NATIONAL ACADEMY OF SCIENCES

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1937-2006

A Biographical Memoir by

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Biographical Memoir

HANS JÀNOS KENDE

January 18, 1937–September 26, 2006

BY JAN A. D. ZEEVAART AND MAARTEN J. CHRISPEELS

HANS JÀNOS KENDE, a University Distinguished Professor Emeritus in the Department of Energy Plant Research Laboratory (PRL) and the Department of Plant Biology at Michigan State University, East Lansing, died September 26, 2006, at the age of 69. Hans was widely known for his work on the biosynthesis and mode of action of the plant hormones gibberellic acid and ethylene. The elucidation of the hormonal control of stem elongation in deepwater rice earned him international acclaim. In addition to being an excellent plant scientist, Hans had a strong sense of community and was a vigorous promoter of plant biology at Michigan State University as well as at national and international levels.

VERY CHALLENGING EARLY YEARS

Jànos was born in Székesfehérvár, Hungary, in 1937. A happy, comfortable life was interrupted in 1941 when his father was sent to a forced labor camp as part of the Hungarian army, where he died in February 1943. In 1944 after Germany invaded Hungary, Jànos and his mother were evicted from their home and sent to a ghetto, then to the local brick factory to await deportation. When the train of boxcars arrived, 30 people, including Jànos, his mother,

and a few relatives, were called forward from the group of nearly 3,000 people. This fortunate group of 30 was taken to Budapest instead of Auschwitz, where the other people were immediately exterminated. In Budapest, Jànos and his mother became part of a group that was to be sent to a neutral country as a "goodwill" gesture by the Germans to support the rescue negotiations of Rezso Kasztner and Joel Brandt with Adolf Eichmann. The group, however, was first taken to Bergen-Belsen, where Jànos and his mother were kept for over six months until their rescue from almost certain death (due to starvation and disease). At the end of December 1944 they were finally transported to Switzerland, where Jànos was given the name "Hans." His ordeal was not over, for after a few days the children were separated from their mothers and sent to children's homes. This painful separation lasted almost three years for Hans, until his mother remarried and he could join her in Zürich. Although he had taught himself to read and write in Hungary, he had little formal education. One source of delight for Hans was learning *The Odyssey* by heart from a scholar at the children's home. In Zürich, Hans was enrolled in fourth grade and quickly made up for the slow start in his formal education, becoming the first student of that elementary school to pass the entrance exam to the *gymnasium*. Like many young people of his generation he was turned on to biology by reading Paul de Kruif's *Microbe Hunters*. He set up a small laboratory in his basement and did all manner of simple biology and chemistry "experiments" and vowed to become a physician.

When he was 16, Hans spent a summer on a kibbutz in Israel as part of a group from Switzerland that included Gabriele Guggenheim, who was to become his lifelong partner. They married in 1960, and over 40 years later Hans related that since they had gotten together not a day had gone by that he wasn't happy. When Hans graduated from

gymnasium in 1956, he and Gaby had decided that eventually they would live on an Israeli kibbutz after their marriage. So Hans contacted the kibbutz and asked what skills were needed. The answer: we don't need physicians, but we do need experts in agriculture and dietetics. Hans put aside his interest in becoming a brain surgeon (a decision he never regretted) and delved into plant science, while Gaby studied dietetics. In fact, they never made it to that kibbutz. The kibbutz's loss was plant biology's gain.

BECOMING A SCIENTIST

Hans did his university studies at the University of Zürich and majored in plant biology (*botanik*). He earned his Ph.D. in 1960 under the mentorship of Professor Hans Wanner. His dissertation research focused on the biosynthesis of trigonelline in the coffee plant. Trigonelline, a natural product found in many plants, is N-methyl nicotinic acid. Nicotinic acid had been identified as a vitamin for humans (antipellagra factor) and the question arose whether trigonelline might also be a vitamin and how it is synthesized. Many laboratories were trying to understand biochemical pathways, and the issue here was whether trigonelline could be a methyl donor like betaine. In the process of doing his dissertation research Hans acquired skills in organic chemistry, paper chromatography, and the purification of small amounts of chemicals from plants. He learned to feed radioactive precursors to growing plants and became interested in growth factors and the role that light plays in the synthesis of growth factors. All this helped set the direction for his later work.

While Hans was studying in Zürich he met Professor James Bonner from Caltech and they talked about a postdoc position in California, but unfortunately there were no available funds for the next year. So Hans accepted a postdoctoral position with A. S. Holt at the National Research Council

(NRC) in Ottawa, Canada, where he studied chlorophylls in green photosynthetic bacteria. He was supported by an NRC fellowship, but by his own admission this research did not really turn him on and he only stayed one year. Hans had received a letter from Professor Anton Lang (NAS member elected in 1967) at Caltech offering him a position as a postdoctoral research associate, which Hans accepted with enthusiasm. Their first son, Benjamin, was born just weeks before leaving Canada. Caltech was Hans's entrée into the area of plant growth and development, the field in which he would make many major contributions. In his own words: "Those 20 months at Caltech proved to be the most exhilarating learning experience of my life. This is where my standards were set!" Anton Lang, who was director of the Earhart Plant Research Laboratory ("the Phytotron"), had a grant to work on "chemical curing of climatic lesions." The idea was to grow plants under different temperature regimes that were suboptimal and then "cure" them by spraying amino acids or other metabolic intermediates. The paradigm came out of microbial and plant genetics, of course, where mutants could be rescued with intermediates. Hans told Anton Lang that this was not terribly interesting to him because it would not work, and Anton gave him permission to pursue other avenues as long as he oversaw a technician who would carry out the curing project.

Hans chose to work on the plant hormones gibberellins, which were also of great interest to Anton Lang. The structures of nine different gibberellins were known by then, and Lang was studying their role in stem elongation and flowering. Hans Kende made three important contributions at that time. (1) He developed a new method to isolate gibberellins that minimized losses during the isolation procedure. (2) He studied so-called growth retardants that were widely used in the flower industry to make plants more compact and

in agriculture to reduce the height of cereal plants so they would not lodge before harvest. He found that two widely used retardants with the trivial names of CCC and AMO1618 reduce stem elongation because they inhibit gibberellin biosynthesis; this work was done in collaboration with Jan A. D. Zeevaart (one of the authors of this memoir who was elected to the NAS in 1998) and Helga Ninneman. (3) He studied the role of gibberellins in light-induced retardation of stem growth and showed that this is caused not only by a lowering of the gibberellin content in the light but also by a lowering of the sensitivity to the hormone. That a plant could modulate the sensitivity of its cells to a hormone was a completely new idea at a time when the level of hormone as determined by synthesis and breakdown was thought to be the only important factor.

KEEPING A PROMISE TO RETURN TO ISRAEL

Yoash Vaadia, who was at the University of California, Davis, and had just accepted a position as head of plant biology at the Negev Institute for Arid Zone Research in Beersheba, visited James Bonner's lab at Caltech, met Hans at a barbecue, and offered him a research position in Beersheba. Hans and Gaby Kende had not forgotten their vow to return to Israel, and Hans accepted. He worked in Beersheba for two years, from 1963 until 1965. Their second son, Michael, was born here. Hans turned his attention to the production of hormones by roots and the relation of these root hormones to senescence. Working without much scientific stimulation (there were only five Ph.D.-level scientists at the institute) but also without any outside pressure, he produced in these two years important research that was published as a paper in *Science* and a second one in the *Proceedings (Proceedings of the National Academy of the U. S. A.)*. A. C. Chibnall had shown that roots produce a factor that retards senescence of leaves.

Richmond and Lang had shown that kinetin (6-furfuryl aminopurine) retards senescence of detached leaves. Hans put two and two together and decided to find out whether natural cytokinins coming from the roots and being transported in the xylem sap were retarding shoot and leaf senescence. He continued this work later on and demonstrated that cytokinin production by the root system of whole sunflower plants is down regulated at the same time as they enter the senescent phase of growth.

THE EARLY YEARS AT THE ATOMIC ENERGY COMMISSION PLANT RESEARCH LABORATORY AT MICHIGAN STATE UNIVERSITY

While Hans was in Israel, Anton Lang was appointed founding director of the AEC Plant Research Laboratory on the MSU campus. Even before Lang moved to East Lansing he set about assembling a staff of young assistant professors. Lang convinced Hans to come back to the United States, and Hans agreed on the condition that he had to stay for only five years. Those few years stretched into a lifetime. After joining the Plant Research Laboratory (PRL) in 1965, Hans continued his studies on the role of cytokinin in delaying senescence. During a sabbatical leave in Switzerland (1972-1973) with Professor Philippe Matile at the Eidgenössische Technische Hochschule (ETH), he initiated work on the rapid senescence of morning glory flowers. These ephemeral flowers open and senesce all in the span of one day. They showed that this rapid senescence is accompanied by *de novo* synthesis of vacuolar hydrolases. They used the density-labeling technique developed by Joe Varner (elected to the NAS in 1984) at the PRL to demonstrate *de novo* synthesis of ribonuclease. The next year Thomas Boller from Matile's lab at the ETH joined Kende's lab as a postdoc, and they demonstrated that the hydrolases that increase during senescence are located in vacuoles. This was an important contri-

bution, as it strengthened Matile's hypothesis that vacuoles play an important role in senescence. At this time Andrew Hanson, another postdoc in the Kende lab, confirmed that the ethylene evolved by senescing morning glory flowers originated from the side chain of methionine, as in other senescing systems.

After returning to the PRL, Kende and his lab established that ethylene regulates flower senescence by positive feedback, as evident from the observation that brief exposure to exogenous ethylene strongly induces endogenous ethylene production. As noted above, ethylene is derived from methionine, and shortly after the discovery, by Shang Fa Yang (elected to the NAS in 1990) at the University of California, Davis, that the immediate precursor of ethylene is 1-aminocyclopropane-1-carboxylic acid (ACC), the Kende lab quickly developed a chemical assay for ACC. This assay became widely used around the world.

Hans's group was the first to purify ACC synthase from tomato fruit tissue and to generate monoclonal antibodies specific for ACC synthase. These antibodies proved to be useful for determining that increases in enzyme activity were accompanied by increases in the protein itself. Ethylene is induced by wounding and wound-induced ACC synthase proved to be synthesized *de novo* and to be the rate-controlling enzyme for ethylene synthesis. Given the importance of ethylene in fruit ripening and the prospect of regulating fruit ripening in transgenic plants by modulating ethylene synthesis, the race was on to obtain a full-length cDNA for ACC synthase. Athanasios ("Sakis") Theologis at the USDA Plant Gene Expression Center in Albany, California, was the first to obtain the ACC synthase cDNA; the laboratory of Marc Van Montagu (elected as a foreign associate of the NAS in 1986) in Gent, Belgium, obtained it a few months later. Kende realized that the amino acid sequences he

had obtained from his purified enzyme matched the Van Montagu clone, which was different from the Theologis clone. It later transpired that ACC synthase is encoded by a small gene family whose members are differentially expressed during wounding. Hans Kende's work on ethylene shows a remarkable transition from physiological to biochemical to molecular approaches.

HORMONE RECEPTORS

As a postdoc Hans had found that dark-grown dwarf peas were much more sensitive/responsive to applied gibberellin than light-grown seedlings. One way to interpret such a finding is that in the dark there are more receptors and this kindled Hans's lifelong interest in plant hormone receptors. During the 1970s and 1980s, he synthesized tritiated cytokinin and gibberellin of high specific activities but failed to detect specific binding by classical biochemical methods. Postdoc after postdoc tried and failed and then switched to another project rather than to be sacrificed on the altar of the elusive hormone receptor. In 1982 Chris Somerville (elected to the NAS in 1996) joined the PRL and introduced everyone there to the molecular genetics of *Arabidopsis thaliana*. Hans saw the possibility that hormone receptors might be found in *Arabidopsis* by isolation of hormone-insensitive mutants. In collaboration with Chris Somerville's lab that involved his postdoc Mark Estelle (elected to the NAS in 2008) and Kende's postdoc Anthony Bleecker, a screen for ethylene response mutants was designed. The picture of the ethylene-insensitive etr mutant seedling towering above a canopy of seedlings dwarfed by ethylene treatment is a classic one that has been widely reproduced. This work led in turn to isolation of the *ETR* gene (by Anthony Bleecker and Karen Chang in Elliot Meyerowitz's laboratory at Caltech). Subsequent work demonstrated that the *ETR* gene encodes

an ethylene receptor, the first plant hormone receptor to be identified.

DEEPWATER RICE

In 1982 Hans started an entirely new project, still dealing with stem elongation and hormones, especially ethylene, but focused on deepwater rice. This was truly pioneering work and a considerable switch from the earlier biological systems on which he had worked. Hans was intrigued by the capacity of the stems of deepwater rice to elongate enormously in concert with the rising floodwaters in the areas where it is grown in Southeast Asia. Hans had worked on the promoting effects of auxin and gibberellin on stem elongation and was well aware that ethylene inhibits stem elongation in young stems of terrestrial plants. This inhibition was the basis for screening for ethylene-insensitive mutants (see above). After Alan Musgrave, who worked as a postdoc with Hans Kende in the late 1960s on pea stem elongation and the metabolism of GA, returned to the University of Amsterdam, he published a paper showing that in aquatic plants ethylene stimulates stem elongation by enhancing auxin transport. Earlier there had been one short paper on the promoting effect of ethylene on stem elongation in rice seedlings, and Hans put all his ideas together in a proposal to the National Science Foundation to study stem elongation in deepwater rice. On a trip to Berkeley, California, he met Jean-Pierre Métraux and offered him a postdoctoral position to study deepwater rice in his laboratory.

Deepwater rice is a semiaquatic plant in which ethylene has a stem-elongation-promoting effect, quite the reverse of its effect in terrestrial plants, where it inhibits growth. Métraux, Ilya Raskin, and others in Hans's group subsequently unraveled the chain of events that leads to accelerated stem growth as a result of submergence. Three hormones—ethylene,

abscisic acid, and gibberellin—participate in response to changes in the internal gas composition. Low oxygen tension promotes ethylene synthesis, which reduces the level of abscisic acid and stimulates synthesis of gibberellin, the immediate growth-promoting hormone. Elongation of internodes is based on increased cell division in the intercalary meristem and subsequent elongation of these newly formed cells. Cell expansion is made possible by relaxation of the cell wall, and this cell-wall loosening is at least partially mediated by expansins. Further evidence in support of the role of the cell-wall proteins expansins in growth and development was obtained with transgenic plants that overexpressed those genes. Such transgenic plants grew taller, whereas antisense plants were shorter than control plants. Another important finding in the work with deepwater rice was made by Hans's graduate student Ilya Raskin, who showed in elegant experiments that aeration of partially submerged leaves takes place by mass flow through air layers along the leaves' surfaces. Until this seminal work, aeration had been thought to occur through internal air spaces.

SERVICE TO THE PROFESSION AND AWARDS RECEIVED BY A CONSUMMATE PRACTICAL JOKER AND POLITICAL ACTIVIST

Hans Kende was an untiring advocate for plant biology. He served the plant sciences and science in general in many different ways: as a member of grant review panels and journal editorial boards and 12 times on committees of the National Academy of Sciences and the National Research Council. From 1995 to 1998 he was chair of the Section of Plant Biology. He served the American Society of Plant Physiologists in several capacities: as a member of the Board of Trustees during the critical period when the society was in transition from a semivolunteer to a professional organization and as the chair of the membership committee; his

work led to a significant increase in membership. He further promoted the plant sciences during the early 1990s when funding was dismal, taking the initiative to organize small groups of plant biologists to meet in Washington, D.C., with congressional delegations to request increased funding for agencies that supported plant biology. I had the privilege of serving for two years (1976-1978) with Hans on the National Science Foundation panel for Developmental Biology when Mary Clutter was the panel director. He was conversant with all aspects of plant biology and his comments were always insightful. When in 1998 the Nobel Prize for Physiology or Medicine was awarded for "nitric oxide as a signaling molecule in the cardiovascular system"—representing a new principle (signaling by a gaseous molecule)—Hans was quick to point out in a letter to *Science* that plant biologists had discovered years earlier that a gaseous signaling molecule (ethylene) regulates plant growth.

Hans received numerous honors for his outstanding contributions to science, including election to the German Academy of Natural Sciences, Leopoldina (1985), election as fellow of the American Association for the Advancement of Science (1990), and election to the National Academy of Sciences (1992). He attended NAS meetings regularly, usually with his wife, Gaby. He was awarded a University Distinguished Professorship at Michigan State University (1990) and received the Medal for Research Excellence from the International Plant Growth Substances Association (1995) and an honorary doctorate from the University of Fribourg, Switzerland, in the same year. The American Society of Plant Physiologists awarded him the Stephen Hales Prize in 1998.

More than anything Hans enjoyed spending time with his family. He and Gaby often traveled to Switzerland, especially when Hans's mother was still alive. In winter they went skiing in the Alps and in summer they went hiking. He had

four sabbatical leaves in Switzerland: twice with Philippe Matile at the ETH in Zürich, once with Thomas Boller (his former postdoc) at the Friedrich Miescher Institute in Basel, and once with Nikolaus Amrhein at the ETH in Zürich. A passionate fan of classical music, he often scheduled his vacations to take greatest advantage of Europe's summer music festivals.

Hans and Gaby became U.S. citizens in 1970, and both were highly committed to the American democratic system. While living in Switzerland, Hans was stateless and therefore could not vote, while Gaby could not vote in Switzerland because she was a woman. Perhaps that was the reason for their extraordinary commitment to the electoral process. Together they worked tirelessly in the political campaigns of Michigan Democratic politician Bob Carr and Democratic presidential candidates Jimmy Carter, Al Gore, Bill Clinton, and John Kerry. Together they walked precincts, manned the telephones, and prepared mailers. Time and again they did all the grunt work that accompanies every campaign. Hans rose early to be a poll watcher, and Gaby replaced him at noon so he could go to work. When it was clear that Ralph Nader would play the role of spoiler in the 2000 election between George W. Bush and Al Gore, he urged Nader not to run.

Hans was always fun to be around and no account of his life would be complete without mentioning that he was a consummate practical jokester. Many a scientist was at the receiving end of his jokes. In 1965 when his colleague Phil Filner published a nice paper on the induction of nitrate reductase in cultured tobacco cells, Hans took a reprint request card from the Institut Pasteur, filled in the reference of Filner's paper, signed it François Jacob with the notation "Très bien!" and put it in Filner's mailbox. When Filner found this most impressive request, he immediately went

from lab to lab showing it to all his colleagues, until one of them sowed some doubt by examining the date stamp a little more closely—and the truth came out.

When Winslow Briggs arrived in Germany in 1973 for a sabbatical leave in Rainer Hertel's laboratory, the two of them called Hans who was on sabbatical in Zürich. Impersonating an administrator of the agency that had given Hans a fellowship, they demanded an immediate report on his progress. After some sputtering on Hans's part, Rainer and Winslow identified themselves. A few months later Winslow received a phone call from the Frankfurt airport police (whoever they were) informing him that they had just arrested a former graduate student of Winslow's who was in possession of 2 kilograms of hashish, which the student claimed to be destined for Winslow. It was Winslow's turn to think up excuses and disavow any knowledge or recent communication. Finally a gentle voice said, "Win…this is Hans, it's payback time." Winslow Briggs admitted later that it would not have been out of character for this particular Stanford student. When Winslow Briggs received the call that he had been elected to the NAS at seven o'clock in the morning, he was worried that this was yet another prank from Hans and waited for written confirmation.

Hans Kende's death so soon after his formal retirement and at a time when he still had so much to contribute was a major loss to plant hormone biology and to plant biology in general.

The following resources were used in writing this memoir:
Lang's Gang 1965-1978 at www.prl.msu.edu/LANG/index.htm.
K. Bird and J. A. D. Zeevaart. Hans Jànos Kende. Obituary. Am. Soc. Plant Biol. Newsl., 2007.

The first two pages of this memoir were written by Jan A. D. Zeevaart, who died unexpectedly in 2009 before he could complete this labor of love on behalf of his colleague of 40 years. Maarten Chrispeels completed the memoir and acknowledges help and input from Gabriele Kende, Karen Bird, Joe Ecker, Jean Pierre Métraux, and Andrew Hanson.

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