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Introduction

Miriam Hasson memorial issue

This issue of *Bioorganic Chemistry* is dedicated to the memory of Miriam (''Mimi'') Hasson, who sadly passed away on a January 16, 2006, after a long battle with brain cancer. Mike McLeish, one of Mimi's collaborators, organized this issue and collected articles from her colleagues and friends. In the paragraphs that follow, David Sanders, her husband, Jeremy Thorner, her Ph.D. advisor, Gregory A. Petsko and Dagmar Ringe, her

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post-doctoral research advisors, and Lena Polovnikova, her first Ph.D. student, share memories of Mimi and discuss her contributions to science and humanity. She is missed greatly by all who knew her.

1. From David Sanders

Miriam Hasson was a scientist for all of the right reasons. She loved solving puzzles. Miriam was fascinated by the beauty of nature and always endeavored to reproduce that beauty in her scientific illustrations. Although she received numerous awards during her scientific career, she never measured her success by those awards or career advances. Miriam did not require external validation of her scientific brilliance. She was also very unselfish with her data and her time. She cared deeply about her students and their training.

She was competitive when playing table tennis or backgammon or Scrabble, but there was no sense of competition between us for scientific or academic success. We relished each other's triumphs.

I was initially reluctant to collaborate with my wife. I worried that it would be a source of tension and that we would be unable to leave the project at work in the evening. Our children did become experts on acetate kinase and Ppx, but it was one of the best scientific decisions we ever made. We complemented each other in terms of our expertise and scientific temperaments.

Miriam's computers were named in Hebrew after the seven agricultural products for which the Land of Israel is praised. I do not know what she would have used after those seven, but it would probably have been something to do with our children's names.

Miriam was never afraid to be alone, but she preferred to be with others. For her, sharing a discovery was the most important aspect of making a discovery. When she was diagnosed with an anaplastic astrocytoma, she characteristically investigated everything available concerning brain tumors and their treatment. Her openness about the disease and her battle was both disconcerting to some people and consistent with her approach to science. Her approach did reward Miriam with an additional 7+ years of life—approximately 5 years of which were treatment- and progression-free, although she was taking anti-seizure medicines throughout that time.

She also developed an intense interest in anything concerning the human mind. She began a correspondence with Oliver Sacks. It was sometimes hard to distinguish the effects of the disease itself from those resulting from the treatments and the anti-seizure medicines. She actually experienced less anxiety, especially during presentations, than she had before the diagnosis. It was also uncanny that she did not move while she slept.

With the agreement of Miriam and the department, I began to supervise the Hasson laboratory. A few months before the end, at a time when Miriam could no longer walk without assistance, one of Miriam's students, who had recently joined the laboratory, passed his qualifying examination. Afterward I suggested to him that it would in his best interests if he found a project in a different laboratory for his thesis research. I was not able myself to provide him with the experimental guidance that he required. When I informed Miriam of my conversation with him, her immediate reaction was "What is going to happen to the project?" I explained that I could not supply adequate supervision for it and that it would be best for the student if he began a different project as soon as he could. She accepted the decision with the knowledge that I was going to add one other graduate student of hers and her postdoctoral researcher to my laboratory group.

Her love for crystallography led to a fascination with snowflakes. Her enthusiasm for the beauty of nature made her the best colleague for a conversation about the latest result—hers or someone else's. It has proven very difficult to rekindle that joy we shared in scientific discovery in her absence.

2. From Jeremy Thorner

2.1. Miriam S. Hasson as a budding biochemist

I never saw Mimi Hasson in an unkind mood. She did not have a hostile or malicious bone in her body. To be around Mimi was an opportunity to enjoy some respite from life's all-too-frequent tribulations, as do the storm-ravaged when the eye of the hurricane passes over them. It was my very great fortune to have known and benefited from my association with such a beautiful human being. I became intimately familiar with Mimi's intelligence, talent, and personality traits because she received the bulk of her Ph.D. training under my auspices. In terms of her innate intelligence and imaginativeness, Mimi was one of the most gifted graduate students I had the privilege to train in my laboratory (out of more than 30 total) in my now 32 years on the faculty at Berkeley.

Miriam Sarah Hasson was raised in Chicago. She received her baccalaureate degree from Yale in 1986, where she was an outstanding scholar. Her first exposure to a research laboratory was during the summer after her freshman year at Yale, when she was employed in the Department of Chemistry at the University of Illinois at Chicago, which was near her parents' home. Mimi took her junior year off and was employed as a technician here at Berkeley in the laboratory of my friend and colleague, Randy W. Schekman. She did so because David Sanders, her then-boyfriend and now husband and life's companion of many years, had entered our graduate program in fall 1983. During the following summer, Mimi conducted research at the Weizmann Institute in Rehovot, Israel. Tellingly, Mimi contributed enough in two of those three labs, even at that relatively early stage of her career development, that she was included as a co-author on publications that resulted from her research findings. Her work in the Schekman lab (where, ironically enough, there also was Tama B. Hasson, no relation) was especially significant [G.S. Payne, T.B. Hasson, **M.S. Hasson**, R. Schekman, Genetic and biochemical characterization of clathrin-deficient *Saccharomyces cerevisiae*, Mol. Cell. Biol. 7 (1987) 3888–3898]. Hence, there was every indication, even at that tender age, that Mimi held the promise of becoming an effective and productive independent investigator.

Mimi entered the graduate program of the Department of Biochemistry at Berkeley in fall 1986. Moreover, she was awarded a highly competitive NSF Predoctoral Fellowship to support her graduate studies here. In her first year, she conducted her three, mandatory two-and-a-half-month research rotations in the labs of Randy Schekman and Elizabeth H. Blackburn (who was then on our faculty, but is now at UCSF) and my lab. Remarkably, Mimi again contributed enough during her brief stint in the Blackburn lab to be included as a co-author on a research paper [G.L. Yu, **M. Hasson**, E.H. Blackburn, Circular ribosomal DNA plasmids transform *Tetrahymena thermophila* by homologous recombination with endogenous macronuclear ribosomal DNA, Proc. Natl. Acad. Sci. USA 85 (1988) 5151–5155]. I was very lucky that, at the end of the rotation period, Mimi elected to conduct her doctoral dissertation research in my group.

Although Mimi was not an experimentalist who was blessed with the proverbial "golden hands," her combination of piercing intelligence, sound judgment, and perseverance allowed her to always surmount any adversities she encountered in the performance of her dissertation research. She did an exceptional job in analyzing the post-translational modification, subcellular localization, and physiological function of the *Saccharomyces cerevisiae STE5* gene product, which is an essential component of a signal transduction pathway in the budding yeast, *Saccharomyces cerevisiae*. Her studies employed biochemical, immunological, genetic, and molecular biological methods. Her work, and that of others in the field, led to the important conclusion that Ste5 serves as a docking platform for the protein kinases involved in this signaling module. Thus, Ste5 became the first recognized MAPK scaffold protein and has remained the prototype and paradigm for understanding the function of this class of cellular regulatory molecule.

After her third year in my lab, Mimi's personal circumstances required that she finish her thesis work elsewhere. In brief, her by-then husband, David, who had completed his degree and conducted a successful joint postdoctoral period with Henry R. Bourne and Frank McCormick at UCSF, elected to receive further postdoctoral training in virology with Richard Mulligan at M.I.T. in Cambridge, MA. By that time, Mimi had already given birth to their first child, Honi (and, eventually, she had two more sons). Obviously, it was an untenable situation for her to remain in Berkeley while her husband was in Boston. To resolve this problem, I arranged for Mimi to work with Duane D. Jenness in the Department of Microbiology and Molecular Genetics at the University of Massachusetts Medical Center in Worcester, MA. Duane had been a graduate student here at Berkeley with Howard K. Schachman studying aspartate transcarbamoylase and a postdoctoral fellow with Leland H. Hartwell at the University of Washington in Seattle, where he learned yeast genetics. His research interests overlapped with my own, and Mimi was able to carry out the remainder of her thesis work in Duane's lab on a collaborative basis. Consequently, the major portion of Mimi's thesis research was published, eventually, as a joint paper [**M.S. Hasson**, D. Blinder, J. Thorner, D.D. Jenness, Mutational activation of the *STE5* gene product bypasses the requirement for G protein beta and gamma subunits in the yeast pheromone response pathway, Mol. Cell. Biol. 14 (1994) 1054–1065].

Mimi returned to Berkeley briefly in early 1992 to give a seminar and file her doctoral dissertation, and received her Ph.D. from Berkeley in April 1992. Perceptively seeing that much of the future of biology lay in obtaining structural information at atomic resolution, and always having displayed a true love and gift for mathematics, Mimi chose to switch fields completely for her postdoctoral training. Immediately after receiving her Ph.D., she commenced postdoctoral research in the laboratory of the renowned crystallographer and enzymologist Gregory A. Petsko in the Rosenstiel Basic Sciences Center at Brandeis University in Waltham, MA. To support her postdoctoral training, Mimi was awarded a prestigious and highly competitive fellowship from the Cancer Research Fund of the Damon Runyon-Walter Winchell Foundation. In the Petsko lab, Mimi learned the crafts of protein crystallography, X-ray diffraction analysis, and mechanistic enzymology. She clearly had an aptitude for this kind of work because, until her untimely death on January 16, 2006, she continually made truly unique and important contributions to the fields of enzyme catalysis and protein structure.

Mimi was exceedingly bright, vivacious, and motivated strictly by her curiosity about the unknown, with no thoughts about personal glory whatsoever. The fact that throughout the progress of her career she carried out research of the highest caliber in a wide range

of biological subdisciplines that each utilizes very different methods and experimental approaches demonstrated her depth and versatility as a scientist. She is sorely missed by all whose lives were favored and enriched for having intersected hers.

3. From Gregory A. Petsko and Dagmar Ringe

The first thing you noticed about Miriam (Mimi) Hasson was her size: she was a tiny thing, and probably was easy to overlook in a crowd. But if you got to know her, that impression faded fast. Her personality wasn't small, her intellect was large, and her heart was huge. She came to our lab with absolutely no crystallographic experience, and the project we gave her to teach her structural biology, though we thought would be easy, turned out to be fiendishly difficult. She solved it, of course. She always did what she set out to do. By dint of sheer determination she cracked a problem in symmetry and packing that would have defeated many an experienced crystallographer. At the end of her postdoctoral stay she knew as much about the subject as anyone who had ever worked with us.

It won't surprise anyone who reads the other remembrances of her that she was like a mother to the others in the group. We could always count on her to tell us if anyone was depressed or struggling. When she left to start her own lab at Purdue, she left a mighty big hole.

We decided to contribute a scientific paper to this issue because we thought that she would have appreciated that. It's work we've never published, and that we're rather pleased with. We'd like to think she would have enjoyed reading it, and would have had lots of questions and suggestions–all right to the point. We hope it would have piqued her curiosity, because that was one of her most outstanding qualities. She wanted to know the answer. That's the soul of a true scientist.

Robert Browning once said something to the effect that if you really wanted to know the height of a person's mind, you should measure it by the length of the shadow it casts. He meant, of course, that what counts is the effect a fine mind has on others. When you read the essays in this issue, and the scientific papers sparked by her memory, you will, we hope, realize that Mimi Hasson wasn't tiny at all. By that standard–maybe the only standard that counts–she was a giant.

4. From Lena Polovnikova

In the year 2000 I became Miriam's first graduate student to defend. As such, along with her distinguished mentors and colleagues, I was invited to share my thoughts on Miriam. This invitation was extended under the consideration that I am a part of Miriam's academic family. I imagine that Miriam would have welcomed the thought, as she was a scientist who took family seriously.

She was extremely devoted to her natural family, but also told me several times that, for a scientist, a laboratory is a kind of family. This interpretation of academic family did not require one to give up the personal for the sake of science, but allowed the scientific and personal lives to flow freely without the division or conflict between the two. Miriam's laboratory embodied this almost literally. Miriam's husband, David Sanders, joined the lab lunches and discussed the projects with his wife's students, who, in turn, often freely moved between the two mentors, at liberty to seek the benefit of their joint spousal scientific wisdom. Miriam and David's sons hung out at her office on the school off-days, and

our own spouses felt free to visit the lab whenever they pleased. One internal graduate student marriage and a couple of babies happened during this scientific process. The practice of science under Miriam's mentorship took some clearly familial notes.

While other professors may have been wary of student-sitting and cultivated strictly professional relationships with their students, Miriam was not afraid to get close. She advised us on data interpretation, experimental design, marital disputes and life strategies, freely asked for advice from us, and brought up scientific discussions at any possible moment. She was baffled when others seemed eager to leave the science talk behind the lab doors. To Miriam, there was no such thing as a bad time to discuss research. She was preoccupied with it at all times, just as she was preoccupied with her children and her religion at all times. She clearly could not imagine partitioning science and that other, non-scientific life into separate compartments; all aspects of life seemed to harmoniously mesh and intertwine in her mind. Miriam was a whole person, and her scientific advice stuck. Pay your dues. Take what you do close to heart. Look for beauty. Move with no fear. Give credit to others.

Through luck, I was Miriam's first student to defend. Therefore, formally, I am her first "academic" child. But, in spirit, someone else is more deserving. My friend and fellow graduate student in Miriam's lab, David Cooper, is now at the University of Virginia in Charlottesville. He was the first to join Miriam's new laboratory at Purdue in 1996. More importantly, he chose structural biology as his life's vocation after leaving the nest. Having changed careers after graduate school, I consider myself more of a wayward sibling than a true descendant continuing the distinguished academic line. Nevertheless, the sense of belonging to the bigger scientific family was one of Miriam's greatest gifts to me.

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