



Ray D. Owen 1915–2014

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An appropriate opening here might be “Cent’anni!”—the idiomatic toast invoking an exceptionally long and productive life. Ray Owen, who died on 21 September 2014 at the age of 98, managed exactly that by establishing a governing paradigm of modern immunology, by inspiring generations of students to scientific excellence, and by fostering enlightened social norms in academic science.

Ray Owen was born in 1915, the son of a Wisconsin dairy farmer. The young Ray would rise before dawn to his daily chores and the trip to the two-room schoolhouse he attended for his first 8 years of education. Perhaps this unique personal history instilled in him an ideal mix of strong work ethic, common sense, and keen intellect. Indeed, armed with these traits, he would make one of the most conceptually transformative observations in modern immunology: the discovery of immunological tolerance.

Ray completed his bachelors degree at Carroll College—where he met his wife and lifelong companion, June—followed by a PhD in genetics at the University of Wisconsin. However, it was during his postdoctoral fellowship in the Immunogenetics Laboratory at the University of Wisconsin that Ray was tasked with investigating a puzzling genetic situation brought to their attention by a Maryland cattleman. A pair of twin calves clearly resulting from separate sires each expressed both sets of paternal blood group antigens. Ray’s subsequent analyses revealed that the twins were chimeric, each containing their own blood cells as well as those derived from their twin sibling, apparently as a result of shared circulation during late fetal development. While this resolved the apparent genetic dilemma, it raised a profound immunological conundrum: the blood-group alloantigens from one dizygotic twin did not elicit an immune response in the other but were instead immunologically tolerated. These findings, reported in his 1945 article in *Science* (*Science* **102**, 400–401 (1945)) are his most well known among immunologists, and for good reason, as their conceptual, theoretical, and practical implications have driven thinking for the past 70 years about how the adaptive immune system works.

Foremost, these observations created the need for a mechanistic hypothesis that could account for these new concepts—immunological tolerance and the implication of an immunological ‘self’—and thus drove articulation and acceptance of the clonal selection paradigm, positing that immunological specificities are clonally distributed and undergo somatic selection processes to build preimmune repertoires around the immunological self. This conceptual framework forms the backbone of the overall research program of adaptive immunity and undergirds present-day concepts of selection in development and activation of the immune system.

Furthermore, Ray immediately recognized the translational implications of his work. He was among the first to suggest that mechanisms

of immunological tolerance could be exploited in transplantation settings, and he shared authorship on subsequent publications describing the use of radiation as a means of blocking or resetting the immune system before transplantation of bone marrow or other tissues.

Given the import of his findings, many in the scientific community, including Sir Peter Medawar himself, were perplexed that the 1960 Nobel Prize awarded for the conceptual advance of immunological tolerance was not shared with Ray. But, perhaps not surprisingly, Ray eschewed the trappings of scientific notoriety, remarking in a 1983 oral history project prepared by the California Institute of Technology (Caltech) that he was “...not keen on prizes.” For Ray, the reward was the scientific process itself and the advancement of understanding.

Ray joined the faculty at Caltech in 1946 as a Gosner Fellow, where he spent the remainder of his career. This was a heady era for genetics and the emerging age of new biology at Caltech and, as might be expected for a person of such intellectual and academic stature, Ray assumed increasingly prominent leadership roles at both the institutional and national level. For example, he variously served as chair of the Biology Division of Caltech; Dean of Students of Caltech; President of the Genetics Society of America; and Chair of the National Cancer Advisory Board.

His scientific accomplishments notwithstanding, Ray made equally lasting imprints on scientific training and academic attitudes. Ray authored the major undergraduate text on genetics, and he was a pioneer in broadening access to careers in scientific research. While it is difficult to fathom in the current era, Ray was a key figure in reversing entrenched policies that denied women admission to Caltech. Ray’s profound commitment to mentorship is evident from his impressive group of trainees, not to mention the third- and even fourth-generation scientists who can be traced in his scientific family tree. In all of these people, Ray inspired the need to practice science with both imagination and rigor.

A scientist and scholar of unassuming intellectual strength, Ray was an exemplar to students and colleagues alike. His view that preparing the next generation of thoughtful, collegial scientists is, in the end, the most valuable contribution was nicely summed up during a 2010 interview by Mitch Kronenberg marking the 50th anniversary of the Asilomar Conference (available online at http://www.youtube.com/watch?v=C_9m_f_AKH4). Ray recounted with mild amusement how prominent figures in science have predicted the end of novel discoveries, and reflected: “... I say to my students—don’t be misled by the old timers saying that it’s all over....there will be plenty of things for you to do when we’re out of the picture.”

I therefore propose a toast to the concepts and attitudes that are Ray Owen’s legacy: Cent’anni!

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