Good Times with Don Caspar

It's a special pleasure for me on this occasion to express the admiration I have for Don and for his many scientific accomplishments, and the affection I feel for him. I want to tell you about our early days when many of you here did not know him. We started the Structural Biology Laboratory together at the Children's Cancer Research Foundation (the so-called Jimmy Fund) in Boston in 1959. It began as a small, rather unorthodox, scientific commune (quite marginal to the Harvard Medical School) and continued that way for more than a decade before we moved to Brandeis. Those were the halcyon days in the field of biological structure, because so little was known and relatively few people understood how exciting these problems were. The possibility of determining the structures of very large molecules or assemblies at the atomic level seemed remote, involving tedious methods then being developed by crystallographers. But understanding the overall design of such structures and their modes of assembly for a variety of muscle and virus systems seemed absolutely feasible and of profound interest. There was a lively collaboration between Andrew Szent-Gyorgyi, who was then at Woods Hole, and myself, and Susan Lowey joined the lab as a postdoctoral fellow to work on myosin. Ken Holmes came from England and joined Don to continue his studies of TMV. Well, I said it was a commune, and Ken was soon working with me as well on coiled coils. (I should note that in return I had a contribution to make on the Dehlemense TMV story.) Now in those days, and for many subsequent years, Don would visit Cambridge, England, every summer to converse—at length—with Aaron Klug. The first time I met Aaron (apart from a brief hello at Birkbeck College when I visited Rosalind Franklin) was on his crucial visit to us just before the Cold Spring Harbor meeting of 1962. Don and he had been struggling with the problem of spherical virus construction for many years, and finally they achieved a major breakthrough and were writing it up to present at the meeting. As you all know, the solution was precise and powerful, with profound implications for the assembly of other biological systems. I think that was certainly a high point of Don's (and the laboratory's) accomplishments. I should add here that Steve Harrison, then a Harvard undergraduate, wandered into the lab one day a few years later. I think he was in search of distilled water, but in addition to the water, he found Don and became his graduate student. In that poorly equipped lab, Steve began to tackle the heroic problem of determining the first high-resolution structure of a spherical virus. Steve's brother, Rick, also joined Susan and myself and worked on muscle, and a bit later, Don Wiley enjoyed the unconventional atmosphere of the place as well.

In the late 1960s Don and I began a wonderful collaboration on tropomyosin that dated back to a visit I paid him about 1957 when he was an assistant professor at Yale, and I was a research associate (like all staff women, of course) at MIT. I brought some tropomyosin crystals to him (probably prepared for me by Andrew Szent-Gyorgyi). I should remind you that one of the few experimental undertakings of Francis Crick in the early 1950s when he was thinking about coiled coils was to attempt to take an x-ray photograph of a tropomyosin crystal in Cambridge. But with 95% solvent content in the lattice, he succeeded only in boring a large hole through the crystal with the x-ray beam. Don had a precession camera but with no cooling, so he and Bob Langridge (then his graduate student) opened the window of the laboratory and left the crystal on the x-ray machine overnight in the cool breezes of New Haven. The next day we saw the wonderful set of spots forming a cross. (When Max Perutz first saw that photograph he said, "Oh a helix." Well it *was* a helix, but not at all like DNA!) About a decade later, I was struggling in our laboratory with the tropomyosin crystals and Bill Longley (who had taken his degree with Aaron) joined us in that work. We were getting lots of puzzling x-ray patterns. Now Hugh Huxley had taken electron micrographs of such tropomyosin crystals, and had shown that they displayed a wonderful open mesh. I remember that Don, Bill, and I were getting nowhere when I said, in exasperation, "Look, Don, we have to connect *this* mesh with *those* x-ray patterns." And lightning struck and Don took a discarded, poorly developed x-ray photograph out of a waste basket and saw the correspondence between the crossed arms of the mesh and the cross on the x-ray pattern. Soon we had the low-resolution structure solved. That was another happy time and another exciting Cold Spring Harbor presentation. I should note that the work on the viruses and the muscle proteins kept Don busy with Charlie Ingersoll, our exceptional machinist (who is still with us), fabricating a variety of delightful mechanical models. One newspaper article at the time described "Dr. Caspar and his tinker toys." That was very apt, because those models were a great source of pleasure and fun, as well as being instructive. In some ways the models epitomize the happy and playful spirit in the laboratory.

There are a few more points about Don's special qualities that I must make. I think that everyone here knows that Don is, and always was, a great explainer. In fact, a marathon explainer. Here I am reminded of what Gertrude Stein said of Ezra Pound. I paraphrase: "Ezra is the village explainer. Excellent if you are a village, but if not, not." But Stein did not admire Ezra Pound as we admire Don. Don's prolonged musings and analyses have always been to many of us an engaging characteristic of this man who essentially loves to think aloud, in order to understand the answers to difficult problems and to make others understand as well.

The final point I want to make is perhaps the most telling one about his creative gifts. Don has always had an aversion to mysticism and magic, ever since his early interest in symmetry. Don's favorite terms of scorn in dealing with bad ideas in science are "preposterous" or "irrational." Yet Don is certainly a magician himself. Anyone who has worked closely with him has recognized that in some ineffable and

marvelous way he has arrived at a series of beautiful and profound insights about the construction and functioning of biological molecules. I am convinced that scientists who make such special contributions use not only the rational part of the mind, but the romantic, poetic, and visionary part as well. (The two parts are what Pascal called "l'esprit de finesse and l'esprit de géométrie.") In one of our papers, Don and I quoted Coleridge's famous "coincidence of contraries" in describing the many dualisms in molecular biology. I believe that that generative dualism is the fount of his inspiration as well.

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