with *Circulation Research*, Swirski described his path into science, from his early childhood in Communist Poland to his education in Canada. His interests are unusually broad, with a passion for both science and the arts. But his deep focus has led to a uniquely modern approach to research and academic life.

Where Did You Grow Up?

I was born in Poland behind the iron curtain. I lived there until I was 9 years old when my parents were able to escape Communist Poland. We moved to West Germany for a year and then immigrated to Canada. We settled in the Toronto area, and that's where we stayed. Even though I was born in Poland, I would say I grew up in Canada.

What Was It Like to Make Such Big Moves at a Young Age?

The most difficult transition was from Poland to Germany. I was very comfortable in Poland, and Germany was a completely different country. When we came to Canada, I was already hardened by the experience—learning English wasn't as hard because I

(*Circ Res*. 2018;122:1334-1337. DOI: 10.1161/CIRCRESAHA.118.313204.)

Circulation Research is available at http://circres.ahajournals.org DOI: 10.1161/CIRCRESAHA.118.313204

already spoke Polish and German. It was certainly not easy, but I had a very loving family.

Why Did Your Family Move?

They were propelled by a combination of factors. My dad had a very serious car accident when I was 7 years old, and this was, of course, a major upheaval that set in motion a number of things. Poland was under martial law. It was a very dim and grim time in Poland. I was only 9 years old, so I didn't understand fully then, and I'm sure I still don't understand all the reasons.

They had the opportunity to immigrate. We had family members in Canada, and my dad had visited for a holiday as a teen. He loved it. It was always a place that my parents talked about moving if they could.

With Moves to Two Different Countries in One Year, How Did You Keep Up With Schooling?

My education was quite good. School in Poland was stricter than in Canada, with more emphasis on rote memorization. Math and science were more advanced. Because of that, when I came to Canada, I was strongest in math. I didn't speak English, but the math in grade 4 was what I had learned a year before in Poland. It made me feel comfortable and very confident.

In Canada, there was a greater emphasis on personal exploration. I remember my parents were amazed when I came home with an assignment to choose a country and then profile it. I chose Australia. That would have been unheard of in Poland. You were told what you needed to learn rather than exploring on your own. That was a key difference.

In Retrospect, Did You Prefer One Form of Education Over the Other? Was One Better Preparation for the Career of a Scientist?

I think it's very important to cultivate creativity. That's essential. At the same time, it must be balanced with learning the critical things that you need to know. You need the background and foundation to allow your creativity bear the most fruit.

When Did You Become Interested Science?

As far as I can remember, I've always been interested in the physical sciences and the natural world. But I've also always been very interested in the arts. I participated in theater and dance. I play music and I love literature. I've had many interests, but immunology and the natural sciences won out.

I sometimes wonder whether my interest in the natural sciences was catalyzed by my dad's accident. I was only 7, and I realized that perhaps my father survived because of the doctors and nurses who helped him. It was their knowledge about how the body works that allowed them to treat him. The connection to medicine and human health is what won me over to science.

With Such Broad Interests, When Did You Narrow Your Focus on Science?

When I was choosing my university, I picked McMaster University in Hamilton specifically for the Arts and Science undergrad program. The purpose of the program is to give students a broad education, with equal emphasis on the arts and sciences. It is a wonderful program—exactly what I was craving.

In my third year, I took an immunology course and I immediately knew this was something I wanted to do.

As I finished my undergraduate courses, I felt torn in different directions. I was considering theater or even film school, but I had also done some laboratory work as part of my thesis. I got to know some of the faculty at McMaster as well as grad students and postdocs. I decided to apply to the graduate program at McMaster, and I was accepted.

But I was still unsure of what to do next—theater or science. In Canada, you have to first complete a 2-year masters before you start a PhD program. I decided to do the masters and then figure out what I wanted to do with my life.

When it came time to decide, I chose to just take my masters and leave science altogether. At the time, I was thinking I would do theater. I began writing my master's thesis, and as I confronted the possibility of leaving science altogether, I realized that I couldn't do that. Even now, I need to do science and cannot imagine doing anything else.

At the last minute, I called my supervisor and said I wanted to transfer to the PhD program. I've never looked back—I've never had any regrets. That was the moment that I made the decision to be a scientist.

Has Your Passion for the Arts Influenced Your Career As a Scientist?

They are obviously two very different careers, but my training in theater and the arts have been profoundly important to my career as a scientist. For example, as a scientist, it is important to communicate your work through writing and speaking. Theater has helped train me to communicate my ideas in front of people. My participation in the arts also involved a lot of writing. It is so important in science to be able to write well and convey your work in grant applications and papers. The arts were also a place for creativity, and I think that allowed me to grow as a scientist.

Do You Still Participate in the Arts?

No, I don't do any theater work or dance anymore—except maybe with my children at home.

I have a few other hobbies now. I run—for 20 years now. It isn't a competitive sport for me. I've done a half marathon and other races, but mostly I run for myself. It makes me feel good and I just love it.

I also cook. In many ways, it has replaced bench work for me. As a postdoc, working in the laboratory was soothing. It may sound strange, but cooking is similarly relaxing. I make many different types of dishes, but lately, I've been working on using a scientific method to perfect my hamburger. They've been getting better and better every time. Sometimes you can find a whole world of complexity in the things that seem to be the simplest.

Those are my primary hobbies. I love the ancient board game Go, and I play the piano a little bit here and there. But really, I'm a full-time scientist at this point.

What's Your Family Life Like Now?

I have a wife, Kaley, and two kids, Elinor and Tullin, ages 10 and 7. We also have a dog named Hercules. It's a full house!

My wife has a PhD in English. Right now, she is working as a medical writer and academic editor part time, which gives her the flexibility to take care of our kids. She works on science and economics papers and grants. She very much enjoys it.

My kids are very interested in science. Just this morning, my son had a show and tell at school. He brought in a conical tube and an ice bucket to show the other kids what a scientific experiment looks like. We talk about all kinds of things in the natural world. His favorite cell is the macrophage—for some reason, he finds them fascinating, but so do I!

How Do You Balance Your Life at Home and at Work?

This is very important to me. As a postdoc, I was working 12 to 15-hour days. It was very difficult to do anything else. As faculty, I'm not bound to the bench anymore, and I have the luxury of being able to be with my family. Weekends, for example, are time for my family—I don't go to the laboratory. It's not always easy because work is demanding, and there are all sorts of responsibilities, but it is a priority. And sometimes other things have to be pushed aside.

There is a metaphor about how you can think of life as four burners on a stove. One burner is for your friends, another for your family. One is for work, and one for health. You can't do all four of these extremely well—the best you can do with all of them is just ok. But if you remove one, then you can do the other three relatively well. If you do only two, you can do both very well. Or if you remove all three, you can be extremely successful in just one. For me, the priorities are family and work. Health comes in third. And friendship has become my fourth burner that I pay less attention to now.

How Hard Do You Work?

I don't think this is the right question. It should be not how hard but how intensely you work. We should not count hours but instead, measure concentration and focus. That is not to say that I don't put in 12-hour days when it is required. But it is the quality of work that is important rather than the quantity.

We have so many distractions all the time, and I try very hard to limit that. When it comes to writing a paper or a grant or even meeting with my team, I give it my undivided attention. When I write something, I shut off my email and my phone. I have a policy in my laboratory meetings that you do not look at your phones unless a baby is being born or you have a sick grandma. I try to cultivate this focus both in myself and my trainees. You can sit through a whole day and still be entirely unproductive. That is not helpful.

In some ways I am always at work: in the morning when I'm taking a shower I'm thinking about a problem; if I'm going for a run, I'm thinking about how to structure a paper or what question to ask. But I don't spend 12 to 15 hours in the laboratory every day like I did when I was a postdoc.

How Do You Spend Most of Your Time As a Principal Investigator, Now That You Are Largely Away From the Bench?

So much of our training during grad school and the postdoc years is about sitting at the bench and doing the experiments. We spend hours analyzing data, making figures, and if we are lucky writing about them. As I transitioned to an independent position, I stopped doing benchwork. My primary responsibility is to keep my laboratory going and publish papers. I have a lot of meetings with my team, analyzing and discussing data and projects, and writing. This is really my bread and butter, the essential components of my daily work.

But my research is balanced with participating in education and community service. Right now, I codirect a course Harvard Medical School called Immune and Inflammatory Diseases along with Mikael Pittet. It is required for first-year graduate students.

I'm also very active in reviewing grants. I am a standing member of the Atherosclerosis and Inflammation of the Cardiovascular System Study Section in the Center for Scientific Review at the National Institutes of Health. It's a 4-year tenure, and I attend study sections every 4 months.

I travel quite a bit to present my work at conferences or various institutions. I also participate in some of the administrative tasks of the hospital, serving on several committees. This includes the committee for fundamental research, which promotes basic, PhD research within the hospital.

Is It Hard to Handle So Many Different Responsibilities?

I love the diversity—there are so many different things to do. I think one of the beauties of this job is that you can really shape what you want to do. Some professors become very involved in administrative aspects of the institution because it is what they enjoy. Others enjoy being in the laboratory and continuing to do benchwork. I think it's possible to shape your career with the right mix of things. Overall, I love what I do.

What Advice Do You Have for Junior Scientists?

There are the classical elements of success, like hard work and a bit of luck. But in science, I think enthusiasm and perseverance are essential. This is not a career that you can do in a perfunctory way. You have to really love what you are doing. There are so many challenges in this career: scientific, administrative, and monetary. To keep going, you have to love the topic and have an unbounded enthusiasm for what you are doing.

You also need to have a little bit of impatience. In science, you are asking difficult, important questions and the successful researcher will be dying to know the answer. That can be very motivating. For me, it is the mixture of enthusiasm, perseverance, and impatience that has helped me along in my career.

Community is also very important. It is crucial to surround yourself with people who you can trust and with whom you can work. At work, my immediate community is my laboratory, where I aim to foster a spirit of openness. I am also very fortunate to be part of the Massachusetts General Hospital community and a broader community of friends and collaborators in Boston: Matthias Nahrendorf and Peter Libby among them. Finally, there's my community of fellow scientists at-large, many of whom are friends. Science is a group effort and it is important to cultivate this.

I think it is also important to mention that there's more to science than research. A PhD graduate has many more options beyond academia or industry. The key is to find a path that best balances your strengths and interests.

Are There Common Pitfalls Junior Scientists Should Avoid?

My biggest piece of advice is don't be married to your hypothesis. When you get your data from an experiment, your next goal should be to devise the best experiment to destroy your hypothesis. How can we disprove my idea? Eventually, after repeatedly failing to disprove a hypothesis, then maybe what you have on your hand is right. You've learned a bit of truth, a bit of knowledge.

Sometimes, people are too committed to an idea and want to pursue it at all costs. It can be difficult to walk away, but it is important that you do. I've seen people spend years and years holding on to an idea and they just can't let go of it. Just because you've put a lot of time into an idea does not mean that you should continue. Walking away doesn't come naturally, so it is important to maintain a healthy distance from your hypothesis.

Are There Any Personal Mistakes You've Learned From?

As you do experiments, you can only interpret them with the tools you have at the time. I always want to correctly interpret my data. But sometimes, as a project or a field matures, you realize that maybe your interpretation wasn't the best. But then you correct it. That's the beauty of science. It's self-correcting. So, we approach our questions with the best tools we have but always maintain a healthy reserve of skepticism.

Disclosures

None.

References

1. Swirski FK, Pittet MJ, Kircher MF, Aikawa E, Jaffer FA, Libby P, Weissleder R. Monocyte accumulation in mouse atherogenesis is progressive and proportional to extent of disease. *Proc Natl Acad Sci USA*. 2006;103:10340–10345. doi: 10.1073/pnas.0604260103.
2. Swirski FK, Libby P, Aikawa E, Alcaide P, Luscinskas FW, Weissleder R, Pittet MJ. Ly-6Chi monocytes dominate hypercholesterolemia-associated monocytosis and give rise to macrophages in atheromata. *J Clin Invest*. 2007;117:195–205. doi: 10.1172/JCI29950.
3. Robbins CS, Hilgendorf I, Weber GF, et al. Local proliferation dominates lesional macrophage accumulation in atherosclerosis. *Nat Med*. 2013;19:1166–1172. doi: 10.1038/nm.3258.
4. Swirski FK, Nahrendorf M, Etzrodt M, Wildgruber M, Cortez-Retamozo V, Panizzi P, Figueiredo JL, Kohler RH, Chudnovskiy A, Waterman P, Aikawa E, Mempel TR, Libby P, Weissleder R, Pittet MJ. Identification of splenic reservoir monocytes and their deployment to inflammatory sites. *Science*. 2009;325:612–616. doi: 10.1126/science.1175202.
5. Robbins CS, Chudnovskiy A, Rauch PJ, et al. Extramedullary hematopoiesis generates Ly-6C(high) monocytes that infiltrate atherosclerotic lesions. *Circulation*. 2012;125:364–374. doi: 10.1161/CIRCULATIONAHA.111.061986.
6. Nahrendorf M, Swirski FK, Aikawa E, Stangenberg L, Wurdinger T, Figueiredo JL, Libby P, Weissleder R, Pittet MJ. The healing myocardium sequentially mobilizes two monocyte subsets with divergent and complementary functions. *J Exp Med*. 2007;204:3037–3047. doi: 10.1084/jem.20070885.
7. Rauch PJ, Chudnovskiy A, Robbins CS, et al. Innate response activator B cells protect against microbial sepsis. *Science*. 2012;335:597–601. doi: 10.1126/science.1215173.
8. Weber GF, Chousterman BG, He S, et al. Interleukin-3 amplifies acute inflammation and is a potential therapeutic target in sepsis. *Science*. 2015;347:1260–1265. doi: 10.1126/science.aaa4268.
9. Theurl I, Hilgendorf I, Nairz M, et al. On-demand erythrocyte disposal and iron recycling requires transient macrophages in the liver. *Nat Med*. 2016;22:945–951. doi: 10.1038/nm.4146.

Circulation Research
JOURNAL OF THE AMERICAN HEART ASSOCIATION

American Heart Association®

Filip Swirski: Understanding How Inflammation Both Heals and Hurts the Heart

Jaclyn M. Jansen

Circ Res. 2018;122:1334-1337
doi: 10.1161/CIRCRESAHA.118.313204
Circulation Research is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231

Print ISSN: 0009-7330. Online ISSN: 1524-4571