An Interview with Dr. David Scadden, MD, Recipient of the 2019 ISEH Donald Metcalf Award

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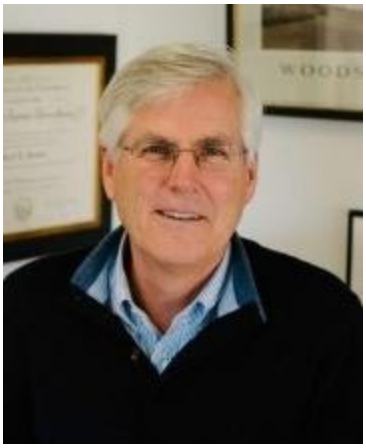
Interviewed by Stephen Loughran of the ISEH New Investigators Committee



If you had to pick one discovery, what do you think has been your greatest contribution to science to date?

How did you get into the field you are working on?

What advice can you offer aspiring new scientists?

What was the biggest challenge that you had to face in your career?

What do you think will be the next big trend in the field of hematology in the coming years?

Hoping to connect with Dr. Scadden in person?
You can do that in Brisbane at the 2019 ISEH Annual Scientific Meeting!

At the risk of being grandiose, I would like to think that my lab helped open up the field of niche biology. First, by using an engineered mouse to alter a specific subset of bone marrow stromal cells and showing a hematopoietic phenotype. And, second, by showing that perturbing a specific set of stromal cells leads to disordered hematopoiesis and myeloid malignancy. I think these studies helped define elements of hematopoietic niches and

perhaps, encouraged others to study mammalian niche biology more broadly. I don't think there were any in vivo studies defining a mammalian niche before the work from my and Linheng Li's labs.

I have a very practical orientation driven by my training as a physician so I was interested in hematopoiesis as a way to create more rationale treatments for blood disease; particularly in the setting of stem cell transplantation. Doctoring is horribly unsatisfying when done in the dark. I had to move more to the lab, not because I thought I could be a good scientist; I had no such pretensions; but because I couldn't stand saying "we don't have anything to offer" to patients.

Two things: 1. Ask for advice. I was shy and never wanted to bother anyone with my dumb questions or naivete about career choices. Now that I have plenty of white hair, I realize that most experienced people in the field enjoy helping junior people, love kicking around ideas and are happy to give guidance. I know I missed some key opportunities because I didn't dare ask for any. 2. Love ideas but don't fall in love with your own. Nimbleness of mind is a key attribute in science. You have to be willing to invest in creative solutions to big problems, but it is solving the problem that should steady you, not the particular idea you hatched. The mantra of 'stay focused' can also be a trap. 'Stay awake' may be more on target as you need to be alive to what the data tell you and where opportunities for new insight might reside; you need to change lanes now again to get anywhere.

I am a lunch-pail carrying physician who studied literature as an undergraduate, hardly the background of a scientist. I never thought I would do much in laboratory science and others' expectations were the same. But I knew I had to try because I watched my mother die by inches from cancer through my clinical training and so knew very well that what we had to offer was mostly useless. If it was going to change, I had to count myself among those hammering away. When I tried to get into big-name labs for a post-doc, I was repeatedly turned down. My early mentors thought I was mostly a clinical person and should do clinical research. I did manage to get a NIH physician-scientist grant that gave me a start and I gradually figured out how to get funding doing clinical research that allowed me to also do lab work. Eventually that worked out well enough for me to grow a real lab and build some momentum. I was lucky enough, believed in my goals enough, had support from my wonderful spouse enough and worked with and at institutions that were committed to research enough, that I could get through an inauspicious start.

I'd like to think that hematology will lead the way in going from mostly descriptive biology to predictive algorithms allowing us to control cellular events—a true and useful systems physiology. Right now we are still describing the parts at the cell and molecular level but have very little understanding of tissue biology. Where we have gained understanding about how specific molecules govern cellular responses that drive tissue biology, enormous benefit has been gained. Erythropoietin and G-CSF are great examples. Now we have increasingly

learned about specific genetic alterations misguiding cellular responses and tissue function. Soon we will learn about how to shift events within tissues to change events. We can only do that in tissues where we can understand the individual parts and how they function coordinately in a tissue. Blood is the place where the field has laid a fabulous foundation to make it happen. I think future gains will give us ways of predicting bad outcomes before they arise and possible tweaks to change their inevitability.

You can do that in Brisbane at the 2019 ISEH Annual Scientific Meeting!

Dr. Traver has graciously volunteered his time and talents for many sessions and events at the ISEH Annual Scientific Meeting. You'll find him:

- Giving the keynote speech and judging posters at the Pre-Meeting Workshop for new investigators.
- Delivering the closing keynote presentation in the McCulloch & Till Award Lecture.
- Meeting with new investigators as one of 11 renowned experts at the New Investigator's Meet the Exper Mixer.
- Mingling at the welcome reception, poster sessions, and social event!

But hurry - most of these popular events require preregistration and space is limited! So REGISTER NOW!