

### **AWARD LECTURE**

# Lessons from a red squirrel, mentors, and the pathway to success<sup>1</sup>

Reinhart A.F. Reithmeier

**Abstract**: In this article I will review my personal career path starting with how a red squirrel got me interested in research, and the vital role that mentors played in my pathway to success — a pathway that taught me many lessons that I would like to share with the reader, particularly graduate students and post-doctoral fellows who are just starting down their own unique pathways.

Key words: biography, careers, graduate studies, mentors, professional development.

**Résumé**: Dans cet article, l'auteur effectuera un retour sur son cheminement de carrière personnel, en commençant par expliquer comment un écureuil roux a éveillé son intérêt pour la recherche, et en soulignant le rôle crucial joué par ses mentors dans son cheminement vers le succès – un cheminement qui lui a appris plusieurs leçons qu'il voulait partager avec le lecteur, notamment avec les étudiants des cycles supérieurs et les stagiaires postdoctoraux qui entreprennent tout juste leur propre cheminement particulier. [Traduit par la Rédaction]

Mots-clés: biographie, carrière, études supérieures, mentors, développement professionnel.

### Lesson No. 1: Follow your passion

It all started with a red squirrel.

I grew up in Ottawa and went to Bell High School where I was a solid B+ student. Mr. Gibson was my Grade 13 Biology teacher, and he was inspiring. Near the end of the course, students had to carry out an independent research project of our own design. My parents were nature lovers and growing up in the countryside outside of Ottawa I had lots of time to explore my environment. So, I decided to do a comparative population study of red and black squirrels.

Every weekend in the spring I trotted around the forests that surrounded our house and catalogued every squirrel sighting on a map. I found plenty of black squirrels, but I could not find any red squirrels. As my project consisted of comparing the two populations, I was sure my project would fail. In the last week before the project was due, I roamed further afield into a grove of old pine trees, a climax forest. When I entered I was greeted by incessant chattering. There, high up in a tree was a red squirrel holding a pinecone.

I searched and searched the pine forest for another but could not find any other squirrels, red or black. So I wrote up the project expecting my usual B\*. Boy, was I amazed when Mr. Gibson gave me an A\*. He said that I had discovered a fundamental principle of biology: black squirrels are gregarious and live in communities in deciduous forests, while red squirrels are solitary, live in coniferous forests, and defend their territory even from other red squirrels. It is amazing what you can learn by just looking around, even from a single red squirrel. From that moment on, I was passionate about discovering things on my own and decided research would be my life.

# Lesson No. 2: Find something you like and are good at

I went to Carleton University in Ottawa and switched majors *three* times. I started out in Honours Chemistry but found the mathematics too hard. In 2nd year, I switched to Honours Biology, which I really liked and was good at. In 3rd year, Carleton created an Honours Biochemistry Program, a perfect combination of my love for biology and the rigors of chemistry.

I did my 4th year project on lysozyme with Stan Tsai in Chemistry. He taught me enzyme kinetics and how to come up with a well-designed experiment. I graduated in the first Biochemistry class in 1972 that celebrated its 40th anniversary in 2012. I married Kathleen Devlin in the summer of 1972, and she has been my greatest supporter ever since. In fact, a supportive and understanding partner is an essential key to success.

### Lesson No. 3: Research is hard work but should be fun too

In the summers of 1971 and 1972, I was fortunate to work at the NRC labs in Ottawa in an historic building on Sussex Drive. The 1st summer, I worked on sequencing ribosomal proteins from diverse bacteria with Mak Yaguchi. Mak taught me that research was hard work, and it paid off a decade later with a paper on *Escherichia coli* S14 (Yaguchi et al. 1983). The next summer I was back at NRC and worked on plant histones with Lou Visentin. Lou taught me that research was fun. He had a real enthusiasm for research and it was infectious. The sequence of a pea plant histone had just come out, and I was amazed that it was identical to the animal histone, a lesson in protein conservation. Lou encouraged me to apply to graduate school and to write to Gordon Dixon, a leading histone expert at University of British Columbia (UBC). As my professional

Received 25 April 2014. Revision received 26 April 2014. Accepted 2 June 2014.

R.A.F. Reithmeier. Department of Biochemistry, University of Toronto, 1 King's College Circle, Toronto, ON M5S 1A8, Canada.

E-mail for correspondence: r.reithmeier@utoronto.ca.

I dedicate this article to my late parents, Friedrich and Reinhilde Reithmeier of Ottawa, who taught me the value of hard work and encouraged me to find my own path to success. Based on an Honorary Lecture given at the 57th Annual Meeting and Conference of the Canadian Society for Molecular Biosciences (CSMB) held 9–12 April 2014 at Banff, Alberta, Canada. This article is part of a Special Issue commemorating the conference.

Biochem. Cell Biol. Vol. 92, 2014

golf (another early passion) career was going nowhere, graduate school, not Q-school, it was!

# Lesson No. 4: "When you come to a fork in the road, take it" (Yogi Berra)

I heard back from Gordon Dixon, but he was moving to England. He had passed my letter on to Phil Bragg, an expert in bioenergetics who worked on membrane proteins. I won an Medical Research Council (MRC) Studentship and joined the Bragg lab to work on outer membrane proteins of *E. coli*. My first paper was published in FEBS Letters in 1974 (Reithmeier and Bragg 1974). Forty years later, I am pleased that outer membrane proteins are still of broad interest. Little was I to know that membrane proteins were to become my life's work. Had Gordon Dixon stayed at UBC, I might well be working on the "histone code" and epi-genetics today.

## Lesson No. 5: Aim high and do not be afraid to move afar

When I started looking for a post-doctoral fellowship, one of my committee members, Denis Vance, a new faculty member at UBC (now at the University of Alberta), recommended that I apply to Harvard to work with Guido Guidotti, who led a large lab working on red cell membrane proteins. Denis had been at Harvard with Nobel Prize winner Konrad Bloch, and he praised the high-powered research environment. There was a postal strike on, and I remember driving down to Bellingham, Washington to send in my application to MRC for a post-doctoral fellowship and my letters to Guidotti.

# Lesson No. 6: Come up with your own ideas, but work with smart people

Guido told me he had space but wanted me to design my own project, just like Mr. Gibson! I knew nothing about red cell membrane proteins. I took what I had learned in the Bragg lab and decided to apply the same sort of methods (hydrodynamics, crosslinking, biophysical techniques) to the Band 3 protein of the human red cell membrane. Again, little did I know that Band 3 would be my life's work right up to today (Shnitsar et al. 2013).

The Guidotti lab was indeed big with over 20 members, and he encouraged interaction and collaboration. So, beside my own project I developed joint projects with Anjana Rao and Lew Cantley, two of the smartest people I have ever met. Guido never put his name on papers unless he actually did experimental work, so I learned how to design my own experiments, carry them out, write up the paper, and get it published. I published four papers, two with Anjana, one with Anjana and Lew, and one as a solo author (Reithmeier 1979).

### Lesson No. 7: Be ready to go out on your own

Due to budget cuts, my MRC Post-doctoral Fellowship was only for two years rather the normal three. I knew that I wanted to return to Canada and decided to apply for a Best Fellowship to work with David MacLennan at the University of Toronto, an expert in muscle proteins of the sarcoplasmic reticulum (SR). David was doing the kind of structural studies I like, but importantly he was also looking at the biosynthesis and assembly of membrane proteins, using techniques like cell-free translation that I was keen to learn. These approaches led to the cloning and sequencing of the proteins of the SR. David was a leader and he was always one step ahead of the competition.

The MacLennan lab was big and well-funded, but more importantly it was like a big family with social events organized by David's late wife Linda and always included all the spouses and young children. I had the good fortune of working with three star technicians: Stella DeLeon, Vijay Khanna, and Kaz Kurzydlowski. The MacLennan lab was always full of smart people (early on, Paul Holland, Amira Klip, Annelise Jorgensen, Kevin Campbell, Marek Michalak, and Denis Lebel, and later, Chris Brandl, Jonathan Lyt-

ton, Larry Fleigel, Balwant Tuana, Wayne Chen, and David Clarke, to name a few), many of whom have gone on to successful research careers and often into leadership positions. David was an inspiration and a mentor to us all. After a couple of years with more publications under my belt, David said I was ready to go out on my own, and he encouraged me to look at the Department of Biochemistry at the University of Alberta.

### Lesson No. 8: When opportunity knocks, open the door

In 1980 there were no faculty jobs in Canada, and research funding was very tight. Alberta had just created the Alberta Heritage Foundation for Medical Research (AHFMR). John Colter, Head of Biochemistry (for life!), invited me out to the University of Alberta for a visit. To say that John was persuasive is an understatement. He pulled out all the stops to recruit me (and more importantly my wife Kathleen) to the Department that he had built up since the early 1960's. With the Heritage funding about to follow and a stellar MRC Group in protein structure forming the core, the choice was easy. John convinced me that the opportunities were perfect for me to start my independent research career. I was lucky to win an MRC scholarship and get my MRC grant (\$28,500 prorated to 1.5 years, since I started in September not April) on my first try.

With the support of AHFMR, I recruited my first star technician (Debra Lieberman), graduate students (Pamela Werner and Sanjay Pimplikar), post-doctoral fellows (Valet Gregg, Jamie Craik, and Mamoru Ohnishi), and a raft of undergraduate summer and project students.

The first three papers (Gregg and Reithmeier 1983; Lieberman and Reithmeier 1983; Reithmeier 1983) from my own lab were published in 1983, based on quite simple and straightforward experiments on Band 3 that I performed on my own, with Debra, and with my first post-doc, Valeta Gregg.

Joel Weiner had arrived previously from Stanford, and like Phil Bragg, was an expert in bioenergetics. We share a common interest in membrane proteins that stands until this day. Along with Carol Cass and Ron McElhaney, we made up the core of membrane biochemistry at University of Albeerta in the early 1980s (Fig. 1).

### Lesson No. 9: Face the class and speak up

I was a terrible lecturer. I was nervous and spoke very quickly. I used the blackboard and had my back to the class most of the time. Early on I watched Cyril Kay, a Professor in biochemistry, in action and asked him to sit in on one of my introductory biochemistry lectures on metabolism. Cyril gave me some tips that have made me a better lecturer. First, be very well prepared and do not lecture from notes. Make it interesting but do not dumb it down, these kids are smart and eager to learn. Face the class and speak clearly. Do not try to cram too much into a lecture, summarize as you go along. Finish on time. Design exams that allow students to apply what they learned to real problems. Along with Charles Deber and Roy Baker, two superb lecturers, I now teach biochemistry to over 1000 undergraduate students in Convocation Hall at University of Toronto and enjoy every class. All three of us have won teaching awards, and for me the credit goes to Cyril Kay. We have even been asked to perform in fund-raising concerts in Convocation Hall as the Pro-Teens, and I have the

I have even produced a youtube video titled How to Sleep in Biochemistry Class (http://www.youtube.com/watch?v=s0tgnJtUgdU).

#### Lesson No. 10: Mentors are essential

For personal reasons, we moved back to Ontario in 1986. Mel Silverman, a nephrologist in the Department of Medicine at the University of Toronto, lead a research group in Membrane Biology Reithmeier 3

Fig. 1. The membrane group in the Biochemistry Department at the University of Alberta at a Banff Membrane Meeting in the early 1980s. From left: Joel Weiner, Carol Cass, Reinhart Reithmeier, Ron McElhaney.



and was looking for a membrane protein biochemist, and I fit the bill. Mel was a clinician-scientist who was creating a grouping within a clinical department where basic research could flourish. Being trained in physics, he believed in the interface of theoretical and experimental approaches. Mel was a mentor to me. He helped to develop my career and was a ready source of advice and encouragement. We created an MRC Group, and I developed a research stream looking into the role of membrane proteins in kidney and other diseases. I again built up a research team of excellent technicians, students, and fellows. Some stayed in academia like Joe Casey, Emmanuelle Cordat, and Rongmin Zhao, some like Jeff Charuk and Yuka Okawa went into the biotech business world, and others like Hilario See, Carol Landolt, Alison Pang, Lisa Tam, Milka Popov, John Vince, Janne Quilty, Joanne Cheung, Sian Patterson, Susan Bustos, and Homa Kameh became doctors, dentists, teachers, lecturers, science writers, and research administrators. I am proud of them all. My technician, Jing Li, has been with me for over 15 years, and she is the backbone of my lab today.

### Lesson No. 11: Follow the leaders and become one

Cathy Whiteside was a member of the Membrane Biology Group and a very successful clinician-scientist like Mel Silverman. I followed Cathy as Graduate Coordinator of the Institute of Medical Sciences (IMS), where I continued to formalize procedures and raise standards for over 300 graduate students. Cathy went on to be Dean of the Faculty of Medicine, where she provided tremendous support to Basic Sciences Departments like Biochemistry.

One day in 2001 I received a call from then Dean David Naylor asking me to apply for the Chair of Biochemistry as Chair Peter Lewis' term was coming to an end and he had moved to a Vice-Dean Research position. At that time, Mel was busy with administration, Cathy was already in the Dean's Office, and the MRC no longer funded groups, so I applied and landed the position. My first year was very stressful, but eventually with a lot of support from colleagues like David Williams (and my wife Kathleen), and by building consensus, the department was able to accomplish a great deal. We hired new recruits including a CERC, captured and renovated new space, developed new undergraduate programs, and increased graduate enrolment and funding. I was Chair for over 10 years, and I happily declare: "It's the best job I have ever had". I am even looking forward to new administrative challenges.

# Lesson No. 12: Develop collaborations and use sabbaticals to enrich your life

Sabbaticals are a way to enrich your research and personal life, yet most people do not take them, and if they do they stay in their own labs. Sabbaticals are certainly disruptive and can be expensive. I have used sabbaticals to develop new research skills: the first in molecular biology with Jacques Pouysségur in Nice, France, where I worked with graduate student Laurent Counillon; the second in membrane protein crystallography with Natalie Strynadka at UBC, where I worked with the magnificent Trevor Moraes; and the third in molecular dynamic simulations of membrane proteins with Mark Sansom at Oxford, where I worked with an outstanding (and patient) post-doc Antreas Kalli. All three labs were big and full of bright people. In all cases, I developed collaborative projects with members of the lab that led to publications (Babu et al. 2010; Counillon et al. 1994) and friendships that last until today. I encourage graduate students and post-doctoral fellows to initiate collaborations.

### A Final Lesson: Develop your skill set and build a network

The majority of graduate students today will obtain jobs outside of academia. This is not necessarily bad news, as graduates have been able to carve out their unique pathways to very diverse and successful careers. Universities but also business, government, the charitable sector, etc., need to hire PhDs who are trained to be deep thinkers, problem solvers, innovators and most importantly, leaders.

First, it is more vital than ever to use your graduate education to develop your skill set (see http://www.conferenceboard.ca/topics/education/learning-tools/employability-skills.aspx), a diverse skill set that goes beyond technical expertise or knowledge of a system. Skills that employers are looking for include communication skills, working as an effective member of a team, time and project management, analytical, and problem solving skills.

Second, you need to build a network beyond the confines of your research project. Do you have any contacts in business, biotech, government, hospitals, etc.? A good place to start is with your own alumni. You will find many people who have developed successful career paths inside and outside of academia. These folks are usually more than willing to give back in terms of their

Biochem. Cell Biol. Vol. 92, 2014

Table 1. Lessons from a red squirrel.

Follow your passion
Find something you like and are good at
Research is hard work but should be fun too
"When you come to a fork in the road, take it."
(Yogi Berra)
Aim high and don't be afraid to move afar
Come up with your own ideas, but work with
smart people
Be ready to go out on your own
When opportunity knocks, open the door
Face the class and speak up
Mentors are essential
Follow the leaders and become one
Develop collaborations and use sabbaticals to
enrich your life
Develop your skill set and build a network

time and experience. Contact an alumnus and arrange a meeting over lunch or a coffee. Do your research and arrive prepared with your cv or a targeted resumé. Interview the person and ask about their career path and how what they learned in graduate school helps them in their job today. Follow-up by e.mail and a Linkedin connection. You never know where this simple conservation can lead and what doors it could open. To get started, make a "cold call" to an alumnus.

Dr. Nana Lee and I created a graduate course in professional development in the Department of Biochemistry at the University of Toronto that was featured in an article in Science Careers: http://sciencecareers.sciencemag.org/career\_magazine/previous\_issues/articles/2013\_10\_01/caredit.a1300216.

The Conference Board of Canada has launched a Centre for Skills and Post-secondary Education in response to the changing educational landscape: http://www.conferenceboard.ca/spse/default.aspx.

The bottom line is that while graduate education, especially at the PhD level, must have a clear focus on research and scholarship, graduate programs should also incorporate professional development into their *curricula* to fully prepare graduates to take advantage of the diverse career and leadership opportunities available to them in today's, and more importantly, tomorrow's global job market.

#### Conclusion

Throughout my career I have been very fortunate to have a supportive partner, excellent mentors, and role models. In turn, I hope that I have been a mentor and role model to my students and fellows, who have supported my career with their hard work and dedication. I have outlined experiences and lessons (Table 1) that I have learned along the way, many that I am sure will resonate with others. There are many pathways to success, you have to find the right one for you. Luckily there are many people and perhaps even a red squirrel to help you along the way.

#### References

Babu, M., Greenblatt, J.F., Emili, A., Strynadka, N.C., Reithmeier, R.A., and Moraes, T.F. 2010. Structure of a SLC26 anion transporter STAS domain in complex with acyl carrier protein: implications for E. coli YchM in fatty acid metabolism. Structure, 18(11): 1450–1462. doi:10.1016/j.str.2010.08.015. PMID: 21070944.

Counillon, L., Pouyssegur, J., and Reithmeier, R.A.F. 1994. The Na+/H+ Exchanger Nhe-1 Possesses N-Linked and O-Linked Glycosylation Restricted to the First N-Terminal Extracellular Domain. Biochemistry, 33(34): 10463–10469. doi:10. 1021/bi00200a030. PMID:8068684.

Gregg, V.A., and Reithmeier, R.A.F. 1983. Effect of Cholesterol on Phosphate-Uptake by Human Red-Blood-Cells. FEBS Lett. 157(1): 159–164. doi:10.1016/0014-5793(83)81137-5. PMID:6862013.

Lieberman, D.M., and Reithmeier, R.A.F. 1983. Characterization of the Stilbenedisulfonate Binding-Site of the Band-3 Polypeptide of Human-Erythrocyte Membranes. Biochemistry, 22(17): 4028–4033. doi:10.1021/bi00286a006. PMID: 6615815

Reithmeier, R.A.F. 1979. Fragmentation of the Band-3 Polypeptide from Human-Erythrocyte Membranes - Size and Detergent Binding of the Membrane-Associated Domain. J. Biol. Chem. **254**(8): 3054–3060. PMID:429334.

Reithmeier, R.A.F. 1983. Inhibition of Anion Transport in Human Red-Blood-Cells by 5,5'-Dithiobis(2-Nitrobenzoic Acid). Biochim. Biophys. Acta, 732(1): 122–125. PMID:6871185.

Reithmeier, R.F., and Bragg, P.D. 1974. Purification and Characterization of a Heat-Modifiable Protein from Outer Membrane of *Escherichia coli*. FEBS Lett. 41(2): 195–198. doi:10.1016/0014-5793(74)81210-X. PMID:4604992.

Shnitsar, V., Li, J., Li, X., Calmettes, C., Basu, A., Casey, J.R., et al. 2013. A Substrate Access Tunnel in the Cytosolic Domain is not an Essential Feature of the SLC4 Family of Bicarbonate Transporters. J. Biol. Chem. 288: 33848–33860. doi:10. 1074/jbc.M113.511865. PMID:24121512.

Yaguchi, M., Roy, C., Reithmeier, R.A.F., Wittmannliebold, B., and Wittmann, H.G. 1983. The Primary Structure of Protein-S14 from the Small Ribosomal-Subunit of Escherichia coli. FEBS Lett. 154(1): 21–30. doi:10.1016/0014-5793(83)80869-2.