

He recognized the need for more leadership at the teaching hospitals proximal to Beth Israel and Harvard Medical School and developed the program at the Boston Children's Hospital, where he was made chief of the Division of Dermatology at the Children's Hospital Medical Center and dermatologist at the Boston Hospital for Women.

When Irwin announced he was leaving Harvard, I was in disbelief. Why would he give up such a successful position, by then in a rapidly growing prestigious program? We both had looked at other job offers, but in my case mostly as an ego trip. These past two years before and since his death I have thought a lot more about what the Boston experience was about and how it molded him. The years at Harvard were like basic training, and Irwin had strong role models in academia in and outside of dermatology at Beth Israel and Harvard Medical School. He was ambitious, but in a very special way. He was confident about himself and his ideas of where dermatology and skin research should move. He felt he could put ideas into action by attaining leadership positions in the organizations that established or influenced policy in the clinical and research areas, such as the Society for Investigative Dermatology, the American Academy of Dermatology, the American Dermatological Association, and the National Institutes of Health. Irwin eventually assumed leadership positions in the Society for Investigative Dermatology and was editor of the *Journal of Investigative Dermatology*. He had the people skills, which are critical for such an undertaking, but I think he felt he needed the platform of chairmanship at a strong university to carry out his ideas. With Tom Fitzpatrick firmly in place at Harvard, moving to another institution was a necessity. Irwin already had leadership experience and was known and respected in the scientific community, and taking over a program would not be unduly challenging to someone with his ability, energy, and healthy self-esteem. Furthermore, his personal life with his children and his wife Irene was rock solid. When I look

at pictures of Irwin from our medical school years at Harvard and New York University, I see the same man but with different ambitions and academic research accomplishments. The outpouring of emotion at his passing

was not merely for the friend whom we loved and who left us too soon but was also an expression of gratitude for the man who contributed so much to the growth of dermatology as a clinical specialty and science.

Irwin Freedberg: Keratins Before the Beginning

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It was through my meeting Bill Montagna in Cambridge, UK, in 1955 that I met Irwin Freedberg some eight years later. It happened this way.

In 1954, when Irwin would have been in the middle of his medical studies at Harvard, I was a research student in Cambridge, UK. I was using the new electron microscope techniques of Porter and Palade to investigate hair ultrastructure and to see if biochemical information could be correlated with it. Montagna was working in London with Geoffrey Bourne; I had published some work using the new tetrazolium salts, and for that reason he visited me in Cambridge. That meeting and subsequent friendship initiated my entrée into the bigger world of investigative dermatology in the USA to view the excitement about basic research on skin hallmarked by Stephen Rothman's 1954 book, *Physiology and Biochemistry of the Skin*.

Montagna invited me to his 1959 meeting in New York on Hair Growth and Hair Regeneration when Irwin would have begun his dermatology residency at Massachusetts General Hospital. However, it was not until 1963 at the Lake Arrowhead conference organized by Montagna and Lobitz (published as Montagna and Lobitz, 1964) that I met him. Irwin Freedberg was one of a group of young investigative dermatologists, including Howard Baden, who were present at

the conference and entering the new era of keratinology. The conference was a landmark because the invitees included older and newer faces in the field, the older including Stephen Rothman, Honor Fell, Howard Mercer, Elizabeth Hay, Albert Kligman, Izzy Bernstein, Eugene van Scott, Peter Flesch, and Ruth Freinkel, covering a wide range of the biology of skin — I was somewhere in between.

Howard Mercer and Birbeck in 1957 published their work on the ultrastructure of the hair follicle and had visualized cortical filaments, or microfibrils as they were then called. Their findings, incidentally, confirmed Mercer's conclusion, made in the 1940s from his viewing degraded wool fibers on a grid in one of the first postwar electron microscopes, that the fiber cortex was an admixture of filaments with a matrix. In 1959, I made the matrix more reactive with osmium and lead in ultrathin sections of mature wool and hair fibers and other "hard" keratins such as nail, horn, and echidna quills, thereby enhancing contrast and visualization of the ultrastructure of mature hard keratins. Because of the narrowed focus on them, several years had to pass before it was realized that the microfibrils of wool, hair, and hard keratins generally, were members of the wider family of intermediate filaments.

Hard keratins were solubilized by Goddard and Michaelis in 1937, but

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it was not until a period of some 25 years beginning in the late 1950s that research, mainly in Australia, made major strides and *inter alia* demonstrated that hard keratins, especially wool, could be fractionated into defined protein groups. Those Australian investigations peaked with the publication of the first amino acid sequence of a type I keratin intermediate filament by the Commonwealth Scientific and Industrial Research Organisation group in Melbourne. During this period the epidermal cyokeratin family of epidermis was defined by Moll, Franke, and others; monoclonal antibodies prepared by Henry Sun in Irwin's department enabled tissue localization. "Soft" and "hard" keratins were joined.

I met up again with Irwin because I became more interested in protein synthesis, as the basic mechanisms were known and *in vitro* protein synthesis systems had been established. In 1965 I reported the isolation of ribosomes from hair follicles and, with Peter Steinert, demonstrated the synthesis of both the filament and keratin-associated proteins. Around that time I visited Irwin at the Beth Israel Hospital in Boston, and to my surprise — and some concern, I might add — I discovered that he was doing the same thing! He had wasted no time in beginning his career in research and had earlier begun studies on protein metabolism with Howard Baden. We kept in touch after that, and he was by then developing his profound and lifelong interest in the combination of basic epidermal and hair keratin research and clinical practice. Irwin maintained, over subsequent years, his strong interest in the keratin proteins and their synthesis in hair follicles and in the epidermis. Two of my PhD students, Peter Steinert and Peter Gibbs, collaborated and published with him. He gathered into his department many excellent researchers with whom he collaborated, including Arthur Bertolino, Miroslav Blumenberg, and Henry Sun, and he rapidly moved into the frontiers of epidermal keratin gene cloning and the control of keratin gene expression, at the same time maintaining his influential hand in clinical dermatology.

Over the years I had the pleasure of Irwin's friendship. He kindly read a paper for me at a meeting in Hamburg in 1979 when I was unable to attend. I visited him when he was at Johns Hopkins and in his department at New York University, and we met on many occasions at meetings in Japan and at Epithelial Differentiation and Keratinization Gordon conferences, which he had been instrumental in setting up in 1979. It was a disappointment for us in Australia that he was unable to be present at a conference held in 1989 in Adelaide on the biology of wool and hair growth.

Irwin Freedberg: Physician-Scientist and Mentor

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He may not have known exactly what the future would look like, but he knew how to get us there.

—David Polsky

I met Irwin Freedberg in 1977 when he offered me my first "real" job, as an assistant professor in his new Department of Dermatology at Johns Hopkins Medical School. In his letter offering me the job, Irwin said, "We shall look into the matter of grant support, and I will be back in touch with you as soon as we have identified the appropriate sources. I am certain that the relationship we have discussed will be a mutually productive, extremely fruitful one for all of us. I am very much looking forward to the adventure." Indeed, that offer began my own fruitful, 28-year association with Irwin, first at Hopkins and later at New York University (NYU).

When Irwin informed me he would "look into the matter of grant support," I assumed he would simply provide me with the names of funding agencies to

Through the course of his life Irwin oversaw and participated at all levels in the remarkable increase in our knowledge of the epidermis and its appendages and the impact of these advances in explaining the causes of skin diseases, in particular those resulting from faulty keratinization. He had an illustrious career in dermatology and was outstanding in his breadth of molecular and clinical knowledge. I feel very privileged to have known him.

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which I could then apply. However, Irwin's involvement in my initial grant application process was much more extensive than that. Irwin provided me with some of his own grants as examples, and he then carefully reviewed my writing, which, I must say, was pretty awful (and still is). Irwin was an amazingly effective editor; without his painstaking work, I am certain that my first grants would never have been funded. From this experience, I learned from a master the skills of writing and good grantsmanship.

Irwin was committed to supporting research because of his deep conviction that research ultimately holds the key to improved clinical care. Shortly after his arrival at Hopkins, he recruited Arthur Bertolino, Gopal Bhatnagar, Peter Gibbs, and Mary Gilmartin to set up a laboratory located on the ninth floor of the Blalock Building to perform pioneering studies on the biosynthesis and posttranslational modifications of keratins. These researchers were the first to demonstrate that

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