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RETROSPECTIVE

Fred Sherman (1932–2013)

Susan W. Liebman^{1,2} and James E. Haber³

Fred Sherman, a brilliant geneticist who popularized the use of baker's yeast, *Saccharomyces cerevisiae*, as a genetic model system of eukaryotic cells, died on 16 September at the age of 81. Budding yeast are now used at virtually all research centers worldwide, largely due to Fred's efforts and mentoring of many of the leaders in the field. Indeed, Randy Schekman, who shared this year's Nobel Prize in Physiology or Medicine, was introduced to yeast in the Cold Spring Harbor course that Fred taught for 17 summers with his friend and colleague Gerald Fink. Many students and postdoctoral fellows who were trained in Fred's own laboratory also helped shape the field of yeast genetics. Fred taught by example how to think about science, how to do it, and how to enjoy it. He lived life fully, with joy, humor, and dance (ballet), and without ever really separating life from science.

Fred was born in 1932 in Minneapolis, Minnesota, to Jewish Ukrainian immigrant parents. The family lived in a few rooms behind his father's grocery store. "Freddie" (the name on his birth certificate) grew up thinking he was one of richest kids in the world because, unlike his friends, he always had enough to eat. Fred graduated magna cum laude with a B.A. in chemistry from the University of Minnesota in 1953. He obtained his Ph.D. with Robert Mortimer at the University of California, Berkeley in 1958, where he was introduced to yeast and then studied with two other founding yeast geneticists, Herschel Roman at the University of Washington in Seattle, and Boris Ephrussi at the Lab Genetique, Gif-sur-Yvette, France. In 1961, Fred took a faculty position at the University of Rochester in the Department of Radiation Biology and Biophysics, where he remained for his entire career and served as chair of the Department of Biochemistry for 15 years. He often said of this job, "I can't believe they are paying me to do this!"

A long time before DNA could be sequenced, Fred devised a method to deduce



the DNA sequence of the first 15 amino acids of the yeast gene *CYC1*, which encodes iso-1-cytochrome c. He did this by isolating and fine-structure mapping many *CYC1* mutations and reverting nonfunctional mutations back to functional, pseudo-wild-type proteins. Changes in these revertants could be identified by sequencing the amino terminus of these proteins, using the laborious chemical process of Edman degradation, carried out with the help of his long-time collaborator, John Stewart. The pattern of amino acid changes from single mutants allowed Fred to establish that the genetic code used in eukaryotes was the same in all key respects with the code that had been deciphered primarily in genetic and biochemical studies with the bacterium *Escherichia coli* and its bacteriophages. He established that AUG was the only start codon in eukaryotic protein translation and that UAA, UAG, and UGA were chain-terminating "nonsense" mutations. He also identified transfer RNA genes by isolating extragenic suppressors of the nonsense mutations and determining the amino acid inserted at the nonsense codon. His work deciphered the rules for transcriptional starts and termination. His deduction of the *CYC1* DNA sequence led to the synthesis of a synthetic oligodeoxyribonucleotide that could for the first time identify the messenger RNA of a specific yeast protein

A geneticist championed baker's yeast as a model system and inspired and trained many scientists in the field.

gene. Studying gene structure and function by genetic approaches inevitably led Fred to investigate gene conversion and to make important contributions to understanding mechanisms of recombination.

The importance of Fred's work was recognized by his election to the U.S. National Academy of Sciences in 1985, his receipt of an honorary doctorate from the University of Minnesota in 2002, and his election as a fellow of the American Association for the Advancement of Science in 2006. In 2006, he also was awarded the George W. Beadle Award from the Genetics Society of America in honor of his outstanding contributions to the community of genetics researchers.

Fred's impact on the scientific community extends far beyond his individual scientific achievements and organized service on editorial and society boards and scientific review panels. Unlike many leading scientists, Fred answered his own telephone, where he spent hours each week helping colleagues with all sorts of scientific problems. In these and other conversations, he might ask seemingly naïve questions and then come up with stunningly profound suggestions. Fred promoted a culture of sharing ideas, reagents, and strains that is still prevalent in the yeast community. He loved to travel and shared his ideas all over the world at conferences and at universities where he visited colleagues and gave many seminars. He welcomed many of the students he met abroad into his laboratory for a year or two of critical training before they returned to their home country for successful careers.

No reflection of Fred Sherman would be complete without mention of his inclusiveness. He ate lunch with his students and postdocs most days. Fred used his famous wit and humor to make people feel included and comfortable. For example, he would break the ice with a lonely graduate student at a meeting by asking "How are you doing?" The surprised student would often respond "I'm fine, how are you?" to which Fred would say "Well, I think I'm fantastic. ... But not everyone agrees with me."

Fred Sherman was an exemplary scientist. His memory is a blessing for us all.