Chris Lamb: A Visionary Leader in Plant Science

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Abstract

Christopher John Lamb (1950–2009) made major contributions to the field of plant defense gene activation, particularly through his studies on signal transduction mechanisms. Between 1994 and 2004, he published a series of seminal papers that outlined the involvement of hydrogen peroxide, nitric oxide, lipid transfer proteins, and aspartic proteases as critical components of local and/or systemic resistance during plant-microbe interactions. Prior to this, he had been one of the first to establish the fact that induced defense responses resulted from transcriptional activation of sets of coordinately regulated genes. Chris obtained his B.S and PhD degrees in biochemistry from the University of Cambridge, United Kingdom, moving to the Botany School at the University of Oxford as a postdoctoral fellow in 1975 and to the Biochemistry Department in Oxford as a Departmental Demonstrator in 1978. He was appointed founding director of the Plant Biology Laboratory at the Salk Institute for Biological Studies in La Jolla, California in 1982, and occupied the last ten years of his life as Director of the John Innes Center, Norwich, United Kingdom. In spite of spending most of his career as a director at two of the world's most prestigious institutes, formal recognition of his achievements came late in life, with election to the Royal Society of London in 2008 and endowment of the honor of Commander of the British Empire (CBE) for his contributions to British plant science by Queen Elizabeth II in 2009. Sadly, Chris did not live to attend the official ceremony at which he would receive his CBE.

INTRODUCTION

Chris Lamb was a giant in the field of plant pathology and one of a handful of individuals who can truly be said to have moved the field into the molecular era. The specific questions he set out to address during his career were conceptually quite simple, but the answers that he uncovered had far-reaching consequences for, and beyond, the field of plant pathology. At the onset of his career, a major question that captivated him was whether plant responses to light, wounding, or pathogen attack occurred as a result of activation of preexisting enzyme systems, or arose through de novo gene activation. Assembling the tools to tackle this question made Chris a pioneer in the application of molecular biology to plant defense systems. Once it was clear that the answer to the first question was yes, Chris dedicated much of the remainder of his career to asking how. Although plant defense responses were Chris's major focus, he also made major contributions to the fields of root development, cell wall biology, and metabolic engineering. In addition to possessing a remarkable scientific intellect, he was an outstanding mentor, talent spotter, and administrator. A multitude of the brightest and best young scientists sought out his laboratory for their postdoctoral training, and many have gone on to become scientific leaders in their respective fields. The scientists he hired as permanent faculty at the Salk Institute have made contributions equal to his own, and the two organizations with which he was associated for the majority of his career gained immeasurably from his strategic thinking. For those who did not know him well, Chris was a somewhat enigmatic character whose natural shyness could be hard to read; for those with whom he was close, he was a wonderfully warm, humorous, and supportive colleague. I hope I have been able to capture both Chris's intellectual stature and the sheer fun of doing science with him in this summary of the career of a great man and true friend.

PHD WORK AT CAMBRIDGE

Chris arrived as an undergraduate in Cambridge in 1970, having completed the United Kingdom's equivalent of high school in the industrial town of Middlesborough in northeast England, where he was brought up by foster parents. His adopting father worked for a shipping company. Travel and soccer (he remained always a committed fan of Middlesborough United) were, at this stage of his life, probably greater passions than science. Nevertheless, he responded to the intellectual climate in the Cambridge Biochemistry Department and obtained a first class honors degree. He decided to stay on in Cambridge for his PhD, working with Philip Rubery, then a relatively new faculty member, whose own interests included phenylpropanoid biosynthesis and auxin transport (43, 87). Chris's PhD thesis addressed the mechanisms whereby phenylpropanoid metabolism in potato is induced by light and wounding. In the pre–molecular biology era, the major tools available to address this question were a cut potato tuber system, in vitro enzyme assays, and chemical inhibitors. In spite of these limitations, or perhaps because of them, Chris's creativity shone through. By the use of careful timing of stimulus and inhibitor application, Chris was able to conclude that the abiotic stress–induced accumulation of phenolic acids in potato tubers was associated with the de novo synthesis of L-phenylalanine ammonia-lyase (PAL), the first enzyme in the phenylpropanoid pathway, through a process that also involved control by cinnamic acid, the product of the PAL reaction (51, 52, 53, 60, 62). He also pondered the mechanisms underlying flux control into the pathway based on a careful mathematical consideration of the kinetics of PAL and its inhibition by cinnamic acid (61). The publication of this work in the *Journal of Theoretical Biology* gave Chris much satisfaction. However, by the time he completed his PhD, he was becoming frustrated with the indirect approaches that

were then the state of the art, and endeavored to develop both a better biological system and better tools to address the mechanisms of induced plant defense responses.

THE OXFORD YEARS

In 1975, Chris arrived in Vernon Butt's laboratory in the Botany School at the University of Oxford, where he had been awarded a postdoctoral fellowship supported by the chemical company ICI. He met the present author on his first day in the lab and was almost immediately discussing his ideas on how to address gene activation in plants. I was completing my D. Phil. in the Botany School, and had developed an elicitor-treated bean (*Phaseolus vulgaris*) cell culture system for studying activation of isoflavonoid defenses (20, 21). Chris immediately saw the utility of this system and proposed a collaboration that would ultimately last for 26 years and see the publication of 114 papers and review articles.

Chris's first approach was to apply the deuterium density labeling technique, recently used by Joe Varner and colleagues to demonstrate gibberellin-mediated de novo synthesis of α-amylase in the barley aleurone layer (36), to the elicited bean culture and wounded potato tuber systems. This confirmed de novo synthesis of PAL protein in response to both fungal elicitor and wounding/light (24, 55, 57, 58, 59). Chris took the technique a step further by utilizing potassium bromide rather than cesium chloride gradients to separate the enzyme fractions; the added resolution enabled partial separation of unlabeled enzyme (present at the start of the experiment) from newly synthesized labeled enzyme. Using this clever approach to monitor the distribution of preexisting enzyme over time revealed that, during the period of enzyme activity increase, there was no PAL turnover, but the enzyme reverted to its normal half-life as soon as its activity began to drop (68). This dual control of enzyme synthesis and turnover in elicited cells is a fascinating observation worthy of renewed attention, particularly in light of the advances in our understanding of protein turnover during the three decades since this observation was made (81, 98).

In many ways, Chris's early work on the regulation of phenylpropanoid biosynthesis was an early example of systems biology. Global scale omics technologies were not yet developed, of course, but within the limitations of the more targeted methodologies available at the time, Chris was already thinking about the integration of changes at the transcriptome, proteome, and metabolome.

Chris now had his own laboratory in the biochemistry department at Oxford, where he had received a five-year, fixed-term appointment as departmental demonstrator, with his first PhD students and a fair teaching load. His studies were now raising questions that could only be fully addressed by the application of the newly emerging molecular biology approaches. These were slow to permeate into the plant sciences, and I remember the look of confusion on colleagues' faces when Chris took a swig of his pint of beer and then announced that we needed to adopt cloning approaches. To bring his lab up to speed with the new technology, Chris and his student Mike Lawton traveled to Freiburg, Germany, to the lab of Klaus Hahlbrock, who was applying molecular biology to similar questions of gene activation in illuminated parsley and elicitor-induced soybean cell cultures (37, 49, 92), to learn the in vitro translation technique. This approach, coupled with in vivo labeling and immunoprecipitation, made it possible to directly demonstrate the elicitor-mediated induction of PAL mRNA, and to link this to PAL protein synthesis (66, 67). The work involved Chris and Mike regularly visiting the present author's laboratory at the Royal Holloway College in Egham to help set up 35S-methionine labeling time course experiments with the bean cell cultures, leaving late at night on the train with the results of the day's work safely secured in plastic tubes in a large Styrofoam box leaking dry ice vapor; surprisingly, their fellow passengers never seemed to inquire as to what they were carrying. The departures were often later than anticipated because of a slow start in setting

up the experiment. Chris strongly believed in those days that a couple of pints of beer and several cigarettes in a local pub (either the Happy Man or the Barley Mow at Englefield Green) over lunchtime helped the creative faculties and ensured an optimal design for the experiment.

This work led to a series of publications on the mechanisms of induction of PAL and chalcone synthase, the first enzyme in the flavonoid pathway that leads to the elicitor-induced bean phytoalexins (41), as well as increased profits for the landlords of the aforementioned pubs. Hahlbrock's parallel work with the parsley system, including the use of molecular biology to study both enzyme function and regulatory networks, was a great inspiration to Chris; it showed him a way forward toward the dissection of induced plant defenses. Perhaps more importantly, the connection with Hahlbrock opened a door that was to have profound implications for Chris's future career. Chris also recognized the limitations of working with model cell culture systems, and during his period in Oxford, set up a collaboration with John Bailey at the Long Ashton Research Station near Bristol to develop a system utilizing race-specific interactions between pathovars of *Colletotrichum lindemuthianum* and resistant and susceptible bean cultivars (5, 6, 84). The results of these studies highlighted the importance of the rapid timing of induced defenses at the molecular level in the resistant interaction.

At this early stage in his career, Chris was already showing one of his most characteristic traits, a love and colorful use of the English language. Although he was never much at ease presenting his work orally, occasionally appearing reticent and even poorly organized, his written English was superb. Changes in enzyme activity were "rapid and massive," and terms such as "repertoire," "orchestration," and "rheostat" would color his descriptions of defense gene activation. This occasionally infuriated reviewers, one of whom complained that an early manuscript was designed to impress rather than to inform. Nothing could be further from the truth; throughout his career, Chris's manuscripts were immaculately written, even if a degree in English was sometimes necessary to discern the subtle meanings, which, however, always perfectly explained and illuminated what the data were saying.

ESTABLISHMENT OF THE PLANT BIOLOGY LABORATORY AT THE SALK INSTITUTE

Hahlbrock was a Nonresident Fellow (external scientific advisor) for the Salk Institute for Biological Studies at La Jolla, California. Named after Jonas Salk, developer of the polio vaccine, this world famous institute for biomedical research was then directed by Frederic De Hoffman, a nuclear physicist who had been involved in the Manhattan project at Los Alamos. De Hoffman realized the importance of basic plant science for the betterment of humankind, proposed the establishment of a Plant Biology Laboratory at Salk, and asked Hahlbrock to help the institute recruit a top scientist to direct this new endeavor. Although early in his career, without having yet held a permanent faculty position, Chris was clearly seen as a visionary with extraordinary leadership potential, and Hahlbrock strongly recommended him for the position. Chris agonized over leaving his parents and friends in the United Kingdom, but his excitement over the scope and possibilities of this new opportunity conquered all, and he moved with his family to La Jolla in 1983.

The early years at Salk were hectic but productive. Chris traveled constantly and widely to spread the word about the institute's new research area, and to raise funds to support the Plant Biology Laboratory. He quickly became one of United Airlines' most traveled passengers, and amassed a number of bizarre travel stories, including thinking that he had been kidnapped at gunpoint in Venezuela when his wealthy host sent his personal guards to collect him from the airport. Because of lack of space in the main Salk campus on Torrey Pines Road, Chris's group had to share space with a biotechnology company in a small building in downtown La Jolla (less attractive, but nevertheless just across the street from the ocean,

and thus a very popular venue for sabbatical visitors). Lawton and other students from Oxford had moved with Chris, and the work on defense gene activation continued apace. PAL and the downstream flavonoid pathway genes chalcone synthase and chalcone isomerase were cloned from bean and their expression characterized (15, 22, 80, 89), and the lab's focus now moved to address transcriptional control of coordinated defense gene activation at the gene promoter level, using both fungal elicitors and the tripeptide glutathione as triggers (14–16, 29, 30, 32, 33, 38, 54, 64, 65, 75, 85, 88, 89, 101). New tools, such as plant in vitro transcription systems, were developed to facilitate these studies (2, 103, 104). At the same time, the scope of the lab was expanded to include the developmental control of these same genes (71–73, 91). The group was augmented by a succession of excellent postdoctoral fellows who came from across the world to join Chris's team, and this led to an expansion of the program into further new areas; some, such as the molecular characterization of (hydroxy)proline- and glycine-rich proteins (13, 44–47, 90, 95, 96), were still related to defense; others, such as control of the cell cycle during root development (26) and regulation of vascular development (93), represented a broadening of Chris's research interests and a deepening vision for what the Salk Plant Biology program could become.

The present author visited the Salk Plant Biology Laboratory for a sabbatical in the spring of 1987. There was a remarkable intellectual atmosphere, where everyone had his or her own project but fed off the expertise on the Salk campus. Chris enjoyed the ethnic diversity of the lab, but was sometimes worried that small groups who tended to speak their native language in the lab might be plotting against him. One or two "secret projects" were certainly going on, but once the instigators had obtained the necessary data to convince Chris that their crazy idea actually had scientific merit, they would confess and show him the data. In this way, Mike Lawton's "project X" led to the first paper reporting the cloning of protein kinases in plants (69), to be followed later by the demonstration of a kinase cascade in the control of phenylpropanoid defense gene promoter activity (28). Because of the physical separation of the Plant Biology Laboratory from the main Salk campus, the social interactions were particularly close. The whole lab met on Friday evenings at a Mexican restaurant and bar in La Jolla, and much beer and chili were consumed. The British contingent also spent many evenings at a hole-in-the-wall Indian restaurant, where the most horrendously hot curries were served, to be followed by a cooling-off session at a nearby ice cream parlor. This was something of an initiation for new postdocs, and many were the casualties. I will always remember Chris, with sweat pouring down his forehead, excoriating some referee for a less than positive review of a recent manuscript; the proprietor of the restaurant played along by seemingly increasing the heat of the curries weekly, such that, by the time my sabbatical was nearing an end, little meaningful discussion was possible at these sessions.

Eventually, the Plant Biology Laboratory moved to the main Salk campus, occupying two wooden "temporary" buildings on the ocean side. These were not as architecturally satisfying as Louis Kahn's masterpiece, but provided spacious accommodation and a fabulous view over the cliffs to the ocean from Chris's office. Chris saw this move as an acceptance by the prestigious Salk faculty, which included Nobel laureates Francis Crick and Renato Dulbecco, of the maturity and intellectual rigor of the Plant Biology program, and this realization resulted in the institute's administration giving a green light for additional faculty hires. Chris was an outstanding talent spotter, and Joanne Chory was hired in 1988 to start a program on the genetic dissection of photomorphogenesis, with Detlef Weigel following in 1993, initially working on the genetic dissection of flowering. Chris collaborated with his new hires where appropriate (39, 99), utilized the techniques they were developing, such as T-DNA activation tagging, in his own work (8), and was delighted to see their programs rapidly

and independently develop to a stature equal to that of his own.

LOCAL AND SYSTEMIC SIGNALING IN PLANT-MICROBE INTERACTIONS

During his tenure as director of the Plant Biology Laboratory at Salk, Chris's lab published a series of seminal, highly cited papers describing how plants orchestrate their defense response following pathogen attack. At the time of Chris's death, the five most important of these papers had collectively been cited by other scientists nearly 4,500 times. This was remarkable for the field of plant pathology and was the basis for Chris's recognition by the Institute for Scientific Information as one of the most highly cited authors in the plant and animal sciences.

The story began with Chris's decision to start looking at inducible cell wall proteins in addition to the phenylpropanoid pathway genes that had occupied his time in Oxford. This work led to early molecular descriptions of cell wall proline- and hydroxyproline-rich proteins and studies on their expression during plant development and biotic stress (13, 44, 95, 96). On examining the induction of a particular proline-rich protein in cell suspension cultures, Desmond Bradley, a postdoc from the United Kingdom, found that, although the *PRP* gene was being induced by fungal elicitor, the protein itself seemed to disappear (9). Careful analysis indicated that the protein had become insolubilized into the cell wall and that hydrogen peroxide was the catalyst for this insolubilization, which strengthened the wall against pathogen ingress through cross-linking (9). Hydrogen peroxide was subsequently shown to be generated, at least in part, by a plant homolog of the mammalian neutrophil NADPH oxidase gp91 (48). The next step was to link the generation of hydrogen peroxide to other aspects of induced defense, such as the hypersensitive response (HR). Subsequent studies by Massimo Delledonne, a visiting scientist from Italy whose several visits to La Jolla were generously supported by Chris from his own lab funds, revealed that defense gene induction and the hypersensitive response were also triggered by nitric oxide, one of the first reports of a function for this gaseous regulator of mammalian stress responses in plants (19). Together, a burst of metabolic activity (the oxidative burst) elicited by attempted infection led to rapid accumulation of hydrogen peroxide and nitric oxide, which initiated the hypersensitive cell death program and activation of downstream defense response genes (10, 70, 97) This suicide by infected cells helps prevent the pathogen from spreading into healthy parts of the plant.

Stimulated by the emerging details of the biochemical responses associated with the expression of systemic acquired resistance (SAR) in noninoculated plant tissues, particularly the work from John Ryals' group at Syngenta linking salicylic acid (SA) production to systemic activation of pathogenesis-related protein genes (18), Chris's group made three more seminal discoveries. The first was stimulated by an unexpected observation that glutathione S-transferase (GST) transcripts were very rapidly induced in systemic, noninfected leaves following an initial inoculation with pathogen on a lower leaf, and that this induction proceeded in waves (1). GST induction is associated with oxidative protection and occurs during a regular HR. This observation caused much excitement and speculation in the lab, and led to the important demonstration that the oxidative burst not only occurred in directly infected cells, but could also be observed in noninfected cells in upper leaves of the plant, associated with the onset of SAR. These systemic microbursts occurred rapidly after a primary infection on a lower leaf, and were shown by an elegant series of pharmacological studies to be associated with establishment of SAR by a reiterative signal network (1). Work with soybean cell suspension cultures then demonstrated an unexpected link between SA and the oxidative burst; when applied alone, SA is a relatively weak inducer of defense responses. However, at low concentrations, it potentiates hydrogen peroxide production by pathogen signals in a manner dependent upon a protein kinase cascade (94). To quote a

fine example of Chris's narrative style, ". . . .SA potentiation of an intrinsic gain control acting upstream of PAL induction subsumes further, extrinsic amplification by creating a positive feedback loop regulating SA synthesis." At this time, it was not known that there were routes other than through PAL for defense-associated synthesis of SA in plants (100), and present day reviewers would likely have complained about the reliance of these papers on essentially pharmacological approaches. Chris's genius, however, was to apply very simple approaches to attack a problem from multiple angles, such that a series of clearly thought through predictions could be generated and tested. This thinking was still essentially that of a biochemist, but Chris also realized that genetic approaches were now becoming essential for this area of research to progress, and he therefore began a gradual move from the legume systems with which he had worked since his first days in Oxford to the more genetically tractable model system *Arabidopsis*.

I don't think that Chris was fully happy with *Arabidopsis* as a model during the 1990s, as early attempts to replicate, in different laboratories, genetic screens for mutants in the establishment and maintenance of SAR proved frustrating. Finally, however, the system began working (11, 17), and exciting new findings were published concerning the involvement of both a lipid transfer protein and an aspartic protease in systemic signal transduction based on isolation of SAR mutants and cloning of the mutated genes (79, 102). Chris continued to follow up on these findings for the remainder of his life.

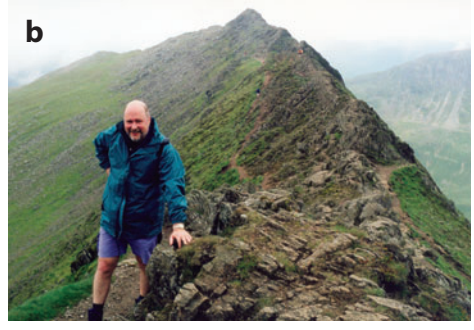
FROM BASIC TO APPLIED

Chris was never happier than when sitting with a cup of coffee in one hand arguing with a postdoc or student about the interpretation of a new piece of data that seemed to upset his current model of the fine details of how things worked. He did, however, also have a strong appreciation for the broader applications of molecular biology for crop improvement, and several projects during his years at Salk developed beyond the purely basic. These centered around the defense response genes that were the targets for the deciphering of signal transduction pathways. In the late 1980s, a visiting scientist with a background in quantitative genetics, Yonatan Elkind, had convinced Chris that it would be interesting to look at the phenylpropanoid pathway from the perspective of how its flux responded to changes in PAL expression. Elkind set up a simple experiment to overexpress PAL in transgenic tobacco; surprisingly, however, the To transgenics were uniformly dwarf, with curled leaves bearing small white lesions, and the extractable PAL activity was strongly reduced (31). This turned out to be among the first reported examples of epigenetic gene silencing in plants (82), soon to become a major research field in its own right (4). Chris saw the possibility of exploiting this system to better understand metabolic flux control, and this became possible when it was found that continued selfing of the plants resulting in progressive loss of silencing, with eventual generation of PAL overexpressing plants (3). These various generations of plants became the subjects of a series of studies addressing topics from metabolic engineering of lignin and other phenylpropanoid compounds (3, 42) to impacts of altered phenylpropanoid metabolism on local and systemic virus resistance (86), fungal resistance (78), or insect herbivory (7, 35). Other applied studies developed gene promoter-reporter fusions as tools for screening novel inducers of defense (27). Although Chris did not pursue the applied aspects of these finding to their ultimate ends, these studies provided early proof of concept for future plant metabolic engineering approaches (12, 83). His early work on chitinase gene structure and function in rice, initially supported by a grant from the Rockefeller Foundation, was developed to demonstrate engineered protection of other species against fungal infection (40, 63, 105).

THE NOBLE CONNECTION

Returning to the early days of the Salk Plant Biology Laboratory, a twist of fate helped

strengthen the long-term research collaboration between Chris and the present author. Salk president De Hoffman was friendly with a member of the Board of the Ardmore, Oklahoma-based Samuel Roberts Noble Foundation, and through this link the Foundation had provided a significant five-year start-up grant for the new Plant Biology Laboratory at Salk. In 1987, Noble's Board of Trustees had completed an external review of its own in-house programs, which at the time focused on agricultural consultation and biomedical research, and De Hoffman strongly encouraged them to move some of their resources into basic plant science, to complement the efforts at Salk. Walking through Old Town San Diego one Saturday afternoon, Chris suggested to me that I should take a look at the possibility of moving to Noble to establish their efforts in plant biology; he could clearly see the potential for building a world-class program, supported by significant interactions with Salk. After my move to Ardmore in 1988, Chris was a constant visitor (**Figure 1*a***) and was instrumental in making the 1,000-mile relationship work. The Noble Foundation renewed its five-year support for the Salk program and established a joint postdoctoral fellowship program whereby selected fellows spent 18 months in Ardmore and 18 months in San Diego. This was critical for nurturing the Noble Plant Biology Division through its formative years. Between 1989 and 1999, 15 postdocs worked as joint Noble/Salk Fellows, during a period that saw over 80 joint publications from the two institutes, with several of the papers already referenced in this article being products of these interactions. One new project involved deciphering the mechanism by which phenylpropanoid pathway intermediates modulate the transcriptional



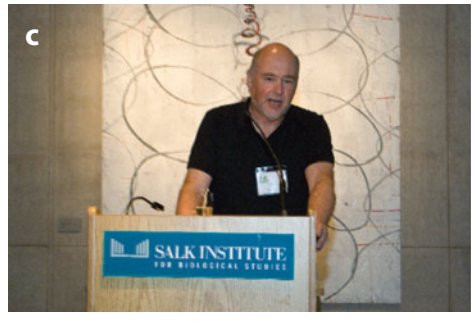


Figure 1

(*a*) Chris with the author on a farm trip, Ardmore, Oklahoma. (*b*) Hiking on Helvellyn in the English Lake District soon after his move to Edinburgh. (*c*) Speaking at the symposium celebrating the 25th anniversary of the Salk Institute Plant Biology Laboratory. (*d*) In the greenhouses at the John Innes Center. Photographs are courtesy of the Samuel Roberts Noble Foundation (*a*), the author (*b*), The Salk Institute for Biological Studies (*c*), and The John Innes Center (*d*).

activation of defense genes following elicitation (76, 77). In addition, a series of highly cited review articles were published (23, 25, 50, 56, 74), one of which, "The Oxidative Burst in Plant Disease Resistance" (50) remains the second most highly cited paper ever published in *Annual Review of Plant Physiology and Plant Molecular Biology*. The interactions between the two institutes were facilitated by yearly retreats, alternatively in Oklahoma and California, featuring all Salk and Noble faculty, postdocs, and students, and an array of high profile guest speakers. Many of the Noble/Salk postdoctoral fellows have subsequently gone on to faculty positions in top universities and institutes in the Americas, Europe, and Asia.

During this period, Chris's interests in the application of technology for agricultural improvement increased, and he was getting involved in an advisory capacity with several plant biotech start-up companies. These activities likely helped prepare him for his subsequent and unexpected career move, where his critical faculties would now turn towards matters of science policy and its implementation.

BACK TO THE UNITED KINGDOM: EDINBURGH AND THE JOHN INNES CENTER

Chris often commented on his love of the optimism that seemed to underlie the U.S. science enterprise of the day. He also developed a strong liking for American football. It was therefore with much surprise that his colleagues learned of his decision to return to the United Kingdom to accept the Regius Chair in Botany at Edinburgh University in late 1998. His reasons were both scientific and personal; he felt that the Salk program was now fully established and able to move forward under new leadership, he saw an exciting potential for developing plant sciences at Edinburgh with several recently recruited younger lecturers and links to a world-class botanical garden, and his mother had recently passed away and he wished to be closer to his father.

Although he stayed for only nine months in Edinburgh, he left a strong legacy centered around his coordination of a major infrastructure grant to focus the department on signal transduction and plant development. This was further supported by his obtaining funds for growth room facilities and large-scale plant genomics efforts.

Doubtless, the members of his group who moved with him from the United States were frustrated at having to pack up and move again after only just having set up their first experiments in their new environment. Chris was now becoming interested in nonhost resistance because of its potential agronomic importance, and the small group that moved with him to Edinburgh was starting to pursue the underlying mechanisms primarily through *Arabidopsis* genetics. Chris was also still interested in chasing up the signaling mechanisms partially revealed by the discoveries of the roles of the DIR-1 lipid transfer protein and the CDR-1 aspartic protease in disease resistance in *Arabidopsis*. These projects finally found a home in Norwich, England, where Chris assumed the directorship of the prestigious John Innes Center (JIC) in 1999. However, his new position left little time for his personal research.

Chris's 10 years in charge of the JIC revealed a very different side to his talents, that of a politically astute and engaged public servant, as well as a newfound passion for cycling. Soon after taking the position, a combination of financial issues and a realization that the institute needed to refocus its efforts and make room for a new cadre of young scientists saw Chris taking on a major reorganization, creating six new departments from the existing ten. Such reorganizations are always more difficult than building programs from the bottom up, as Chris had done before, but he rose to the occasion and put the institute on a sound footing, both scientifically and organizationally. He also became a major advocate for basic plant science and its practical application, at times a difficult sell in the United Kingdom with its staunch anti–genetic modification lobby.

Through a series of dinners in the House of Commons organized through a local Member of Parliament, Chris helped communicate the importance of plant science to U.K. legislators. His being honored with the title of Commander of the British Empire was a direct result of his tireless efforts to promote British plant science. Although his personal research had to take a backseat during these final years of his life, he still attended international scientific conferences and presented work from his lab with the same enthusiasm as during his days at Salk. He presented his research at a symposium to mark the 25th anniversary of the Salk Plant Biology Laboratory in 2008 (**Figure 1***c*). His final publication, in Plant Physiology, described hitherto unsuspected roles of abscisic acid in the control of plant defenses (34).

A RICH LEGACY OF SCIENCE AND SCIENTISTS

Throughout his career, Chris Lamb showed the highest degree of scientific integrity and was a tireless campaigner for support for plant science research. He did things on the grand scale, such as building and effectively leading programs at two of the world's major institutes, and the rise of La Jolla as a major center for plant science research is one significant component of his legacy. La Jolla currently boasts sixteen principal investigators in the plant sciences between Salk, the University of California-San Diego, and the Scripps Institute, seven of whom have been elected by their peers to membership in the U.S. National Academy of Sciences. Between them, La Jolla plant scientists have published more than 1,500 primary publications, which have been cited in the literature close to 100,000 times.

Chris was also attentive to the smaller, more personal details, and was remarkably generous to those who worked in his lab as students, postdoctoral fellows, or visiting scientists; it is notable that he freely allowed many of these people to take the projects they had initiated under his supervision to their new jobs. Another of his major legacies is therefore the number of careers he nurtured that are now flourishing at major universities and research institutes throughout the world. There are also the memories that many people have of the sheer fun of doing science with someone who is at once a great leader, a visionary, a lover of the good things in life, and the possessor of a most wonderful sense of humor. Chris's natural reticence could make him seem somewhat aloof to those who did not know him. Those who did know him, however, were touched by his wisdom, his underlying kindness, and his striving to always support excellence. Great love and respect for a remarkable personality were visibly and movingly apparent at his memorial symposium held at the JIC in April 2010. Chris's final legacy is the family that was so important to him; his wife Jane, who he married during his first year as an undergraduate at Cambridge, his daughter Catherine, and his sons William and Donald.

DISCLOSURE STATEMENT

The author is not aware of any affiliations, memberships, funding, or financial holdings that might be perceived as affecting the objectivity of this review.

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LITERATURE CITED

1. **Alvarez ME, Pennell R, Meijer P-J, Ishikawa A, Dixon RA, Lamb C. 1998. Reactive oxygen intermediates mediate a systemic signal network in the establishment of plant immunity. *Cell* 92:773–84**
2. Arias JA, Dixon RA, Lamb CJ. 1993. Dissection of the functional architecture of a plant defense gene promoter using a homologous in vitro transcription system. *Plant Cell* 5:485–96
3. Bate NJ, Orr J, Ni W, Meroni A, Nadler-Hassar T, et al. 1994. Quantitative relationship between phenylalanine ammonia-lyase levels and phenylpropanoid accumulation in transgenic tobacco identifies a rate determining step in natural product synthesis. *Proc. Natl. Acad. Sci. USA* 91:7608–12
4. Baulcombe DC. 1996. RNA as a target and an initiator of post-transcriptional gene silencing in transgenic plants. *Plant Mol. Biol.* 32:79–88
5. Bell JN, Dixon RA, Bailey JA, Rowell PM, Lamb CJ. 1984. Differential induction of chalcone synthase mRNA activity at the onset of phytoalexin accumulation in compatible and incompatible plant-pathogen interactions. *Proc. Natl. Acad. Sci. USA* 81:3384–88
6. Bell JN, Ryder TB, Wingate VPM, Bailey JA, Lamb CJ. 1986. Differential accumulation of plant defense gene transcripts in a compatible and an incompatible plant-pathogen interaction. *Mol. Cell. Biol.* 6:1615–23
7. Bi JL, Felton GW, Murphy JB, Howles PA, Dixon RA, Lamb CJ. 1997. Do plant phenolics confer resistance to specialist and generalist insect herbivores? *J. Food Agric. Chem.* 45:4500–4
8. Borevitz J, Xia Y, Blount JW, Dixon RA, Lamb C. 2000. Activation tagging identifies a conserved MYB regulator of phenylpropanoid biosynthesis. *Plant Cell* 12:2383–93
9. Bradley DJ, Kjellbom P, Lamb CJ. 1992. Elicitor- and wound-induced oxidative cross-linking of a proline-rich plant cell wall protein: a novel, rapid defense response. *Cell* 70:21–30
10. Brisson LF, Tenhaken R, Lamb C. 1994. Function of oxidative cross-linking of cell wall structural proteins in plant disease resistance. *Plant Cell* 6:1703–12
11. Cameron RK, Dixon RA, Lamb CJ. 1994. Biologically induced systemic acquired resistance in *Arabidopsis thaliana*. *Plant J.* 5:715–25
12. Chen F, Dixon RA. 2007. Lignin modification improves fermentable sugar yields for biofuel production. *Nat. Biotechnol.* 25:759–61
13. Corbin DR, Sauer N, Lamb CJ. 1987. Differential regulation of a hydroxyproline-rich glycoprotein gene family in wounded and infected plants. *Mol. Cell. Biol.* 7:4337–44
14. Cramer CL, Bell JN, Ryder TB, Bailey JA, Schuch W, et al. 1985. Co-ordinated synthesis of phytoalexin biosynthetic enzymes in biologically-stressed cells of bean (*Phaseolus vulgaris* L.). *EMBO J.* 4:285–89
15. Cramer CL, Edwards K, Dron M, Liang X, Dildine SL, et al. 1989. Phenylalanine ammonia-lyase gene organization and structure. *Plant Mol. Biol.* 12:367–83
16. Cramer CL, Ryder TB, Bell JN, Lamb CJ. 1985. Rapid switching of plant gene expression induced by fungal elicitor. *Science* 227:1240–43
17. de Maagd RA, Cameron RK, Dixon RA, Lamb CJ. 1993. Screening methods for *Arabidopsis* mutants affected in the signal transduction pathways leading to defense responses. In *Advances in Molecular Genetics of Plant-Microbe Interactions*, ed. EW Nester, DPS Verma, pp. 445–49. Dordrecht, Netherlands: Kluwer Acad. Publ.
18. Delaney TP, Uknes S, Vernooij B, Friedrich L, Weymann K, et al. 1994. A central role of salicylic acid in plant disease resistance. *Science* 266:1247–50
19. **Delledonne M, Xia Y, Dixon RA, Lamb C. 1998. Nitric oxide functions as a signal in plant disease resistance. *Nature* 394:585–88**
20. Dixon RA, Bendall DS. 1978. Changes in the levels of enzymes of phenylpropanoid and flavonoid synthesis during phaseollin production in cell suspension cultures of *Phaseolus vulgaris*. *Physiol. Plant Pathol.* 13:295–306

1. The seminal finding that inoculation at a single site can lead to systemic oxidative bursts that underlie the expression and spread of SAR.

19. The first demonstration of a role for nitric oxide as a signal molecule in induced antimicrobial defenses in plants.

21. Dixon RA, Dey PM, Murphy DL, Whitehead IM. 1981. Dose responses for *Colletotrichum lindemuthianum* elicitor-mediated enzyme induction in French bean cell suspension cultures. *Planta* 151:272–80
22. Dixon RA, Gerrish C, Lamb CJ, Robbins MP. 1983. Elicitor modulated induction of chalcone isomerase in *Phaseolus vulgaris*. *Planta* 159:561–69
23. Dixon RA, Harrison MJ, Lamb CJ. 1994. Early events in the activation of plant defense responses. *Annu. Rev. Phytopathol.* 32:479–501
24. Dixon RA, Lamb CJ. 1979. Stimulation of *de novo* synthesis of L-phenylalanine ammonia-lyase in relation to phytoalexin accumulation in *Colletotrichum lindemuthianum* elicitor-treated cell suspension cultures of French bean (*Phaseolus vulgaris*). *Biochim. Biophys. Acta* 586:453–63
25. Dixon RA, Lamb CJ. 1990. Molecular communication in plant: microbial pathogen interactions. *Annu. Rev. Plant Physiol. Plant Mol. Biol.* 41:339–67
26. Doerner P, Jørgensen JE, You R, Steppuhn J, Lamb C. 1996. Control of root growth and development by cyclin expression. *Nature* 380:520–23
27. Doerner PW, Stermer BA, Schmid J, Dixon RA, Lamb CJ. 1990. Plant defense gene promoter-reporter gene fusions in transgenic plants: tools for identification of novel inducers. *Bio/Technology* 8:845–48
28. Dröge-Laser W, Kaiser A, Lindsay WP, Halkier B, Loake GA, et al. 1997. Rapid stimulation of a soybean protein-serine kinase that phosphorylates a novel bZIP transcription factor, G/HBF-1, in the induction of early transcription-dependent defenses. *EMBO J.* 16:726–38
29. Dron M, Clouse SD, Dixon RA, Lawton MA, Lamb CJ. 1988. Glutathione and fungal elicitor regulation of a plant-defense gene promoter in electroporated protoplasts. *Proc. Natl. Acad. Sci. USA* 85:6738–42
30. Edwards K, Cramer CL, Schuch W, Lamb CJ, Dixon RA. 1985. Rapid transient induction of phenylalanine ammonia-lyase mRNA in elicitor-treated bean cells. *Proc. Natl. Acad. Sci. USA* 82:6731–35
31. **Elkind Y, Edwards R, Mavandad M, Hedrick SA, Ribak O, et al. 1990. Abnormal plant development and down regulation of phenylpropanoid biosynthesis in transgenic tobacco containing a heterologous phenylalanine ammonia-lyase gene. *Proc. Natl. Acad. Sci. USA* 87:9057–61**
32. Faktor O, Kooter J, Dixon RA, Lamb CJ. 1996. Functional dissection of a bean chalcone synthase gene promoter in transgenic tobacco plants reveals sequence motifs essential for floral expression. *Plant Mol. Biol.* 32:845–59
33. Faktor O, Loake G, Dixon RA, Lamb CJ. 1997. The G-box and H-box in a 39 bp region of a French bean chalcone synthase promoter constitute a tissue-specific regulatory element. *Plant J.* 11:1105–13
34. Fan J, Hill L, Crooks C, Doerner P, Lamb C. 2009. Abscisic acid has a key role in modulating diverse plant-pathogen interactions. *Plant Physiol.* 150:1750–61
35. Felton GW, Korth KL, Bi JL, Wesley SV, Huhman DV, et al. 1999. Inverse relationship between systemic resistance of plants to microorganisms and to insect herbivory. *Curr. Biol.* 9:317–20
36. Filner P, Varner JE. 1967. A test for *de novo* synthesis of enzymes: density labeling with H_2O^{18} of α-amylase induced by gibberellic acid. *Proc. Natl. Acad. Sci. USA* 58:1520–26
37. Hahlbrock K, Lamb CJ, Purwin C, Ebel J, Fautz E, Schäfer E. 1981. Rapid response of suspension-cultured parsley cells to the elicitor from *Phytophthora megasperma* var. *sojae*. *Plant Physiol.* 67:768–73
38. Harrison MJ, Choudhary AD, Dubery I, Lamb CJ, Dixon RA. 1991. *Cis*-elements and *trans*-acting factors for the quantitive expression of a bean chalcone synthase gene promoter in electroporated alfalfa protoplasts. *Plant Mol. Biol.* 16:877–90
39. He ZH, Wang ZY, Li JM, Zhu Q, Lamb C, et al. 2000. Perception of brassinosteroids by the extracellular domain of the receptor kinase BRI1. *Science* 288:2360–63
40. Hedrick SA, Bell JN, Boller T, Lamb CJ. 1988. Chitinase cDNA cloning and mRNA induction by fungal elicitor, wounding, and infection. *Plant Physiol.* 86:182–86
41. Heller W, Hahlbrock K. 1980. Highly purified "flavanone synthase" from parsley catalyzes the formation of naringenin chalcone. *Arch. Biochem. Biophys.* 200:617–19
42. Howles PA, Sewalt VJH, Paiva NL, Elkind NL, Bate Y, et al. 1996. Overexpression of L-phenylalanine ammonia-lyase in transgenic tobacco plants reveals control points for flux into phenylpropanoid biosynthesis. *Plant Physiol.* 112:1617–24
43. Jacobs M, Rubery PH. 1988. Naturally occurring auxin transport regulators. *Science* 241:346–49
44. Keller B, Lamb CJ. 1989. Specific expression of a novel cell wall hydroxyproline-rich glycoprotein gene in lateral root initiation. *Genes Dev.* 3:1639–46

31. A key publication providing a novel approach for genetically testing the roles of phenylpropanoid compounds in plant defense, and one of the first examples of epigenetic gene silencing in plants.

45. Keller B, Sauer N, Lamb CJ. 1988. Glycine-rich cell wall proteins in bean: gene structure and association of the protein with the vascular system. *EMBO J.* 7:3625–33
46. Keller B, Schmid J, Lamb CJ. 1989. Vascular expression of a bean cell wall glycine-rich protein-ß-glucuronidase gene fusion in transgenic tobacco. *EMBO J.* 8:1309–14
47. Keller B, Templeton MD, Lamb CJ. 1989. Specific localization of a plant cell wall glycine-rich protein in protoxylem cells of the vascular system. *Proc. Natl. Acad. Sci. USA* 86:1529–33
48. Keller T, Damude HG, Werner D, Doerner P, Dixon RA, Lamb C. 1997. A plant homolog of the neutrophil NADPH oxidase gp91^{phox} subunit gene encodes an intrinsic plasma membrane protein with Ca^{2+}-binding and RanGAP1 domains. *Plant Cell* 10:255–66
49. Kreuzaler F, Ragg H, Fautz E, Kuhn DN, Hahlbrock K. 1983. UV-induction of chalcone synthase mRNA in cell suspension cultures of *Petroselinum hortense*. *Proc. Natl. Acad. Sci. USA* 80:2591–93
50. Lamb C, Dixon RA. 1997. The oxidative burst in plant disease resistance. *Annu. Rev. Plant Physiol. Plant Mol. Biol.* 48:251–75
51. Lamb CJ. 1977. Phenylalanine ammonia-lyase and cinnamic acid 4-hydroxylase: characterisation of the concomitant changes in enzyme activities in illuminated potato tuber discs. *Planta* 135:169–75
52. Lamb CJ. 1977. *trans*-Cinnamic acid as a mediator of the light-stimulated increase in hydroxycinnamoyl-CoA: quinate hydroxycinnamoyl transferase. *FEBS Lett.* 75:37–39
53. Lamb CJ. 1979. Regulation of enzyme levels in phenylpropanoid biosynthesis: characterization of the modulation by light and pathway intermediates. *Arch. Biochem. Biophys.* 192:311–17
54. Lamb CJ. 1994. Plant disease resistance genes in signal perception and transduction. *Cell* 76:419–22
55. Lamb CJ, Dixon RA. 1978. Stimulation of *de novo* synthesis of L-phenylalanine ammonia-lyase during induction of phytoalexin biosynthesis in cell suspension cultures of *Phaseolus vulgaris*. *FEBS Lett.* 94:277–80
56. Lamb CJ, Lawton MA, Dron M, Dixon RA. 1989. Signals and transduction mechanisms for activation of plant defenses against microbial attack. *Cell* 56:215–24
57. Lamb CJ, Lawton MA, Shields SE. 1981. Density labelling characterisation of the effects of cordycepin and cycloheximide on the turnover of phenylalanine ammonia-lyase. *Biochim. Biophys. Acta* 675:1–8
58. Lamb CJ, Merritt TK. 1979. Density labelling studies of the photocontrol of L-phenylalanine ammonia-lyase in discs of potato (*Solanum tuberosum*) tuber parenchyme. *Biochim. Biophys. Acta* 588:1–11
59. Lamb CJ, Merritt TK, Butt VS. 1979. Synthesis and removal of phenylalanine ammonia-lyase activity in illuminated discs of potato tuber parenchyme. *Biochim. Biophys. Acta* 582:196–212
60. Lamb CJ, Rubery PH. 1976. Differential effects of cycloheximide on the activity of phenylalanine ammonia-lyase and cinnamic acid 4-hydroxylase in light- and dark-incubated potato tuber discs. *Plant Sci. Lett.* 7:33–37
61. Lamb CJ, Rubery PH. 1976. Inhibition of co-operative enzymes by substrate-analogues: possible implications for the physiological significance of negative co-operativity illustrated by phenylalanine metabolism in higher plants. *J. Theor. Biol.* 60:441–47
62. Lamb CJ, Rubery PH. 1976. Interpretation of the rate of density labelling of enzymes with ^2H_2O: possible implications for the mode of action of phytochrome. *Biochim. Biophys. Acta* 421:308–18
63. Lamb CJ, Ryals JA, Ward ER, Dixon RA. 1992. Emerging strategies for enhancing crop resistance to microbial pathogens. *Bio/Technology* 10:1436–45
64. Lawton MA, Clouse SD, Lamb CJ. 1990. Glutathione-elicited changes in chromatin structure within the promoter of the defense gene chalcone synthase. *Plant Cell Rep.* 8:561–64
65. Lawton MA, Dean SJ, Dron M, Kooter JK, Kragh KM, Harrison MJ, et al. 1991. Silencer region of a chalcone synthase promoter contains multiple binding sites for a factor, SBF-1, closely related to GT-1. *Plant Mol. Biol.* 16:235–49
66. Lawton MA, Dixon RA, Hahlbrock K, Lamb CJ. 1983. Rapid induction of phenylalanine ammonia-lyase and of chalcone synthase synthesis in elicitor-treated plant cells. *Eur. J. Biochem.* 129:593–601
67. Lawton MA, Dixon RA, Hahlbrock K, Lamb CJ. 1983. Elicitor induction of mRNA activity: rapid effects of elicitor on phenylalanine ammonia-lyase and chalcone synthase mRNA activities in bean cells. *Eur. J. Biochem.* 130:131–39
68. Lawton MA, Dixon RA, Lamb CJ. 1980. Elicitor modulation of L-phenylalanine ammonia-lyase in French bean cell suspension cultures. *Biochim. Biophys. Acta* 633:162–75

50. One of the most highly cited review articles in the plant sciences, providing an in-depth analysis of the generation and role of hydrogen peroxide in defense.

69. Lawton MA, Yamamoto RT, Hanks SK, Lamb CJ. 1989. Molecular cloning of plant transcripts encoding protein kinase homologs. *Proc. Natl. Acad. Sci. USA* 86:3140–44

70. An analysis of the multiple roles of hydrogen peroxide in the HR, emphasizing the importance of a balance between induced cell death and cellular protection mechanisms.

70. Levine A, Tenhaken R, Dixon RA, Lamb CJ. 1994. H_2O_2 from the oxidative burst orchestrates the plant hypersensitive disease resistance response as a local trigger of programmed cell death and a diffusible inducer of cellular protectant genes. *Cell* 79:583–93

71. Leyva A, Liang X, Pintor-Toro JA, Dixon RA, Lamb CJ. 1992. *cis*-Element combinations determine phenylalanine ammonia-lyase gene tissue specific expression patterns. *Plant Cell* 4:263–71

72. Liang X, Dron M, Cramer CL, Dixon RA, Lamb CJ. 1989. Differential regulation of phenylalanine ammonia-lyase genes during plant development and by environmental cues. *J. Biol. Chem.* 264:14486–92

73. Liang X, Dron M, Schmid J, Dixon RA, Lamb CJ. 1989. Developmental and environmental regulation of a phenylalanine ammonia-lyase ß-glucuronidase gene fusion in transgenic tobacco plants. *Proc. Natl. Acad. Sci. USA* 86:9284–88

74. Lindsay WP, Lamb CJ, Dixon RA. 1993. Microbial recognition and activation of plant defense mechanisms. *Trends Microbiol.* 1:181–86

75. Lindsay WP, McAlister FM, Zhu Q, He X-Z, Droge-Laser W, et al. 2002. KAP-2, a protein that binds to the H-box in a bean chalcone synthase promoter, is a novel plant transcription factor with sequence identity to the large subunit of human Ku autoantigen. *Plant Mol. Biol.* 49:503–14

76. Loake G, Choudhary AD, Harrison MJ, Mavandad M, Lamb CJ, Dixon RA. 1991. Phenylpropanoid pathway intermediates regulate transient expression of a chalcone synthase gene promoter in electroporated protoplasts. *Plant Cell* 3:829–40

77. Loake GJ, Faktor O, Lamb CJ, Dixon RA. 1992. Combination of H-box ($CCTACC(N_7)CT$) and G-box (CACGTG) *cis*-elements is necessary for feedforward stimulation of a chalcone synthase promoter by the phenylpropanoid pathway intermediate *p*-coumaric acid. *Proc. Natl. Acad. Sci. USA* 89:9230–34

78. An early genetic demonstration of the importance of induced phenylpropanoid compounds in plant disease resistance.

78. Maher EA, Bate NJ, Ni W, Elkind Y, Dixon RA, Lamb CJ. 1994. Increased disease susceptibility of transgenic tobacco plants with suppressed levels of preformed phenylpropanoid products. *Proc. Natl. Acad. Sci. USA* 91:7802–6

79. Genetic evidence for the role of a lipid transfer protein (and therefore possibly oxylipin signal molecules) in long distance signal transduction to establish SAR.

79. Maldonado AM, Dixon RA, Lamb C, Doerner P, Cameron RK. 2002. A putative lipid transfer protein is involved in systemic signaling to establish acquired resistance in *Arabidopsis thaliana*. *Nature* 419:399–403

80. Mehdy MC, Lamb CJ. 1987. Chalcone isomerase cDNA cloning and mRNA induction by fungal elicitor, wounding and infection. *EMBO J.* 6:1527–33

81. Moon J, Parry G, Estelle M. 2004. The ubiquitin-proteasome pathway and plant development. *Plant Cell* 16:3181–95

82. Napoli C, Lemieux C, Jorgensen R. 1990. Introduction of a chimeric chalcone synthase gene into petunia results in reversible co-suppression of homologous genes in *trans*. *Plant Cell* 2:279–89

83. Niggeweg R, Michael AJ, Martin C. 2004. Engineering plants with increased levels of the antioxidant chlorogenic acid. *Nat. Biotechnol.* 22:746–54

84. O'Connell RJ, Bailey JA, Vose IR, Lamb CJ. 1986. Immunogold labelling of fungal antigens in cells of *Phaseolus vulgaris* infected by *Colletotrichum lindemuthianum*. *Physiol. Mol. Plant Pathol.* 28:99–105

85. Ohl S, Hedrick SA, Chory J, Lamb CJ. 1990. Functional properties of a phenylalanine ammonia-lyase promoter from *Arabidopsis*. *Plant Cell* 2:837–48

86. Pallas JA, Paiva NL, Lamb CJ, Dixon RA. 1996. Tobacco plants epigenetically suppressed in phenylalanine ammonia-lyase expression do not develop systemic acquired resistance in response to infection by tobacco mosaic virus. *Plant J.* 10:281–93

87. Rubery PH, Northcote DH. 1968. Site of phenylalanine ammonia-lyase activity and synthesis of lignin during xylem differentiation. *Nature* 219:1230–34

88. Ryder TB, Cramer CL, Bell JN, Robbins MP, Dixon RA, Lamb CJ. 1984. Elicitor rapidly induces chalcone synthase mRNA in *Phaseolus vulgaris* cells at the onset of the phytoalexin response. *Proc. Natl. Acad. Sci. USA* 81:5724–28

89. Ryder TB, Hedrick SA, Bell JN, Liang X, Clouse SD, Lamb CJ. 1987. Organization and differential activation of a gene family encoding the plant defense enzyme chalcone synthase in *Phaseolus vulgaris*. *Mol. Gen. Genet.* 210:219–33

90. Sauer N, Corbin DR, Keller B, Lamb CJ. 1990. Cloning and characterization of a wound-specific hydroxyproline-rich glycoprotein in *Phaseolus vulgaris*. *Plant Cell Environ.* 13:257–66
91. Schmid J, Doerner PW, Clouse SD, Dixon RA, Lamb CJ. 1990. Developmental and environmental regulation of a bean chalcone synthase promoter in transgenic tobacco. *Plant Cell* 2:619–31
92. Schröder J, Kreuzaler F, Schäfer E, Hahlbrock K. 1979. Concomitant induction of phenylalanine ammonia-lyase and flavanone synthase mRNAs in irradiated plant cells. *J. Biol. Chem.* 254:57–65
93. Seguin A, Laible G, Leyva A, Dixon RA, Lamb CJ. 1997. Characterization of a gene encoding a DNA-binding protein that interacts with vascular specific *cis*-elements of the phenylalanine ammonia-lyase promoter. *Plant Mol. Biol.* 35:281–91
94. Shirasu K, Nakajima H, Rajasekhar VK, Dixon RA, Lamb CJ. 1997. Salicylic acid potentiates an agonist-dependent gain control that amplifies pathogen signals in the activation of defense mechanisms. *Plant Cell* 9:261–70
95. Showalter AM, Bell JN, Cramer CL, Bailey JA, Varner JE, Lamb CJ. 1985. Accumulation of hydroxyproline-rich glycoprotein mRNAs in response to fungal elicitor and infection. *Proc. Natl. Acad. Sci. USA* 82:6551–55
96. Templeton MD, Dixon RA, Lamb CJ, Lawton MA. 1990. Hydroxyproline-rich glycoprotein transcripts exhibit different spatial patterns of accumulation in compatible and incompatible interactions between *Phaseolus vulgaris* and *Colletotrichum lindemuthianum*. *Plant Physiol.* 94:1265–69
97. Tenhaken R, Levine A, Brisson LF, Dixon RA, Lamb CJ. 1995. Function of the oxidative burst in hypersensitive disease resistance. *Proc. Natl. Acad. Sci. USA* 92:4158–63
98. Vierstra RD. 1993. Protein degradation in plants. *Annu. Rev. Plant Physiol. Plant Mol. Biol.* 44:385–410
99. Weigel D, Ahn JH, Blazquez MA, Borewitz J, Christensen SK, et al. 2000. Activation tagging in *Arabidopsis*. *Plant Physiol.* 122:1003–13
100. Wildermuth MC, Dewdney J, Wu G, Ausubel FM. 2001. Isochorismate synthase is required to synthesize salicylic acid for plant defence. *Nature* 414:562–65
101. Wingate VPM, Lawton MA, Lamb CJ. 1988. Glutathione causes a massive and selective induction of plant defense genes. *Plant Physiol.* 87:206–10
102. Xia Y, Suzuki H, Borevitz J, Blount JW, Guo Z, et al. 2003. An extracellular aspartic protease mediates disease resistance in *Arabidopsis*. *EMBO J.* 23:980–88
103. Zhu Q, Chappell J, Hedrick SA, Lamb CJ. 1995. Accurate in vitro transcription from circularized plasmid templates by plant whole cell extracts. *Plant J.* 7:1021–30
104. Zhu Q, Dabi T, Lamb C. 1995. TATA box and initiator functions in the accurate transcription of a plant minimal promoter in vitro. *Plant Cell* 7:1681–89
105. Zhu Q, Maher EA, Masoud S, Dixon RA, Lamb CJ. 1994. Enhanced protection against fungal attack by constitutive co-expression of chitinase and glucanase genes in transgenic tobacco. *Bio/Technology* 12:807–12

94. Evidence that salicylic acid acts in an amplification loop during transduction of pathogen signals for induced defense responses.

102. Genetic evidence of a key role for host-associated proteolytic reaction as an early step in defense gene induction by pathogen signals.