**Invited paper**

Barbara A. Baird*

# My path in the company of chemistry

https://doi.org/10.1515/pac-2021-1205

**Abstract:** Experiencing the honor of this international recognition in chemistry, I wonder how this came to be. I reflect on my imperfect but rewarding path to where I am now, and on those who have helped me along the way.

**Keywords:** Career journey; IUPAC award; IUPAC Distinguished Women in Chemistry and Chemical Engineering; women in chemistry; women in science.

It has been a terrific honor to be nominated for and to receive IUPAC's Distinguished Women in Chemistry and Chemical Engineering Award for 2021. A significant part of this honor is my cohort of 12 amazing women from all over the world who received this award with me, as well as the amazing women who preceded us. We've all had such different experiences as we've managed to succeed despite multiple stumbles along the way. As I read about my cohort's accomplishments and listened to their stories at the 2021 IUPAC Symposium, I thought about the path I've taken, the support I have had along the way, and what I would tell others who might think about taking a similar route. "Just get lucky!" wouldn't be much help to them (or to me, as I think about my own path going forward), although good fortune is surely a boon for success. As I recount my own story, I pick out some lessons I've learned as I found and pursued my way in chemistry.

## Early years

Although my path winds through chemistry, there is more of course, and I have to step back to what I learned growing up in the middle of a big family in central (Decatur) Illinois of midwestern United States. Both of my parents grew up during the depression and participated in the effort of World War II. My mother earned a degree in sociology, then trained to be a registered nurse and worked in a navy hospital. My father had a degree in history and after law school and four years of overseas service in the army initiated his law practice in our town. While we were growing up my father worked hard as a generalist attorney, and my mother put her career aside to focus on family; both parents were active as volunteers in the community. We five children witnessed how our parent's partnership in resilience, resourcefulness, work ethic, community spirit, and positive attitude not only helped solve the daily problems but allowed us to do things that we wouldn't be able to do unless we all worked together. During the 1950s and 60s we took camping trips all over the U.S., piling into our station wagon and pulling a tent trailer. My mother did all the planning and made sure that we

I dedicate this account to my scientific and life partner, Dave, and to the memory of my sister Carolyn, an artist and teacher who gave invaluable perspective to me as a scientist.

**Article note:** A special collection of invited papers by recipients of the 2021 IUPAC Distinguished Women in Chemistry and Chemical Engineering Awards.

***Corresponding author: Barbara A. Baird**, Department of Chemistry and Chemical Biology, Cornell University, Ithaca NY 14853, USA, e-mail: bab13@cornell.edu

© 2022 IUPAC & De Gruyter. This work is licensed under a Creative Commons Attribution-NonCommercial-NoDerivatives 4.0 International License. For more information, please visit: http://creativecommons.org/licenses/by-nc-nd/4.0/

learned the context of our journeys to civil war battlegrounds, routes of western migration, national parks, and much more. As soon as we were old enough, we all took turns driving, and we all set up and dissembled our camp daily. Boys and girls shared equally in the tasks. When the car broke down along the way, our father figured out how to get it fixed, and our mother figured out how to keep us active by taking us on a hike or organizing a game of frisbee. Our mother always expected us to engage to do the best we could, and she could be critical of some of the things we did. From her I learned how to take criticism as well as its value in trying to do better. Our father also had a strong sense of fairness and high standards but was typically gentler in his comments. From him I learned that a sense of humor often brightens the picture and lightens the load. Both my parents were interested in and relished history, current events, and the natural world around us. Also, from them we learned the value of clear communication, both verbally and in writing – even though we had to work at it. Clearly, I was fortunate to be born into my family then and we remain close as an unconditional source of love and support. My growing-up experience gave me basic skills that I've continuously tried to improve on in my work and with my own husband and children. Through the years I have also become aware of so many others who have not been as fortunate in family and opportunities as I have been and yet succeeded mightily through their own fortitude and drive. I also have grown to appreciate the sad loss from the scientific community of others less fortunate who were not able to get there for reasons beyond their control.

Like many who became scientists, I was an avid reader and curious about the world around me. I had great, good, and OK teachers in my public schools, and I learned from all of them. I enjoyed learning and doing well on tests, and I don't recall ever feeling that I shouldn't be as good as or better than the boys at math or any other subject. For this, I give credit to my family and to my teachers. Several of my teachers stand out, and one I must mention is my high school chemistry teacher. Although I wanted to be a veterinarian as I started to high school, it was in Mr. Earl Rudolph's chemistry class that I found the problems I liked to think about and solve. This was a science that I could get into in a way that I could not with biology or physics. At that time the US National Science Foundation (NSF) supported summer science programs for high school students in college venues. With Mr. Rudolph's encouragement, I applied as a high school sophomore and the following summer went to Manchester College in Indiana. This was my ticket out of my home town and the chance to get together with other adventurous teenagers. We had fun making polymers, living in dorms, and pretending we were college students. After my junior year I attended another program at Kansas University learning microbiology and sociology. It is too bad that these NSF programs for high school students no longer exist; they catalyzed my growing interest in science and my realization that collaborative scientific endeavors are both fun and can take you to new places.

When it came time to become a real college student in 1969, I chose Knox College in Galesburg, Illinois, and a chemistry major. The beauty of a small liberal arts school like Knox is that a student can be immersed in a rigorous science, working closely with professors, and still explore the humanities, working closely with different professors. I truly enjoyed moving through the diverse mix of students and disciplines. I was fascinated most by physical chemistry, in part because of my professor Dr. Bob Kooser who set high standards and gave beautifully clear lectures. The problem sets and exams were difficult, so I really had to dig deep, and the more I thought about the concepts and equations, the more I liked it. As in high school, I grabbed for the opportunity to go somewhere else for a summer program, and went to an NSF-sponsored program at Lawrence Berkeley Laboratory to try out nuclear chemistry. This was my ticket out of the Midwest. That summer I carried out neutron activation analysis to determine the origin of archaeological pottery shards. I also enjoyed living in a Berkeley co-op and exploring the bay area with fellow students. This was interesting new science for me – and this was fun. Less scientific, but also important for my journey were college summers spent at the National Outdoor Leadership School in Wyoming. These were five-week backpacking trips in wild mountainous areas, far away from civilization. We learned how to hike and camp with minimal gear under all kinds of conditions, cross streams, climb rocks, and preserve the beauty of the wilderness. We learned how to make responsible leadership judgements under challenging circumstances. Traveling and surviving in the wilderness is sometimes hard; it is eminently rewarding.

Although I took biology in college, I determined that counting fruit flies was not for me (remember this was the early 1970s), but biochemistry got my attention when taught for the first time by my organic chemistry professor at Knox, Dr. Leland Harris. Through him, I saw biology on a molecular level, and it began to make more sense to me. In fact, it was very interesting to think about living processes as a chemist. For some reason, unknown to me at the time, I became fascinated by the subject of cell membranes. These mysterious lipid bilayers somehow protect the cell from its environment and also allow specific environmental stimuli to be communicated into the cell.

## A Budding Scientist

As for so much of my journey, I followed my nose and moved directly from college to chemistry graduate school in 1973 (Looking back from the present, I might have beneficially opted for one or more gap years). I chose Cornell University because of the quality and breadth of its chemistry PhD program and because of the natural beauty of the Ithaca area. The one factor surely balanced the other: when my chemistry courses got very tough or my research got very discouraging, I could easily get on my bike and ride through the hills or walk along the waterfalls or Cayuga Lake. Although I and my grad student cohort were more narrowly focused on chemistry, rather than across the liberal arts, we shared with mostly good humor the challenges of rigorous courses, teaching assistantships, and budding research experiences. Backpacking and cross-country skiing groups formed, and we took days away-from-it-all on Finger Lakes trails or Adirondack Mountains.

Cornell has had for many years exceptional strength in biophysical chemistry, and that is the research area that attracted me. When Dr. Gordon Hammes told me about the chloroplast coupling factor ($CF_1$), which catalyzes formation of ATP by transporting protons across the membrane, I was hooked and joined his group. In fact, this was a golden time in the emergence of oxidative phosphorylation: Peter Mitchell won the Nobel Prize for the chemiosmotic mechanism for ATP synthesis in 1978, and Cornell played a leading role on the experimental side with collaborations across Biochemistry, Plant Science, and Chemistry. I had the good fortune to play a small role in these Cornell collaborations, and found myself most fascinated by the role of the membrane in the ox-phos process. I grew immeasurably as a scientist during my graduate studies with Dr. Hammes as my mentor. His foresight and critical thinking toward understanding key enzyme systems, and application of rigorous physical chemistry approaches to solve these problems, continue to serve as a model for me. As a highly understated acknowledgement in my PhD thesis, I thanked him for his “overall support and encouragement and an occasional push.” The “support” and “encouragement” are real (and continuing); the “push” part is also important because, like other key mentors, Dr. Hammes challenged me to take on opportunities I thought might be beyond my capabilities.

My final PhD project used fluorescently labeled immunoglobulins (specific antibodies) and fluorescence resonance energy transfer (FRET) to measure the distance from labeled sites on $CF_1$ to the membrane of reconstituted vesicles, so as to determine this enzyme’s orientation [1]. Although antibodies were simply a labeling reagent in these experiments, I became fascinated by their immunological origin. This interest was inspired further by a postdoc in the Hammes group (and a fellow outdoors person), Dr. David Holowka, who helped me and had experience in immunological systems from his PhD work. And so, very naively, I decided to carry out postdoctoral studies in cellular immunology. This also gave me opportunity to follow Dave Holowka to the National Institutes of Health (NIH) in Bethesda, Maryland where he continued postdoctoral studies with Dr. Henry Metzger on the cell membrane receptor (FcεRI) for immunoglobulin E (IgE). My own naive dive into immunology was almost overwhelming because I had never worked with cells or animals before, and the connection with biophysical chemistry was far from clear in the late 1970s. My good fortune at this time was that the molecular level of immunology was just beginning to emerge with the cloning of a key immune receptor (the T cell receptor), and I had the opportunity to begin to learn about mechanistic foundations of these complex systems at an early stage. I was tentative and tenuous as rooky chemist in the Immunology Branch of the National Cancer Institute [2], but I received a lot of kind help finding my way from colleagues there. Although I was far away from what I could do well, this became a lasting connection to immunology.

Dave and I solidified our partnership in life and science by marrying while at the NIH. When it came time to apply for jobs, we decided to go for what was best for both of us. We were not given the opportunity for two equal positions, but we did get some joint offers where he had the senior position and some where I did. Dr. Hammes encouraged me to apply for a faculty opening in the chemistry department at Cornell. My research proposal, which Dave and I wrote together, included using FRET to determine the orientation of the receptor-bound IgE to the cellular membrane [3]. Somehow, I got the offer and accepted it as the first woman faculty member in our department. Although the plan was for Dave to get a second faculty position in biochemistry or immunology at Cornell after we arrived, we set up our research laboratory and found that our complementary strengths worked well together. Within the first year, we each applied for and received NIH grants for our respective favorite projects. While I took on teaching and other faculty responsibilities, Dave could spend his time carrying out his own experiments as he worked closely with our growing research group members. Another aspect of our fortunate work partnership was that we could be flexible and cover for each other on a moment's notice. This flexibility and collaborative spirit became especially important while raising our three sons. We've had a good life.

Although Dave and I were happy to come back to the beauty of Ithaca and to Cornell, returning to my PhD department as a faculty member was initially frightening. Indeed, I felt like an imposter. This was also the first time I can recall feeling like an underrepresented minority as the only female faculty member. "Code-switching" is the term I've learned more recently that describes how I interacted with my chemistry colleagues during those first years. None-the-less, they were truly supportive in their individual and collective ways as I worked on developing my own departmental voice. When I became pregnant with twins shortly before my tenure review, our chemistry chair said to me: You are going to have to tell us how to support you because we've never had this situation before and we don't know how to handle it. This was eye-opening, because I realized I had to put forward my own solutions, rather than expect others to figure out what I needed to be successful under my individual circumstances.

In our research laboratory, Dave and I worked to develop biophysical approaches to investigate the role of the cell's outer (plasma) membrane in transmitting an environmental signal to the interior of the cell so that the cell would respond appropriately. The system we chose, built on the seminal work of Dr. Metzger (and others) to determine how a small particle (e.g., pollen) acts as an antigen to cause a specialized (mast) cell to release histamine to initiate allergic and inflammatory responses. Continuing as Dave's (and then my) mentor, Dr. Metzger was both supportive and unsparingly (but constructively) critical of our work; he was generous with many reagents that made our work possible. From previous studies we knew that specific cell membrane receptors (IgE-FcεRI receptors) bound to and were clustered specific antigens but the question is: what is it about clustering of outside-facing receptors that carries the stimulus across the membrane such that intracellular components are released? We started with this simple question when we established our Cornell chemistry lab in 1980, and we have been teasing apart its actual complexity ever since. We developed quantitative fluorescence spectroscopy [4] and microscopy [5, 6] as primary approaches. This has been stimulating work as we expanded our own multidisciplinary efforts and jointly with collaborators at Cornell (and elsewhere) across chemistry [7–9], biochemistry [10, 11], immunology [12, 13], applied physics [14, 15], materials science [16, 17], and theoretical biology [18–20] to grasp new concepts and develop new tools of investigation. Many outstanding students and postdoctoral associates joined our group in this quest, some of whose names are included in representative publications referenced. A key achievement has been characterizing phase-like behavior within the membrane such that clustering of IgE-receptors results in co-sequestration with a signaling kinase (to phosphorylate receptors) while excluding a contra-balancing phosphatase (preventing dephosphorylation of receptors). Tipping the balance to phosphorylation of intracellular components of the receptors initiates transmembrane signaling. Our current model is shown in Fig. 1 [21].

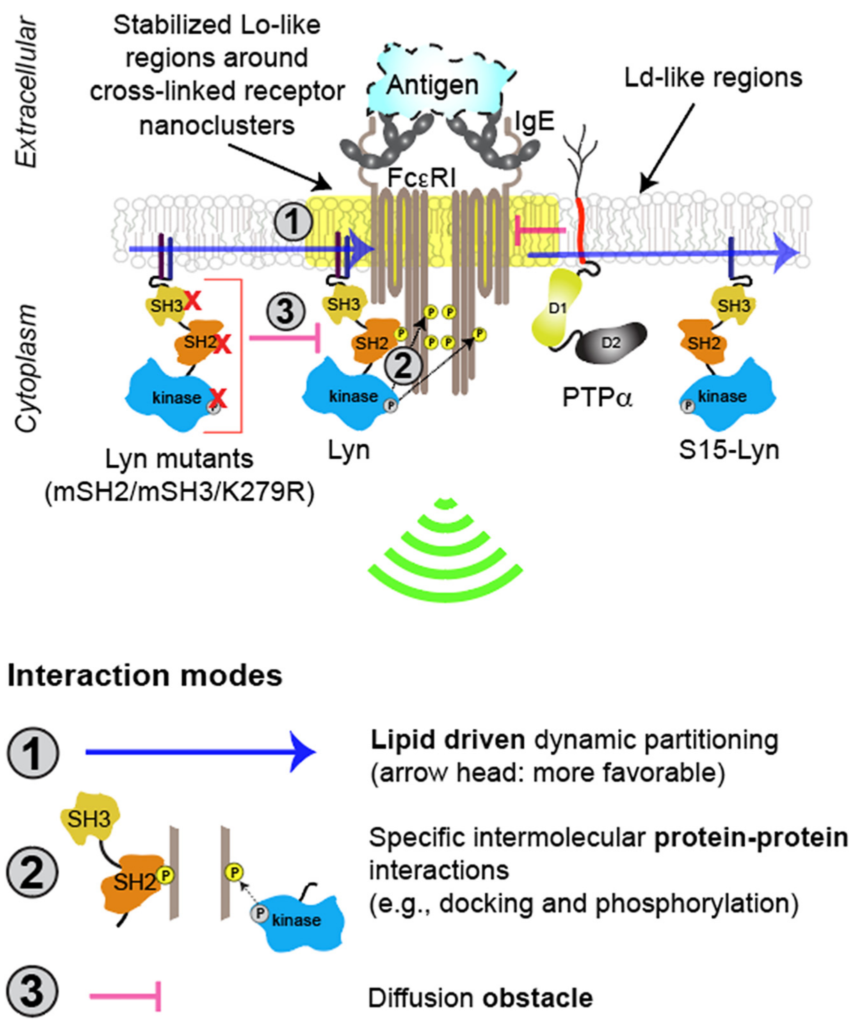


**Fig. 1:** Antigen-mediated crosslinking of IgE-receptors (IgE-FcεRI) stabilizes phase-like separation in the plasma membranes of mast cells, causing distinctive liquid-ordered (Lo) and liquid-disordered (Ld) nanodomains. This results in dynamic lipid-based and protein-based interactions that target key components and leads to supra-threshold phosphorylation of receptors by Lyn kinase and initiation of transmembrane signaling. Proposed interaction modes leading to functional coupling of Lyn with clustered FcεRI: Stabilized Lo-like environment preferentially includes Lo-preferring Lyn and excludes Ld-preferring S15-Lyn and transmembrane phosphatase PTPα (interaction mode 1). Preferentially proximal Lyn (interaction 1) phosphorylates clustered FcεRI via its kinase module and then binds to pTyr via its SH2 module as facilitated by its SH3 module (interaction mode 2); these cumulative interactions stabilize the coupling. Lyn variants with impaired kinase, SH2 or SH3 modules are sterically hindered by cytoplasmic segments of clustered FcεRI (interaction mode 3). PTPα, which is preferentially excluded from Lo-like environments (interaction mode 1), has also limited access to FcεRI-pTyr likely due to steric and hydrodynamic obstruction by clustered FcεRI-TMDs (interaction mode 3). Schematic reproduced from Reference [21].

## Part-time Administrator

Despite being an introverted scientist by nature, I found I enjoy working with other people as a team, and this inevitably led to opportunities for administrative leadership. Who will take the responsibility for success of the collective task? When asked, I wasn't sure I would be able to fulfill these positions satisfactorily, but why not try? Initially with some trepidation, but then with increasing confidence I became Director of Graduate Studies and later Chair of my department, followed by serving as Senior Associate Dean of Science and Math in Cornell's College of Arts and Sciences. A challenge and reward of these positions is working to understand the needs and points of view of other players in the academic enterprise, both in the trenches (faculty, students, and staff) and in the upper administration who are all responsible for the overall success of our very complicated department, college, and university. I have been further rewarded by combination of scientific and administrative tasks, such as (co-)leading NIH training grant in molecular biophysics and a Keck Foundation-funded program in biophysics research that spanned Cornell's Ithaca and Manhattan Medical College campuses. My most daunting and ultimately rewarding challenge was serving as Director of NSF Science and Technology Center in Nanobiotechnology, which spanned multiple institutions. Daunting, because I was neither proficient in nanotechnology nor a recognized leader among the engineers who offered these exciting new tools to biological and biomedical communities. Rewarding, because this was my opportunity to help form powerful collaborations across these communities, as well as invaluable new collaborations with my own research group.

Becoming a female scientist with some administrative skills put me on the lists of academic recruiters. However, although I've come to appreciate this hard work and admire those who do it well, I've never aspired to be an administrator. Rather, I've remained primarily dedicated to Dave's and my research laboratory and our best scientific efforts to advance understanding of cell membranes and transmembrane cellular mechanisms. Leadership of our research group has allowed us to help form strong bonds within our international group of more than a hundred undergraduate, graduate, and postdoctoral trainees as we strive to bring out the strengths of these amazing individuals in our collective scientific endeavor. Beyond the scientific advances our group has contributed over the years to the overall progress of our research field, Dave and I are grateful for the lasting connections to the individuals we had the privilege to mentor. We watch with parental pride as our past trainees move ahead to contribute in research universities, liberal arts colleges, big companies, start-ups, consulting, medicine, and law.

## Lessons learned

Reflecting on my story, I am struck again by my good fortune, including my extended family, the mentors who have stepped up to encourage me, and my life/scientific partnership with Dave. I have found continuing joy and balance within my family and in the natural beauty outdoors. From the beginning of my journey, I did not have a long-term plan but continued along a winding road following leads I thought were interesting and worthwhile. I've made a lot of mistakes and some wrong turns along the way, but found that this is inevitable, that I learn from these errors, and that I can move on a little stronger and more confident from the experience. I learned to accept and value kernels of truth in criticism of my efforts from others. I learned to grab opportunities appealing to my curiosity or sense of responsibility, realizing that, despite some disappointments or failures, these lead to appealing other opportunities that further stimulate and challenge me. I learned to seek out mentors whose work I admire, who hold high expectations for me, and who encourage me in efforts to do my best and rise to new challenges. I have been accompanied and supported by strong women in my cohort, and through our efforts and good fortune we increasingly have the privilege and responsibility to serve as effective and caring mentors, helping to create opportunities for others across a diverse community.

**Research funding:** This work was supported by National Institute of General Medical Sciences (grant number: R01GM117552).

## References

[1] B. A. Baird, U. Pick, G. G. Hammes. *J. Biol. Chem.* **254**, 3818 (1979).
[2] B. Baird, P. Henkart. *Cell. Immunol.* **75**, 312 (1983).

[3] B. Baird, Y. Zheng, D. Holowka. *Acc. Chem. Res.* **26**, 428 (1993).
[4] D. Holowka, B. Baird. *Biochemistry* **22**, 3475 (1983).
[5] A. K. Menon, D. Holowka, B. Baird. *J. Cell Biol.* **98**, 577 (1984).
[6] S. A. Shelby, S. L. Veatch, D. A. Holowka, B. A. Baird. *Mol. Biol. Cell* **27**, 3645 (2016).
[7] E. K. Fridriksson, P. A. Shipkova, E. D. Sheets, D. Holowka, B. Baird, F. W. McLafferty. *Biochemistry* **38**, 8056 (1999).
[8] E. J. Baird, D. Holowka, G. W. Coates, B. Baird. *Biochemistry* **42**, 12739 (2003).
[9] M. J. Swamy, L. Ciani, M. Ge, A. K. Smith, D. Holowka, B. Baird, J. H. Freed. *Biophys. J.* **90**, 4452 (2006).
[10] K. A. Field, D. Holowka, B. Baird. *Proc. Natl. Acad. Sci. U.S.A.* **92**, 9201 (1995).
[11] R. M. Young, X. Zheng, D. Holowka, B. Baird. *J. Biol. Chem.* **280**, 1230 (2005).
[12] N. Calloway, M. Vig, J.-P. Kinet, D. Holowka, B. Baird. *Mol. Biol. Cell* **20**, 389 (2009).
[13] R. Cohen, A. Torres, H.-T. Ma, D. Holowka, B. Baird. *J. Immunol.* **183**, 6478 (2009).
[14] J. L. Thomas, D. Holowka, B. Baird, W. W. Webb. *J. Cell Biol.* **125**, 795 (1994).
[15] M. Wu, D. Holowka, H. G. Craighead, B. Baird. *Proc. Natl. Acad. Sci. U.S.A.* **101**, 13798 (2004).
[16] A. Burns, P. Sengupta, T. Zedayko, B. Baird, U. Wiesner. *Small* **2**, 723 (2006).
[17] W. Senaratne, P. Sengupta, V. Jakubek, D. Holowka, C. K. Ober, B. Baird. *J. Am. Chem. Soc.* **128**, 5594 (2006).
[18] B. Goldstein, R. G. Posner, D. C. Torney, J. Erickson, D. Holowka, B. Baird. *Biophys. J.* **56**, 955 (1989).
[19] L. A. Chylek, D. A. Holowka, B. A. Baird, W. S. Hlavacek. *Front. Immunol.* **5**, 172 (2014).
[20] E. D. Mitra, S. C. Whitehead, D. Holowka, B. Baird, J. P. Sethna. *J. Phys. Chem. B* **122**, 3500 (2018).
[21] N. Bag, A. Wagenknecht-Wiesner, A. Lee, S. Shi, D. A. Holowka, B. A. Baird. *Proc. Natl. Acad. Sci. U.S.A.* **118**, e2026583118 (2021).