The remarkable influence of Paul M. Doty on the heat shock field

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We have lost a pioneer of molecular biology and a larger-than-life player on the world stage. Paul Mead Doty died on 5 December 2011 at the age of 91. Douglas Martin's article in *The New York Times* hits the high notes (Martin 2011). Here, I would like to add a few personal memories and thoughts about Paul along with his link to the origin of the Cell Stress Society International (CSSI). Paul's 1960 paper (Doty et al. 1960) describing some remarkable physical properties of double helical DNA that we know today by the heading nucleic acid hybridization and the even more remarkable property of specific recombination was required reading by graduate students in biochemistry and molecular biology when I was a graduate student. Now, this information is taught in high schools as part of the molecular basis of life.

The Doty laboratory was centered on physical chemistry. The pioneering work of Paul and Helga Boedtker Doty included the gene structure of collagen as well as the properties of DNA. Several of the founding members of the CSSI studied in the Department of Biochemistry and Molecular Biology started at Harvard by Paul Doty. In the words of Richard I. Morimoto, "I had the good pleasure to work with Paul and Helga and published a paper with them (Wozney et al. 1981). I would wander frequently to the Doty tearoom at Harvard as they seemed to have better cookies. Moreover, to have Helga and Paul hold court was special as through him and Matt Meselson, I was exposed to the world of the scientist-public citizen. At that point in his career, Paul was deeply interested in world policy issues on disarmament and to hear him expound on this and other topics was inspiring." Indeed, Paul Doty facilitated relations

Paul Mead Doty (1920–2011) circa 1960. Harvard University Archive

between US and Soviet scientists during the cold war and he was credited with contributing to the Anti-Ballistic Missile Treaty signed between the Soviet Union and the USA in 1972. In 1974, Paul Doty founded the Center for Science and International Affairs at Harvard.

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Paul Doty was instrumental in recruiting Professor Matthew Meselson, who was also a mentor to Susan Lindquist. She carried out her pioneering work on heat shock RNA in Meselson's lab (McKenzie and Meselson 1977). Earlier this year, Dr. Meselson's thoughtful retrospective on the life of Paul Doty was published in *Science* (Meselson 2012). Paul helped me establish my graduate study at Harvard during the very difficult year of 1968. Not only did I learn the physical and biological properties of DNA from Paul, but he took the extra time to write a letter for me in an effort to hold off my draft board long enough to allow me to finish my first semester. I decided then and there that if I survived Vietnam, I would come back to his department to restart my life as a scientist.

I did return to Harvard soon after serving 13 months in Vietnam as an enlisted draftee in the US Army. When I took my oral examination to continue in the Ph.D. program, Paul Doty was present as a supportive member of my committee to question me on eukaryotic chromatin structure. He was one of those faculty members whose influence was life changing. After passing my orals, I concentrated on my doctoral research in virology with Professor Michael Bratt at Harvard Medical School. I became involved in research on the heat shock response several years into my assistant professorship at the University of Connecticut. One of my graduate students, Ivone Takenaka, wanted to study the effects of transforming growth factor- β (TGF- β) on the induction of heat shock proteins in chicken embryo cells. As a positive control, we decided to measure the effects of TGF- β on collagen gene expression, a gene known to be strongly activated by this factor. Helga Doty generously sent us their plasmid containing a chicken procollagen cDNA that allowed us to quantify collagen mRNA production in our experiments. It was the findings on the melting and reannealing of the strands of the DNA double helix described in Doty's 1960 paper that provided the foundation for the blotting techniques that Ivone used in her successful study (Takenaka and Hightower 1993). This is just one of countless examples of the experiments made possible by the pioneering work of the Doty laboratory.

As Rick Morimoto recalled above, I too was struck by Paul Doty's efforts to use science as a positive force in international policy. I began to view science as potentially the most powerful unifying influence in a world torn by divisive sociopolitical, economic, and religious dogma. I am convinced that this was a formative influence on my own decision to invest time and energy in the founding and development of the CSSI and its professional journal *Cell Stress & Chaperones*.

Paul Doty also recruited James D. Watson to Harvard and this is where the history holds additional interest for our field and professional society. Professor Doty and several

colleagues were successful in forming the Committee on Higher Degrees in Biochemistry in 1954–1955. James Watson was recruited in 1956 to establish molecular biology. Watson invited Alfred Tissières to spend time in his laboratory as a visiting scientist, the same Alfred who later discovered the *Drosophila* heat shock proteins (Tissières et al. 1974). When colleagues studying heat shock genes and proteins decided to organize the first international meeting, it was Alfred who went to his old friend and mentor Jim Watson, then Director of Cold Spring Harbor Laboratory, to make the case for a meeting at this prestigious laboratory. It was not a given that the director would agree because at the time, many scientists still considered the heat shock response at best a curiosity of *Drosophila* biology and at worst a laboratory artifact. But Alfred was convincing and the first of many meetings in an ongoing series was held at Cold Spring Harbor (Schlesinger et al. 1982).

Without Paul Doty then, the meeting that galvanized the field of cellular stress responses arguably would not have taken place. Later, scientists from around the world who had met each other at the Cold Spring Harbor heat shock meetings became friends, colleagues, and collaborators and joined together to form the editorial board of *Cell Stress & Chaperones* journal in 1995. Indeed, the first meeting of the editorial board was held at Cold Spring Harbor the following year. Several years later in 1999, the organizing meeting for the CSSI was held in Grace Auditorium at Cold Spring Harbor Laboratory. It is very doubtful that this chain of events would have occurred without the nucleating links laid down by Paul Mead Doty.

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