ASCB AWARD ESSAY

A Developmental Journey and Lessons Learned Along the Way

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A career in science is a journey of wonder and discovery. To succeed in science requires curiosity, perseverance, a good dose of luck, and wise guidance from those who have taken the journey ahead of you. We also need to use our science skills to contribute to public debate on complex issues of the day.

Being honored by the 2009 American Society for Cell Biology Women in Cell Biology (WICB) Senior Award has provided me with an opportunity to look back and examine the importance of mentorship and role models, both female and male, in my career. I am fundamentally a basic biologist, driven by my curiosity about how the world works. The question that has fascinated me for over 30 years is one that we can all relate to: How is it that complex, rational organisms such as ourselves can arise from a single cell, the size of a speck of dust?

Over the years my lab colleagues and I have explored many aspects of that question, using mice as our model system, and we've discovered more and more about the hierarchy of cell decisions that begins when sperm hits egg. Along the way we have contributed to the development of techniques for manipulating the mouse genome, helped identify key signaling pathways that control blood vessel development, and isolated novel stem cells from the mouse blastocyst. But I always return to the fundamental questions of lineage development in the early embryo, attacking the problem with new tools as they become available.

EARLY INSPIRATION AND GUIDANCE

A life in science is not a journey you take alone. At all stages, mentors are key. No one in my family had ever been to university, let alone undertaken a Ph.D. It was a female high school teacher who encouraged me to set my sights high and apply to Oxford University for undergraduate studies, and it was the sister of a school friend who first showed me by example that it was possible to have a career in research. At Oxford I attended lectures by John Gurdon on frog development and became fascinated by developmental biology. Chris Graham had just joined the faculty in the Department

of Zoology and gave some lectures on new approaches to studying the mammalian embryo. I decided there and then that this was a system with a great future. I joined Richard Gardner's lab in the Marshall Laboratory of Reproductive Physiology at the University of Cambridge for my Ph.D. in 1972. Richard had made a big impact with his studies on lineage development in the early mouse embryo, performed by injecting cells into blastocysts, and I became his first graduate student.

The Marshall lab at that time was really at the center of new developments in technologies to study mammalian development and reproduction, and it was a very exciting and challenging place to work. Bob Edwards was close to refining in vitro fertilization techniques in humans. David Whittingham was able to successfully freeze and recover mouse embryos. Matt Kaufman was developing parthenogenesis in mice, and Richard Gardner and Martin Johnson were making interspecies chimeras to follow cell fate in situ. All this was carried out in a very collegial environment where a shy new graduate student was able to mingle and learn from the experts. So when I am asked how students should choose a lab for their graduate studies, I tell them to find an area of science that fascinates them and find a leading lab working in the area, but also to make sure that they will be in a collegial working environment where people are ready and willing to talk and share expertise.

ACROSS THE OCEAN WITHOUT A LIFE JACKET

After my Ph.D. and postdoc in Cambridge and Oxford, I married a Canadian, whom I met through a college rowing team in Cambridge, and moved to Canada. This was a leap into the unknown. Moving to Canada without a job was probably a dangerous way to start a marriage and definitely not the best way to start my academic career. However, I rapidly obtained my first faculty appointment and over the years have built and sustained my research program in the Canadian system (and remained happily married!).

Success was not without its challenges, especially in the early years, and the importance of mentors comes to the fore again. Richard Gardner introduced me to Verne Chapman in Buffalo and Tom Wegmann in the University of Alberta,

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both of whom were inspiring scientists and fantastic mentors. They went out of their way to forge collaborations with me and to get me invited to meetings, grant panels, etc., in the United States and Canada. This enabled me to expand my network of contacts and allowed my science to thrive and make an impact. Verne and Tom both died too young, but their selflessness in promoting me has been my touchstone as I try to guide the careers of people around me.

WOMEN IN DEVELOPMENTAL BIOLOGY

So far this look back at some of the role models and mentors in my career has largely focused on men, but men who were completely gender-blind in their support of good science. But developmental biology in general and mammalian development in particular have always had a very high quotient of successful women at all levels, who provide role models for aspiring young scientists. There is no question that this preponderance of females makes it easier for a woman to feel that this is an area of research where she can be accepted and made welcome. A positive feedback loop is thus set up, and the field continues to recruit strong females to its ranks. Joining the research profession is challenging and tough, and it is important to have support networks where problems can be shared and worked through.

GIVING BACK AND GOING FORWARD

I have always tried to give back to the community of science that has been so good to me and am continuing this path in my current endeavor as head of one of Canada's biggest and most successful hospital-based research institutes at the Hospital for Sick Children. It is a very challenging opportunity to try to make a difference for a broad range of scientists

and clinician-scientists and to have real impact on major problems in children's health—and, of course, one more challenge in terms of being able to balance science, administration, outside commitments, and family. I was told the other day that I should write a book on how to be a successful scientist and leader who gets things done. Of course, that immediately made me think of all the things I have not managed to get done! In the end, nobody can do it all, but I have a few small pieces of advice in lieu of an entire book. First, compartmentalize your activities as much as possible and try not to let one activity take over the time set aside for the other. Second, make lists and check them off. Third, take time to smell the roses. And fourth, always keep science front and center.

We are extraordinarily privileged to work in this era of great scientific discovery and to be able to contribute in whatever way we can. Science is an international language. It knows no barriers of race, religion, or creed. I can go anywhere in the world and immediately have a point of contact and common values with people there. I strongly believe that science has a major role to play in promoting harmony and peace across the world. Educating world citizens in common cause to pursue knowledge and apply it to human welfare not human warfare is a goal to which we can and should all aspire. Life in science is a journey of discovery. The road is tortuous, but the rewards are great!

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