ELIZABETH (TIBBY) S. RUSSELL

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ELIZABETH BUCKLEY SHULL was born into a family of scientists on 1 May 1913. Elizabeth's mother, Margaret Buckley, had an M.S. from Columbia University and taught zoology at Grinnell College before her marriage. Elizabeth's father, Franklin Shull, was a professor of zoology and genetics at the University of Michigan. Close relatives included a physicist, a geneticist, a plant physiologist, and a botanical artist. Elizabeth's proclivity toward science was fostered by a teacher in a grammar school associated with the University of Michigan, who encouraged students to make hypotheses, to design methods to test the hypotheses, and to evaluate and report the results.

Despite significant exposure to genetics, her University of Michigan A.B. was in zoology. Not until she read a paper by Sewall Wright entitled "Physiological and Evolutionary Theories of Dominance" during her tenure as an M.S. degree student at Columbia University was Elizabeth's interest piqued. She subsequently obtained an assistantship with Dr. Wright at the University of Chicago and began her lifelong study of genetic principles by assessing the inheritance of guinea pig pigmentation patterns.

Elizabeth received her Ph.D. in 1937, married a fellow graduate student, William L. Russell, and moved to the Roscoe B. Jackson Memorial Laboratory in Bar Harbor, Maine. As an independent and unsalaried investigator in her husband's laboratory, she received the first of many monetary and scientific awards. Her work on the genetic control of tumorigenesis in Drosophila was supported by an Elizabeth Pemberton Nourse Fellowship from the American Association of University Women (AAUW). As one of three "Elizabeths" at the laboratory, she was nicknamed "Tibby" to differentiate her from her colleagues. For the rest of her life this amiable, highly intelligent woman was known as Tibby.

Three boys and a girl were born to the Russells. The informality at the laboratory allowed Tibby to continue her active, although part-time, role in science. During the 1940s, she helped generate inbred populations of laboratory mice, characterizing each strain for physical characteristics and disease. In 1946, she was appointed to the scientific staff. A Finney-Howell Research Fellowship allowed her to complete a microscopic analysis of the pigment granules of thirty-six mutant stocks of mice. This monumental work, published in four parts during 1946, 1948, and 1949, showed that color, size, clumping of pigment granules, and degree of pigmentation are controlled by relatively independent entities.

The Russells divorced in 1947, leaving Tibby with four children under the age of seven. In the same year, the laboratory was destroyed by fire. During rebuilding, Tibby was selected to coordinate importation

of mice from outside the laboratory. Scientists worldwide, who had either purchased or been given stock, offered to return pedigreed breeders. Tibby fought for better animal health programs and maintenance of a separate inbred nucleus of founder mice for crisis situations. Health monitoring and revival of Tibby's inbred mouse nucleus were accomplished at the laboratory long before these issues became international concerns. In recognition of her foresight, the much expanded inbred nucleus was moved in 1990 to a new Foundation Stocks Building named for Tibby and her colleague Margaret Dickie.

Tibby's interest in education extended far beyond the needs of her own children. While she chaired the local PTA, she also accepted summer students for training in scientific principles. In 1937, she had twelve summer students and established herself as an excellent and inspiring mentor. Until her retirement forty-one years later, she welcomed prebaccalaureate students, Ph.D. candidates, postdoctoral fellows, and visiting investigators into her laboratory. Here, they were nurtured and supported in their career goals. One of these, Nobel laureate David Baltimore, when asked what stimulated his interest in science, noted that it was his summer experience at the Jackson Laboratory. She also developed a course in mouse genetics presented alternately with the Hopkins/Jackson Laboratory human genetics course.

Her enthusiasm, potential for stimulating discussion, and ability to pull together people with similar interests were among her many strong points. One example was the collaboration she organized with a premedical student and a visiting investigator; the three colleagues described the first mouse model for muscular dystrophy, a monumental discovery for the medical research community. In typical Tibby fashion, the student was first author of the paper published in the *Proceedings of the National Academy of Sciences* in 1955. In 1957, Tibby was promoted to senior staff scientist. In 1958, she received a Guggenheim Fellowship to review the current status of physiological genetics.

Tibby was ahead of her time in her persistent and persuasive argument for the importance of mice as models of human disease. Many inspired scientists visited her laboratory, bringing with them new diagnostic techniques and approaches. A dominant white spotting mutation, *W*, created a flurry of activity in the 1950s. The mutant mice had germ cell and red cell as well as pigment cell deficiencies. The pleiotropic effects allowed Tibby to assess functional differences and similarities of a single locus in each developmental pathway. Drs. Beatrice Mintz, Willys Silvers, and Seldon Bernstein worked with Tibby and contributed significantly to the analyses. New tenets were established with each paper published between 1956 and 1959. First, primordial germ cells do not differentiate in situ but migrate long distances to

reach the genital ridges. Second, the donor germ cells determine the developmental potential of the gonads. Third, the cell-intrinsic action of the *W* locus results in hematopoietic cell defects that are cured by transplantation of normal cells.

The cure effected by normal cell transfer preceded the first therapeutic transplantation in humans. It also provided an impetus to collect and assess other mutant mice with anemias. A seminal observation in 1961 presaged the current interest in secondary genes that modify disease expression. Tibby and her colleagues showed the extreme variability in the incidence and severity of disease when a single mutation was fixed on different genetic backgrounds. Secondary genes, not primarily responsible for the disease, have since become suspect in patients carrying identical disease-causing DNA alterations but showing extreme diversity in disease presentation. This observation, coupled with Tibby's guiding principle to "seek the optimal system" for the solution of any problem, caused her to move each anemia mutation onto a common genetic background. The analyses of differences and similarities between genetically determined traits without complication from secondary gene effects and the cross-transplantation between anemic mice without graft rejection became routine thereafter. Choice of the appropriate background was a monumental task, requiring Tibby's brilliant insights into problems of genetic diversity. Tibby received one of the first DOE grants for studies on the effects of irradiation on anemic and normal mice. Her DOE and NIH grants were funded continuously until her retirement.

One of the new anemias, Steel, had a *W* phenotype but mapped to a different chromosome. Tibby and her colleagues discovered in the 1960s that Steel and W mice differ in their acceptance of hematopoietic stem cell transplants. W mice are repopulated in the long term with both Steel and normal cells, but Steel mice are resistant to transplants from all donors. Tibby hypothesized that the W defect was intrinsic to blood cells, while Steel had a defective environmental milieu. Transplantation of normal hematopoietic spleen into the Steel mice alleviated the anemia, providing support for Tibby's theory. A review she published in 1979 was prophetic. Tibby suggested that the products of the two normal genes might interact, as acceptor and ligand, to activate the hematopoietic cells. Within eleven years both genes were cloned and Tibby's hypothesis proved correct. W was a signal receptor for the Steel ligand.

In the 1960s, Tibby's studies progressed to the analysis of hemoglobins in different mouse strains. She fixed an electrophoretic hemoglobin variant on her common stock background. She then used the "marker" to confirm that the cure initiated by transplantation of Steel cells into

W mice is due to the cells themselves and not to normalization of host cells. Tibby and associates mapped the variant gene to the beta globin locus. Another physiological variant, solubility (*sol*), was mapped to the alpha globin locus. Mapping of *sol* was a heroic effort since variability at the beta globin locus had an independent effect on solubility. Again, Tibby had to jockey genes to eliminate the complication.

In the late 1960s, Tibby showed that embryonic hemoglobins are expressed only in the large nucleated red blood cells from the yolk sac, while adult hemoglobins are produced in the fetal liver. This was especially important since it supported arguments that differential gene expression is dependent on factors intrinsic to ontogenic stages.

Tibby was extremely active on both the local and national levels during the 1970s. She was a member of an informal advisory council on aging at the National Institute of Child Health and Development. It was largely through her efforts that the National Institute of Aging (NIA) was established as a separate institute with the primary goal of performing research on the genetic principles of aging. A book chapter by Tibby became the most quoted reference in aging research. She served on the council of NIA and received one of the first program project grants. As she herself aged, she volunteered for the NIA on-site program to monitor human health.

In 1972, Tibby was elected to the National Academy of Sciences. As a council member, she waged a vigorous battle for preservation of live animal and plant germ plasm. She was president of the Genetics Society of America in 1975, and chaired a committee in 1976 to draft a position paper on race and IQ. Because of her leadership, the final document, on a highly sensitive issue, was supported with little discussion. In 1978, the secretary of health, education, and welfare invited Tibby to co-chair a committee to assess the future needs of biomedical researchers.

Locally, Tibby was appointed to the Bar Harbor Planning Board, on which she protected two local landmarks that were havens for wild birds and animals, served on the Somes Meynell Wildlife Refuge Board, was a local and state officer in the AAUW, and sang a rich alto in the Episcopal choir. In 1972, she became a founding trustee of the College of the Atlantic in Bar Harbor, which focuses on human ecology. In 1980, she became a trustee of the University of Maine, and argued vehemently for local branches to educate employees left jobless as businesses moved south.

Tibby became senior staff scientist emeritus in 1978. With papers and reviews yet to publish, she worked several days each week at the laboratory until 2000. She was a marvelous resource for the next generation of scientists, some of whom had been her students. Tibby traveled

to China, Russia, and Egypt to assess concerns about radiation and science. She taught genetics and global ecology at the College of the Atlantic. In 1988, she taught embryology and genetics at Cuttington College in Liberia, a sister diocese of the Episcopal Church in Maine. A return in 1990 ended in near disaster as Tibby, with the help of faithful students, fled to the coast through inland areas occupied by rebellious troops. She caught the last plane out of Liberia. She felt her toll was the loss of her bright students and of an opportunity to establish an African-based medical school. More serious to her friends and family were her two life-threatening malaria attacks.

Tibby was elected to the American Academy of Arts and Sciences and to the American Philosophical Society in 1983. Local and national groups honored her by inclusion in the book *Contemporary Women Scientists of America*, dedication of the Sixth Anniversary Symposium of the Jackson Laboratory to her, selection for Woman of the Year Awards from five local and state associations, and presentation of honorary degrees from three Maine colleges.

Tibby was interested in diverse disciplines, listened before commenting, always asked perceptive questions, supported and expedited her students' careers, and provided a rich environment that encouraged discussion for her natural and scientific children. Her youngest son, Jim, noted at her memorial that the household was often chaotic but always interesting. The same could be said by her scientific family. She was a wonderful mentor!

A minor fault was her absent-mindedness. I first experienced this affliction during my postdoctoral fellowship. In 1966, she invited me to her laboratory, apparently forgetting that her whole family was moving to the California Institute of Technology for two years in 1967. She greeted me with the news as she was exiting and I was arriving at the Jackson Laboratory. It was still a marvelous experience for me to be at the Jackson Laboratory and work with Tibby's group. Jim's comment on this particular failing was quite vivid. He said that Tibby could make a major breakthrough in science one day and back through the closed garage doors the next.

Jim also noted that Tibby rarely used the *me* word. She never discussed herself or seemed concerned about her own health—often to her own detriment. Later in life when she had a series of illnesses, she discussed the diseases clinically, not as they related to her. After a double hip replacement, she fell while exiting her home in Somesville on Thanksgiving eve. She tried several ingenious methods to stand—piling snow up beside her and trying to climb up the resultant slippery slope—and failed. Realizing she might freeze, she put on her hat to retain heat and hollered for help. Her boarder in a cabin about a

hundred feet away finally heard her call and came to the rescue. What interested Tibby was not that she was close to death, but that the local policeman who answered the emergency call knew he should keep the windows open in his patrol car so she would not warm up too fast!

Tibby died peacefully on 28 May 2001 at her cottage overlooking Echo Lake. She was predeceased by her eldest son, Dr. Richard Russell, a developmental biologist at the University of Pennsylvania, and by her brother, a physicist.

Elected 1983

JANE BARKER
Senior Staff Scientist
The Jackson Laboratory