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IN MEMORIAM

Ernst Joachim Ungewickell: 1950–2020

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Ernst Ungewickell, a remarkable contributor to our knowledge of intracellular transport coats, died in Hannover, Germany on August 19, 2020. He leaves behind Huberta, his wife of 45 years; his three children, Alexander, Charlotte, and Veronika; and five grandchildren. His life's work was encapsulated by the broad cellular question: How does soluble clathrin bind and assemble into rigid polygonal coats and then reverse? From discovering the three-legged structure of the clathrin triskelion (which he said "fell like a ripe plum into his lap"; Ungewickell and Branton, 1981) to revealing that live cells lacking clathrin still produce incipient puncta where other coat components concentrate (Hinrichsen et al., 2003), to reconstitution of coat assembly and budding with minimal purified protein cofactors (Dannhauser and Ungewickell, 2012), Ernst spent decades pouring his considerable analytical intellect into vesicle-mediated transport research. His efforts elucidated the structural and operational boundaries of the clathrin molecule during clathrin-mediated trafficking, ushering clathrin into the molecular era.

Ernst was born in West Berlin, Germany on January 6, 1950. He was fiercely proud of his hometown. At the second European workshop on endocytosis in 1990 in Paris, Ernst described his joy at finally being able to cycle across boundaries that were forbidden to him as a child. And in later years, he made a habit of escorting friends and colleagues to important city sites he felt should not be left unknown. Ernst's graduate studies were at the Freie Universität Berlin, followed by a first postdoctoral stint with Walter Gratzer in London (Ungewickell et al., 1979). Pursuing an urge to join Daniel Branton's laboratory at the Biological Laboratories at Harvard to master Branton's innovative EM technology, Ernst crossed the Atlantic for additional postdoctoral training in the late 1970s.

Upon arriving in the Branton laboratory, Ernst was captivated by the technology there, but less so by the project he was meant to pursue, leaving him open to inspiration from invited seminar speaker, Joe Goldstein, describing the molecular connection between receptor uptake and clathrin-coated vesicles. Combining his biochemical perspective from studying spectrin in the Gratzer laboratory (Ungewickell et al., 1979) with his newly acquired expertise in platinum shadowing, Ernst immediately set out to explore the morphology of purified clathrin and produced the now-classical first images of the triskelion, indelibly so named in the paper he published with Branton in 1981 on "assembly units of clathrin coats" (Ungewickell & Branton, 1981). One can only imagine the scientific thrill and excitement Ernst experienced upon looking into the glowing window on the electron microscope and seeing the metal-coated, symmetrical, three-legged triskelion macromolecule. Once Ernst showed others in the field what they were looking for, everyone could then see it in their own images. Following up this initial work, which also identified the light chain subunits as components of the triskelion, Ernst later published, with his wife Huberta, a definitive study demonstrating the regulatory effects of clathrin light chains on clathrin assembly (Ungewickell & Ungewickell, 1991), stimulating others (including one of us—F.M.B.) to address the nature of their regulatory function both in vitro and in cells.

After a year (1982) at the MRC Laboratory of Molecular Biology in Cambridge with clathrin pioneer Barbara Pearse, Ernst moved back to Germany, affiliated with Klaus Weber at the Max Planck Institute (MPI) for Biophysical Chemistry in Göttingen. With highly purified preparations of clathrin and the so-called associated proteins (APs) in hand, in one experimental thrust, Ernst chose to make a panel of monoclonal antibodies. This decision launched him into daily battle with advancing mold contamination—promptly sealed off with liquid paraffin—as he raced to screen the hybridoma clones. The end result was a panel of well-categorized monoclonals against the fundamental AP constituents. These antibodies were key in establishing the subunit architecture of heterotetrameric adaptors and were indispensable tools for the community. In 1986, Ernst started his own laboratory at the MPI for Biochemistry in Martinsried, Munich. Toiling away in the cold room with Suzanne Ahle, they purified and mapped functionally the activity of both multimeric and monomeric APs from brain clathrin-coated vesicles (Ahle, 1986; Ahle, 1990) and began to clone the encoding cDNAs. This work led to a clear and concise biochemical understanding of the clathrin-AP compartment.

Emil Unanue, whom Ernst had "mentored" at the bench while he was doing a sabbatical in the Branton laboratory at

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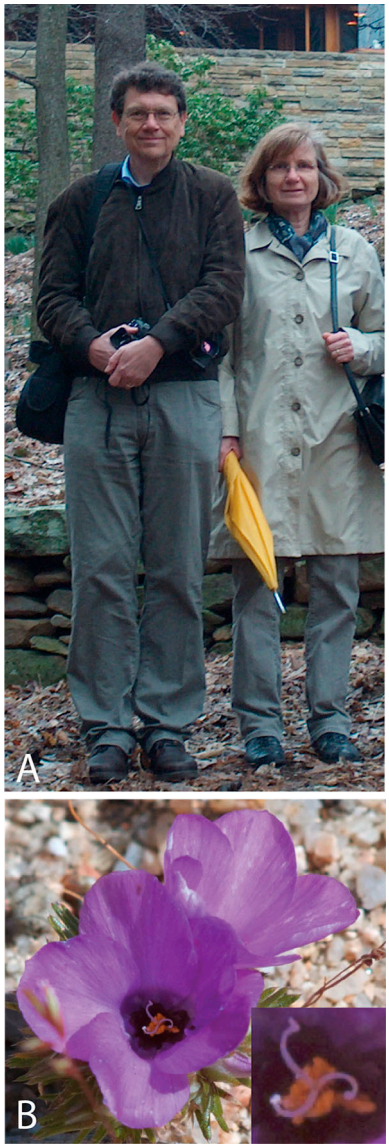

(A) Ernst (with ever-present camera) and Huberta at Frank Lloyd Wright's Kentuck Knob in Pennsylvania. Photo courtesy of Linton Traub. **(B)** Even while Ernst was pursuing his other interests, science and clathrin were never far from his thoughts. Over the years, he sent his family and friends numerous detailed photos of plant stamens and various architectural details on buildings, in which he recognized the triskelion shape. Flower image by Ernst Ungewickell courtesy of Alexander Ungewickell.

Harvard (Unanue et al., 1981), recruited Ernst to the Department of Pathology and Immunology at Washington University, St. Louis, in 1993. Ernst's five years "back in the USA" was a period of notable scientific advance for him, unraveling the fine molecular details of clathrin coat uncoating by the auxilin-Hsc70 complex (Holstein et al., 1996; Ungewickell et al., 1995). Those superficially acquainted with Ernst might be surprised to learn that he enjoyed driving a roomy (second-hand) American car and listening to rock-and-roll "oldies" on the radio but, to us, this illustrates how he embraced the freedom that global scientific enterprise enables, as well as his appreciation of "culture" in its multifaceted forms.

Ernst was comfortable with what he contributed to science without feeling the need to promote himself, admirably so in the climate of competition that increasingly prevailed. Indeed, Ernst was not competitive, and his relationship with one of us (F.M.B.) exemplifies his magnanimity. Frances contacted Ernst early in her foray into clathrin research and he was responsive and happy to meet to discuss mutual, if overlapping interests. She then invited herself (!) to a meeting that he organized in the early 1990s in Germany, and Ernst was not only a gracious host under the circumstances, but introduced her to German cell biology colleagues, whom she would not have met otherwise in those early days of European Union science. Over the years, three of Ernst's trainees joined the Brodsky laboratory after their time in his laboratory, and it was clear he had been (and continued to be) an influential mentor. When Frances met Ernst's son Alex, during his medical internship at Stanford after his MD-PhD studies, she could see that Alex had also benefitted from a strong "second supervisor" in his father, whom he continued to consult frequently throughout his training as a physician-scientist in oncology and beyond.

In 1998, Ernst moved to the Medizinische Hochschule Hannover to head the Cell Biology Department in the Center for Anatomy. It was another period of terrific graduate student attraction to his laboratory, as his interests in cellular mechanisms blossomed. His students were devoted to him and benefitted much from his continual presence in the laboratory and his personal commitment to wet bench research. Ernst was always interested and eager to use novel ideas and technologies that would advance his burning research questions. He was fascinated by Sayda Elbashir and Tom Tuschl's pioneering siRNA work in Klaus Weber's laboratory, and he was the first (Hinrichsen et al., 2003), with Sasha Sorkin (Huang et al., 2004), to use mRNA transcript interference, which subsequently swept the field of intracellular membrane traffic.

With his open-door policy, Ernst was a wonderfully kind and encouraging mentor and discussion partner. Walter Gratzer would give Ernst books to read and discuss while Ernst was using a spectrometer in Walter's office. Ernst would likewise expand his trainee's minds by doing the same. Ernst wanted his people to be the best they could be. He set high standards of excellence for himself, as well as for those around him under his supervision, and those of us who were his colleagues feel honored to be acknowledged as such.

Despite his impressive vertical and horizontal impact on the field, and his use of biochemistry with aplomb, Ernst was never far from the electron microscope. In a lovely recent collaboration with David Owen at Cambridge (Kelly et al., 2014), the beautiful ultrastructure is all from Ernst's laboratory. Gratifyingly, his daughter Charlotte spends her days in Munich with state-of-the-art Titan Krios cryo-electron microscopes, coming full circle.

Ernst was fascinated and delighted by science. On reading a top-tier journal biophysical article on the motions of the F_O-F_1 ATP synthase, Ernst quipped "I wish I'd done that!" He was patient and tolerant to the point when, in his judgement, Evan Eisenberg and Lois Greene at the National Institutes of Health were just taking too long to biochemically dissect the role of auxilin (a protein he discovered and named; Ahle and

Ungewickell, 1990) in Hsc70-mediated clathrin uncoating. The consummate intellectual, he could no longer wait and, with due deference, Ernst went ahead and performed critical studies in his own laboratory to bring the project to fruition as a successful collaboration (Ungewickell et al., 1995).

Retired, Ernst shifted his interests and pursued them with characteristic enthusiasm and drive. Travel, reading, cycling, running, enriching his local community with discussions and lectures, and photography. He also learned to read and write anachronistic German text (Sütterlin and Kurrent) used in old family letters and historical documents in order to trace his family history. Ernst will be remembered by all those whose lives he, and his wife and laboratory soulmate Huberta (see figure), touched as an outstanding and laudable member of the cell biology scientific community. Over their years of work, Huberta, herself a trained laboratory technician, was his steadfast partner at the bench. Ernst was a marvelous raconteur who strangely disliked public speaking, yet he made an indelible impact on our lives and our science.

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