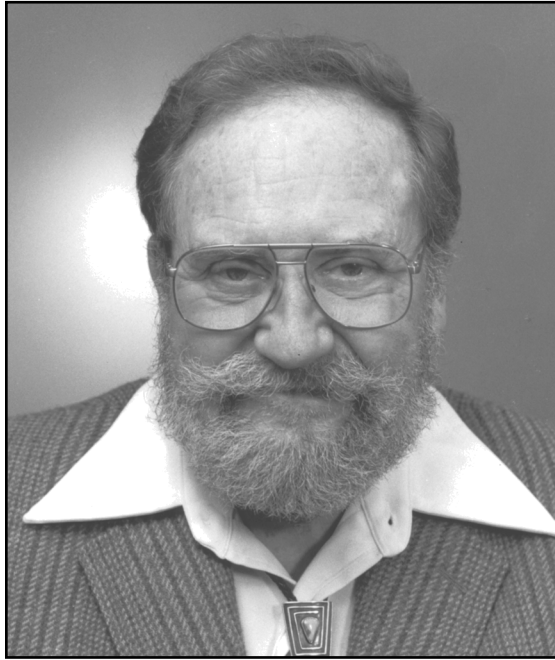


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RAY DAVID OWEN



CALTECH

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The authors are among many indebted to Ray Owen for his unique and endearing responses to students and his incredible mentorship. To his friends (and that included almost everyone), Ray was a complex man with a simple affect. He was an uncommon mixture of a highly critical and careful scientist overlaid on the soul of a mensch. We recall Ray's many and important scientific accomplishments below, but will finish with a particular trait of the Owen lab: twice daily coffee.

Ray David Owen was born in rural Geneseo, Wisconsin (population 180) on October 30, 1915. His father was a dairy farmer, and Ray grew up with a farmer's habit of early rising and hard work. He helped work the family farm through three years at nearby Carroll College (Waukesha, Wisconsin), where he majored in biology; the biology department there consisted of a single faculty member. Ray had planned to become a teacher and even went so far as to practice teaching in his hometown. Perhaps most importantly, he met his future wife—June Weissenberg—at Carroll College. He was married to June in 1938, a marriage that lasted for 74 years, until her death.

Ray began graduate work at the University of Wisconsin, and his earliest work that we could locate was on the iris color in pigeons (Hollander and Owen 1939a, 1939b). This study using chemical approaches to understand genetics proved to be an important harbinger of his later studies—an approach that he never gave up on. His early fondness for pigeons and doves continued in his own PhD work on the expression of hybrid antigens on crosses between guinea fowl and domestic fowl. This work represents first use of specially produced antibodies that detected neo-antigens on the hybrids that were not present on either parent, and this result foreshadows much of the work of the late twentieth century on the detection of neo-antigens in cancer. He also brought the pigeon models to his graduate students later in his career.

Ray's most important single contribution is the famous twin cattle observation. It is important to note that this was not an experiment *per se* but an observation: an experiment of nature that only a thoughtful observer could interpret. Ray noticed that each of the twin offspring of a cow inseminated by two different bulls expressed blood groups consistent with both sires (Owen 1945). This observation could not be accounted for by then-current Mendelian genetic understanding. Ray, with his previous knowledge of cattle development, surmised that two things had happened: first, that there was a colonization of the blood system of each calf with its co-twin's hematopoietic stem cells; and second, that these acquired cells are capable of becoming established to provide a source of blood cells throughout life, despite their difference from the "host" blood cells. In Ray's oral history, he describes his

development in 1946 of the idea of acquired unresponsiveness for a seminar at Caltech. These studies led to the idea of acquired immunological tolerance, which was profound. The paper was recognized but not widely cited until the observations of Anderson et al. (1951) and Billingham, Brent, and Medawar (1953). It is clear that the Medawar group appreciated the importance of the cattle observation. This is stated explicitly in Brent's obituary of Owen published in *The Independent*, as well as in a letter from Medawar to Owen after the awarding of the Nobel Prize to Medawar and Burnet.

In 1946, with the blessing of his department chair, Ray took a leave from the University of Wisconsin and came to Caltech on a short-term appointment as a Gosney Fellow. The appointment transformed into a permanent faculty position a couple of years later, and Ray never returned to Madison.

Although the discovery of acquired tolerance is of vast importance, Owen made many other contributions. During a sabbatical at Oak Ridge National Laboratory to work with Dan Lindsley (a Caltech PhD who became a noted *Drosophila* geneticist), he performed seminal experiments on bone marrow transplantation. He provided the direct demonstration that bone marrow cells can give rise to an entirely new hematopoietic system in the recipient animal and that this new blood system persists for the life of the animal.

A characteristic of Ray's scientific career was to use whatever experimental system seemed best for the question at hand. Ray worked with pigeons, doves, chickens, rats, mice, goldfish, nematodes, tetrahymena, sea squirts, yeast, and, of course, cattle. Ray himself said:

I never adopted the principle that grad students should work on a problem for which I was getting research grant support and be components in some kind of machine, all of them working on the same highly focused area. I don't mean to imply that the way I structured things is better than other ways. But it does have some advantages, because each grad student had his or her own material and problem and area, often things that they had dreamed up for themselves, and we talked over and tried very diverse kinds of things. (Owen 1983)

This philosophy was coupled with his decision to have his students and postdocs generally publish without his name on the papers. He had decided that his contributions did not merit authorship, so a generation of students published their work without any attribution to Ray, thus defying the still-current convention that the lab director serves as the senior author on every publication coming from that lab. As Ray himself acknowledged, this convention provides a useful paper trail of continuity

of the contributions from the research group. Nonetheless, Ray felt it undervalued the contributions of his postdocs and students.

Ray made major contributions nationally. At the National Institutes of Health, he chaired both the Genetics Study Section and the Allergy and Immunology Study Section. He viewed this kind of service as a necessary and appropriate activity for successful practicing scientists—a view he impressed on his students and postdocs. In addition to this “first line” service, he had higher visibility national jobs. He served on the advisory council of the National Institute of Allergy and Infectious Diseases (NIAID), which is directly advisory to the director of the NIAID.

Arguably, his most prominent role was as a member of the inaugural President’s Cancer Panel, which was created as part of President Nixon’s War on Cancer. On the panel, he had a major impact, making sure that there was an appropriate balance between translational and basic research—a tension that persists to the current day.

Ray was not only elected to the National Academy of Sciences (NAS) in 1969 but also served as the Chair of the Genetics section of the Academy. He held this position while several of the authors were in the lab, and we came to appreciate the arcane mechanisms of NAS election.

Ray balanced his many obligations, most of which were on the East Coast, with aplomb. On one occasion, Ray was at coffee (more about this below) on Monday morning; left for Geneva, Switzerland; and was back in the lab Thursday afternoon. It was clear Ray always felt a strong obligation to his students and colleagues at Caltech.

Ray made many contributions to Caltech. He was a tireless teacher, teaching Immunology (Bi 114) for many years. Ray also initiated and taught Bi 2, a freshman elective during which students met with faculty in small groups (named jokingly after 1950s first-grade reading groups as “Robins” and “Bluebirds”). At the start, most Caltech freshmen were not interested in biology as a career—physics and engineering were much more popular (and remain so)—but his course was very popular. The class met on alternate weeks at his home on Rose Villa near the Institute and on campus. This interaction gave new undergraduates a connection with faculty that largely never ended.

Ray made big-picture contributions to Caltech in two areas—the first was the transformation of the freshman year, and the second was the admission of women as undergraduates. Both of these events were transformative to the undergraduate experience at Caltech.

At Caltech, the freshman year is a trying time for students. Young people (or young men at the time of Ray’s tenure) have been thrown together after stellar high school careers. Often, their entire sense of self-worth is wrapped up in the knowledge that they were one of the smartest students (if not *the* smartest student) in their schools.

During Ray's time at Caltech, many students arrived to find they were in the bottom half of their classes, surrounded by students who were their intellectual equals or superiors. Grades made the comparisons easy, and the pressure was intensified by the fact that these young people were (and still are) often driven by grades. Ray, however, spearheaded a significant change in the 1960s when he chaired the *ad hoc* Committee on the Freshman Year. This group of faculty carefully considered how to improve the experience of Caltech freshmen, and they devised a plan to abandon letter grades during the first year and instead grade pass/fail. Ray describes the long process in his oral history and recalls the lively debates. In the end, in a very Caltech fashion, the Institute performed an experiment—they agreed to use pass/fail for two years and then evaluate how the students did in terms of their social, psychosocial, and academic adjustment. There had been dire predictions that the students would become lazy and thus unprepared for their second year at Caltech. However, this turned out not to be the case, and the pass/fail grading strategy continues to the present day.

The second contribution—admission of women as undergraduates—seems self-evidently correct in retrospect that it is difficult to imagine any discussion at all. Nonetheless, Ray again led the charge and further worked hard on the implementation. This endeavor required long discussions among the faculty and trustees to make this momentous change occur. Surprisingly, an argument that was effective was: Caltech was losing some of the most qualified men because they wanted a coeducational opportunity. Surprisingly, the then-president of Caltech, Lee Dubridge, was not a proponent, and the decision to admit women was driven by the Committee on the Freshman Year that Ray chaired. Ray made the presentation to the Board of Trustees. In commenting on his presentation to the board, Ray used the “bright guys want girls” argument, but it is clear he felt uncomfortable. In his oral history, he says:

I didn't feel that that was a legitimate basis for deciding whether women should have suffrage or not, but it was helpful. Anyway, the decision was that we'd do it—we would admit women in two years. I got back on the Freshman Admissions Committee then, because I was very much interested in promoting—you know, we were told we wouldn't get many female applicants; and those that we did get would wear thick glasses and not be able to dance, and things like that. That's proved to be so wrong. (Owen 1983)

Ray then returned to the Freshman Admissions Committee and set about recruiting outstanding freshmen of both sexes. Among the class of 1973 was a student named Sharon Long. Long is currently Professor at Stanford, NAS member, and MacArthur prize winner, and she was

also a frequent coffee visitor as an undergraduate. So much for unqualified women. We are confident that Ray would be well pleased with the increasing proportion of women undergraduates at Caltech, an area to which he devoted much of his effort.

Coffee. This was an event much more than a beverage. Those who worked with Ray knew that he had very few requirements, but one was attendance at morning and afternoon coffee. Imbibing the coffee itself was not required, but that was a good thing. Because Ray was an early riser and was in his office by (we are told) 7:00 a.m., he made coffee in a large coffee urn. By the time of the official event at 10:00 a.m., it required substantial fortitude to drink. Ray, at the time a pipe smoker, was believed to fortify the coffee with pipe tobacco. Maybe the use of pipe tobacco was only apocryphal, but the coffee was bad enough to believe it.

Coffee was held in Ray's small outer office, which had a round table that could seat maybe five or six people. The Dutch door that separated Ray's inner office (also small) from his outer office bore testimony to his early life on the farm. Numerous bracket-and-board shelves were filled to capacity with back issues of immunology journals. Other items, including a reproduction of Dürer's painting of a young hare and copies of *Biology of the Laboratory Mouse* (the "Mouse Bible") and *The Pigeon* (a large-format compendium of everything from pigeon breeds' characteristics to pigeon feeding, veterinary care, and even recipes), paid tribute to animals that were important to the lab's research. A blackboard featured ephemera of the "Hungry Owen Group" (H.O.G.), including a set of make-believe, graduate-student-size pigeon leg bands.

What happened at coffee? Coffee was the central experience of working in the Owen lab. Postdocs, graduate, and undergraduate students from all over the Institute visited during coffee and found a genial and supportive mentor in Ray. He usually let the lab members listen and learn from how Ray dealt with other people's problems, including career advice. It was clear that Ray was not out to replicate himself but sought to help others reach their own goals. As a result, Ray often began conversations with visitors with: "Tell me about what you are doing, and what you want to do." His careful listening to the visitors always left a lasting impression on them. Ray almost never gave direct advice. He just continued asking questions until the visitor had reached their own conclusion (often clearly determined by Ray much earlier in the conversation). As a result, all of his visitors loved him.

It goes without saying that Ray was a pillar of integrity and wisdom. One of us (LH) had the interesting experience of giving Ray a paper to review that was an intellectual analysis of Jerne's network theory of immunity and why it was wrong. Ray read the paper carefully

and returned it without a single red-line comment. He said that it was his belief that you never should publish a paper without new data. He was convinced that theories were disproved by experimentation and not by intellectualization. It was a lesson the author (LH) never forgot.

The people in his lab also loved Ray, but differently. Although part of coffee was devoted to non-science and non-career topics (mostly the future of his beloved California Angels), most of the time was dedicated to science, which could be a description of a new interesting paper someone had read. Those many conversations always started with the big picture (why was this interesting?) and quickly shifted to the smallest experimental details. As with visitors, Ray rarely ventured direct comments but asked increasingly probing questions about the work. He would often mention that this problem had been considered before by the giants in biology. Ray would describe how they had addressed the problem with the tools they had and pressed us into asking how new tools might be used to solve the old problem. Clearly, Ray's goal was for each of us to learn how to think and be armed with all the relevant facts.

Because Ray was an internationally respected scientist, he was always on the visitor schedule for Caltech seminar speakers. In addition, he often had visitors who came to see him. A surprising number of the latter were (among the few) women prominent in their field at the time. He always had the visitors come at coffee time, during which the schedule was clear. Ray would introduce the visitor to the group, and then each of the members had about three to five minutes to present their work to the visitor and get feedback. This continuous honing of a young scientist's ability to present the essence of their work was the forerunner of the now-fashionable elevator pitch—before it was trendy. Again, these very brief presentations had to go from 30,000 feet to the nitty gritty of the experiment. Everyone took a turn, and Ray never interrupted—for good or ill, you were on your own, and we all got good at this. The result was we met famous scientists and basically had a chance to be remembered. Similar to many aspects of Caltech, it was a wonderful but incredibly stressful experience.

The final facet of coffee was the evolution of our own work. Here, the always supportive face of Ray seen by the outside world vanished. In its place was a truly critical and thoughtful scientist's evaluation of work—independent of the person. Although Ray's comments were gentle, they were not superficial. He probed for controls, then controls of the controls, and finally the statistical evaluation of the data. Although Ray was not a great statistician, he often sent us to Ed Lewis, who certainly understood statistics. These sessions always focused on the experiments, not the person. This approach taught us that the work

did not equal the person, which was important to remember when our dissertation drafts came back from Ray heavy with his red ink.

Ray was an avid gardener. He specialized in camellias and chrysanthemums and introduced us to the vast variety of those two flowers. He bred camellias and was particularly proud of one he named after his wife—June Rose. Ray's office always had flowers on the table, brought from his garden. Winter was camellias and fall chrysanthemums.

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## REFERENCES

- Anderson, D., R. E. Billingham, G. H. Lampkin, and P. B. Medawar. 1951. "The Use of Skin Grafting to Distinguish between Monozygotic and Dizygotic Twins in Cattle." *Heredity* 5: 379–97.
- Billingham, R. E., L. Brent, and P. B. Medawar. 1953. "Actively Acquired Tolerance of Foreign Cells." *Nature* 172: 603–6.
- Hollander, W. F., and R. D. Owen. 1939a. "Iris Pigmentation in Domestic Pigeons." *Genetica* 21: 408–19.
- . 1939b. "The Carotenoid Nature of Yellow Pigment in the Chicken Iris." *Poultry Science* 18: 385–7.
- Owen, R. D. 1945. "Immunogenetic Consequences of Vascular Anastomosis between Bovine Twins." *Science* 102: 400–1.
- . 1983. Interview by Rachel Prud'homme, in *Oral History Project, California Institute of Technology Archives* (October–November). Accessed April 2016. [http://resolver.caltech.edu/CaltechOH:OH\\_Owen\\_R](http://resolver.caltech.edu/CaltechOH:OH_Owen_R).