INTRODUCTION

This essay is a series of events whereby I cover the 30 years (1964-1994) in a ‘transposon odyssey’ in which I sought to learn more on the molecular investigations of transposons that eventually led to collaboration with Professor Heinz Saedler.

Following his stellar career in bacterial genetics, Prof. Saedler embarked in 1980 on a career in plant genetics. Using the tools from bacterial genetics and his work with the IS2 elements, he quickly adapted to the maize genome. In less than half a decade, he organized a laboratory effort to uncover the first investigations in this eukaryotic genome.
A. Awakening to Molecular Biology: Stanford University and Stockholm, Sweden, Leading to a Collaborative Venture with Professor Heinz Saedler

1. January 1964 Stanford: The Freiburg-Cologne connection that led to a joint venture with Prof. Heinz Saedler on a transposon odyssey had its beginnings at Stanford University in Palo Alto, California. The occasion was the time I was invited to teach a course in cytogenetics during the 1964 spring term at Stanford University. The course was developed to provide Stanford genetic graduate students in the Biological Sciences Department a maize geneticist’s perspective on genetics and cytogenetics features. Another purpose of the course was to introduce these perspectives to molecularly oriented students. As such, the course was a challenge but pleasant experience to present this material.

There was however another distinct, and important feature at Stanford. There was a far-reaching benefit with the Stanford teaching venture. This was in 1964 and only 11 years after the revelation of the structure and emerging concepts associated with DNA. Nightly, there were seminars on the many features of DNA and this was attended by hundreds of graduate students, post-doctoral researchers, many Stanford faculty and others in a vast amphitheater-like auditorium on the Stanford campus. This was my first exposure to the extensive and the latest information on DNA and the methods and techniques for the manipulation of DNA. Lectures were given by Prof. Dale Kaiser and by Ken Murray (visitor with wife Noreen from Edinburgh, Scotland and a visitor in the cytogenetics course). For many in the audience including myself this was a wake-up-call for the fast-moving concepts emerging from the novel revelation of the structure and the implications dealing with DNA. At the same time in 1964, in another building, Prof. C. Yanofsky and his research team had demonstrated and published a singularly important concept that the gene sequence was collinear with the protein sequence (Yanofsky et al., 1964). How the whole experience with the seminars and the research in the various departments impacted me was yet to be seen.

The specific event that triggered my awareness of a relation to all that was experienced at Stanford was a personal reaction during a seminar on maize transposons I presented to an audience that included most of the geneticists on the Stanford campus, including those from the Medical School. The seminar covered what was then known about maize transposons in the mid-1960s. (The coverage was entirely genetic as the molecular aspects would not be

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1 Actually, one might say that this quest really began in 1947 when I graduated from Tufts College. It was at this time that Prof. Paul Warren thought I should take a year off (after a stint in the US Navy in WWII) and go to Cold Spring Harbor at the Dept. of Genetics of the Carnegie Institute of Washington located on the North Shore of Long Island, NY. Spending summers at Cold Spring Harbor were a number of geneticists that were beginning their discoveries that led to major genetic concepts: Delbruck, Luria, Watson, Mark Adams and a number of others. McClintock was a permanent member of the CSH staff. There were also seminars by noted visitors, for example Sir Ronald Fisher attending the United Nations spoke at Cold Spring Harbor.

2 Some of the students were from Charlie Yanofsky’s, Dow Woodward’s, David Perkins’ laboratories, and from other molecular labs in the biological sciences department. (One of the students, Tom Creighton, became a prominent protein-folding expert and the author of a noted book on the subject).

3 By 1964, emerging techniques and concepts were brought forward to augment the DNA view of life’s processes. This included the sequence of proteins, and the language of reading and copying the sequence of nucleotides (Sanger and Tuppy, 1951a,b; Crick, 1958; Lehman et al., 1958; Hayes, 1963).

4 In the following years, several Stanford faculties made key discoveries leading to the awarding of Nobel Prizes (A. Kornberg and Paul Berg.).

5 While in graduate school at the University of Illinois, the Avery et al. (1944) experiment confirming DNA as a hereditary component of bacteria was discussed. This experiment was thought interesting but not important and consideration for this discovery was to change in the coming years.

6 (This was 4 years after joining the Agronomy Dept especially as so many cytogenetics concepts were established in maize) 1964 was 11 years after the discovery and presentation at the 1953 Cold Spring Harbor Spring Symposium. Though teaching Genetics at Ames from 1956-1960, there was little or no mention of DNA or its relation to heredity either in the Genetics course or in the Genetics Seminars. Much was probably due to the “protein syndrome” whereby it was difficult to comprehend how a string of nucleotides could lead to development of complex organisms. Only when the amino acid changes were shown to cause mutants and phenotypic changes (Ingram, 1956, 1957) it was obvious that proteins derived their activity from specific arrangement of elements in the protein. And the understanding of the machinery that leads to proteins was this universally accepted. (Lehman et al., 1958). So, I was surprised, and indeed, impressed by the nightly revelations during the seminars. The Stanford speakers were on top of the subject.

7 This paper made it clear that nucleotide changes in a codon results in a change in enzyme performance.
What was bothersome to me occurred at the end of the seminar. There was a lack of probing questions. More significant to this author was the exit at the end of the seminar by Prof. Josh Lederberg (then the Chairman of the Dept. of Medical Genetics). (This had a noted effect on the speaker as detailed in a note, “Did I fail to get the transposon concepts across to the audience?”). With this concern I approached a colleague in the audience, Prof. Dale Kaiser, for his ideas and reaction to the seminar. Kaiser then suggested that I should join a working DNA lab to appreciate their thinking and procedures. With Kaiser’ suggestions of various laboratories that would provide a DNA perspective, I chose the Bertani lab in the Karolinska Institute in Stockholm, Sweden.

2. Stockholm: The Karolinska Institute in Stockholm, Sweden appeared to fit the need to relate the maize transposons to bacterial mobile elements. The Bertani lab was investigating the P2 phage that, unlike the lambda phage (for example, the Paris lab of Jacob and Monod), was random in site phage deposition. That is, that any gene could be a site for mobile element insertion.

I prepared a proposal that outlined the goals and procedures for study at the Stockholm laboratory. This proposal was submitted to the National Institute of Health (NIH). Surprisingly, this proposal was approved and a one-year program was granted.

(Surprisingly, because it was a long shot that NIH would approve a grant to one in Agronomy). The goal of the proposal was to demonstrate that any gene could be a site of mobile element deposition. On arriving in Stockholm, experiments were initiated to target a gene and rescue an insert (P2) in that gene. The targeted locus needed special anaerobic conditions that appeared (to this experimenter) to be insurmountable. And, before one could visualize it, the year was over. It appeared a difficult task for someone new to develop and finalize this bacterial experiment within one year.

Upon my return to Ames in January 1970, after a year in Stockholm, it seemed prudent to summarize and report on Stockholm DNA experiments, research on the manipulation of DNA handling and the research conducted in other labs. The Agriculture Dean (Andre) listened but did not seem interested. So, the effort was dropped. That was early 1970 so I returned to his laboratory to continue with genetic analysis of maize genetic crosses dealing with the transposon En.

3. A slight diversion from transposons: The Corn Blight epidemic: In 1970, the Southern corn blight (Bipolaris maydis) was prevalent in the United States Corn Belt. There was a hurry-up call from the US Department of Agriculture in Washington to the State Agriculture Experiment Stations to initiate investigations into this problem that was devastating.

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8 At this time in 1964, maize transposons were the only “game in town”. Not until 1980 did geneticists gather at Cold Spring Harbor, N.Y. (Cold Spring Harbor) to discuss transposons in maize, Drosophila, yeast, the nematode and other organisms. (Cold Spring Harbor Symp. 45, published in 1981). Currently, mobile elements are known to be universally present in all organisms including the human DNA. Obviously, the various reporters that report the movement of transposons in maize were not adequately explained to this audience. The molecular biology of transposons did not become apparent until 1982 when the cin1 element was identified (Sheppard et al., 1982). In 1983, the Ac transposon system was described (Fedorkov et al., 1983) and in 1984 a derivative of the En/Spm transposon system was cloned (Schwarz-Sommer et al., 1984).

9 It would be some years before mobile elements were demonstrated to be universally present in all organisms (see note 8). At this time in 1964, mobile elements were actively studied in the maize genome though a year before Taylor (1963) reported that bacterial mutations were induced by a mobile element.

10 Because of the Lederberg exit at the seminar (Lederberg later told me that he had urgent tasks in his office.), I inquired from Prof. Kaiser as to the lack of inquiring questions on the genetics of transposons and the Lederberg exit. What he said was significant to me and led me on a quest to learn more. He said it was difficult to see how we (in maize genetics) could conclude the findings of genetic material “moving in the genome from one location to a defined location elsewhere with only spots on corn kernels and ratios”. How could a maize geneticist deduce an insertion from these observations? Kaiser said “what you should do is go and do research in a molecular laboratory and learn how molecular researchers think”.

11 It is obvious that the Lederberg incident set off a series that will be detailed in the next few paragraphs leading to Stockholm and several other places in the coming years.

12 At this time, I was disputing the thinking on transposons relating to controlling elements. The critical paper that was pivotal in altering this thinking was a paper written by Taylor (1963) indicating Mu element in bacteria was mobile and could induced mutations. During the leave in Stockholm, I wrote a paper detailing how maize transposons related to a number of mobile elements in bacteria and the lambda phage. This relation to lambda was made because this phage was the only mechanism known at that time of insertion. As was later learned, it is too specific in site deposition and not like the maize transposons. This paper was read by B. McClintock and many years later I learned of her reaction to the ideas in the paper (Peterson, 2002).
to corn production. It was determined early that the susceptible plants contained the T cytoplasm\(^{13}\). Many corn companies quickly produced their popular hybrid combinations in winter nurseries in Chile and Argentina that avoided the use of T-cytoplasm female parents. As the target (mitochondria) was known, research was quickly focused on that organelle. The Illinois Agronomy group had advanced the notion that the target of the fungus was the mitochondria. A grant was prepared and with funds available, a post-doc joined the project. We too supported the cytoplasmic aspect of the Southern corn blight problem (PETERSON et al., 1975). To advance this problem, I sought a leave to join a lab to learn more on mitochondria.

With the advice of several, the Tuppy laboratory (The Medical School in Vienna, Austria) was chosen. The leave included both the Tuppy lab in Vienna and the Flavell lab at the Plant Breeding lab in Cambridge, England. The Tuppy\(^{14}\) lab introduced this author to mitochondrial handling and a Friday afternoon custom. The Friday noon custom involved the whole lab driving to a countryside wein-stube for knodell and spritzer. It was a way for Prof. Tuppy to converse with his students and post-docs in his lab in an informal setting.

With the Vienna experience, there was in addition to the mitochondria handling, more chemistry at the Flavell lab with the production of three papers relating the Southern corn blight toxin effects on cell activity (PETERSON et al., 1975)\(^{15}\). By that time other labs were into this study. Because of limited resources in Ames I had little chance to succeed in the mechanisms in the Southern corn blight effect, though the Cambridge lab continued on the T cytoplasm project that was initiated by this author.

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\(^{13}\) The T cytoplasm was widely used by commercial corn companies as female plants in the production of hybrids. The T cytoplasm induced the abortion of pollen with this cytoplasm.

\(^{14}\) Prof. Tuppy was a post doc associate in Fred Sanger’s lab when the Sanger lab established the first sequence of a protein (STRETON, 2002). They showed the first complete sequence of amino acids of the Beta chain of insulin. This, more than 6 decades ago, was the example showing that proteins had a unique sequence that formed the protein function. (SANGER and TUPPY, 1951a,b).

\(^{15}\) PETERSON et al. (1974, 1975); BARRATT and PETERSON (1977). Barrett came to Ames as a post-doc to continue some of this work.

\(^{16}\) The week-long symposium in 1973 was welcomed. Transposon genetics was languishing at this time. From peer reviewed comments on grant proposals, it appeared that there was little support for these studies. Other organisms had not progressed very far at this time to generate more support for the maize transposons. (FINCHAM and SASTRY, 1974).

\(^{17}\) When plating gal\(^{-}\), mutants arose and expressed as red colonies on a white colony. These red colonies could be isolated and tested for inheritance and molecular investigation. When plating for mutants, I decided to adopt a maize genetics winter nursery routine. As colonies showed mutants at 4PM, I recollected the mutants and replated. By 11 pm I replated again so that colonies would be ready the next morning. The morning, Heinz Saedler had already seen the plates to tell me about them. I saw this many times in Cologne. This made me realize that he had his hand on the tiller (see section D).

\(^{18}\) PETERSON et al. (1979). This was my first molecular paper.

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B. Freiburg and Cologne: Reawakening of molecular genetics of Transposon Biology

1. The Saedler-Freiburg lab: In the following year (1973) Prof. Fincham organized a week-long symposium on plant variegation\(^{16}\) in Leeds, England. Everything that led to variegation was discussed but the focus finally came down to mobile elements of plants and bacteria. The Leeds session was significant as it reawakened an interest in transposons. Included among the participants in the sessions were two geneticists from Germany, Prof. Peter Starlinger and Heinz Saedler. Saedler discussed the IS2 mobile element and its activity. From the experiments that Saedler described, I saw an opportunity to join the Saedler microbial lab in Freiburg Germany to learn more molecular tools to introduce into studies of maize transposons.

With this reawakened interest in mobile elements, a grant to work with the IS2 element in the Saedler lab at the Botanical Institute, Freiburg, Germany was obtained (Humboldt Fellowship) and a leave requested for me to participate in microbial spring of 1977. Of course, there was concern in that lab (as I heard later) “what would they do with a visitor to the lab who was a maize geneticist?” Arriving in Freiburg, a research problem was presented and experiments were arranged to introduce me to microbial handling (Fig. 2). The Freiburg experiments were more readily handled than the experiments in Vienna (or were the experiences in Vienna that helped here). But, isolating gal\(^{-}\) mutating to gal\(^{+}\) was both aesthetically pleasing and relative easier to handle\(^{17}\). In the end, a mutant was isolated that formed a new promoter and this was published in MGG (PETERSON et al., 1979\(^{18}\); SAEDLER et al., 1980).
Something more interesting and unexpected, however was happening in the Freiburg lab. I was asked to provide a general discussion on corn production and breeding which interested several in the group. What I did not know, was that Saedler was negotiating with several offers to be a Max Planck director either in Munich or in Cologne. In the end, he was offered and accepted the directorship at Cologne at the Max Planck Institute (MPI) in Vogelsang, Germany.

The MPI in Vogelsang was a Plant Institute for Crop Improvement and the concern was how to get plant experiments started by someone with a microbial background. According to Prof. Lothar Willmitzer (of MPI-Potsdam), the discussion at MPI was on the coming appointment of Heinz Saedler. What Saedler needed and what he saw as an opportunity was the plant genetic resources in Ames in the Peterson laboratory. So a contractual arrangement was signed19 and experiments began in 1980 in the outskirts of Cologne, Germany.

Saedler assembled a research team (Fig. 3) and the transposon project was started. The immediate goal was to isolate the $En$ transposon. With $En$ available as a probe; several genes in the maize genome could be probed and eventually cloned and described. This study was the first that led to one of the most productive investigations of the maize genome.

![The Freiburg group in 1978.](image)

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19 Of course, this arrangement needed an agreement from Iowa State University. The Agronomy Dept. head was approached and the request was made. There was a question of an unlimited leave (2 weeks, 4 X a year to Germany) that seemed to be questioned and the Dean to approve. This author offered to take vacation leave in order to pursue this research if the request was denied.

In order to retain continuity in the Ames lab and Lectures in teaching, a typical Cologne trip included a Thursday class at 7:30-9:00 AM and then head to the airport at 11 AM for a 14:00 flight from Des Moines to Frankfort and the train on Airport Express train to Cologne. Returned a week later for a 7:30 AM Tuesday class.
2. Cologne-MPI

a. An approach to isolating En: In 1980 in Cologne, strategy sessions began on the transposon project which was the isolation of the transposon En. With the transposon in hand, this En-DNA would be used as a probe to extract the several genes with En inserts. With an En probe, these genes with En inserts could be extracted and cloned in order to study maize gene structure and function. It seemed that with all these genes with En inserts available, that it would be a multi-year project. As the culture of maize in the Cologne greenhouses would need care and guidance as well as constantly changing strategies, I periodically traveled to Cologne. The joint venture continued until 1994 when the transposon project was completed.

By 1982, the first plant mobile element in maize (cin1) was isolated and described (Shepherd et al., 1982). But to get to the individual genes in maize, the En transposon was needed and so a strategy was developed to get at the En transposon.

b. The wx strategy

To gain access to the En transposon, two fea-
tures had to be considered. (1) To get to the DNA of the waxy gene to use as a probe and to (2) to get a full-sized En inserted into the waxy gene.

The Wx gene. Saedler’s MPI group reasoned that the most abundant activity in the maize endosperm was starch development\(^{23}\) and thus decided to concentrate on the Wx gene. With this developed strategy at MPI, Zsuzsana Schwarz-Sommer et al. (1984) could capture the RNA messages in the developing endosperm and search for a Wx transcript. These RNA transcripts were converted to cDNA’s. The MPI Cologne group concentrated on the waxy gene. It was assumed that as endosperm developed in the growing kernel, extensive starch production would take place and this tissue would have abundant transcripts of the Wx gene. By capturing the RNA products and converting them into cDNAs, they could then be used in an expression transient assay in producing the waxy protein product, thereby confirming the waxy cDNA. With thousands of cDNA’s, the Cologne group ran these through the \(\text{in vitro}\) assay system.

These double-strand cDNA’s (there were thousands); could be run in a rabbit reticulocyte \(\text{in vitro}\) translation protein forming system. Approximately, more than 800 cDNA’s were run before the first Wx cDNA was confirmed by the appropriately correct identified protein. This provided the opportunity for Zsuzsana Schwarz-Sommer et al. (1984) to use this small probe to clone the \(\text{wxm8}\) allele (a 2.2 bp derivative receptor of the \(\text{En/Spm}\) system\(^{24}\)). With this \(\text{wxm8}\) allele, some of the basic structures of the \(\text{En}\) transposon were identified including the target site duplication (TSD 3+3 bp) and terminal inverted repeats (TIR 13 bp).

c. En inserted in Waxy (Wx)

The full-sized \(\text{En}\) insert in the Wx gene was still needed. This was dependent on the Ames part of the project.

To obtain the \(\text{En}\) transposon inserted into the waxy gene, field isolation plots were developed in the Ames nursery plots. The plot would include the \(\text{En}\) transposon in the female parent that included one or more \(\text{En}\)’s. The specific cross in the isolation plot was as follows:

\[
\text{CI}/\text{CI} \; \text{En} \; \text{Wx} \; \text{Wx} \times \text{CI} \; \text{sh} \; \text{bz} \; \text{wx} \rightarrow \text{F1} \; \text{search for } \text{wxm}
\]

FIGURE 4 - The parents in the crossing plot searching for the \(\text{En}\) inserted into Wx.

d. The \(\text{wx-844}\) allele: Massive isolation plots (approximately 10,000 \(\text{En}\) containing female plants) (Fig. 4) were used that were detasseled\(^{25}\) and crossed as shown followed by laboratory screening of F1 ears for \(\text{wxm}\). Of course, a colorless kernel was needed in order to detect any changes in Wx. As most of the available \(\text{En}\)’s were in color lines, a dominant colorless line with \(\text{En}\) was the obligate genotype. This was solved by introducing \(\text{En}\) into a \(\text{C1}\) color suppressing line\(^{26}\) (This was already done years before for another experiment). In the first 1982 run of the isolation plot, several candidates were detected and isolated but they were not confirmed to be mutable alleles. The following year with a scan of over 3 million kernels\(^{27}\), one candidate was isolated and this was sent to Cologne and identified as \(\text{wx-844}\). Mutant \(\text{wx-844}\) became the standard that was used for \(\text{En}\) size and structure (Pereira et al., 1985; 1986) and as the probe for the other genes containing \(\text{En}\) inserts. At this time, one of the Ames project’s graduate students (Andy Pereira) was in genetic analysis. Pereira went to Cologne to continue his graduate program and to research this \(\text{wx}\) mutant. The mutant was cloned and shown to include an 8.4 kb insert (\(\text{wx-844}\) in

\(^{23}\) The most abundant protein in starch granules is the \(\text{Wx}\) product, the granule-bound NDP sugar-starch glucosyl-transferase.

\(^{24}\) In 1965, it was shown that \(\text{En}\) (First identified and named in 1953), and \(\text{Spm}\) were homologous transposon systems (Peterson, 1965). This was discussed with B. McClintock, but she indicated that \(\text{Spm}\) was used so long in her work that she would continue to retain that nomenclature (Peterson, 1961).

\(^{25}\) The detasseling was done during morning “break” (0:30-10) after the early morning ritual of shoot bagging and before pollinating when the graduate students and summer helpers went to the isolation plots for walking the rows and pulling off the tassels from the female plants.

\(^{26}\) The \(\text{CI}\)’s were necessary in the cross: \(\text{CI}/\text{CI} \; \text{En} \; \text{En} \times \text{CI} \; \text{sh} \; \text{bz} \; \text{wx} \rightarrow \text{CI} \; \text{sh} \; \text{bz} \; \text{wx}\).

This was to facilitate seeing \(\text{wxm}\). It would be difficult to detect \(\text{wxm}\) in a colored background. It was fortunate in 1980 to have \(\text{En}\) in a dominant colorless background. This availability was prompted by a goal of getting \(\text{En}\) in the \(\text{CI}\) allele to target the \(\text{CI}\) allele. At that time, the \(\text{CI}\) allele was considered bipartite and bifunctional and attempts were made to separate the two components of this allele (Cox, 1964).

\(^{27}\) Even with the \(\text{CI}\) genes in the F1, the heavily mutating \(\text{wx}\) allele was difficult to detect because of the heavily mutating expression which appeared to be wild type. In the isolation of \(\text{wx-844}\), the detection was aided by the presence of \(\alpha 1\) in the genotype which modified the heavy mutability allowing easier ability to isolate the mutant (Cuypers et al., 1988).
the Wx gene28 (Pereira is presently a research professor at VirginiaTech).

c. Isolating other genes in the maize genome:
Now with this En DNA used as a probe, the a1 gene was isolated and cloned (O’REILLY et al., 198529; SCHWARZ-SOMMER et al., 198730. The a1 gene was the first description of an important gene in the maize anthocyanin pathway that is part of the defense tools in maize to resist disease infection.

Soon after, the C1 gene with an En insert in the c1m1 1701 allele31 was cloned (PAZ-ARES et al., 1986, 1987). The C1 is the first cloned regulatory gene in maize and in plants. The C1 gene is one of the genes that regulate the genes in the anthocyanin pathway. The C1 provided the first glimpse of the activity of regulatory gene control. There was another aspect of the C1 gene. The C1 includes a series of alleles, one of which is the C1-dominant allele32. PAZ-ARES et al. (1990) described this allele and showed that the dominance arises from a truncated transcript resulting in a predicted protein truncated in the C-terminal activation domain whereby transcription starts but cannot activate transcription. Sometime later (SINGER et al., 1998) this was proven by the isolation of new C1-d alleles. Later it was shown that the original C1-d allele has a unique promoter that over-expresses mRNA that provides an advantage in binding to promoters of the pathway (SCHEFFLER et al., 1994). This is the first explanation of how a plant dominant repressor allele functions33.

Other genes and transposons were cloned and described; A2 gene-Messsen et al 1990); C2 gene (WIENAND et al., 1986); Uq reporter (PISABARRO et al., 1991). Further aspects of the domains of the C1 gene were also related to the domains of the protein (FRANKEN et al., 1994). The interesting interactions between the C2 and Whp genes were deciphered (FRANKEN et al., 1991). The Saedler group dissected and analyzed the detailed structure of the En/Spm transposon to determine the fine structure of the excision process (GRANT et al., 1990).

f. Final proof of the M and S functions of En:
The En/Spm transposon is unique in possessing two functions: a suppressor function (S) (TNPA) and mutator (M) function (TNPD). These two functions were verified with the isolation of the En2 mutant which severely impaired the expression of TNPD. With the sequencing of En2, the nucleotide limitations of the two functions were verified (CUYPERS et al., 1988).

Definitive proof of the two functions was provided by FREY et al. (1990) in their experiment with TNPA and TNPD sequences in tobacco (Nicotiana tabacum). With this experiment, they were able to demonstrate that excision of the En/Spm transposable element requires two element-encoded proteins. With reference to TNPA, it was demonstrated.

28 PEREIRA et al. (1985). The isolation of En in this wx844 allele provided opportunities to go after the genes with En inserts.
29 The MPI lab was attracting a number of post-graduates eager to develop their skills in molecular genetics. C. O’Reilly was one of the first and the a1m (PETERSON, 1961) was available for her to research.
30 This was the first of a number of genes isolated and this was quickly followed by others. The a1 gene was sequenced and the publication was sent to EMBO. In her paper (SCHWARZ SOMMER et al., 1987) described the structure of the A1 locus and all the many other inserts in the gene. One finding in the 4th exon was the c1n 4 element. This element in addition to the extra elements in the vicinity of the tex locus (SCHWARZ SOMMER et al., 1984) indicated as was learned in further exploration of the maize genome (SONG and MESSHING, 2002), the abundance of element throughout the maize genotypes.
31 In the review process, another lab was alerted to the sequence and the a1 clone was requested before publication. This was granted. The a1 clone was a prime target for this other lab so that they could embark on a number of McClintock’s interesting A1 mutants that she had accumulated (BANKS and FEDOROFF, 1989).
32 This was anecdotal, but the C1-d allele is one mutant of the early maize collections in the maize Cornell stock collections. Very likely, it originated in the collection by the early plant explorers in So. America. It is assumed that there was strong selection against color bearing kernels for their use in the cuisine of the indigenous inhabitants. Another mutant in the Cornell collections was an ear with kernels with dots on a colorless background (RHOADES, 1938).
33 This description of the mechanism of how a dominant allele is expressed provided an insight into the complexity of activity in the maize genome.
34 With the Pisaborro molecular paper, the relation between Uq and Ac was clarified. It became clear why the genetic tests did not reveal this relation. Ac recognizes the ac-rag reporter (Ds1) but Uq does not recognize the Ac reporter Ds2. Extensive discussion of the mechanisms distinguishing Ac vs. Uq activity in detailed in PISABARRO et al. (1991).
that the En/Spm encoded protein requires a specific target sequence for the suppression to function (Grant et al., 1990).

**g. MPI visitors from Ames:** Since the Cologne lab could use frequent guidance, the lab welcomed a number of Ames graduate students to Cologne for further molecular-oriented research. This arrangement also provided the Ames students with an opportunity to participate in DNA molecular experiments. With this arrangement, Andy Pereira was the first Ames student to join the MPI lab. This was followed by other Ames students from the Ames lab namely, Pat Schnable (Schnable et al., 1989), B. Scheffler (Scheffler et al., 1994), Yong Bao Pan, Michael Muszynski (Muszynski et al., 1993) and others. Equally significant, a number of the MPI students and technicians came to Ames in the summer to help in the summer field nursery.

This joint venture did not accomplish the original purpose of my Freiburg study-leave, that is, to develop the molecular expertise to initiate such a lab in Ames. However, having seen the enormous resources in the Saedler lab (5 labs each with 10-15 in each lab tackling various aspects of the project) it was prudent to join in this venture.

**C. Summary**

1. **The maize genome:** The isolation of the En transposon was a significant achievement followed quickly by the cloning of a number of genes of the anthocyanin pathway. The isolation and description of these genes provided the first insight into maize gene structure and function. Further, the description of a dominant gene provided an insight into the mechanism of a dominant allele and explained many aspects of the maize genome interactions. The Cologne initiative was the first and most productive investigation into the maize genome.

2. **Ames Graduate Students:** Probably, an unexpected and important aspect of the MPI-Ames connection as we now see in 2009 was the training of the Ames graduate students. All went on to make significant careers in molecular genetics. They are in Ames, Blacksburg, Va, Mississippi, and other parts.

**D. Heinz Saedler: A Lasting Legacy:**

1. **The maize genome:** Every scientist in career tenure looks back on a legacy left in its wake. The exploration of the maize genome by the Saedler group is a most significant achievement. This was the first insight into maize genes, their structure, size, composition, and their interaction in cellular processes as well as the first description of the mechanism of the action of a dominant gene. These early revelations of the maize genome attracted world-wide attention as attested by the requests for probes (Peterson, 1991).

2. **A Career’s Output:** This essay concentrated on the maize aspect of the Saedler career. Yet, there were other areas that included the IS elements, the cin elements, *Antirrhinum* elements, paramutation, transposon systems in heterologous plants, and mechanisms of transposition and potential in evolution (see Quelle in the citations).

3. **Future scientists:** But in any scientists career, there is a lasting legacy that will impact many future generations of developing scientists. Saedler’s MPI-Cologne lab trained hundreds and developed many that went on to initiate their own research labs in many places. These labs are spread widely in various parts of the world though most are in Europe. This is an important part of Prof. Heinz Saedler’s legacy. Those trained in Saedler’s MPI lab will live on by training others and continue their scientific progeny. But, going back to note 19, this rapid success in uncovering the details of the maize genome in the Saedler lab was that he had his hand on the tiller. By this he was able to steer the research progress moving productively and effectively.

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35 This was the first case of a 3-element control of mutability and indicated the preciseness of the protein binding in the excision event.

36 The graduates and others trained at the Saedler MPI lab are now in diverse sites that includes in Germany: Braunschweig, Düsseldorf, Bremen, Gossweierer, Munich, Berlin, Osnabrück, Kaiserlautern Hamburg, Jena; in Spain: Pamplona, Madrid, Valencia, Cartagena; in other parts of Europe: Leuven, Verona, Leeds, Liege, Vienna; in the United States: Ames, Mississippi, Maine, Blacksburg; and in other parts: New Delhi, Saskatoon, Peking, Sendai.
Appendix A

The Max Planck Institute at Cologne (Vogelsang).

The successes, and there were many, that arose out of this Institute (MPI) were likely due to the "culture" that existed at this research site. There exists a flow of communication among the several departments. Every technique and strategy used in DNA protocols from any department was shared with all. There were several features that aided in this cooperation.

One important feature was the physical connection between five sections of the MPI. One could walk through corridors undercover from one to the other with your test tube and with your lab coat on as if one was in their own department.

One other feature was the lunch hour. Here, members of different departments could sit in the same table and exchange news or of science or of experiments or other matters. This led to a compatibility among the MPI researchers.

In fact, the MPI as most MPI's throughout Germany, included a guest house for visitors. Thus all of Germany and beyond had a fruitful network of cooperation in advancing their research goals.

As a visitor to a number of campuses and an observer on his own campus, this author finds the features described above lacking and missing the synergy that comes with a free flow of communication so strikingly evident at the MPI-Vogelsang.

Appendix B

The Saedler Family:

In the span of twenty years that this author was intermittently in the Saedler laboratory, the Saedler family was very generous in their hospitality inviting this author to their home and family gathering. Joining this family with their children in their meals and holidays was a special treat. A chance to listen to Anni on the piano was especially enjoyable.

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