Joseph G. Gall Retirement Celebration

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Website: https://sites.google.com/carnegiescience.edu/gall-celebration

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Welcome (Yixian Zheng)

Welcome friends and colleagues. My name is Yixian Zheng. As director of Carnegie’s embryology department, it is a great pleasure for me to welcome all of you to today’s symposium in honor of our dear colleague Joe Gall’s retirement. In the midst of the pandemic, I am very touched by the enthusiasm and care that Joe’s former trainees and friends have shown in organizing this Zoom based symposium to celebrate Joe’s contribution to science. The symposium is organized by Joe’s former trainees, but in the process, many Joe’s science friends have reached out to express interest to participate in today’s celebration. We are seeing many of them dialing in today.

We want to thank Mr. Navid Marvi, our communications coordinator, for helping with all the logistics of the Zoom symposium and our IT staff for supporting the Zoom behind the scenes. I also want to thank the organizing committee: Susan Gerbi, Ginger Zakian, Ji-Long Liu, and Zehra Nizami for putting this symposium together. The organization was challenging because the committee members live in three different continents. Luckily, we have Susan Gerbi. As Joe puts it, as long as you have Susan, you will have a great event. Please check your email for today’s meeting agenda as a PDF file. We had some minor changes. To ensure the smooth running of the talks, we decided to use the time in the beginning to coordinate speakers. This took the time away from the welcome slide show. The event is fairly long so the organizers have scheduled a few breaks.

Our department has gotten to know many of Joe’s former trainees throughout the years, particularly by attending the past symposia the trainees organized for Joe’s birthdays. Joe’s academic family has become part of the extended academic family of our department and our institution. We have learnt a lot about Joe’s amazing legacies in scientific discoveries and in training generations of scientists. Many of Joe’s trainees have themselves been contributing to science throughout the world. For such a long and truly amazing career, Joe had made so many contributions to science, each time when a symposium like this is held, I find myself learning something that Joe discovered I did not know before. I am sure today’s symposium is no exception.

Although many of us had not had the fortune to train and study with Joe, we treasure having Joe as our colleague. I have learnt a lot from Joe in the last 24 years at Carnegie. Each of us have our own memories about Joe. For me, Joe had played an important mentoring role in helping me to cope with stress as a beginning faculty. He has always encouraged me to explore the biological problems that are important but under studied. We are lucky that in retirement, Joe will continue to do research. So we will continue to enjoy discussing science and life with Joe at lunch and at our Friday gatherings once our life returns to normal. We also look forward to interacting with Joe’s former trainees as part of our extended family in years to come.

Now, I would like to introduce our President, Dr. Eric Isaacs, who will give some remarks. Eric joined our institution over two years ago. He is a physicist and had directed research at the famous Bell labs before joining the Argonne National lab. Prior to coming to Carnegie, Eric was Provost and Vice President for Research at University of Chicago. We are very happy that Eric is able to find time in his very busy schedule to help us kick start this symposium.
Introductory Comments (Eric D. Isaacs)

It's an honor to be here today as we gather together to honor our colleague Joseph Gall on his retirement. I want to begin by offering my sincere congratulations and best wishes to Joe and Diane. I think I speak for everyone at Carnegie in saying how much we admire Joe, and how much he has inspired all of us --- through his work, and also through his character.

In 2003, the Journal of Cell Science celebrated Joe’s 75th birthday by publishing a tribute from two of his former students, who called him "a scientist's scientist". I can't think of higher praise. At events like this, I know it's considered appropriate to offer some flattering assessment of the guest of honor and his work --- A little polite exaggeration of their achievements, but it is simply impossible to overstate the impact Joe has had on life science.

When he won the Lasker Award, in 2006, he was called the founder of modern cell biology. Think about that. When Joe was a student, biologists were just starting to ask basic questions about DNA, RNA, and protein were just beginning to be asked --- and that research focused on single-cell organisms. Then Joe Gall took a microscope that he had built himself, and started looking at cell nuclei. He began carefully, methodically, and brilliantly transforming our understanding of the mechanics of life itself.

His contributions to microscopy alone would have made him a luminary in his field. Throughout his career, he has had an extraordinary gift for asking important questions --- identifying the most appropriate organisms and model systems, and then developing novel and ingenious tools and techniques to find the answer. But beyond his own work, Joe has transformed biology through his exceptional teaching and mentorship, especially of women scientists. In one interview, Joe credited his mother for instilling his lifelong belief that women could – and should – be great scientists. So as an adult, he saw nothing unusual in a woman excelling in a science career. He opened the doors of his lab to any brilliant researcher who wanted to join --- male or female. He treated all his students with respect, he set high standards, and he nurtured their talent. The results speak for themselves. Generations of women scientists have credited Joe for training them, launching their careers, and then continuing to offer support, advice, and encouragement. Some of them are here today to honor Joe. Three of his women students - Mary Lou Pardue, Susan Gerbi, and Elizabeth Blackburn – have gone on to serve as President of the American Society for Cell Biology. Mary Lou Pardue has noted that, the year she was elected to the National Academy of Sciences, there were three women in the class, and two of them (Mary Lou Pardue and Joan Steitz) had worked with Joe. And his former postdoc, Elizabeth Blackburn, shared the Nobel Prize in Medicine in 2009. In recognition of his superlative record of training and mentoring women scientists, Joe received the AAAS Lifetime Mentor Award and the ASCB Women in Cell Biology Lifetime Achievement Award. He is also a member of the Rosalind Franklin Society, whose mission is to promote the contributions of women in the life sciences.

I want to mention here just a sample of the many other honors Joe has received throughout his career. In addition to the Lasker Foundation Special Achievement Award, he has received

- Society for Developmental Biology Lifetime Achievement Award
- E. B. Wilson Medal from the American Society for Cell Biology
- Wilbur Cross Medal from Yale University
- Shared the 2007 Louisa Gross Horwitz Prize from Columbia University

He also is a Member of the American Academy of Arts and Sciences, the National Academy of Sciences, and the American Philosophical Society.
And of course, since 1983, Joe has been our highly valued colleague here at the Carnegie Department of Embryology. You know, I am sometimes asked to define the "Carnegie Difference". As has been said in other contexts, "I know it when I see it". And when I look at Joe Gall, I see the Carnegie difference personified. His brilliance, his independence, his innovative approach to research, his generosity to his colleagues, and his steadfast commitment to the highest principles of scientific integrity.

Joe - as President of the Carnegie Institution for Science, it is my honor and my privilege to thank you for your many years of exceptional service and to wish you a happy, healthy, well-earned retirement.

**Introductory Comments (Donald D. Brown)**

Joe Gall was a Professor at Yale when he came to our department on sabbatical in the late 1980s. When his year was up he returned to Yale, but he was in line to be Chairman of Biology and he rebelled against that idea. I got wind of his dilemma and offered him a staff position. Without a doubt this was one of the best things that I did as Chairman of the Department of Embryology. It meant reducing the size of his lab and the number of students but it also meant no administrative duties. He wanted to stay in the lab and certainly not become a Chairman. I am proud of my decision to hire Joe. He may be retiring at the age of 92 but he is still working in the lab. He remains the expert on anything optical and that includes the latest innovations. In fact, Joe has given the only course in our Department taken by all of our graduate and postdoctoral students. Joe will continue working at the bench doing important research. Congratulations, Joe, on a wonderful and continuing career.
I call this presentation “Through the Looking Glass”, which many of you will know is the title of the 19th century book by Lewis Carroll that describes the adventures of Alice, who enters through a looking glass (what we would call a mirror) into a strange and wonderful world of mythical creatures and events. In much the same way the microscope for me, and for many others, has been the way we have entered the wonderful world of microscopic objects and phenomena.

Here is a photograph of me taken when I was about 14, looking through my real microscope, not a toy one. This was in the middle of the second world war, and I was fortunate not only to be too young to be drafted, but to have resourceful parents, who were able to find and purchase this instrument for me. I spent many hours looking through this microscope, preparing specimens for observation, reading about the things I was observing, and becoming a scientist on my own. I think one of the greatest things about this experience was the independence that it fostered. If I wanted to know something, I had to either find it out myself or read about it in one of the books my parents were able to provide for me.
Skipping ahead a number of years to the time I entered graduate school in the old Zoology Department at Yale, my advisor, Donald Poulson, was a *Drosophila* geneticist and for a long time I thought I would do a thesis in genetics. But somehow I came across a text-book that contained this image of a chromosome from a salamander oocyte. It was made by an investigator by the name of William Duryee and it showed a chromosome from an oocyte of a salamander being stretched between microneedles. I thought surely the scale marker was wrong, that the chromosome couldn't be this large. But this set me on a literature search and I found that indeed giant chromosomes had been observed in the oocytes of frogs and salamanders as far back as the late 19th century. They had been given the quaint name of "lampbrush chromosomes" because of their imagined resemblance to the brushes used at that time for cleaning the soot from oil lamps. This has remained the name for these remarkable structures.

Giant lampbrush chromosomes have been found in the oocytes of frogs and salamanders, and indeed in a variety of other organisms that have giant germ cells. Although not so well known as those from amphibians, lampbrush chromosomes are found in many birds, fishes, and even in a few plant species. Most of my work has been done on the two species shown in this slide, the frog *Xenopus* and the salamander *Ambystoma*.
Here we see a bit of ovary from the frog *Xenopus*, showing oocytes of all different sizes, from the very small transparent ones to the largest, yolk filled ones which reach a size of a millimeter or so in diameter. For those of you not familiar with animal reproduction, I remind you that, despite their size, these are single cells with a single nucleus.

This slide shows how easy it is to remove the giant nucleus by poking a hole in the oocyte and squeezing. The nucleus pops out, often completely free of adhering yolk, as in this example. This nucleus is almost always called the germinal vesicle, or GV, a term that actually goes all the way back to the early 19th century. It was first described from oocytes of the chicken, long before it was recognized as the nucleus, and even before the oocyte itself was recognized as a single giant cell.
This slide shows the contents of a single GV of the frog *Xenopus*. At this stage of early meiosis, the maternal and paternal chromosomes are paired. That is, each nucleus contains the haploid number of paired chromosomes. I point out the numerous small bodies in the background, as we will come back to these a bit later.

Here is a higher magnification image of a portion of one chromosome pair from the salamander *Notophthalmus*. *Notophthalmus* is also known as the newt, and is a fairly common inhabitant of ponds and streams throughout eastern North America. Here you can see loops of chromatin extending laterally from the axis of the chromosome. Each of these loops represents a single active gene, visible because it is covered with the ribonucleoprotein products of transcription.
Here is a diagram of lampbrush chromosome structure. At the right is shown a single pair of loops, which represents an active gene covered with the products of transcription. Transcription begins at the thin end of the loop and continues all the way around the loop to the thick end. It should be noted that, despite the size and prominence of the transcription loops, most of the DNA of the chromosome is tightly wound up and is transcriptionally inactive.

In addition to the lampbrush chromosomes, each oocyte nucleus contains hundreds to thousands of small bodies of several different types. The largest of these have been called nucleoli since the 19th century, although the relationship to the nucleolus of ordinary somatic cells was not clear at all.
To illustrate the extreme difference between an oocyte and a typical somatic cell, I show you here an image taken from a classic paper by Barbara McClintock of the nucleolus of maize (or corn, if you prefer that name). Here there is a single nucleolus attached to a specific point of one chromosome, the so-called nucleolus organizer region. What, then, is the relationship between the single nucleolus shown here and the hundreds of nucleoli in the amphibian oocyte?

The answer to that question takes us to the earliest stages of the oocyte, long before the giant lampbrush chromosomes are so prominent. At this time we can see the chromosomes as thin fibers. On one side of the nucleus, however, is a large mass of chromatin; that is, DNA plus protein. To make a long story short, what has happened here is that somehow the genes coding for ribosomal RNA have gotten out of the chromosome and replicated independently. They have formed a large mass on one side of the nucleus consisting of thousands of copies of the genes coding for ribosomal RNA. This mass of DNA is referred to as amplified rDNA.
Here is another view of early oocytes from *Xenopus*, showing the stages of rDNA amplification. In this case the rDNA has been labeled with a radioactive tracer (H3), shown here as black dots in the photographic emulsion that records the radioactive molecules. This technique of autoradiography would have been familiar to an earlier generation of cell biologists, but is much less commonly used nowadays. (Comment: The technique of autoradiography using hybridization with a radioactive tracer (H3) followed by detection with a photographic emulsion is seldom used in 2020. This use of a radioactive tracer for *in situ* hybridization was the precursor to the now-familiar fluorescent *in situ* hybridization, known as FISH.)

Another way to look at the amplified ribosomal RNA genes is by electron microscopy. This image is a quite famous one produced by Oscar Miller and reproduced in numerous cell biology texts. It shows individual ribosomal RNA genes undergoing active transcription. The active transcripts get longer and longer as they move down the gene, giving rise to these iconic “Christmas trees.”
Most of the early studies on specific genes were carried out on the genes coding for ribosomal RNA. This was because these genes were present in hundreds to thousands of copies per nucleus. One other type of DNA was available for molecular analysis in these early studies. This is the DNA known as "satellite" DNA. This image of satellite DNA would have been familiar to an earlier generation of cell biologists, whose only way to separate different fractions of DNA was by centrifugation. It turns out that about 10% of the DNA in the mouse genome has a different density from the rest of the DNA and can be separated by centrifugation.

When this “satellite DNA” was purified and used as a probe on a cytological preparation, it hybridized to the centromeres at the ends the chromosomes. Satellite DNA was found to consist of very simple sequences and essentially defines large regions of gene-free chromatin.
It turned out that chromosomes of many organisms had regions of satellite DNA. Here is another well known example from the fly, *Drosophila virilis*. Roughly half of each chromosome consists of simple-sequence DNA that does not contain genes.

I want to make a digression here to look at the single celled organism *Tetrahymena*. For a period of about ten years starting in the early in the 1970’s, I turned my attention to *Tetrahymena*. It had been known for many years that *Tetraymena* had two nuclei, a small genetic nucleus or micronucleus, and a larger macronucleus that contains a massive amount of DNA. I was struck by the fact that the macronucleus had multiple nucleoli and in fact looked very much like the nucleus of an oocyte. To make a long story short, it turned out that the macronucleus of *Tetrahymena* contains many thousands of copies of the genes coding for ribosomal RNA. These are present in multiple nucleoli on the periphery of the macronucleus, very similar to the situation in the amphibian oocyte.
When we isolated the ribosomal genes of *Tetrahymena*, we found that they were in pairs located head to head. The tails turned out to be quite interesting.

The tails contained many copies of a repeated sequence, as shown by Elizabeth Blackburn, at that time a postdoc in my lab. That sequence was C4A2 on one strand and G4T2 on the other. At that time we did not know it, but later Liz Blackburn and her student Carol Greider found that this and similar sequences characterize the ends of chromosomes, or telomeres, in many other organisms. As many of you know, this finding led eventually to the Nobel Prize for Liz, Carol and Jack Szostak.
In closing, I want to come back to the germinal vesicle and the organelles that it contains. We already talked about the many free nucleoli that occur in the germinal vesicle. There are two other major bodies in the germinal vesicle, which we call the histone locus body and the speckle. The histone locus bodies get their name from the fact that one or two are attached to the lampbrush chromosomes at a specific locus, in addition to the several hundred copies found free in the nucleoplasm.

Here is a histone locus body with attached speckles shown by differential interference microscopy in the upper left, and after specific staining in the other three panels. The histone locus body contains the well known protein named coilin as well as SM proteins associated with small nuclear RNAs.
I want to close this presentation by briefly mentioning molecular studies on isolated GVs. As I showed earlier, we used isolated GVs for cytological studies of the chromosomes and nuclear organelles. We have also studied isolated GVs by molecular techniques, which I can only touch upon here today. This slide shows isolation of the GV from a *Xenopus* oocyte and removal of the nuclear envelope to give a fraction of pure nuclear RNA.

One of the surprising findings from studies of isolated GVs is the occurrence of stable intronic sequences derived from splicing of many genes. These intronic sequences are found not only in the nucleus, where they are formed, but in the cytoplasm. At the moment we have no good hypothesis for the occurrence of these sequences. I wanted to close on something we know very little about to emphasize that the oocyte contains many secrets and that we can expect many surprises as we continue to study the oocyte, its wonderful chromosomes, and the many molecular processes occurring during in it.

So, thank you all for being a part of the lab on this incredible journey — “Through the Looking Glass”. There are so many of you that I could not name each of you in this brief presentation. But, please know how much I appreciate each of your individual contributions. Our collective work, followed by your work after leaving the lab, and the work of the students you have trained, will continue to push the boundaries of our knowledge of the cell. I am looking forward now to the presentations, pictures, comments—and especially to the anecdotes—that will follow. Thank you again.
Joe won the 1996 AAAS lifetime achievement-mentoring award. The following speakers are all former Gall lab members, and their accomplishments provide a wonderful example of Joe’s mentoring abilities.

1. **Joan Steitz**, *Early Years at the University of Minnesota.*
   Joan’s family lived in Minneapolis. She spent the summer after college graduation (1963) working in Joe’s lab. She received her PhD from Harvard where she was the first female graduate student in Jim Watson’s lab and then did a postdoc with Francis Crick at the MRC. She joined the Yale faculty in 1970 where she is a HHMI-supported researcher. Her research focuses on RNA, where she has made multiple pioneering findings. Among these was the technical tour de force demonstration that the initiation of bacterial protein synthesis involved base pairing between 16S rRNA and mRNA. Joan went on to discover and characterize the small nuclear RNAs involved in splicing. Her large number of awards include Membership in the National Academy of science and the British Royal Society and receipt of the National Medal of Science.

2. **Liz Rodgers,** (MARY ELIZABETH ROGERS) *The transition from Minnesota to Yale.*
   After her undergraduate years in Zoology at Oxford, Liz came to Joe’s lab in Minnesota in 1962 for her PhD and then moved with him to Yale in 1963. Her graduate research focused on ribonucleoprotein particles in the nucleoli of amphibian oocytes. She continued to study RNPs first as a postdoc at U of Edinburgh and then as a member of its academic staff. Far ahead of her time, she also developed and ran a 13-year program that was a collaboration between the University and the city primary schools on environmental issues. Later, she reinvented herself as a primate biologist. For 20 years, she studied great apes in central Africa.

3. **Susan Gerbi,** *In situ hybridization with input from Mary Lou Pardue.*
   Susan came to Yale in 1965, the same year as her fellow graduate student and good friend Mary Lou Pardue. Susan and Mary Lou played key roles in Joe’s development of in situ hybridization, one of the most impactful contributions of his career. A version of this method called FISH continues to be used worldwide. Susan and Mary Lou both assumed faculty positions in 1972, Susan at Brown University and Mary Lou at MIT. As a bit of an aside, Joan Steitz at Yale, Susan at Brown, and Mary Lou at MIT were among the first women to get tenure track faculty positions at major research institutions and they were important role models for the next wave of female students in Joe’s lab and elsewhere. Susan has led her department and university in many ways, including as Founding Chair of the Department of Molecular Biology, Cell Biology and Biochemistry. Research in Susan’s lab focuses on ribosomal RNA (she generated the first sequence of a metazoan 28S rRNA) and various aspects of DNA replication. Susan has also been a national leader in biomedical graduate education, guiding FASEB in developing best practices for graduate education. Like Mary Lou and Liz Blackburn, Susan followed in Joe’s footsteps by serving as President of the American Society for Cell Biology. Although there are four organizers for this celebratory meeting, Susan was the driving force. Thank you, Susan.

4. **Sir Adrian Bird,** *ribosomal DNA (rDNA) structure and amplification.*
   Adrian did his PhD with Max Birnstiel at U of Edinburgh on amplification of amphibian ribosomal DNA, a subject dear to Joe’s heart. He came to Yale as a postdoc in Joe’s lab in 1972. Here he continued his work on rDNA. In a wonderful collaboration with fellow postdocs Jean Rochaix and Aimee Bakken, he used EM autoradiography to demonstrate that rDNA amplification proceeded by a rolling circle mechanism. Adrian has spent most of his career at the University of Edinburgh where he helped set up and served as Director of the Wellcome Trust Centre for Cell Biology.
Adrian’s research focuses on DNA methylation. He identified CpG islands as gene markers in the vertebrate genome and pioneered the discovery of proteins that read the DNA methylation signal, such as MeCP2, whose mutation causes the severe autism disorder Rett Syndrome. Like many of Joe’s progeny, Adrian has a long list of honors, such as membership in the Royal Society and the US National Academy of Sciences, but I believe he is the only former Gall lab member to be knighted by the Queen for his services to science.

5. Elizabeth (Liz) Blackburn, Heterochromatin and repeated DNA.
Liz was raised in Tazmania, Australia. She did her PhD with Fred Sanger at the MRC Laboratory of Molecular Biology, Cambridge. Here she was part of the pioneering work that led to the sequencing of the DNA genome of \( \phi x174 \) bacterio-phage. When she came to Joe’s lab in 1975, she was one of the few people in the world who knew how to sequence DNA. She told Joe, she wanted to sequence something important. This was before cloning, so Joe suggested that she sequence the ends of \( Tetrahymena \) rDNA, as he had recently isolated these 22 kb molecules by CsCl centrifugation. The telomere sequencing work was described in a 1978 paper by Blackburn and Gall that began the molecular era of telomere biology. In her own lab, Liz continued working on telomeres, first at Berkeley where she and her grad student Carol Greider discovered telomerase, the activity that lengthens chromosome ends in almost all eukaryotes and then at UCSF. Her pioneering work on telomeres has been recognized in innumerable ways, including with the 2009 Nobel prize in Medicine, which she shared with Carol Greider and Jack Szostak. Joe was her guest at the Swedish award ceremonies.

6 Giuseppina Barsacchi, Lampbrush chromosomes.
Giuseppina was educated at the U of Pisa, where she became a faculty member in 1969. In the first part of her career, she studied amphibian lampbrush chromosomes. Because of this shared interest, in 1969, she spent time as a visiting scientist in the Gall lab. This visit must have been fun for both Giuseppina and Joe because she returned to his lab four times. In 1990, she set up the developmental biology lab at the U of Pisa and switched her research to the development of the vertebrate eye. She held multiple important positions in her university and in European science. Among her many honors, in 2005, she was elected to the Italian equivalent of the US National Academy of Sciences (“Accademia Nazionale dei Lincei”). Although this organization was founded in 1603, Giuseppina was the first female member of the Academy’s council.

7. Ji-Long Liu, Cajal and other nuclear bodies.
Ji-Long, a co-organizer of this meeting, received his Ph.D. from the Chinese Academy of Sciences Institute of Zoology in 2000. He was a postdoc in Joe’s lab from 2003 to 2007. Here he identified the long-sought-after Cajal body in \( Drosophila \). He must be a discoverer at heart because he identified two additional subcellular structures in egg chambers during his postdoc: the nuclear histone locus body and the cytoplasmic U body. Ji-Long set up his first lab at the MRC Functional Genomics Unit at the University of Oxford. Here, he discovered yet another new structure, the filamentous cytoophidium, and showed that it contained CTP synthase. In 2016 he moved to Shanghai Tech University where in addition to being a Professor, he is also Vice Dean. His current research focuses on how the assembly of metabolic enzymes into specific structures affects metabolic regulation. He still collaborates with Joe.
8. Gaëlle Talross, RNomics.
Gaëlle who is from France was Joe’s last PhD student, working with him from 2012-2017. One of the things she discovered during her thesis work was that some sisRNAs (stable intronic RNAs) are located in the cytoplasm, being exported there via the mRNA export machinery. Gaëlle is currently a postdoc in John Carlson’s lab at Yale, where she is using insect models to test if non-coding RNAs have a role in the diversification of the olfactory system.

9. Allan Spradling will provide closing remarks for this part of the program. Allen first met Joe when he was a graduate student at MIT where he did his PhD with one of Joe’s former graduate students, Mary Lou Pardue. Thus, although Allan did not have the good fortune of being a student or postdoc in Joe’s lab, he is Joe’s scientific grandson. Allan came to the Carnegie as a staff member in 1980 and later served as its director for over 20 years (1994-2016). He is also a Howard Hughes Investigator (since 1988). Allan’s research focuses on oocyte development in both flies and mice. Among his many honors, Allan is a member of the National Academy of Sciences and recipient of the Genetics Society of America Medal and the CF Conklin award from the Society of Developmental Biology.

10. Zehra Nizami will lead the open mike session. Zehra, who is also a co-organizer of this meeting is from Hong Kong. After graduating from Princeton, in 2005, she became a grad student in Joe’s lab where she worked on nuclear bodies in Drosophila and Xenopus. Among her PhD achievements was her co-discovery of sisRNAs (stable intronic RNAs). After her PhD, she stayed in Joe’s lab as a postdoc, switching to the study of gene expression in amphibian germinal vesicles using genomics and super-resolution microscopy. In 2012, she was awarded the Johns Hopkins Service to Science award in recognition of her science outreach. In 2016, she won the Carnegie Postdoctoral Innovation and Excellence Award (abbreviated PIE; the award ceremony apparently involves eating a lot of pie). The PIE award recognizes achievement in science, education, and service. Zehra is currently an Applications Development Scientist at a British biotech company called Oxford Nanoimaging (ONI).
Remarks from Joan Steitz

Congratulations Joe!

An example to emulate......
THE ISOLATION OF CILIARY BASAL BODIES (KINETOSOMES) FROM TETRAHYMENA PYRIFORMIS

JOAN ARGETSINGER. From the Department of Zoology, University of Minnesota, Minneapolis. Miss Argetsinger's present address is The Biological Laboratories, Harvard University, Cambridge, Massachusetts

Joe Gall    Joan Steitz    Mary Lou Pardue    Oscar Miller
probably 1983
I went to the Department of Zoology at the University of Minnesota to work with Joe in fall 1962, with a degree in Zoology from Oxford University, UK. I came to work with Joe after hearing a talk by Mick Callan (Professor of Zoology, St Andrew's University, Scotland) while I was at Oxford, which fascinated me with its slides of lampbrush chromosomes. I had not enjoyed or understood the Genetics lectures we had as students. Their approach was very classical, and DNA was hardly mentioned, even in 1960/61. To actually see living chromosomes at work was unforgettable, and I wanted to learn more (as well as travel).

To give this talk, I wondered how to jog my faded memories of Joe’s lab in the early 1960s. Fortunately, I knew I had a potential treasure trove in the form of the letters I wrote every week to my parents back in the UK, which my mother kept. Through them, I’ve got a sense of what being in Joe’s lab meant, though there’s not much scientific detail. I clearly found it very enjoyable talking to Joe about his work from day one, because of his enthusiasm and clarity. I had studied the whole animal kingdom as a student, and I was delighted to find that Joe had worked, or was working, not only on amphibians, but also on insects, snails, cycads and ferns. He chose species with characteristics that were key to solving each cellular puzzle he decided to investigate – like, for example, the origin of centrioles, for which he needed cells with many cilia or flagella, such as spermatozoa or protozoans.
In Fall 1962, Joe was also interested in the nuclear membrane and nucleoli in newt oocytes, as was Mick Callan, who was visiting Joe’s lab then as well. For instance, there were new technical possibilities with the electron microscope, which they wanted to exploit. One of the over-riding questions that we were discussing was: what was all the protein on the lampbrush chromosomes doing? First, I had to learn how to use the inverted phase contrast microscope and isolate oocyte nuclei and chromosomes. To advance this process, Joe presented me with my own disarticulated Zeiss microscope, which I had to assemble from scratch! Having mastered this, I wrote to my parents about my first isolation of oocyte nuclei and then chromosomes with wonder and amazement, wanting to find out more: “Very carefully you tear open the nucleus, which floats before you, pale blue, under the microscope. If you do the tearing properly, you see the chromosomes unfolding, and everything moves. The loops move in and out as you watch. I could have watched those things for an age – in fact, I did sit and watch them for at least half an hour. I thought, what are they doing, those chromosomes, and why?” It wasn’t until later in the 1960s that exquisite EM photographs of transcribing genes in the oocyte nucleolus were published, most notably by Oscar Miller, a previous postdoc of Joe’s, who had been visiting the lab in Minneapolis just before I arrived there.

By January 1963, I knew Joe was moving to Yale, and that I might be able to go too as his assistant. That was confirmed in February, and Joe’s appointment to Yale Faculty as Professor in the Departments of Cell & Molecular Biology was eventually made official. My position as TA in Joe’s future Cytology course at Yale was confirmed in April 1963. At the same time, we started experiments with radioactive isotopes to try and work out what was going on in the amphibian oocyte, in terms of the movement of RNA and protein from the nucleus to the cytoplasm. Through June and July 1963, research on this progressed well, if sometimes puzzlingly!
In August 1963, we packed up everything and prepared to move to Yale. My sister and I drove to New Haven via Vancouver Island in ten days, discovering the immensity of the N American land mass in the process! When the fall semester started, we plunged into Joe’s Cytology course, and I had to worry about Comprehensive exams and reading scientific literature in French & German. For this, I exploited Joe’s large collection of antique books on 19th century cytology, which I could translate. I commented to my parents that “my life whizzes by in a turmoil of nuclei, seminars, German and men!” Notice that nuclei came first and men last, so I had my priorities right. Comb jellies (Ctenophores) arrived in my lab unexpectedly as part of the cytology course, and we found ourselves looking at their ciliated ‘combs’ under the microscope. Joe’s lab was always wonderfully prone to housing a menagerie of living things. Research continued, and the incorporation of radioactive amino acids into proteins on the lampbrush chromosomes, and of tritiated uridine into nuclear RNA, is mentioned in my letters home. So is Joe’s ‘excellent’ talk at the ASCB meeting in New York in November 1963, which made me proud to be supervised by him.

Early in 1964 is the first mention in my letters of ‘isolating the particles responsible for protein synthesis’, and this is what continued as the subject of my doctoral research. At that time, although it was known ribosomes were in the cytoplasm, it wasn’t clear whether they were assembled there or exported fully formed from the nucleus. The amphibian oocyte, with its multiple nucleoli containing the amplified genes for ribosomal RNA, was a perfect tool for research on ribosome synthesis, especially as the nuclei could be isolated in a pure form by hand. I switched from working on newts to axolotls for various practical reasons. By October 1964, I was doing polyacrylamide gel electrophoresis of nuclear and cytoplasmic proteins, and expressing joy at being a ‘full-blown researcher’ at last.
And so, life in Joe’s lab at Yale continued. We were soon joined by many more people interested in Joe’s work, as you will now hear from others who came after me.

THANKS, Joe, you were a great supervisor, supporter and friend.

Liz Rogers, August 2020.
Joe Gall’s Early Years on the Faculty at Yale

Recollections from 1965-1970

Susan A. Gerbi

Mary Lou Pardue

Amphibian “Lampbrush” chromosome (during meiosis)

Lampbrush chromosome loops spool out from the main axis

axis = 2 chromatids
loop = 1 chromatid

How many strands of DNA are in one chromatid?

Kinetics of DNase digestion of newt lampbrush chromosomes


Development of in situ hybridization

• New method of biochemical molecular hybridization (RNA to single-stranded DNA)
• How to adapt this to chromosomes? South American meeting – ideas for in situ hybrid. Others tried acridine orange to assay denaturation of chromosomal double-stranded DNA
• Joe Gall – let biology be your guide.
He used a biological system where he knew the answer to work out details of the method
• Ribosomal DNA (rDNA) associated with the nucleolus organizer region:
Multiple nucleoli in amphibian oocytes --- do they contain DNA?

- Painter TS and Taylor AN (1942) Proc Nat Acad Sci 28:311–317. Toad (*Bufo*) oocytes – each nucleolus shows a Feulgen positive (DNA) granule directed towards the nuclear wall.
- Joe Gall and Mick Calian could not repeat this on salamander.
- BUT then Joe got decades old dyes from TS Painter and saw Feulgen positive DNA in newt extrachromosomal nucleoli (he showed me this result and I was late for class)

- Oscar Miller showed DNA in nucleoli by EM –

Amplified rDNA in *Xenopus* oocytes


*Xenopus* pachytene oocyte - Black silver grains 3H-T lie above the cap of darkly stained amplified rDNA. Note that the chromosomes are not labeled. Thymidine is normally incorporated into DNA during the S phase of mitosis, not during prophase, as in these nuclei.

Hybridization of radioactive ribosomal RNA (blue line) to *Xenopus* ovarian DNA (red line) after centrifugation on a CsCl density gradient. Note the detectable peak of DNA in fractions 6–11, which represents amplified rDNA.
**In situ hybridization to amplified rDNA in Xenopus extrachromosomal nucleoli**

- Mary Lou Pardue thesis project – is rDNA excised from chromosome or copied to form extrachromosomal amplified rDNA in oocytes?
- Mary Lou blows up ultracentrifuge with SW25 rotor (Joe was on sabbatical in UK)
- Joe invites Mary Lou to switch thesis project to work with him on *in situ* hybridization


**In situ hybridization to rDNA genes in chromosomes**

**Polytene X chromosome of the fly Sciarag**


No patent filed for *in situ* hybridization method to identify genes in chromosomes

**In situ hybridization shows mouse satellite DNA in centromeres**


Guinea pig intended for satellite DNA experiment became lab pet instead
A biologist extraordinaire, Joe Gall has worked on many diverse organisms:

- Amphibians (newt - Notophthalmus, frog - Xenopus)
- Protozoans (Tetrahymena)
- Insects (fruit fly - Drosophila, fungus fly - Scara, water beetle – Dytiscus)

Search for a red eft (juvenile newt)

Gordon conference –
hike with Joe Gall and Oscar Miller
to find red eft

Congratulations to my “Doktor Vater”
for a spectacular career full of scientific discoveries.

All best wishes for a very happy retirement, including continued microscopy to view your favorite slides!
Adrian Bird Reflections on rDNA Structure and Amplification

Chromosome biology in 1971

- How many genes? Do Drosophila polytene chromosome bands signify genes?
- How many copies of each gene? Master-slave hypothesis
- Do all cells in the body have the same genome?
- Chromosome structure: Uninemy:
  - Herbert Taylor's autoradiography
  - Joe's DNase I experiment
  - Dupraw's folded fibre model
- What makes a centromere, telomere, origin of replication?
- What are lampbrush chromosomes doing?

Transcription visualized

Oscar Miller's Christmas trees

Electron microscopic spread preparations of lampbrush chromosomes from Plesioptera vulgar. Bars, 1/20. L. Schaefer
Differential Synthesis of the Genes for Ribosomal RNA During Amphibian Oogenesis

By Joseph G. Gall

Department of Biology, Kline Biology Tower, Yale University

Communicated by Norman H. Gill, November 7, 1967

- Only one or two types of genes could be studied
- These were multi-copy genes that could be isolated by physical methods
- In amphibian and fish eggs, ribosomal RNA genes are amplified 1000s of times

Rolling Circles
- a salutary lesson and Route 66

\[ \text{\textsuperscript{3}H-thymidine incorporation} \]

In situ hybridization
Gall & Pardue 1969

Jean-David Rochaix
Aimée Bakken
Frogs do it, fish do it, even water beetles do it

Fig. 1. Apocrine oocyte. Epithelium showing the large oogonia of mitochondria, modified rRNA (left) and Secret.


The Macronuclear Ribosomal DNA of *Tetrahymena pyriformis* is a Palindrome

KATHLEEN M. KARRER and JOSEPH G. GALL

Department of Biology

Yale University, New Haven, Conn., U.S.A.

Fig. 11. *Tetrahymena* rDNA following heat-denaturation and intranuclear reassociation. Single-stranded DNA can be distinguished from double-stranded molecules by its thinner, more kinked appearance.

(a) An rDNA molecule from *Tetrahymena* strain BVI which is fully double-stranded but half the length of native rDNA and a molecule which is fully single-stranded.
Un-amplification of α–heterochromatin

Emil Heltz
1892-1965

Theophilus Painter, 1934

Gell, Cohen and Polan 1971
Repetitive sequences in Drosophila

Joe’s unique approach

- Use knowledge of biology to find informative outliers
- Combine microscopy with molecular biology (the new cell biology)
- Experimental rigour
- A lab of equals
- Clear thinking – and presentation (“limpid”)
- Infectious enthusiasm
- Place in history
Liz Blackburn Reflections on Heterochromatin and Repeated DNA

First – my warmest congratulations and best wishes to you, Joe on your retirement - and we look forward to the science still to come from you! And what a wonderful opportunity today to celebrate all your great science that has happened.

My assignment for this talk is to briefly highlight the research into heterochromatin and simple repeated DNA sequences in Joe’s lab, Although I can only include just a couple of the wonderful reminiscences by some of you involved in those studies, that you recently shared with me, don’t worry: Ginger Zakian is compiling the full set of great stories and reminiscences that we’ve collected.

But I’ll start by reminding us that Joe is a superb, scholarly historian of science. Witness this marvelous book that Adrian Bird alluded to, that Joe created – if you don’t have it, find it and give yourself a real treat and education, and share it.

In the collection of plates illustrating this “Views of the Cell” book I’m holding, just one plate has original photomicrographs taken by Joe himself:

Notably, it relates to Joe’s area of long fascination: highly repetitive DNAs --- many of which are satellite DNA sequences, so called, as Joe has reminded us this morning, [because simple sequence DNAs often have a different buoyant density from the majority of the genomic DNA, and form a satellite band when subjected to cesium chloride or cesium sulphate density gradient centrifugation.]

On top you see the darkly staining, heterochromatic regions of chromosomes in D. melanogaster and D. virilis. Previously, as we heard, Joe and Mary Lou Pardue had shown, initially in mouse chromosomes, that, to quote Joe: "Clearly, the satellite sequences were located in the heterochromatin"
And Joe has just told us about these Drosophila chromosomes. Moreover, Joe wrote about these Drosophila chromosomes: “CsCl fractionation quickly showed that DNA from D. melanogaster, like that from the mouse, contained a satellite fraction of low buoyant density. Early cytological studies had shown that another species of Drosophila, D. virilis, had even more prominent segments of heterochromatin in its mitotic chromosomes. By CsCl centrifugation we found that roughly 40% of all D. virilis DNA consisted of satellite sequences.”

Furthermore, shown below (image above) is Joe’s picture – related to the point made by Adrian was that satellite DNA was underreplicated in the Drosophila polytene chromosomal heterochromatin.

So, through the early 1970s, Joe went on multiple explorations of simple sequence satellite DNAs as well as other repeated DNA sequences - especially with lab members Ed Cohen, Diane Atherton, Mary Lake Polan, Ronald Eckhardt, Sharon Endow, Ginger Zakian - they addressed fascinating and important biological questions about satellite DNAs: Their biophysical and DNA sequence characteristics, and their replication patterns, their amplification, their chromosomal locations, sometimes their extrachromosomal nature. And even in recent years Joe has not forgotten them, as witness his 2016 paper on genome evolution of multiple Hawaiian Drosophila species and particularly their various expansions of satellite DNAs.

How I came into the world of these simple repetitive DNA sequences: was because they turned out to converge with Joe’s other fascination then – ribosomal RNA gene amplification. Back in 1974, I was completing my PhD in Fred Sanger’s lab in Cambridge, UK, where new methods for RNA, and then DNA, sequencing were being developed, using prokaryotic systems. First, I was greatly impressed by Joe’s ready development and adoption of always the latest and greatest techniques to address interesting biological questions - particularly nucleic acid sequencing, AND in eukaryotes to boot!

And here’s the other thing that absolutely riveted me: Joe’s 1974 electron micrograph, again, it’s one that Joe himself took, that I’ve also put in my virtual background. This is from Joe’s 1974 PNAS paper showing the amplified Tetrahymena rDNA was in the form of many copies of extrachromosomal short, linear, apparently identical 20 Kilobase-pair rDNA molecules, some fraction of which could be found as circles under the electron microscope. Why did this rivet me? Because this DNA form was superficially like that of linear bacteriophage lambda DNA, which could form circles via its cohesive complementary DNA sequence single stranded DNA ends. AND, the very end sequences of the linear 50 kb lambda bacteriophage DNA had recently been laboriously sequenced - by Ray Wu and Dale Kaiser in 1968, using repair reactions by DNA polymerase, and by Ken Murray in 1972. I was excited because back then, there weren’t many ways to get directly at DNA sequences,
apart from copying them into RNA and piecing together the RNA sequences, as Joe and his lab had done in their pioneering satellite DNA repeat sequence characterizations. SO – I thought – well, it had been possible for 50 kb lambda phage DNA, and here Joe had succeeded in preparing homogeneous populations of an even shorter – 20 Kb - DNA, the *Tetrahymena* rDNA. Critically, Joe strongly urged me to use these *Tetrahymena* rDNA linear molecules for my DNA terminal sequencing effort – rather than the even shorter *Oxytricha* macronuclear linear DNAs, that I had briefly contemplated for this purpose. So, as so often, Joe made the absolutely right call.

The icing on the cake when I joined Joe’s lab was that Kathy Karrer had just demonstrated that the rDNA molecule was palindromic - so the two ends might even be identical, which would make it even more technically attractive as a DNA whose ends could potentially be sequenced. Extending Wu’s, and Murray’s, leads with lambda DNA, I could then stitch together a terminal sequence, adding in some additional techniques for DNA sequence determination that had been developed in Fred Sanger’s lab group. Following Wu’s, and Murray’s, leads with lambda DNA, I could use polymerization – as was done for the single strand overhangs of lambda DNA, which are 5’ end overhangs and therefore can be templates for primer extension synthesis in vitro by DNA polymerase, and use radiolabeled dNTPS so the next neighbors and other sequence features could be deduced. And add in some techniques for DNA sequence determination that had been developed in Fred Sanger’s lab group – such as depurination, depyrimidation, endonuclease IV partial nuclease digestions, plus a whole raft of nucleases with various sequence specificities for cutting the DNA backbone.

So it was in the *Tetrahymena* rDNA molecules that Joe’s interests in rDNA amplification and repetitive DNAs converged – in this case the repeat sequences turned out to be the simple sequence telomeric C4A2 repeats that I was able to sequence at the ends of this rDNA. Then, in Joe’s lab, Meng-Chao Yao and I were able to show, that C4A2 repeats were also at the ends of the processed non-rDNA macronuclear genome linear DNA molecules in *Tetrahymena*.

**Reflecting on the methods** Joe and his lab members brought to bear on repetitive eukaryotic DNAs, it was completely characteristic of Joe that he was a very early adopter of the newest of molecular and biophysical techniques for nucleic acid sequence analyses.


“In retrospect, I realize that most of my knowledge of the outside world was coming through my eyes, and that has been the story of my life.”

We’ve all seen the beautiful demonstrations that Joe’s evidence is often highly VISUAL: of hybridization of satellite DNA to heterochromatin regions of chromosome spreads, or of ribosomal RNA to nucleoli, or 5S RNA to lampbrush loops for example. It struck me how visual also, in a different way, was the first data from his lab that some repeated DNAs were actually very simple sequences.

Here’s Sharyn Endow’s anecdote: how an audience reacted, in the very early days of DNA sequencing.

“My first conference talk was at the Gordon Research Conference on Nucleic Acids in 1974. When I showed my sequence data, there was a low murmur across the audience, as there were only 3 or 4 spots since my data were for simple sequence satellite DNAs by contrast to the promoter and other sequences that the other conference attendees were reporting.”
Sharon’s spots were of a 2 D fractionation of fragments of 32P labeled RNA copies of the DNA],

Tetrahymena telomeric sequences also first revealed their simple sequence, and highly repeated nature, to me as a major single spot on a 2 D fractionation of 32P labeled products - in this case from cleavage of depurinated DNA, which led to a prominent C4 spot on an autoradiogram, showing that they contained a Purine CCCC Purine sequence that was present in many copies.

Ed Stephenson wrote me recently:

“I have a vivid memory of Liz wandering the 4th floor Kline hallway with an X-ray film, still wet from the wash tank, and explaining to anybody who would listen the experiment that showed that Tetrahymena telomeres are composed of the sequence C4A2.”

Finally, in Joe’s lab

We all cared about the success of ALL Joe’s projects.

Once I volunteered to go newt hunting in the woods near New Haven to provide animals for Joe’s lampbrush chromosomes studies. Funnily enough, like Sue Gerbi’s, my animal hunting story is also a newt story!

Armed with a Styrofoam collecting box on this hot humid day, one newt looks pretty much like another to me, and I sweated mightily as I captured one newt after another and as I raised the lid to put it in, the one I’d just caught jumped out. So after a long sweaty hunt, I was feeling pretty incompetent, but I had a grand total of a few, and proudly brought them in to Joe’s lab. He opened the box and said: “oh yes, that’s the fast species”.

I’ll close with two important things that have stayed with me from being in Joe’s lab, because I’ve heard them from so many other past members of Joe’s lab too:

First, his supportiveness and kindness to everyone in his lab, and the spirit of good interactions among the lab members.

Second, when encountering some lab, or research-related, situation, we always think: what would Joe do?

So, I join every one of us in saying: I am so grateful to you, Joe, for so much, and thank you.
I met Joe Gall.... thanks to the lampbrush chromosomes!

It happened that my supervisor in Pisa, Giorgio Mancino – here looking for newts in a water tank on the Apuan Alps, Tuscany – was interested in amphibian cariology and joined Mick Callan in St. Andrews, where he learnt how to make lampbrush preparations.
When Giorgio Mancini came back to Pisa we began studying the morphology of lampbrush chromosomes in different newt species - and also drawing them ourselves, as exemplified here-, and I began reading the pertinent literature.

This 1954 review paper, where I first met Joe! I truly admired this and Joe’s other papers for both content and style, and I remember thinking: “if this person is anything like his writings, I would like to work with him at some time!”
However, when I won a scholarship to spend a year in the States, my supervisor and I agreed that a jump directly to Yale was probably too soon for me, and I started working with Alan Humphries – a very nice gentleman and scientist – on oocyte maturation. This was in Atlanta, Georgia, where, incidentally, I took part in many anti-racism and anti-Vietnam-war demonstrations, as later I continued to do both at Yale and back home – those were the post-1968 years!

From Atlanta I also went to visit Oscar Miller in Oak Ridge, Tennessee, and I was so fortunate that he showed me personally how to make the famous “Miller’s spreads” for both ribosomal DNA and lampbrush chromosomes.

Lampbrush chromosomes were involved in my oocyte maturation research and I kept reading up on the Joe’s work, so that, when I felt more confident about myself in the States, I wrote him a letter saying “… I am here in the States, I am doing this and this, I am interested in lampbrush chromosomes, I really admire your work, I would like to visit your lab, can I come??” I thought that most probably I was not going to receive any answer… but, to my surprise, Joe called me back – I was so excited… after reading his papers for such a long time I was eventually talking to the real Joe Gall!! In that conversation we arranged my first visit to Yale, where I spent 3 months on the famous 4th floor of Kline Tower - depicted in the image above by Manuel Diaz (tilted as “my” leaning tower of Pisa) and discovered science – something for which I will be eternally grateful to Joe.
It was a very exciting time in Joe’s lab – the time of ribosomal gene amplification, *in situ* hybridization and so on... and I met many nice, interesting people and also...I was introduced to the Model E ultracentrifuge and I fell in love with it - actually, a mixture of love and hate since, when I was running it overnight, I had nightmares of the centrifuge exploding because I had not assembled its cell properly.... and where, in any case, we isolated a satellite DNA component.

**Repetitive DNA in the newt, *Notophtalmus***

was located at the centromeres and the sphere loci by *in situ* hybridization.

You can appreciate that the morphology of these lampbrush chromosomes isn’t great, and the loops are almost invisible.

During one of my subsequent visits, in 1979, this was the morphology obtained in the lab after *in situ* hybridization with different probes – just beautiful. In these experiments it was discovered that histone genes and highly repetitive satellite sequences are intermingled and jointly transcribed at the sphere loci. These findings had a bearing on our ideas on transcription units and are also related to the impressive subsequent studies of Joe and his collaborators on the nuclear coiled bodies, or Cajal bodies, and Histone Locus Bodies.
The centrifuge incident

The miraculous change in morphology of the lampbrush chromosomes was achieved by centrifuging the lampbrush slides – according to an idea and design of Joe - on especially made swinging platforms, in a swinging buckets rotor, and the platforms were held by rods made of aluminum in a first version. However, things didn’t go smoothly at first. In fact, during the very first test of these devices Joe started the large Sorvall centrifuge, we were around and everyone held their breath: no problem at 1, 2, 3 K rpm, smiles all around. At this point, guests arrived for an office appointment and Joe went away with them. When the speed reached 5K, we heard a huge, horrendous noise and saw the centrifuge rattling and jumping a little: some of the aluminum rods had broken and the devices flew all around. Joe’s face appeared at the window between the lab and his office, he grimaced for a moment, and then returned his attention to his guests, displaying admirable self-control. We kept a very low profile for the rest of the day.

Fortunately, the centrifuge could be repaired, the aluminum rods were replaced with steel rods and the centrifuging went well in the successive tests, but the lampbrush preparations were far from satisfactory - they were distorted to some extent, with the loops all “combed” towards the superior edge of the centrifuged slide. This was frustrating and Joe wanted to understand what was wrong: going inside the centrifuge himself (as suggested in the cartoon above!), Joe discovered that the devices did not go all the way horizontal, so that the slides never reached a perfectly vertical position but remained tilted, “leaning” to some extent.

PERFECTION requires that NO DETAILS are left to CHANCE…

Therefore, to obtain “near perfect lampbrush chromosomes preparations”, as Joe writes in this autographed letter, he added a metal wedge to keep the slides at a small angle over the platforms, so that the lampbrush preparations reached a perfectly vertical position – perpendicular to the centrifugal force - and he was delighted to observe that the chromosomes were now “beautifully displayed”!

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This episode exemplifies Joe’s general attitude to cultivate great issues in science while personally taking care of all related technical details: we all remember Joe on Saturdays or Sunday mornings in his lab, playing with staining jars or saline conditions for in situ or whatever else related to research projects under way in the lab at that time – and doing this with great pleasure!

Superresolution imaging of transcription units on newt lampbrush chromosomes
Centrifuging lampbrush chromosomes on a slide reduces their complex three-dimensional organization to two dimensions, allowing Joe and his collaborators, more recently, to examine transcription on the loops by superresolution microscopy and to propose a model, that has a bearing on the way we think about transcription in general.

Friendship in Science
We all know that a fundamental byproduct of being in science is that we make strong, sometimes lifelong friendships, and before concluding, I wish to recall here two of the best friends – lampbrush friends, I would say! - of Joe and of many of us, Herbert Macgregor and Mick Callan.
I had the privilege to overlap with Mick and Amaryllis Callan during some visits to Baltimore and I have fond memories of the time we spent together. Mick and Joe were extremely good friends even though of different personalities and, for instance, it was somewhat of a problem that Mick kept smoking in the lab. Chris Murphy recalls that it took him many visits before stopping and I remember Mick – this imposing, authoritative person – hiding his cigarette behind his back, when he met Joe in the hall - like a child caught with his fingers in the cookie jar!

Acknowledgements. I gratefully acknowledge recollections from Celeste Berg, Manuel Diaz, Brian Kay, Kathi Mahon, Chris Murphy, Ed Stephenson and Martha Wild. I am especially grateful to Manuel Diaz for his charming cartoons.

Pisa, 15/04/2011
I was honored and happy when Joe and Diane attended my retirement meeting in 2011, where Joe delivered a beautiful plenary lecture.

I conclude with the Joe’s acronym I dedicated him for his 90th birthday.
Thanks Joe and best wishes to you, your family and everyone! Giuseppina
Ji-Long Liu Reflections on Cajal Bodies and Other Nuclear Bodies

Good afternoon, Joe. Hello, everyone. This is Jilong. It's midnight in Shanghai.

It's my great honor to speak here to celebrate Joe's remarkable career with astonishing discoveries. In the next 10 minutes I will introduce: “7 Theorems of Joe”.

Amphibian oocytes are big. Their nuclei, or germinal vesicles are huge. You can dissect them by hand, just as Joe did.

In 2003, Korie and Chris published a paper in JCB, showing that Cajal body components can come from nucleoplasm into the Cajal body dynamically. That year, Sveta, a girl from Russia joined Joe's lab. Her question was to see if Cajal body components can come out from the body. She used photoactivable GFP to do the experiment. But nothing happened. Then she decided to repeat Korie’s experiment. She couldn't. She couldn't repeat Korie’s experiment. She was so frustrated.

She asked Joe. Immediately, Joe realized mineral oil was kept in a plastic container, which made mineral oil toxic. So a new batch of mineral oil in a glass bottle solved the problem.
Theorem #1: If you have trouble, ask Joe!

On the first work day of 2003, I joined Joe's lab. One question in the lab was:

**Does Drosophila have Cajal bodies?**

It was difficult, because the signature protein coilin has not been identified in *Drosophila*. People started to believe there is no coilin in *Drosophila* at all. But luckily, U7 and U85, these RNAs supposed to be markers for Cajal bodies, have been identified in *Drosophila*. And the strategy was to use RNA, instead of protein, to identify the Cajal body in *Drosophila*. I started to learn the *in situ* hybridization technique, which was invented by Joe many years ago. To make a long story short, eventually I got it done. I got U7 showing one dot in the nucleus, and U85 showing one dot in the nucleus. Joe said, “Perhaps you can see if these two dots colocalize. Then we'll be convinced”. I did.

But…you see… Two-color FISH of U7 and U85 shows two dots in one nucleus. Sometimes they are close together, but many times they are far away. I remember that Friday afternoon. I talked to Joe. I said, “Joe, I don't know why. There are two dots, not one”. I was so disappointed. But Joe was excited. He said, “This is unexpected. This is something interesting!” So he encouraged me to do the following experiment using different markers.
Eventually, we realized that there are two separate bodies in the nucleus. For one we decided to keep the name “Cajal body”, and for the other one we named it the “Histone locus body”, because of its association with histone gene clusters. In addition, we found a third body in the cytoplasm and called it the “U body”.

Theorem #2: If you are disappointed, talk to Joe!

We also look into nuclear bodies in the Drosophila GV. Alison Singer had just gotten her bachelor’s degree from Brown University, and recommended by Susan Gerbi, Alison joined the lab. Encouraged by Joe, Alison looked at the Drosophila GV and found inducible nuclear bodies there. They published a research paper together.
The next question was: **Does Drosophila have coilin?** I remember the last two days of 2005, using a new strategy, I found a putative hit. Only one, out of several hundreds. On the first workday of 2006, I talked to Joe. I said, “I found one putative hit of *Drosophila* coilin.” But I was skeptical. Joe said, “mmm, this is something suspicious. We should go for it.” Encouraged by Joe, we made transgenic flies. When the flies were available, Joe and I looked at them and found there were bright dots in the nucleus. Immediately we realized that we had identified coilin in *Drosophila*.

In the following year, we collaborated with Dana Carroll and used zinc finger nuclease to generate mutants for coilin. This was one of the first genes in *Drosophila* being targeted by zinc finger nuclease, leading to two publications in PNAS and MBOC.

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**Theorem #3:** If you have doubts, Joe pushes you!
Thus, we had an issue of two bodies, the Cajal body and histone locus body. So, Zehra and Sveta decided to look back into amphibian oocytes. Their conclusion was: “The coilin-positive bodies in late-stage *Xenopus* oocytes should be considered HLBs, not CBs”. And then Zehra looked at early-stage oocytes and found a third type of structure that has coilin. They call them “Pearls”, because coilin stays in the periphery.
This was NOT unexpected. In 2000 and 2003, Joe wrote two review articles, talking about Cajal bodies have been studied for 100 years.

**Theorem #4: 100 years isn’t enough for CB studies said Joe!**

Last year, Joe and I were invited by the Editor-in-Chief of *Experimental Cell Research*, Andras Simon, to organize a special issue on *Amphibian Model Systems* for 2020. I dug out my notebook from 2003 and 2004, the first two years when I was in Joe’s lab as a postdoc. It was a 5000+page notebook, but I dug out the data, analyzed them, prepared a manuscript and sent it to Joe. Two weeks ago, Joe sent me back his last edit, Version 21. So we found a new structure. I called it C-ball, but Joe renamed it as “C-body”. We aim to submit this manuscript later this month.
Theorem #5: In Joe’s lab, the due date is 15+ years later!
Theorem #6: Joe does not age!

Theorem #7: Joe likes glass!
(microscopes, lenses, microscope slides and coverslips. Like the mirror for Alice in Wonderland, the microscope is the looking glass for Joe)

Happy Retirement, Joe! I am lucky to be your trainee. Ji-Long Liu
Gaëlle Talhouarne Talross Reflections on the Gall Lab in the RNomic World

The Gall lab in the RNomic world:
Discovery of stable intronic sequence (sis)RNA

sexiRNA


Joe's contagious curiosity

A curiosity that leads to unexpected science

Talhouane and Gall. 2018. RNA Talross*, Deryushova* and Gall. In prep
These pictures/slides highlight 3 important characteristics of Joe (out of many)

1. His unique perspective/approach to biological questions
   - An example of this output was his discovery of sisRNA

2. Curiosity
   - An example is the pursuit of side projects (7SL in mature red blood cells + stable lariats bearing a snoRNA)

3. Tenacity
   - An example is an application of complex new techniques like single molecule FISH and Omics approaches

Thank you, Joe!
Allan Spradling: Concluding Remarks

This afternoon, it has been deeply satisfying to hear Joe recount his career, and illuminate with characteristic modesty and humor some of the philosophy that has guided it so unerringly. We listened with equal fascination to reminiscences and anecdotes from many of you who have played key roles in Joe's stellar scientific accomplishments. We heard repeatedly about the joy of doing science within the Gall universe. It was fun just working together in the lab, and we have seen today that your camaraderie is still going strong, despite the passing of years and lab generations. Training with Joe was not just exciting, but also the source of a uniquely valuable scientific worldview that has allowed so many Gall graduates to pursue wonderful careers of their own--like newly forming galaxies shooting in all directions after the Big Bang.

We were further privileged to become better acquainted with Joe's childhood experiences that shaped his scientific and personal style. He found that one learns best by doing, and that you should trust what you see with your own eyes even more than what you read about the observations of others. Joan described Joe's early interest in astronomy (which, incidentally, continues to this day), and Larry will tell us later how Joe ground the lenses for his own telescope and peered at the wonders of the night sky. Joe was flabbergasted when it was discovered that the main Hubble Space Telescope mirror, with all its big science sophistication, had a defective curvature. "Anyone who has ever ground a lens could have easily detected that problem" he explained. However, Joe had chosen to study biology rather than astronomy, so he was not available to prevent that particular near disaster. But Joe has nonetheless taken on a unique astronomical role, within the field of biological science.

For in the universe of biology, Joe is the North Star. The scientific heavens may turn and swing with the fashion of changing seasons. But those of us who know Joe understand that the things he stands for in science hold steady and are always there to inspire and guide us. Are gravitation-like forces suggesting that groups need to congeal together into large masses in order to compete? Large groups and projects have made wonderful contributions to the advancement of our fields. None of us would want to live without genome sequences, strains from stock centers and soon, single-cell RNAseq of every tissue and developmental stage. But, Joe's work and voice reminds us how simplicity can be even more powerful and original. Joe asked: If you can hybridize probes to DNA on a Millipore filter, why not to DNA on a microscope slide? If an oocyte nucleus has thousands of nucleoli maybe nucleolar genes have been amplified. If some introns are preserved and move into the cytoplasm, maybe they are doing something interesting.

We need simplicity and clarity because if all we have is stellar data, there may be no one around who can interpret them productively. Data are a given that will always get bigger and better. But scientists cannot wait and hope that data quality will eventually improve until some meaning becomes self-evident. Science is about developing the novel ideas needed to
understand our world, something that data only enable. It has often been said, "Oh you couldn't do anything with the technology available back then." But Joe never seemed to notice such limitations. He showed that no matter where a field's development stands, there are simple, revealing experiments to be done based on what is known and available. Yes, you may have to change the question you most want to address, but there are always interesting, unexpected and important results waiting for someone who knows the right answerable question to ask.

For example, it's great to hear the excitement about unconventional model organisms today, but also a little amusing. Yes, it's becoming easier to work with these systems now using genomic techniques. But for his entire scientific life Joe has done important work mostly outside the specially favored model systems such as *Drosophila melanogaster*, with which he started his career. Joe wanted to make use of each organism's special properties, and was therefore drawn to newts with chromosomes more tractable than polytene chromosomes; Tetrahymena with telomere proliferation; the water beetle *Dystiscus*, whose oocytes had a giant DNA staining body; *Drosophila virilis* with disappearing polytene heterochromatin; *Sciara coprophila* and *Rhynchosciara* with DNA puffs; as well as *Xenopus*, salamanders, *Paramecium, Euplotes*, mice, snails, coelacanths, *Gastrothecae*, and even human cells, to mention just the animal kingdom. Throughout his career Joe has made research on unconventional creatures seem simple and normal. He showed us that whatever the current level of technology, by choosing the right organism and right question one can uncover a new aspect of nature.

Ultimately Joe and his career also guide us beyond just the subject matter and questions of scientific concern. The way you carry out your scientific activities can be as important as the subjects you study and the discoveries you make. Very few of us are able to add anything to the existing body of knowledge on our own. Doing science, is largely about the people we work with: in our laboratories, in our institutions, and in our disciplinary communities around the world. Working with others adds immeasurably to the value and joy of science, but also raises the question of who is selected to be part of our ventures and how the rewards of success are shared among our group members. Our understanding of social organization seems to have much in common with scientific knowledge itself. We start out believing that we have a better grasp of what is fair than in previous eras, but then over time we realize that much still remains to be improved. Joe has always run his laboratory in a humane manner far ahead of his time, in a way that benefits both science and all the participants of the enterprise. Finally, scientists need and deserve to take pleasure and pride in what they have accomplished. Knowledge is not acquired easily, or without many disappointments along the way. Joe shows us how to enjoy the thrill of discovery while remaining humble and recognizing the many contributions of others who worked on the same questions.

In closing, Joe, we thank you again for making us better scientists, and better human beings, and for all the good times we have shared together.
Remembrances

LAB MEMBERS

Elizabeth (Liz) Rodgers
PhD student from 1962-63 (Minnesota) and 1963-1967 (Yale)
Senior Lecturer Emerita Zoology and Biological Sciences, U of Edinburgh 1969-2004

“Joe in the news”
Here’s a newspaper cutting announcing the appointment of Joe to Yale Faculty as Professor of Biology in 1964. I found it in a box of papers from the 1960s, but I don’t have a record of which publication it came from. What I like about it is that it highlights so many of Joe’s strengths at that time, which of course continued throughout his life. For example, how his research crossed boundaries which then seemed to exist between Cell Biology and Molecular Biology, and how new it then was to be able to connect the activities of chromosomes to what was happening in the rest of the cell. Joe’s ‘hope to get a fair amount of research done’ came to the most wonderful fruition, as we can all testify!
Susan A. Gerbi  
1965-1970 graduate student  
Professor of Biochemistry, Brown University

Joe has been active in the American Society for Cell Biology (ASCB) since its beginnings. When he was the Program Chair for an early ASCB annual meeting, I recall that he single-handedly sorted the few hundred abstracts into appropriate categories, placing them as piles in the hallway outside his office in the Kline Biology Tower (KBT) at Yale. The number of abstracts was manageable compared to current ASCB meetings with ~10,000 participants. Joe served as ASCB President, and three of his scientific progeny (myself, Mary Lou Pardue and Liz Blackburn) became ASCB Presidents in the decades that followed. At ASCB meetings Joe generously introduced his students to luminaries in the field --- I recall meeting Hewson Swift (who later served as the outside reader for my PhD thesis), Oscar Miller, Bob Perry and others. At the ASCB annual meetings, Joe would bring an album filled with wonderful photos of his latest findings, and at evening parties in a hotel room, these scientific advances would be shared with other scientists at the meeting. This was before the days of poster presentations. Those of us in the Gall lab made a point of sitting in the front row to hear the last speaker in the last session of the meeting (to give them an audience as many had already left the meeting). Students from Hewson Swift’s lab also joined us for this final event of the meeting, and someone in the Swift lab (perhaps Marty Gorovsky?) dubbed us the “Gall girls” since we were an all female contingent (Liz Rogers, Nancy Lane, Linda Hufnagel, Mary Lou Pardue, me, and others).

The following year, Hans Laufer (from U. Conn) visited the Gall lab for the day. This happened to be the day before Joe was leaving for a sabbatical in the UK. We (the 7 Gall girls) had planned a farewell surprise for Joe. After lunch with Joe and Hans Laufer, we sang a song we had written and we did a can-can dance performance to go with the song. Hans Laufer was amazed and wondered if the Gall girls entertained Joe like this every day after lunch!

While Joe was away on sabbatical two lab incidents happened, but we did not tell him about them until after he returned to Yale. One was that the SW-25 rotor flew off the spindle when Mary Lou was doing an ultracentrifuge run, destroying the rotor and the centrifuge. As soon as Joe walked in the lab on his return from his sabbatical, Mary Lou ran up to him to explain what happened. I recall her relief that he kept his cool after learning about this expensive mishap. Evidently there was a special tool to tighten a screw at the base of the rotor spindle and it was supposed to be tightened before each run --- but none of us know about that so it had never been tightened and by bad luck for Mary Lou, it came loose during her run. You will read in some of the anecdotes from others about other ultracentrifuge stories in the Gall lab. I was lucky to be given for my lab at Brown a gift of some model E ultracentrifuge cells that Joe no longer needed. Also, Joe gave me a specialized rotor he had designed for lampbrush chromosome preparations and this was valuable for our experiments spinning down amplified nucleoli from Xenopus oocytes to discover the sequence in snoRNAs that targets them to nucleoli.

The other lab incident when Joe was away on sabbatical was that my boyfriend who was in charge of some Freshmen boys at Yale helped them with a skit for their college. The skit included a baby pig from a local pig farm. After the skit, we needed a place to house the pig overnight, and the only place available was my office in KBT. To contain droppings of pig manure, my boyfriend went to Macy’s and asked the salesgirl for diapers. In reply to her question about the age of the infant, he replied 8 weeks so she brought out small diapers ---- but he exclaimed that they were way too small. She then asked the weight of the infant, and he said 40 pounds. She looked amazed but gave him the extra large size. He asked her for a demo of how to fold
and fasten the diapers. When he asked her where the tail should go in the diapers (not having disclosed that the infant was a baby pig), she threw up her hands in disbelief! In addition to the diapers, as an added precaution we laid down some newspapers on my office floor, left the piglet for the night and closed the door. The next day, unaware of the new occupant of the office, my office-mate (Masha Etkin) arrived and found the piglet who had kicked off the diapers, torn up the newspapers and deposited manure everywhere. Masha blurted out: “How can I finish writing my PhD thesis with a pig in my office!” We shared this story with Joe when he returned from sabbatical.

I had a serious hobby of horse-back riding, but thought Joe might not approve of my spending several afternoons a week away from lab, so my classmates all covered for me and said I must be at the library if Joe asked where I was. I subscribed to the “Chronicle of the Horse” magazine and by mistake once it was put in Joe’s mailbox instead of mine. In conversation when giving me the magazine, the cat was let out of the bag that I was a horse-back rider. Joe was not angry, and was fascinated to learn that the magazine was published in Berryville, Virginia, a few miles from his family’s farm where he grew up. At subsequent lab parties at his home, his daughter Barb would sequester me in her bedroom to play with her toy horses! Later, Barb got a real horse named Major (Barb now has several horses on her farm and is a vet). Barb helped to organize a local 4H club horse show and asked me to be the judge and Joe served as the ringmaster --- what fun! Some years later when I was a postdoc in Germany, I visited Joe and his family when he was on sabbatical in the UK. Barb was excited to show me how she could do flying changes at the canter on a reluctantly willing pony. Also on that visit, I brought as a gift for Joe a “mid-wife toad” that Joe had expressed an interest in and a fellow scientist (Claus Pelling) in Germany had collected the toad from a pond near his house. I transported the toad in a jar with my carry-on bag, but the stewardess spotted it and asked if she could take the jar to show the pilot --- I was worried that the pilot would become so fascinated that he would lose control of the plane, but luckily we landed ok.

Joe --- thanks so much for your mentorship throughout my career. You are such an amazing role model and an inspiration to all of us. Using the German term, you are my Doktor Vater (doctor-father) and I am your Doktor Tochter (doctor-daughter). It is a privilege to be part of your scientific lab family. I wish you continued enjoyment in looking through a microscope in your “retirement”.

Susan

Linda Hufnagel
Postdoctoral fellow, 1967-69
Professor Emerita, University of Rhode Island,

In reviewing my experience of working with Joe, my memories are dominated by two things: first and foremost, was his strong support of the women working with him as students and postdocs. It was the first time in my educational experience that I found myself surrounded by numerous intelligent and motivated female colleagues, some of whom have continued to be important in my life. And those of us who were postdocs were given private research rooms in which to do some of our work! What luxury, when previously, at the University of Pennsylvania, my “private” research space and office was a desk that I shared with another graduate student!

Second and certainly also at the fore, is my memory of the day when Joe emerged from his lab to excitedly announce the results that showed that he had succeeded in developing in situ hybridization. Since I was still new in his lab, I had not been aware of the quest that had
sequestered him so frequently in his private lab room, and I certainly was not aware of how significant this technical advance would become! How lucky I was to be there for that momentous occasion!

The lowest point in my experience with Joe came when, in the summer of 1969, after having done a series of microscopic and model L experiments with *Tetrahymena pyriformis* that helped to convince Joe and me at the time that Tetrahymena’s ciliary basal bodies do not contain DNA, events in my private life led me to leave Joe’s lab, and move to New York to undertake a new research goal: the structural and functional mapping of nervous systems in small invertebrates. While leaving Joe’s lab was the most difficult life decision I ever had to make, I am happy to report that what I learned while in Joe’s lab has had lasting effects on my later career and personal decisions, and on my commitment to mentor over 100 graduate and undergraduate students, both women and men, who have worked in my own laboratory, at the University of Rhode Island.

I wish to express my best wishes for Joe’s retirement. Also, I want him to know that I enjoyed hearing and reading (in "Chromosome Odds and Ends") about Joe’s memories of being a young scientist on the farm. It brought back my own memories of growing up on a farm in Vermont, where I collected butterflies, dissected insects, tried out taxidermy and saved allowances for two years to buy my own microscope. The microscope was a Gilbert and was a big disappointment because of its poor resolution. The protozoa I raised, from a hay infusion set to incubate behind the wood stove, were moving around but that was it! But it still led to my dream to view cells through better microscopes and to my later career as an electron microscopist! I am forever grateful that Joe enthusiastically supported my efforts to conduct experiments following up on my earlier thesis work on *Paramecium* by searching further for evidence of basal body DNA in *Tetrahymena*. While my results were not what I had hoped for, they allowed me to move in new and rewarding directions in my scientific career.

**Edward (Ed) Cohen:**
Graduate Student 1968-72
Phage Display Scientist now retired

“*Three new grad students*”
One day Joe very unexpectedly came into the office that Brian Spear and I shared as graduate students. He said something to the effect that he had a major problem. He felt he really could add only one new graduate student to the lab in the upcoming year, but that three very qualified students wanted to join it. He just did not know how he was going to select one from the three. This was the first and only time I remember Joe in such an indecisive state. Brian and I were not going to be able to advise him, and as I recall said few if any words. I do not remember Joe even mentioning the names of the students, and at that time at best I might have met each of them only briefly.

Shortly thereafter all 3 students joined the lab: Sharyn Endow, Ginger Zakian and Pat Pukkila.

**Giuseppina Barsacchi**
Professor Emerita, University of Pisa Italy, Lab of Cell and Developmental Biology and Department of Biology

How lampbrush chromosomes mediated my meeting with Joe
In the early sixties, my supervisor at the University of Pisa (Italy), Giorgio Mancino, was interested in amphibian karyology and joined Mick Callan in St. Andrews, where he learnt how to make lampbrush preparations. Therefore, when he came back to Pisa, we began studying the morphology of lampbrush chromosomes in different newt species. I began reading the pertinent literature, including Joe’s 1954 review paper in J. Morphology – that was a turning point for me. I truly admired this and other of Joe’s papers on lampbrush chromosomes for both content and style, and I remember thinking: “if this person is anything like his writings, I would like to work with him at some time!”

However, when I won a scholarship to spend a year (1969) in the States, my supervisor and I agreed that a jump directly to Yale was probably too much for me, and I started working with Alan Humphries – a very nice gentleman and scientist – on amphibian oocyte maturation. This was at Emory University, Atlanta, Georgia, where, incidentally, I took part in many anti-racism and anti-Vietnam-war demonstrations.

From Atlanta I also went to visit Oscar Miller in Oak Ridge, Tennessee, and I was so fortunate that he showed me personally how to make the famous “Miller’s spreads” for both ribosomal DNA and lampbrush chromosomes. (The late Oscar Miller, former chair of the department of Biology at the University of Virginia, was a postdoc with Joe at the University of Minnesota in 1960-61).

Lampbrush chromosomes were involved in my oocyte maturation research. I kept reading Joe’s work, so that, when I felt more confident about myself in the States, I wrote him a letter saying “… I am here in the States, I am doing this and this, I am interested in lampbrush chromosomes, I really admire your work, I would like to visit your lab, can I come??”

I thought that most probably I was not going to receive any answer…… but, to my surprise, Joe called me back – I was so excited… after reading his papers for such a long time I was eventually talking to the real Joe Gall!! In that conversation we arranged my first visit to Yale, where I spent 3 months on the famous 4th floor of Kline Tower and discovered science – something for which I will be eternally grateful to Joe.

It was a very exciting time in Joe’s lab – the time of ribosomal gene amplification, in situ hybridization and so on, and I met many nice, interesting people. Among others, I was introduced by Susan Gerbi to the Model E ultracentrifuge and I fell in love with it - actually, a mixture of love and hate since, when I was running it overnight, I had nightmares of the centrifuge exploding because I had not assembled its cell properly. Here we isolated a satellite DNA component, which was located at the centromeres and the sphere loci of the newt Notophtalmus by in situ hybridization (Mary Lou Pardue was at hand to provide advice!).

During one of my subsequent visits, in 1979, the morphology of lampbrush chromosomes obtained in the Gall lab after in situ hybridization with different probes was improved: those experiments showed that histone genes and highly repetitive satellite sequences are intermingled and jointly transcribed at the sphere loci.

The miraculous change in morphology of the lampbrush chromosomes was achieved by centrifuging the lampbrush slides – according to an idea and design of Joe - on especially made swinging platforms, in a swinging bucket rotor, and the platforms were held by rods made of aluminum in a first version.
However, things didn’t go smoothly, at first….

In fact, during the very first test of these devices, Joe started the large Sorvall centrifuge, we were around and everyone held their breath: no problem at 1, 2, 3 K rpm, smiles all around. At this point, guests arrived for an office appointment, and Joe went away with them (1). When the speed reached 5K, we heard a huge, horrendous noise and saw the centrifuge rattling and jumping: some of the aluminum rods had broken and the devices flew all around.....

Joe’s face appeared at the window between the lab and his office, he grimaced for a moment, and then returned his attention to his guests, displaying admirable self-control. We kept a very low profile for the rest of the day.

Fortunately, the centrifuge could be repaired, the aluminum rods were replaced with steel rods and the centrifuging went well in the successive tests, but the outcoming lampbrush preparations were far from satisfactory - they were distorted to some extent, with the loops all “combed” towards the superior edge of the centrifuged slide.

This was frustrating and Joe wanted to understand what was wrong: Joe discovered that the devices did not go all the way horizontal, so that the slides never reached a perfectly vertical position but remained tilted, “leaning” to some extent. Therefore, to obtain “near perfect lampbrush chromosomes preparations”, as Joe wrote me in a hand-written letter enriched by original cartoons (Jan. 21, 1980), he added a metal wedge to keep the slides at a small angle over the platforms, so that the lampbrush preparations reached a perfectly vertical position – perpendicular to the centrifugal force - and was delighted to observe that the chromosomes were now “beautifully displayed”!

This episode exemplifies Joe’s general attitude to cultivate great issues in science while personally taking care of all related technical details: we all remember Joe on Saturday or Sunday mornings in his lab, playing with staining jars or saline conditions for in situs or whatever else related to research projects under way in the lab at that time – and doing this with great pleasure!

Centrifuging lampbrush chromosomes on a slide reduces their complex three-dimensional organization to two dimensions, allowing Joe and his collaborators, more recently, to examine transcription on the loops by super-resolution microscopy and to propose a model, that bears on the way we think about transcription in general.

Before concluding, I wish to recall here two of the best friends – lampbrush friends, I would say! - of Joe and of many of us, Herbert Macgregor and Mick Callan.

During a visit to Carnegie in 1986-7, I had the privilege to overlap with Mick and Amaryllis Callan during their visits to Baltimore and I have fond memories of the time we spent together. Mick and Joe were extremely good friends even though of different personalities and, for instance, it was somewhat of a problem that Mick kept smoking in the lab…. Chris Murphy recalls that it took him many visits before stopping and I remember Mick – this imposing, authoritative person – hiding his cigarette behind his back, when he met Joe in the hall - like a child caught with his fingers in the cookie jar!

I conclude with an acronym for Joe, which I dedicated to him for his 90th birthday:
Notes (1) Kathi Mahon remembers the centrifuge incident well since she was one of the "guests" at the meeting in Joe's office: "It was in fact my very first meeting with Joe and my advisory committee. Afterwards, Joe and I went into the lab to inspect the damages. I was very impressed with Joe's calmness at such destruction of a rotor. Most people would be very upset! I knew right then that the rotor explosion was an auspicious sign that I belonged in Joe's lab".

Elysse Craddock
Visiting Postdoctoral fellow, Fall of 1972
Professor Emerita, Purchase College, SUNY

Dear Joe,

Sending you my greetings on your non-retirement, along with sincere thanks for your generosity, supportiveness and enduring intellectual stimulation.

One of the many memorable highlights of my all too brief stay in your lab was the afternoon when you invited me to watch you dissect Xenopus oocytes and reveal their beautiful lampbrush chromosomes. This remains the only time I have observed them firsthand down the microscope! Thank you too, for introducing me to the intricacies of the Model E and so much more, and for your enthusiasm and interest in my research on the evolution of chromosomes and genomes.

You remain the most insightful and inspirational scientist I have ever encountered!

With my very warmest wishes,

Elysse

Sharyn Endow
Graduate Student, 1970-1974
Professor of Cell Biology, Duke University

“Diane’s polytene chromosomes preparations (with Diane’s note on her DIS methods paper)”

When I first arrived in Joe’s lab, my assigned office space was in the fly room, which was a small room just large enough for the fly bottles, myself and Diane who worked as a technician (this was pre-Joe & Diane). Diane came to the fly room whenever she had a few minutes to spare to make polytene chromosome spreads. She was very skilled at doing this and would often show me the slides. I was there the day that she made an especially beautiful chromosome spread from D. virilis. She immediately saw that the chromosomes were unusually well spread with each arm extended and only let me look for a few moments before she went quickly to find Joe and asked him to come and admire the preparation, and then finished fixing the chromosomes. I recall that
Joe then took the slide and carefully stained it for further examination. Sometime after leaving Joe’s lab, I heard that Joe and Diane were a couple. I could only conclude that the way to Joe’s heart was by producing beautiful scientific data.

Diane’s methods with one of her especially well-spread polytene chromosome preparations - this time from *D. melanogaster* - were later published in DIS 49,131 1972.

“**Phenol-extracted pipette drawer**”
I walked into the main lab at Yale one day to find Joe standing off to one side and Diane (this was pre-Joe & Diane) wearing heavy gloves and removing all the glass pipettes from the pipette drawer. It turned out that Joe had spilled phenol into the drawer and Diane was called upon to help clean up the phenol-extracted drawer.

“**Worn Corex tube**”
As a graduate student, one of my thesis projects was to survey *D. virilis* tissues for differences in satellite DNA levels. I found that pupal ovaries showed significantly increased amounts of satellite DNA, rather than decreased amounts as in many tissues with polytene chromosomes. This required purifying DNA from a large number of pupal ovaries to analyze on the infamous Beckman Model E analytical ultracentrifuge. I set out to dissect ovaries from 1000 pupae, which required a week or more of long hours of nonstop exacting dissections. There was only a minor mishap around pupal ovaries #850 or so, when I almost spilled the collection tube. After DNA extraction and EtOH precipitation, I centrifuged the EtOH mix to recover the DNA. Upon opening the rotor, I found that the Corex tube had shattered during the spin. Since it was not possible to recover the DNA, I cleaned up the broken glass and went for a walk down to the New Haven Green, where I sat on a bench and watched the men on the Green playing board games. I thought about science and life, and board games that I did not know how to play, and, after about an hour, realized that I did not want to learn how to play. I walked back to Kline Tower and went into the lab, where I saw Diane, who told me that Joe said he was sorry about my DNA prep and that the old Corex tubes really needed to be thrown away. The next day I started the dissections for the pupal ovary DNA prep again.

“**Joe’s Duke seminar trip**”
At some point after I moved to Duke as a faculty member, I invited Joe for a seminar, which was probably one of the low points of his travel that year. First, after I introduced him, he thanked me for my “effusive” introduction. Then, in the evening, I had an open house for him and he stayed overnight in my guest room, where I have a duvet on the bed. Joe didn’t ask for milk and cookies, as he did at Brian and Helen’s, but he did ask for a blanket, with which I wasn’t able to provide him. He was not able to sleep well that night - he said the next morning that he got too hot under the duvet, then too cold after throwing it off, and this went on throughout the night. For breakfast in the morning, as a special treat, I served the smoked salmon left over from the open house. Joe asked for cereal and milk, which I did not have, so he nibbled at the salmon. Then he abruptly asked to use the bathroom - not an auspicious sign. Finally, as we were leaving my house, he paused on the doorstep and looked carefully to the side of the door, where there was a large black spider with red markings. After a moment or two, he said, “it’s a black widow” to my horror and shock. This was probably the high point of his visit to Duke.

“**Baggy pants**” (a Don Brown story)
After leaving Joe’s lab, I went first to CSHL and then did a second postdoc under Peter MB Walker in Edinburgh, Scotland, where I was in Ed Southern’s laboratory. Soon after I arrived in Edinburgh, Don Brown came to give a talk at a small meeting. Before the meeting, Ed Southern
remarked to me that I had a lot in common with Don Brown - I asked him why, expecting him to say that we both had worked on changes in chromosomal DNA, or something similar. Instead, Ed replied that we both wore baggy pants. Later, I sat next Don Brown at the meeting and, making casual conversation, remarked that Ed Southern thought that he and I had a lot in common. Don, of course, asked why, and when I said that Ed said that we both wore baggy pants, Don and I both glanced down at his pants, which were not only baggy, but noticeably frayed around the cuffs. The next time I saw Don, later the same day, I noticed that he had changed into a pair of pants without frayed cuffs.

Virginia (Ginger) Zakian
Graduate Student 1970-75
Professor Emerita Molecular Biology and Research Scholar Lewis-Sigler Institute, Princeton University

“Gall girls make good”
Mary Lou Pardue and Susan Gerbi visited the Gall lab several times during my time as a graduate student. They were to me (and I suspect to the rest of the females in the lab) the scientific equivalent of rock stars. Joe would have the whole lab around the table in the food room on the 4th floor when one of them visited so that Mary Lou and Susan could talk to us. They were both so wise. The two of them were my first female scientific role models: they were concrete examples of the possibility of a scientific future for women. Only in retrospect did I realize how important they were for my development as a scientist.

“Gatlinburg TN”
A bunch of the people from Joe’s lab drove down to Gatlinburg TN in Kathy Karrer’s brand-new car for an Oakridge sponsored meeting. I think this was 1973. It was an amazing meeting. Joe gave his speaking slot to Adrian Bird who talked about his recent discovery that amplification of Xenopus rDNA occurred by a rolling circle mechanism. Bruce Alberts introduced the trombone model of DNA replication. But one of the most memorable events occurred at one of the cocktail parties. Ed Southern came up to a bunch of the female grad students from Joe’s lab and asked (paraphrased), “what is it that Joe has that all of you chicks work in his lab.” Sharyn Endow gave the best possible answer. She said, “because when Joe shuts his office door to talk with you, he talks about science.” (this memory was reviewed by Sharyn; details are a bit off as Sharyn doesn’t think she went to the Gatlinburg meeting; she probably said it in a different context, and it was conveyed to Ed by one of the several grad students of Joe’s who attended the Gatlinburg meeting)

“DNA is anti-parallel”
One day Joe called a lab meeting so he could present his work sequencing the satellite DNAs of D. virilis. He had clear data, but it didn’t make sense because the two strands were not complementary. Someone pointed out that he was not considering that DNA was anti-parallel. To Joe’s credit, he didn’t seem embarrassed but rather grateful. For me, it was a wonderful example that anyone can be wrong and that input from others is to be sought after.

“Joe gets into the National Academy of Sciences (NAS)”
This event occurred in spring 1973 or 74. It was a typical late night in the lab. Someone came in and told us that Joe had been elected to the NAS – in his typical modest fashion, he hadn’t told the lab. We were excited and decided that we had to celebrate the next day. Ed Cohen was the designated lab cake maker, but he said it was too late at night for him to make a cake. So, I volunteered to do it. At the time, I was living on Humphrey St; a friend from Cornell who was a
grad student in Psychology at Yale, used to spend two nights a week at my apartment, and this was one of those nights. I made the cake (surely from a mix) and while I was waiting for it to bake, made the frosting (probably premade canned frosting). While Patti and I were waiting for the cake to cool, we ate some of the frosting. It ends up that we ate a lot of the frosting so that there wasn’t enough to cover the whole cake. By this time, I realized this, it was really late, and I decided it would have to do. I brought it in the next day thinking that a partly frosted cake was better than no cake. (I was probably impressed that I had even made a cake.) But Ed was worried that someone would think that he had made this really ugly cake, and after we shouted congratulations, he announced to Joe that Ginger had made it.

“Thinking about something else” (Pat Pukkila joined Joe’s lab at the same time that Sharyn Endow and I did; tragically, Pat died of pancreatic cancer in 2019; this is a story she told me). The skating rink was close to Kline Tower, and Joe often went skating around lunch time. While a graduate student, Pat had season tickets to both the NY Philharmonic and the Metropolitan opera. One day Pat was also skating, and she had this conversation with Joe. Joe asked her how she could concentrate on music during the performances she went to; didn’t she find herself always thinking about experiments? (Pat said no, she thought about the music). Joe said that the only time he didn’t think about science was when he was skating.

“Another story from Pat Pukkila” Pat came in one day (probably early on a weekend morning as she and Joe were the only ones in the lab). Joe had spilled some phenol on the lab bench and was carefully cleaning it up. He told Pat how dangerous phenol was and to impress the point, he put his hands in it!! They quickly got white and then he washed it off!!

“Balancing the tubes” My first project in Joe’s lab was to isolate Drosophila rDNA using differential mobility in CsCl gradients. Soon after I joined the lab, I came in the morning after setting up an overnight run in the ultra-centrifuge. Much to my horror, I learned that the vacuum had failed during the night and the machine had come down. When I came in, Joe was in the midst of removing my samples from the rotor and weighing them. I almost died of relief when he told me that they were properly balanced.

“Visible reminders to be careful” Everyone in the lab before computers will remember developing and printing your own pictures and developing slides in one of the lab’s darkroom. When drying the prints, we had to place them very carefully on the roller drum of the dryer to avoid a big scratch on the drum. We were told that the scratch came when Mary Lou put her keys on it, and they went through the dryer. Joe loved that story. He also saved a blown-up rotor for the ultra-centrifuge. At the time, we all knew whose run had caused the crash, but I no longer remember….

“Call me Joe” We all thought it was strange that graduate students (and certainly undergrads) called Joe “Dr. Gall” while postdocs called him Joe. But once you got your PhD, if you didn’t start calling him Joe, he’d tell you “just call me Joe.” I was later told that when Brian Kay joined the lab, he told Joe that he found it weird to call him Dr. Gall. Joe said to Brian, I find it strange too. When I started out, I kept telling my students to call me Joe, but they wouldn’t do it so I decided to accept it. But I drew the line at postdocs and insisted they call me Joe. Thereafter, students called him Joe.
“The albino axolotl and use of other organisms”
At some point, Joe bought an albino axolotl from (I think) Carolina Biology. When asked what his plans were for this new addition, he said he didn’t have any, but he just wanted it. My love of animals, especially sea life, was what made me decide to be a biologist so I always appreciated the animal room and Joe’s attitude towards new acquisitions!

“Naturalist for a night”
Joe invited the lab to go amphibian collecting, which we did in CT at night. It was a fantastic experience. One of the most memorable parts was that Joe could identify so many critters by their “voice” alone.

“Use the right organism”
I started using budding yeast during my second postdoc and, in my own lab, we used it more than any other organism (I recall being nervous that Joe would be disappointed in me for choosing an organism whose chromosomes were not visible by light microscopy.) However, one of the many things I learned from Joe was to use the organism that was most appropriate for each experiment. So, in addition to budding yeast, my lab also used Tetrahymena (to isolate DNA termini for construction of the first artificial linear chromosomes or YACs, which were propagated in budding yeast), Oxytricha (to isolate the first telomere end binding proteins, the prototype of Pot1), mammalian tissue culture cells (to test if ARSs, autonomously replicating sequences, identified from mouse DNA using a functional assay in yeast could serve as origins of replication in mouse cells; probably not) and to determine the function of human PIF1 (in collaboration with Lea Harrington; this was another disappointment), and fission yeast (used much more successfully than mammalian cells for studies of both telomerase and fission yeast Pif1, Pfh1). I especially enjoyed having ciliates in the lab, as I had ciliate envy during much of my time in Joe’s lab. I made a video of Oxytricha to show my son’s kindergarten class (they were unimpressed).

“Introductory sneeze”
In my early years as an independent investigator (~1980) when I was at the Fred Hutchinson Cancer Center in Seattle, I was scheduled to fly on a Sunday for a New Hampshire Gordon Conference, perhaps the Nucleic Acids meeting. An intestinal bug delayed my departure so I didn’t arrive until the Monday evening session. The session had already started when I entered the darkened room during the middle of Joe’s talk. I sat down in the back and soon gave one of my (in)famous sneezes. Joe stopped his talk and said, “I hear that Ginger has arrived.”

“Grateful”
I will always be grateful to Joe for imbuing me with his love of chromosomes. Although I used different organisms and diverse methods, I always worked on chromosomes. Quite frankly, I’ve never understood why anyone works on anything else...

I am also grateful to Joe for his daily example that it was possible to love your work for its own sake (as opposed to for fame or monetary gain). I feel incredibly lucky to have had the career of scientist-educator.

Finally, I am grateful for Joe’s example that the goal of science is not more of the same but rather quality and that good science is not possible without integrity.

Mary Lake Polan
Postdoctoral fellow, 1971-73
Katharine Dexter McCormick and Stanley McCormick Memorial Professor Emerita in the School of Medicine and Professor of Obstetrics & Gynecology, Stanford University

Here’s an idea that links clinical medicine to research many years ago in Joe’s lab. We were studying mitochondrial DNA and at the time, little was known about it. Now we understand that illnesses that genetic mutations in mitochondrial DNA are responsible for. With new IVF techniques, it is possible to correct those defects by constructing an embryo with the healthy oocyte derived from one person, the sperm from another and the mitochondria from a third person, thus resulting in a healthy baby.

Kathleen (Kathy) Karrer:
Graduate student, 1972-76
Professor Emerita, Marquette University, Department Biological Sciences

“Mentoring, palindromes, TN”
Jan Engberg’s lab in Denmark was working on the structure of the rDNA at the same time we were. On THE VERY DAY (or maybe the next day) that I did the experiment that convinced Joe of the palindromic structure (an experiment Joe suggested), he got a letter from Jan. Jan didn’t actually say what he was thinking, but he asked us a question that would be the counterexample. That is, did we get even numbers of restriction fragments with any of the enzymes we tested. So, it was pretty clear that he was onto the idea. I asked Joe what he thought we should do and he said he wanted to think about it overnight. When we met the next morning, I said that since the EM experiments were 1-day experiments that I thought we had to tell Jan everything we knew, otherwise he might think that we had stolen Jan’s idea. Joe said he had come to the same conclusion. He then (1) Assured me that he knew I had come up with the idea independently, and therefore my dissertation was safe and (2) That a scientist’s scientific reputation never depended on just one experiment. That was a great comfort to me, even though his words of wisdom were a bit more difficult to appreciate when you are talking about your first significant experiment.

There was one remaining issue, which was that our experiments were done on T. thermophila rDNA and Jan was working with the rDNA of T. pyriformis strain GL (the amicronucleate strain). There was always the possibility that there might be a strain difference, so we decided to repeat the experiment on rDNA from strain GL. Joe was in England visiting Mick Callan and he was about to leave to go to Jan’s lab. He called on the telephone (pre-email days) to ask if we had done the experiment. I was melting the DNA in the spectrophotometer at that moment, so I told him it would be an hour or so before I could do the snapback experiment. I told him I would send him a telegram with the results. We did the experiment, and indeed it was a palindrome. Rob Grainger told me that I couldn’t just send a regular telegram. I said, “You mean we should write a palindrome?” When Rob said yes, I reminded him that it had taken him two weeks to write the “Sex aware era waxes” palindrome and told him that if he wanted to send a palindrome, he had an hour to come up with one. Over lunch time he came up with the telegram we sent which said: TODAY DID GL-LG DI DYAD. P.S. SORRY ABOUT THE STICKY END. This was GREAT for the short amount of time Rob had, but a little obscure. GL, of course, was the strain of Tetrahymena. LG was an abbreviation for large, DI referred to the double stranded nature of DNA, and DYAD is the crystallographer’s term for the palindromic structure. Although Joe was expecting this specific piece of information, he told me later that it took him a couple hours to figure out what we were talking about. It took him a couple days to write the answer: DYAD IS NO CILIATED DETAIL I CONSIDAYD. P.S. SORRY ABOUT THE SPELLING.
In the early days of restriction enzyme analysis, there were no commercially available enzymes, so each individual lab had to isolate them from the bacteria. We wanted HindIII, so Art Landy’s lab at Brown sent us some of the bacteria on a plate. Joe came to me in the lab kind of sheepishly at about 4:30 one afternoon and said “The *Haemophilus* have arrived.” I replied, “I'll bet you want me to do something with them.” (He had to leave for the evening). I didn’t know anything about growing and maintaining bacteria, so I went up to see Ben Stark in the Altman lab on the 8th floor. They knew about growing fastidious bacteria and had the appropriate media, etc. Ben showed me how to grow the bacteria in liquid culture and freeze them in glycerol. A couple days later, Joe apparently remembered that he had left me with the *Haemophilus* and asked me where they were. I replied that they were frozen down, and he got this kind of panicky look on his face. I guess he thought I just put the plate in the freezer. I reassured him that I had grown them up first and frozen them in glycerol.

My first scientific meeting was in Gatlinburg Tennessee. I think it was five of us impoverished graduate students drove down in my Chevy Nova. Four or five of us shared a hotel room and we were basically living on graham crackers and bananas. Somehow Joe caught on to this and invited us all out to dinner so we would have a decent meal. That meeting was my first encounter with several prominent scientists. I told Joe that at the next meeting there were lots of people I knew I was supposed to recognize, but I didn’t know who was who. He told me that eventually I would reach the stage when there were lots of younger scientists that I thought I should recognize, but I wouldn’t know who was who.

**Craig Findly**  
Graduate Student: 1972-1978  
Postdoctoral fellow: 1980-1984  
Senior Research Scientist, University of Georgia College of Veterinary Medicine

Dr. Donald Poulson, who had served as Joe’s PhD advisor, was on my committee for my qualifying oral exams. I spent the week proceeding my exam memorizing “Classic Papers in Genetics”. On that cold, snowy January day, I did fine, and felt as if I were undergoing an initiation into a scientific lineage.

**Jean-David Rochaix**  
Postdoctoral fellow 1973-74  
Professor emeritus, Molecular Biology, University of Geneva, Switzerland

Dear Joe, I greatly enjoyed the on-line celebration of your official « retirement » and I was deeply moved by the souvenirs that came back from my marvelous period at Kline Tower almost 50 years ago.

I remember a Cell Biology Meeting in Miami in 1973 I believe. I was sitting next to you in a session in which someone presented EM sections of nuclei from Tetrahymena. At the end of this talk you turned to me and said: There is something intriguing in these nuclei. We must have a look at it. The following week you ordered Tetrahymena in your lab, the start of a new and incredibly successful story. A second event you might remember was in 1975 when you visited us in Geneva. At that time my wife Giustina and I had just moved to a new barely furnished apartment, in particular there was no decent dinner table. Thus, we had dinner sitting on the floor. Fortunately, the food was delicious and we spent an unforgettable evening together.

Best wishes,  
Jean-David
Harry Erba, M.D., Ph.D.
Department of Medicine Duke University; Director of the Leukemia Program and Director of
Phase I Development in Hematologic Malignancies.

“Joe eats DNA”
In the late 70s when the world was worried about all this cloning talk, Joe precipitated and ate
DNA. He was trying to allay the fears of the public about recombinant DNA technology by eating
it to show it was safe. This was reported in the New Haven Register.

“Testimonial for Dr Joseph G. Gall at the occasion of his retirement”:

I enjoyed listening to the stories from your many graduate students, postdoctoral fellows, and
colleagues from the span of your long and productive career. My story is different. You see,
they all sought you out as a mentor or collaborator. But you chose me. I only knew you as the
father of two of my high school friends, Barbie and Larry. My mother was a bookkeeper at
Lender's Bagel Bakery. My father was a truck driver, but usually unemployed. (I later learned
he had spent time in prison during my early childhood). I developed an interest in science and
biology during high school. Somehow, Barbie or Larry convinced you to let me work in your lab
during my senior year at North Haven High School. But why? Maybe you heard that my mother
bought me a microscope with her limited income, just as your mother did for you when you were
a young boy. But I still think you let me work in your lab at Kline Biology Tower to keep me from
“chasing after” your daughter Barbie. You really should have known that nothing would come of
my high school crush, because in the words of Tom Petty, “She likes horses”.

I worked with Kathy Karrer that first year. I learned how to isolate DNA, run cesium chloride
density gradients to prepare satellite DNA, and performed electron microscopy of DNA. It was
an amazing year and solidified my desire to pursue a career in molecular, cellular and
developmental biology. When I was accepted to Yale University (likely based on your kind
recommendation letter), you offered to let me continue working in the lab. I told you that I had to
work during my undergraduate years in order to make my tuition, room and board. You hired me
as a research assistant. I could not believe it…I did not have to work in the dining halls during
my undergraduate days.

My undergraduate years in your lab were inspiring. I learned so much. Sure, I made the 20x
SSC, I fed worms and slices of liver to the Xenopus and cleaned their tanks, I made culture
media, and I cleaned and autoclaved the labware. But I also worked with amazing graduate
students and postdoctoral fellows on their projects. I also learned how to work with proteins. I
made batches of restriction enzymes such as Bgl II, Eco RI, and Taq I. Those batches lasted
years! During the summer, I was your teaching assistant at Cold Spring Harbor Laboratories in
the Molecular Cytogenetics Course. While in your lab at Yale and at Cold Spring Harbor I met
so many incredible scientists: Mary Lou Pardue, Barbara McClintock, James Watson, Francis
Crick, Janet Rowley, Larry Kedes (with whom I would later do my PhD doctoral work at Stanford),
Herbert McGregor (with whom I would work at the University of Leicester on a fellowship the year
after I graduate from Yale), Samuel Lux, Thomas Cech, and so many others.

I started in a Medical Scientist Training Program at Stanford University in 1981. My intention was
to learn more about medicine so that I could apply what I had learned to treating human disease.
As I completed medical school, followed by an internship and residency in Internal Medicine, and
a fellowship in Hematology and Oncology, I discovered that I had a another passion, taking care of people. Ultimately, I did not believe I could pursue both of my passions, patient care and laboratory research, equally well. I then chose to leave my lab career behind. I have been a clinical investigator helping to develop novel therapies for people with leukemias and other myeloid neoplasms since 1996.

I have at times worried that I let you down, leaving the lab behind. But you need to know that you did not waste your time, choosing to mentor this high school student from North Haven. As the basic science curriculum of medical education is becoming more and more abbreviated, the complexity of the science leading to our medical advances has increased. My education that started in your lab in 1974 has allowed me to teach trainees about molecular biology techniques that form the basis of new discoveries and new assays in medicine. I am better able to work with scientists in the pharmaceutical industry in the development of novel therapies for patients because I can understand their language, and I can help them understand clinical issues. I share your love of the microscope. I use a microscope daily as I examine blood and marrow samples from my patients. I not only know where the condenser is, but I know how to focus the condenser. I order fluorescence in situ hybridization almost daily to rapidly identify gene fusions in leukemic blasts that allows me to select the most effective therapies for my patients, helping to improve their chance of survival. I enjoy telling my students, nurses and colleagues that I was fortunate to work with the man and woman who developed the technique.

In my role as Chair of an NCI-sponsored leukemia committee, I have been able to help advance the careers of women from around the country. I learned from your example that gender is an independent variable from determination, passion, and skill in science. I learned from you that women and men are equals in science and medicine. But your greatest legacy for me is with each and everyone of my patients. Every life that I help to extend and every person’s suffering that I can alleviate is because you chose to mentor that young boy from North Haven so many years ago.

And mine is just one of the many stories in your legacy. And no one believes for a second that you have any intention of retiring. Who chooses to retire from doing what they enjoy?

Robert (Rob) M. Grainger
Postdoctoral fellow 1974-76
Professor of Biology, University of Virginia

“Centrifuges and darkrooms”

Last week (written 8/12/20) I had to travel to Baltimore, the first trip out of Charlottesville in months, and while there I had a delightful socially distanced lunch with Joe and Diane in their backyard. Joe seems strikingly unchanged after all of these now many decades. Diane had her iPhone out and the attached image recorded the event; I can assure you, it was taken under appropriately socially distanced conditions.
I have not sent in any of the many memories and anecdotes I could contribute to the group—so many great ones, some of which I was involved in, have already been passed along, but I have three moments in the lab that I would like to mention. It was rare, very rare, when Joe would make anything approaching an error or miscalculation, but it did happen……

The first of the three occurred when we were all in the lab working away one day and Joe was there too, balancing the pH on a new batch of CsCl over at the pH meter. My recollection is that he made a comment about having to add a lot more base (or acid) than usual, but he kept at it until it became ridiculous, potentially diluting many hundreds of dollars of CsCl beyond usability, when he realized that the pH meter was set on the 10X scale. I could be misremembering but I really think I heard a four-letter word burst out of his mouth, a very rare event indeed. But how many senior PI's make up their own CsCl solutions? I daresay not many. What a pleasure to all work together in the lab.

My projects in grad school focused on using the ultracentrifuge and fractionating RNA and proteins by density labeling—but I guess most of us were very familiar with ultracentrifuges back then. Whatever happened to them anyway? One day during one of my runs I was checking the machine in the outer area adjacent to the darkroom and it looked like it had turned off, but it had just been running at top speed as it should have been a short while before. This seemed like an appropriate moment to call in Joe because this just didn’t seem right. So, he came in and also thinking the centrifuge had gone off for some reason, opened the top of the centrifuge and it looked indeed like the rotor had stopped. Joe, confident that it was safe to remove the rotor, reached down to remove it but couldn’t get his hands under the rotor. It was as if there were a sheet of metal interfering. Indeed, there was: rotor buckets still spinning at 55K rpm. The rotor was still running and of course the buckets are not visible at these speeds. I guess we pulled the plug and thanked our lucky stars that the event was not more catastrophic, as centrifuge events can be (and at least in my history, I had seen a few very dramatic examples). But thankfully in this case we were saved by the speed and angular momentum of the spinning rotor. On the positive side then, actually a lesson in physics principles.

The last event was quite memorable, occurring on a Saturday morning I believe when at least a few of us (maybe Rob Steele?) were in the lab. Quieter than it usually was during the week, but we heard what we thought was a familiar thumping coming from above: the folks in Alan Garen’s lab banging their fly bottles against the benches to empty them. But the drumbeat went on and on and we decided that this didn’t seem right. Walking around from our offices to the darkroom area we noticed that the darkroom door was vibrating rather dramatically, exactly in concert, if you will, with the sound that we had heard. Being such sharp folks as we were, it finally dawned on us that something was amiss and indeed discovered that Joe had locked himself in the inner sanctum of the darkroom and was beating on the inner door to get our attention. Well, if he had only screamed or banged in a frantic way, we might have figured this out much sooner but in his inimitable manner, he just calmly and so rhythmically beat on the door that we didn’t appreciate that there was indeed a big problem in the darkroom. But absolutely characteristic of Joe’s ever calm demeanor. [One version of this story, as reported by Brian Kay, is that Joe’s banging was calm and rhythmic because it was in Morse code.]
Martha A. Truett  
Lab technician, 1974-76  
Retired biotech scientist

“My Time in Joe Gall’s Lab at Yale: A lab technician’s tale”

I think the following couple of anecdotes are good ones from my time in Joe’s lab (1974-76). I think it helps to explain a bit about my background first though. My husband, Dave White, and I moved to New Haven after our “sojourn” in the Pine Barrens of NJ so that I could return to work in the lab, decide about taking GREs and applying to a PhD program. My undergrad degree was in Chemistry and although I’d taken a lot of Math and Physics in addition to the Chemistry, I hadn’t taken a single Biology course. I had worked in a Biochemistry & Biophysics Research Lab at Harvard Med School for 3 yrs. while Dave finished his PhD at MIT. I interviewed for several lab positions at Yale in the Biology Dept and Med School and had an offer at the Med School working on a similar project to the one I’d been on at Harvard, but I also got an offer from Joe and wanted to try something different. Joe’s enthusiasm for the science was very appealing and so I took the position he offered. That decision set me on the course that led to my return to school in Biology instead of Chemistry.

My young daughter Stacey often came into the lab with me, which was helpful, and Joe never made a big deal of that. He was endlessly patient with Stacey’s questions. [comment from Ginger: before Stacey, Sooze Hodgson’s dog Britches came to the lab, staying in Joe’s outer office.] Liz (Blackburn), Dave, and I reminisced about the time Stacey got head lice. When informed of this event, Joe immediately pulled a book off one of his shelves and showed us a monograph of a louse. In fact, it was Robert Hooke’s drawing of a human louse (and a flea, for good measure) from the Micrographia. Typical Joe — ever the enthusiastic field biologist, microscopist, and historian. He then gave us a quickie overview of the life cycle and the fact that head lice are different from pubic lice - a fascinating piece of info. And then he urged us to take Stace home and start the shampoo and laundry cycle...as a result of his instruction, delivered calmly as always but with some urgency, and with more details from the local pharmacy, we got things under control and no one else got lice!

Dave too remembers what a great teacher Joe was and how supportive he was of all his students, postdocs and techs, especially of the many women in his lab at a time when female scientists in the hard sciences had a much harder time of it than our male colleagues. Joe turned out to be a mentor not only to me but also to Dave, which is pretty remarkable. I learned so much from him - technical lab techniques and a lot of basic biology as well as how to run a large lab group.

In Joe’s lab, I worked on isolating *Tetrahymena* macronuclear rDNA with the goal of identifying the mechanism of its replication. Once I’d isolated the appropriate fraction that I hoped contained replicating molecules, the work turned to the electron microscope, which I hadn’t had experience with before this project. Joe and I spent a good bit of time on the instrument with him teaching and me learning how to use the instrument, how to prepare my samples and how to scan for molecules that were, hopefully, replicating. Once I’d mastered the instrument, I spent a lot of time alone (hours) scanning for replicating molecules. Finally, I spotted one, then another and then more. I immediately ran to get Joe to show him and get his confirmation that this was indeed what we’d been looking for. He dropped what he’d been doing and followed me back to the EM room and was gleeful when he saw what I’d spotted - replicating rDNA molecules! It was so typical of him to be thrilled with any and all new discoveries and his enthusiasm for the science was catching.
Before we finally found replicating molecules, I spent a LOT of time getting my *Tetrahymena* to conjugate so I could isolate the appropriate molecules. This went along well until, all of a sudden, my *Tetrahymena* stopped conjugating. Joe and I scratched our heads over the problem - I’d already tried different lots of media to no avail. In going over the timing, we realized that some time after Rob Granger started growing *Physarum* in the same flasks I was using, the *Tetrahymena* had stopped cooperating. Eventually we figured out that even with thorough washing and autoclaving, there must still be enough residue from the *Physarum* inside the flasks and that was inhibiting conjugation. I ordered new flasks to be used exclusively for *Tetrahymena* and the problem was resolved! It was a real teaser and Joe just kept calmly asking questions, I kept trying things, and eventually we sorted it out. Both Joe and I were surprised, as was Rob!

There is one other episode that stands out but only indirectly had to do with my project. I'll mention it since it shows how calmly Joe handled all lab mishaps...

I had to distill phenol periodically for everyone’s use. The process usually took 2 days and I’d turn off the still and close the hood overnight. One morning when this was in process, I stepped off the elevator in Kline Tower and immediately KNEW that I must not have turned the still off completely overnight….the phenol smell was incredible! I rushed into the lab and shut it off but couldn’t open the windows - they were locked. I hurried down to the main office to request someone to come up immediately to unlock the windows and by then Joe had come in. He too knew right away what had happened and I filled him in on the window situation. He got a heavy-duty gas mask and brought it to me and told me to put it on and spend as little time in the lab as possible until we could get the windows open. He was calm and although it was a bad situation, his assurances that we’d get it sorted calmed me down. The cleanup was a bitch but, again, Joe was very methodical about waiting until the fumes cleared before starting cleanup and wearing heavy gloves etc. - just reminding me to be careful. Things were in much better shape by the time most of the grad students and postdocs came in to the lab (they tended to work late into the night and come in later than I did in the morning) and Joe was really good about taking the position that “these things happen” and we’d dealt with it.

In that same vein, I was also responsible for oversight and maintenance of all our equipment and there was a rotor/ultracentrifuge episode on my watch too, although, thankfully, not with the Model E. A tube broke and the rotor unbalanced and came off the spindle - the noise was really loud and the centrifuge moved too. I got the repair person right on it and although we lost the rotor, the centrifuge was OK once the spindle was replaced. Of course, Joe was around because he almost always was - and, once again, he took the calm view that “it happens” sometimes and we’d dealt with it and no one was hurt so it was all OK. That calm steady approach was so typical and kept things running much more smoothly than they might have otherwise. I always appreciated that and tried to take the same approach in my subsequent positions, projects and labs.

To say that Joe was a wonderful mentor in all ways, is a gross understatement. He impacted the way I’ve tried to approach both the science and the human interactions. I’m not sure I fully appreciated this until now as I reflect on my time in Joe’s lab. Joe’s approach to science was filled with wonder and enthusiasm that was contagious. He also had a lot of female grad students and postdocs during my time in his lab – something that was striking to me, and also very encouraging to someone who was trying to commit to returning to school after what would be a 9-yr. hiatus. When I started in Joe’s lab, I had a 3yr old, a husband, a German Shepherd and a mortgage! Certainly not typical for grad students, but Joe was encouraging and supportive. I had to decide between taking the GREs in Chemistry and Biology, which reflected my changing scientific interests. When I decided, with some trepidation, to go for Biology, Joe suggested...
several pretty basic Developmental and Cell Biology texts; he also encouraged me to audit Joel Rosenbaum’s Cell Biology course. He, along with Ginger [Zakian], Pat [Pukkila] and Sharyn [Endow], encouraged me to attend and participate in the weekly noontime informal seminars. I eventually became comfortable enough to select and present a paper myself. I was also struck by the fact that Joe’s technicians seemed to always go on from his lab to get PhDs or MDs; how could I do any less! Joe was so supportive and encouraging of my decision to go to grad school. He helped me stay on course for and during graduate school, as graduate school was challenging for me, owing to my having a young daughter and a long commute.

Robert (Rob) E. Steele:
Graduate student Peter Rae’s lab (next door to Joe’s), and honorary Gall lab member, 1974-80
Professor, Department Biological Chemistry, University of California, Irvine

Although I was not a member of Joe’s lab, I will always be grateful for how he and the members of his lab made everyone in Peter Rae’s lab feel included in the 4 th floor family. I have so many good memories of those days, and how they made me the scientist and teacher that I am today. Two memories stand out for me. First, were our lunches on the top floor of KBT. It is so remarkable how inclusive they were. It didn’t matter whether you were a senior professor like Joe, sabbatical scientists like John and Bertie Preer, or a beginning graduate student like me. Everyone was welcome at the table. And the conversations were great. I recall one in which Joe opined that sequencing an entire genome would be a big waste of time and money. Oh well, everyone is allowed to be wrong once in a while. The second memory is of evening gatherings at Joe’s house for desert with seminar speakers. While free food is always welcome for a graduate student, even more important were the opportunities that these gatherings provided for students to meet with outstanding scientists. Finally, I want to congratulate you Joe on still doing science with your own hands at 92. You are an inspiration to us all. Every time I do an experiment myself (which I’m still doing at the young age of 67), I think of you.

P.S. I hope there aren’t any split infinitives in this message. If there are, Joe will surely find them, as he did with my thesis.

“Grants vs grant proposals”
Joe once mentioned to Peter (Rae) about a grant he was writing. Peter’s reply: “Joe, you write grants, I write grant proposals.”

Elizabeth (Liz) Blackburn
Postdoctoral fellow 1975-77
Professor Emeritus, Biochemistry and Biophysics, University California San Francisco

Joe emphasized: Always use the best organism as the experimental system to answer a scientific biological question
Tetrahymena: for rDNA amplification (and telomeres and replication)
When I said I wanted to study chromosome DNA ends, Joe quite firmly encouraged me to use Tetrahymena rather than Oxytricha. (I had considered using Oxytricha because of Oxytricha’s short linear macronuclear DNA molecules). He argued for Tetrahymena because it was much easier to cultivate than Oxytricha, and also had the large copy number of uniform rDNA linear molecules.

Joe was: Early adopter of new technologies to be used in biology research: my choice of Joe’s lab was partly influenced, in addition to his excellent reputation, by reading his paper on (or was
it hearing about?) his sequencing work on *Drosophila* satellite simple sequence DNA, which showed he was an early adopter - and adapter - of the emerging techniques for sequencing DNA.

Joe’s interactions with people: Kindness and encouraging mentor: Very encouraging about applying for Assistant Professor positions.

I had given a practice job talk in which I crammed far too much material and the talk did not go well. After the talk, when I was in tears of despair in my shared office, Joe came by and said something kind and encouraging.

Mentoring: Supportive and good mentor of his lab people's careers.

One day some of us were in the lab when Joe came bounding in and gleefully announced “Mary Lou Pardue got tenure at MIT!” I said (I can’t recall if I said it aloud); “Of course she should have.” I then had little appreciation for how difficult it was for women scientists.

Conduct as a leader of a research lab group: lab atmosphere was congenial and supportive; people in lab interacted well with Joe and with each other. Cohesiveness was engendered by the regular weekday lunches with all lab members sitting at a shared round table or adjoining tables in the top floor cafeteria of Kline Biology Tower.

Joe created a sort of extended "lab family" which included the lab group of Peter Rae, whose lab members were as close as the Gall lab members and the two lab member groups intermingled just as much with each other as with their own labs.

Joe’s integrity: Straight dealing regarding science: Once Joe said he would never accept a gift from a lab equipment vendor, even as little as accepting a lunch with a vendor, so there was no question of compromising his ability to be objective about buying lab equipment.

Joe said he mostly turned down invitations to write articles that were review articles, as he said one’s time was better spent on original research articles themselves.

In the late 70s when the world was worried about all this cloning talk, Joe precipitated and ate DNA. He was trying to allay the fears of the public about recombinant DNA technology by eating it to show it was safe. This was reported in the New Haven Register.

**Meng-Chao Yao**  
Postdoctoral fellow 1975-78  
Professor emeritus and head Institute of Molecular Biology, Academia Sinica, Taiwan

I have learned some of my most important research lessons during the years in New Haven. Two things stick in my mind: Joe pipetting on the bench; we all eating lunch together daily with Joe on the top floor cafeteria. I love that culture of researchers enjoying science and miss it when I failed to emulate it in my lab at times.

**Brian Kay**  
Graduate Student 1975-80  
Emeritus Professor, University of Illinois at Chicago

“Recollections about Joe, 4th floor colleagues, and graduate school”
Saturdays
It was a pleasure to got to lab on Saturdays because Joe was in the lab too. He could often be found in the small room next to his office in Kline Tower, where he would be preparing lampbrush chromosomes and viewing them with his large, fancy microscope. (It was a badge of honor, if he trusted you enough to use his microscope under his supervision.) At noon, everyone would assemble in the small conference/lunchroom down the hall and eat lunch together. Joe would sit at the head of the table, with his brown bag lunch from home, periodically wiping away the homemade yogurt that stuck to his mustache or the tip of his nose. We would talk about science, politics, arts, and a variety of other topics. It was great bonding experience.

Model E
One of the mainstay techniques in the lab was analytical ultra-centrifugation. The Model E centrifuge was something to be loved and feared. Joe was one of the first to own such device (low serial number). Joe would teach each person individually how to assemble and seal the cell with quartz windows, put it in the machine, and get it up to speed. The machine sounded like a jet engine at top speed. I wouldn't sleep well during the three-day run, worried about the cell leaking and machine exploding.

On one Saturday, no one could find Joe. We looked everywhere. Rob Grainger later found him locked for several hours in the autoradiography room. The door was jammed shut, so Joe started tapping out Morse code on the door. But because it was adjacent to the Model E, the tapping sound was drowned out by the scream of the Model E.

On the following Monday, Joe got stuck in the revolving door of Kline Tower. The joke among the graduate students was that Joe was jinxed and no one should get on the elevator with him.

Snowstorms
In February 1979, a heavy snowstorm went through Connecticut, dumping over 20 inches of snow. Governor Ella Grasso closed all the roads and called in the National Guard to deal with this emergency. At the end of the day, my wife, Helen, who was in medical school at the time, walked to Kline Tower from Cedar Street covered with snow. As I packed up to head to our house, Joe asked if he could stay overnight with us as he could not drive home to Hamden. We walked a few blocks to our place and he joined us for dinner. Later in the evening, when it was time to retire, Joe came to the kitchen and asked if he could have some milk and cookies. He said they would help him sleep better.

A series of unfortunate events
One afternoon, Joe was working in the small lab next to his office. He was setting up some in situ hybridizations for lampbrush chromosome using some 3H nick-translated DNA as probe and was at the stage of sealing the coverslips on the glass slides with molten paraffin. He put the metal tray of solid wax onto a stand over a Bunsen burner. While waiting for the wax to heat up and melt, he ventured into the lab to retrieve something. While there, he observes a graduate student from another lab using the pH meter to measure the pH of a 10 M solution of NaOH. Joe gets mildly upset and becomes distracted. Meanwhile, the cytology room fills with black smoke. Joe and Peter rush to the room to investigate, and while Peter tries to open the window to let out the billowing smoke, the window breaks. Thankfully, that was the extent of the mishap and the fire department was not called. The graduate students all kept a low profile for the rest of the day.

Madam, I'm Adam
With the discovery by Kathy [Karrer] that the ribosomal DNA in the macronucleus of Tetrahymena pyriformis was an inverted repeat, the lab went crazy over palindromes. A contest was started to see who could come up with the best palindromes. The list on a hallway blackboard grew every
day. It started with the usual suspects, "Able was I ere I saw Elba,"Was it a cat I saw," and "Never odd or even." With time, there were very many entries. (Remember, this was pre-Google days.) The winner was entered by Rob Grainger (or Little Kathy): "Sex at noon taxes."

**Five second rule**
During the summer months, some of the graduate students would grab dinner together in New Haven and return to the lab for evening work. Our routine was to get a slice of pizza and then head to a creamery for ice cream cones. One day on our walk back to Kline Tower, the scoop of ice cream fell off of Rob Steele's cone onto the sidewalk. We immediately stopped in our tracks. We expressed our condolences and offered to return to the creamery to get a replacement, but Rob picked up the cone, wiped the grass and dirt off on his cargo pants, repositioned it on the cone and proceeded to lick.

**Scarred for life**
To know Peter Rae was to realize he had a wicked sense of humor. He was always quick with a pun, no matter how bad or corny. I never lived it down, when I wrote a term paper about this new technique of copying mRNA into DNA and used "complimentary DNA" throughout the typed document. My bad!!

**Rorschach test**
Liz [Blackburn] joined the lab about the same time I did in the summer of 1975. She set out to sequence the ends of the extrachromosomal rDNA of *Tetrahymena* using the techniques she utilized for her Ph.D. work in Dr. Sanger's group at the MRC in the UK. Since Joe's lab didn't have the high-voltage paper electrophoresis tanks needed for DNA sequencing, she used the tanks in Dieter Soll's lab on the 2nd floor of Kline Tower. She exposed a large (40 x 40 cm) sheet to x-ray film. I remember her coming out of the 4th floor darkroom, with the developed film still dripping wet and clipped in a stainless-steel frame, showing everyone in the hallway the arc of repeating spots. We were all excited by this simple, yet unexpected pattern of dark spots on the clear film. Long live C4A2!

**Purifying genes is hard work**
To study rDNA, we would feed 32P phosphate to cells, purify ribosomes by sucrose gradients, and then extract the rRNA. Separately, one would try several different centrifugation runs, first with the Model E and then later preparative, with CsCl containing various metals (or not), collecting fractions, immobilizing them on filter, hybridizing the filers with the radioactive rRNA, followed by scintillation counting. Nice, clean peaks used to make us happy, as we were ISOLATING GENES! How times have changed, and for the better!!

**What's in a name?**
A guest joined us at one of the large round tables in the Kline Tower cafeteria for lunch. When he/she was introduced to the lab members at the table, we were each introduced by our first name, except for Joe, who was introduced as "Dr. Gall". We all laughed, and I think I said that his full name was “Dr. Gall Dr. Gall.”

Afterward, I asked if I could call him by his first name. Joe replied yes. I then shared his willingness to the other students in the lab and we made an informal pact to address him by his first name.

Speaking of names, I bet we are the only lab that knows the middle name of their advisor:
Self-control
Joe was always thinking of ways to improve how to prepare lampbrush chromosome spreads for cytological experiments. Over a period of time, he came up with the idea of modifying the swinging bucket rotor so that it would accept a swinging tray for a glass slide. He worked with a machinist in the Department to design and fabricate a tray from stainless steel. The big day finally came when it would be tested. Joe and the machinist replaced the four buckets of the rotor with two new trays and started the large, refrigerated, Sorvall centrifuge. Everyone held their breath. The machine started and hummed when it reached the speed 1K rpm. No problem! Smiles all around. At this point, guests arrived for an office appointment and Joe took them away. I watched as the machinist adjusted the speed dial upward to 2K, then to 3 K, and when it reached 5K, there was a huge noise - the hinge on the tray had broken and metal pieces were flying around inside the sealed rotor. The noise was sickeningly horrendous. Joe’s face appeared at the rectangular glass window inset in the closed door that separated the lab from his office. He instantly knew the fate of his design. He grimaced for a moment, and then returned his attention to his guest.

Things I don’t miss from graduate school
• typewriters, white-out, Eaton’s corratable bond paper
• letterset and cannibalizing (A-E) letters
• dark rooms, dodging and burning, resin-coated paper,
• CsCl-EtBr gradients for plasmid preps
• glass pipettes, Lang-Levy pipettes
• 32P and nick-translation
• TCA precipitation, round filters, scintillation

Ed Stephenson
Graduate student 1975-1981
Professor of Biological Sciences Emeritus, University of Alabama

During my senior year in college, 1974-75, I asked my undergraduate research mentor for advice on graduate programs. He mentioned several, including Yale, and said that it would be great if I could work with Joe Gall, whose work he admired. He added however "I’m not sure that he accepts males into his lab.” He may have been joking, but his concern had some basis in fact: in the preceding five-year period a series of wonderful and revolutionary papers had come from Joe’s lab, almost all of them authored by women.

Joe’s support for female scientists is of course one of his greatest legacies, but it was based not on favoritism but on his underlying decency and his desire to treat everybody equally. My undergraduate adviser knew Joe only from his work, not personally. I’m sure if they had been better acquainted, he’d have known that Joe would have never penalized me for being male.

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When I arrived in the lab in the spring of 1976 almost the entire lab was working on Tetrahymena, and my first projects were to clone fragments of the rDNA, and later the 5S gene. I stalled out in trying to characterize the Tetrahymena histone genes, however. During my first couple of years in the lab, newts and lampbrush chromosomes came back in, and Joe suggested that I assume a project begun by Steve Case, a postdoc who had successfully cloned a newt H4 histone gene. Steve was leaving to begin a faculty position and I was lucky to have inherited this toehold in the
project, a same-species probe. This allowed Harry Erba and me to clone and characterize the newt histone gene cluster, a standard cluster with the genes for each of the 5 histones, repeated several hundred times in the genome.

The goal of the histone gene project was, of course, to generate probes that could be used to hybridize to lampbrush chromosomes. With the same goal in mind, Giuseppina Barsacchi and Manuel Diaz had decided to pull random clones from a library, hybridize them to LBCs and follow up on any that looked interesting. In this way, they discovered the satellite sequence that is transcribed from the sphere locus, named by Joe much earlier for the unusual balls that are associated with the loops.

When I used the extreme ends of the histone gene cluster as probes in a Southern blot, I discovered that these cluster flanking sequences hybridized strongly to a satellite sequence with the same repeat length as that of the sphere locus satellite sequence. In a remarkable convergence, we discovered that both the satellite sequence and the histone gene clusters are present at the sphere loci: each histone gene cluster is flanked by and separated from the neighboring cluster by tens of kilobases of satellite sequence. Oddly the satellite sequence, the histone coding sequences, and the histone cluster non-coding sequences are all transcribed from the sphere loci of lampbrush chromosomes.

***

One of my favorite memories from Joe’s lab is a newt collecting trip. The picture here is not my picture, or even a picture from that trip, but it’s representative of our trip: Joe in his waders scooping up newts from the bottom of a crystal-clear pond in Massachusetts. As I remember it (and enough time has gone by that my memory is undoubtedly defective in one or more respects), we drove to a Massachusetts state park (what was the name of that park?) in his Volvo on a Saturday or Sunday, on a clear perfect New England fall day. I remember collecting many newts, re-stocking the newt refrigerator for many future lampbrush chromosome and DNA preps. Thanks, Joe, for letting me be a field biologist for once in my life.

***

My time in the lab represented the first applications of restriction enzyme analysis and DNA cloning. Restriction enzymes and other enzymes were not commercially available at the time – if you needed an enzyme you sponged it from somebody who had some, made it yourself or did without. Harry Erba, working in the lab first as a high school student and later as a Yale undergraduate, became a master at making enzymes. His preparation of BglII was especially successful: when it became commercially available, we calculated that, at its retail price, we had about $75,000 of BglII in the freezer.

***

I have a vivid memory of Liz wandering the 4th floor hallway with an X-ray film, still wet from the wash tank, explaining to anybody who would listen the experiment that showed that Tetrahymena
telomeres are composed of the sequence C4A2. I wish I could claim that I understood the significance of this result and what it would lead to.

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A recollection of the late Pat Pukkila. Pat and I didn’t overlap in the lab; I think she graduated in the fall preceding my joining the lab in the spring. However, a few years later during her postdoc she visited Yale, and Joe had her do the lab circuit, talking to everybody about their projects. I was in the late stages of trying to isolate and characterize the *Tetrahymena* histone genes, an exercise that had frustrated me for over a year, first because the *Drosophila* and sea urchin probes that were available were too divergent, and later because the clones that I had isolated didn’t seem to correspond to what was in the *Tetrahymena* genome. The explanation for the latter was a horrible and embarrassing artifact, but I had failed to recognize it for several months. During my conversation with Pat, a lightbulb came on and I finally figured out the reason for my crazy results. I soon moved on to a project that became my dissertation. I was always grateful to Pat for her accidental role in helping me to move along, and several years later during a visit to UNC, I was able to finally thank her for it.

Martha Wild
Graduate Student, 1976-81
Homework Tutor, City of San Diego (semi-retired from many years in biotech)

“Humanitarianism”
Joe was particularly kind to scientists from many other countries. One of the reasons his lab was so international was that he had so many people from other countries who he found positions for or who came for sabbatical there. As you all are aware since many of these people are our friends and colleagues, some were dissidents or defectors, persona non grata in their own countries. But his aid to others did not stop there. Often if he bought a new piece of equipment, he would find a way to ship an old piece to a deserving lab that had none.

One evening as I left, I found Joe working on a paper. I was curious what paper it was, thinking it was a new one of his. He was actually doing a pretty extensive rewrite on a paper for one of the journals he was an editor for. Papers would be sent to the journal from other countries, often behind the Iron Curtain, or in developing nations. He would read these and if he found their research compelling, but their command of English lacking, he would take the time to make all the necessary corrections to be able to publish the paper, rather than reject it out of hand. I am sure many laboratories around the world who otherwise would have not received recognition for their work benefited from his kindness, and the field of cytology was advanced for all.

“Dipteran rDNA”
Peter Rae’s lab worked on ribosomal DNA as well, but they worked a lot on *Drosophila*. They were also interested in other Diptera. One day there was a bee on the ledge outside one of the windows, or at least, it looked like a bee. Joe told Peter that it was actually a robber fly, as some robber flies are bee mimics, and they sit high on ledges and then swoop out and grab unsuspecting insects in flight. Peter decided to catch it to examine its rDNA. Unfortunately, a short time later he returned and angrily told Joe that it was indeed a bee and had stung him. I was pretty surprised that Joe got this wrong, as he seemed to know so many details about the natural world, even showing us all one evening how to determine the temperature by the chirps per minute of the crickets.

“A place for physics in chromosome research”
While I was in the lab about 1980 or so, Joe and others in the lab were doing a lot of research using hybridization to lampbrush chromosome loops. One of the hurdles to this research was the generation of the lampbrush chromosome loop slides, and Joe sought a way to make more slides quickly. In order to make the slides originally, Joe had been taping single slides on the top of tube holders in centrifuge buckets. Slides had wells in which lampbrush loop material from oocytes had been gently deposited on a slightly viscous solution, and by spinning them on the buckets the material settled nicely to the bottom and splayed the loops out for subsequent hybridization and visualization. But it was a long process, and only four slides could be completed at a time. Joe came up with the idea of creating his own centrifuge rotor "bucket", and he enlisted the aid of one of the skilled mechanical shop guys that Yale had on staff. Together they designed a device that could be put on the swinging bucket holders of a swinging bucket centrifuge rotor. Each "bucket" had four metal pegs hanging from a platform at the top that engaged the rotor knobs all attached to a platform on the bottom. Loop slides could then be stacked on top of each other between the metal pegs in the platforms. I think about 10 slides could be stacked in each "bucket" and so the ability to produce slides would be increased about 10-fold. I remember being present at the maiden voyage of the rotor. I was a little nervous so I watched looking in through the hall door. Joe stood at the centrifuge and slowly turned up the speed. Suddenly all hell broke loose, with a grating, ripping, metal on metal gouging sound that brought people running. Joe just stood there, gripping the centrifuge. The buckets had broken apart. However, though it was loud and the centrifuge was badly gouged, it was not destroyed. Joe realized that he hadn't properly figured out the forces on the four pegs at speed, and it turned out that the tensile strength of the pegs was insufficient for the force involved. Undaunted, he and the shop guy redesigned the "bucket" to account for the tensile strength, and the next iteration worked, and was a great help to making loop slides.

Elizabeth (Liz) R. Gavis  
Undergraduate research student, 1981-2  
Professor of Molecular Biology, Princeton University

Doing my senior thesis research in Joe’s lab was truly one of the highlights of my undergraduate years at Yale. I still don’t know why Joe had faith in me (sadly, I missed out on taking Cell Biology from him since he was on sabbatical) but his trust in my ability to succeed gave me the confidence I needed to pursue a research career. Even then I realized how incredibly special it was to share Joe’s bench in his little personal lab room and to learn how to dip slides in photographic emulsion from the master. Joe’s sheer excitement when I showed him my results was more rewarding than any “A” I received on an exam. The comraderie in the lab sucked me in further and I made lasting friends as well. I’m not sure my roommates ever understood why I happily made the trek up science hill. Thank you Joe for taking me under your wing!

Celeste Berg  
Graduate student 1982-86  
Professor Genome Sciences, University of Washington

“Ethanol and lampbrush chromosomes”
As a graduate student with Joe, I worked on *Tetrahymena* rDNA replication by injecting DNA into *Xenopus* eggs. Although I never had the opportunity to make lampbrush chromosomes myself, I do recall the infamous story about the centrifuge and what an impression it had made on the lab, mainly because several people independently described the incident to me on my first day there.
After graduating, Joe generously let me stay in his lab for several months before spending the summer at Woods Hole and then starting my postdoc in Allan Spradling’s lab. During that time, I worked on a project with Joe and Mick Callan to analyze the distribution of 5S DNA on *Xenopus laevis* lampbrush chromosomes. Mick and Joe prepared the chromosomes, and I made the 3H-labelled probes and hybridized them to the samples they had prepared. When Joe was analyzing the results, he noticed something peculiar. Half of the samples had a much stronger signal than the other half.

Joe called me into his office and asked if I had treated the slides differently in any way. I replied “No, I hybridized them all under the same conditions using the same probes.” Joe became really excited because the distinguishing feature about the slides with the stronger signal was that those slides had been stored in ethanol while he prepared more samples for the experiment. Fortuitously, Joe had discovered that ethanol treatment enhances the hybridization process!

My lab now includes an ethanol-treatment step in all of our *in situ* protocols, both for chromosomes and tissues.

**Alison B Singer PhD, MHS:**

I worked as a research technician in Joe’s lab from 2007 – 2009. I would often return to lab for visits during the midst of graduate school because it still felt like a home to me. Joe enthusiastically set aside his time to catch up about life. One year for my birthday he even invited me back to the lab for a celebration (with a cake, of course). Joe’s kindness impacts everyone around him. He has a way of providing advice that is full of understanding and without judgement. Thank you, Joe, for all your support and guidance over the past 13 years! Best wishes for a happy retirement!"

Best wishes,
-Alison

**COLLEAGUES:**

**Joel Rosenbaum**
Professor Yale University

When the first autoradiographs from the hybridization of labeled rRNA came through following hybridization in situ with Xenopus oocyte nuclei. Joe G came running down the hall "come see this, everyone!" (Pardue and Gall, PNAS).

Susan Gerbi (grad student), was always one week ahead of everyone else with the recent literature, even if it was a pre-print and not yet in the library. One day at lunch I made up a report (phony) that she had NOT seen. After lunch she immediately went down to the library to check (the non-existent paper) it out. After some serious searching she came up and asked me about it and I had to admit I was pulling her chain.

**Thoru Pederson**
Professor Biochemistry and Molecular Biology, University of Massachusetts

Others have touched on this Joe but I think it can never be emphasized enough:
You always displayed an impressive, I would say remarkable, capacity to choose biological material that was ideal for the problem at hand. These included viviparous snails when you studied centrioles in the late 1950s, your beloved lampbrush chromosomes of course, the beguiling genomic gymnastics of rDNA in Tetrahymena and Xenopus oocytes, and so many other examples.

Some scientists adhere to one system or organism and do fine things. But you knew the very creatures and cells you could most profitably engage. Molecular, cell and developmental biology are much the richer for this skill of yours, a key part of your unique signature and legacy, adding to the many other dimensions of our admiration and affection.

Sandra Wolin
Head, Section on Noncoding RNAs and RNPs; NIH National Cancer Institute

I was an M.D.-Ph.D. student at Yale University from 1978 to 1985, carrying out my Ph.D. work in Joan Steitz’s laboratory. Joe was a member of my thesis committee. Celeste Berg was a member of my Ph.D. cohort, and Joan served on her thesis committee. When Joe and Celeste moved to the Carnegie Institution in 1983, Joe graciously agreed to continue as member of my committee. Every six months or so, Joe and Celeste would take the train up to New Haven, and Celeste and I would hold our committee meetings back to back. Joe’s input was invaluable, and his philosophy of choosing the best organism for the biological question at hand has influenced my science to this day.

As an RNA cell biologist, I have had the pleasure of continuing to interact with Joe, and I have benefited from his mentorship throughout my career. I was incredibly honored when Joe invited me to the Carnegie to give a seminar in December 2018. It was a wonderful visit, and I will always treasure the photograph of the two of us that was taken that day.

Thank you, Joe, for all that you have done, and also for just being you.

Sandy

Xin Chen: Professor Department of Biology, Johns Hopkins University

From the neighboring JHU Biology department to Carnegie, many of us including myself, consider ourselves extended trainees of Joe. For example, Joe is the driving force behind the recent collaboration between our labs. Before working with Joe, we had struggled for a couple of years trying to use super resolution microscopy methods, such as PALM and STORM, to visualize histone incorporation patterns during DNA replication in fly germline stem cells. We kept encountering all kinds of technical issues which prevented us from reaching any confident conclusion. Joe was very insightful to point out that a more direct visualization microscopy method, STED, would be sufficient to give us a clear image. We very much appreciate the generosity of Joe for his time and continuous support! A graduate student from my lab, Matthew Wooten, soon teamed up with a very talented postdoc Zehra Nizami from Joe’s lab. Together, they used the STED microscope at Carnegie to obtain beautiful chromatin fiber images. This
collaboration led to very recent publications of a research article (in 2019) and a method paper (in 2020). This chromatin fiber coupled with super resolution microscopy now becomes a standard method in my lab (and hopefully in other research labs soon) to study various chromatin biology questions using small number of cells. We just cannot thank Joe enough for his enthusiasm and inspiration! His eyes are always wide open to new ideas and he is always so curious about looking into "odd" observations. I am truly inspired!

I am also sure that all my colleagues at the Biology Department feel the same way, and so do our graduate students— Joe co-taught the graduate core course on microscopes for many years! He served and is still serving in numerous thesis committees and GBO committees for our graduate students! Thank you, Joe, and happy retirement! We look forward for many more discussions with you on various topics!

Valerie Butler  
BioEYES Program Manager, Carnegie Institution for Science, Embryology

While many know of Joe's outstanding accomplishments and advocacy on behalf of female scientists, he has also been an incredible supporter of K-12 teacher and student education in Baltimore. Every year as BioEYES hosts teacher training workshops and brings students to the Department of Embryology to meet scientists, Joe has volunteered time and again (really, more than anyone else) to talk with these groups and patiently explain his research and answer their questions. Joe, I cannot thank you enough for volunteering, and for allowing your lab members to take part as well. Best wishes on your retirement!

Barbara Wakimoto  
Postdoctoral fellow at the Carnegie, Spradling lab (Allan’s first postdoc, 1980-1984)  
Professor of Biology, Adjunct Professor of Genome Sciences, University of Washington

I first learned about the Gall lab during my graduate training in genetics and cytogenetics at Indiana University. Their papers made a lasting impact on me because they focused on my favorite topics (heterochromatin, repetitive DNA, cytology). So, meeting Joe was a highlight of my training at the Carnegie. His simple act of regularly inviting me and other postdocs, no matter which lab we worked in, to tell him about our projects and progress meant a great deal to us. Joe and Dan Lindsley, whom I continue to miss very much, are my role models for super human beings and mentors with scientific careers well-lived.

Maggie de Cuevas  
I was a Post doctoral fellow at Carnegie (in Allan Spradling's lab) from 1994-1999 and met Joe there.

For me, as for many others, Joe is the epitome of a Renaissance man. His journal clubs at Carnegie were often the starting point for mini-lectures on natural history, etymology, social history, or another of the many topics that interest him. No one ever wanted to miss those journal clubs. I still remember, thanks to one of them, how the word "Neanderthal" should be pronounced.

Joe taught me how to use Carnegie's confocal microscope, and I took his memorable course on microscopes. I cherish my copy of Views of the Cell, which reminds me of the lecture on the history of microscopes - and the thrill of seeing a few treasures from Joe's collection.
Best wishes to Joe for a wonderful, long, and happy retirement.

Robert (Bob) W. Levis
Drosophila Gene Disruption Project, Carnegie Institute
2000 to date

“My Appreciation of Joe Gall”
I’ve been blessed to have been a colleague of Joe Gall for nearly 20 years at Carnegie, from 2000 until now. It’s difficult to put my appreciation for him into words. He was already a legend to me before I met him, because so many of his former trainees over the years have been my friends and colleagues, including Mary Lou Pardue, Ginger Zakian, Meng-Chao Yao, Sharon Endow, Liz Blackburn, and Celeste Berg. It’s hard for me to remember too many anecdotes, but here are a few of my many memories of Joe:

Joe as a softball pitcher – How many of you know of Joe’s athletic ability? I first met Joe during his sabbatical at Carnegie in 1982 or 1983, when I was a postdoc with Gerry Rubin. Our department had a team in the Hopkins intramural slow-pitch softball league. Joe joined as our oldest team member. He pitched on occasion and was nicknamed “Goose Gall” after the Yankees fire balling relief pitcher Rich “Goose” Gossage.

Lunch table discussions - Many of my interactions with Joe have been around a table in the lunchroom. Joe is the only faculty member who consistently eats lunch with other employees in the lunchroom. Everyone feels welcome having lunch with Joe; he is never intimidating. He engages with everyone at the table, be they technicians, front office staff, undergraduates, grad students or postdocs. He never dominates the conversation and always shows a genuine interest in the work, opinions, and personal lives of everyone. His career has spanned so many decades that have given him a perspective on the fads in science and the history of ideas. His knowledge of animals, especially amphibians and insects, is extraordinary. Some of my favorite lunch conversations with Joe have been on Saturdays, when it’s just the two of us.

Animals in and around Carnegie – Joe’s ability to identify animal species is legendary around Carnegie. One morning in 2015, I came to lab in the late morning and saw a large, beautiful moth on the wall of our building, near the entrance. I took this picture of it with my iPad and brought it down the hall to ask Joe what it was. Joe said something like “Oh, you’re the 4th (or 5th or 6th) person to ask me about that moth today.” He then proceeded to tell me not only the common and Latin names, but many other facts about the geographic distribution, diet, and life cycle of the moth. One did not have to bring pictures of animals to Joe to learn about them. The first time I ever saw an axolotl was in Joe’s lab. I once came into his lab to find a net cage of butterflies. I can’t remember whether he had collected a butterfly and let her lay eggs in the cage or whether he had collected the caterpillars or chrysalises. My final memory of Joe’s interest in animals began on a Saturday afternoon when a snake appeared in the lunchroom or in the adjoining atrium. Someone used a broom to gently guide the snake out the door of the lunchroom, across the patio, and into the grass. Joe heard about this and rushed out to look for the snake, because he wanted to bring it back into his lab; I’m not sure what he wanted to do with it (hopefully just for observation and not for an experiment for which he had not filed a protocol with the IACUC).
Joe and Diane’s kindness and hospitality – On another Saturday, in March 2018, my wife, Evie, came to lab with me to escape our cold house during a power outage. Joe happened to see us when we entered. When Joe heard about the power outage, without hesitation he invited us to his house for dinner and to stay for the night. He called Diane to tell her about the last-minute houseguests and there was a wonderful crab cake dinner ready when we arrived. We were watching the PBS news on TV with them after dinner when I got a text message from our neighbor that the power at our house had been restored. We were a little sad to go back home and to have missed the opportunity to spend even longer with them.

In no way can any of these memories begin to convey my respect and admiration for Joe, as a scientist and a person. I thought Allan summed it up well in his remarks at the end of the retirement celebration/symposium when he called Joe the North Star that we depend on for guidance.

Bob Levis

Steve Farber
Faculty Carnegie Institute

Over the years doing zebrafish work - my favorite thing was finding some weird creature in our system and/or tanks and taking them to Joe. He would always stop what he was doing take a look under one of his microscopes, reach for one of his books and then explain in great detail what I had brought him.

Lynne Hugendubler
Carnegie Institute Dept of Embryology

It has been a wonderful pleasure to get to know Joe. His gentle friendship and passion for science and mentoring has contributed greatly to the positive atmosphere at Carnegie. I will fondly remember the many lunchtime chats and his microscope course where he shared his antique microscopes and books. Congratulations, Joe! Happy Retirement! All the best, Lynne
BIOGRAPHICAL SKETCH

Provide the following information for the Senior/key personnel and other significant contributors. Follow this format for each person. **DO NOT EXCEED FIVE PAGES.**

**NAME:** Gall, Joseph Grafton

**eRA COMMONS USER NAME** (credential, e.g., agency login): JGGALL

**POSITION TITLE:** Staff Member

**EDUCATION/TRAINING** *(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable. Add/delete rows as necessary.)*

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**A. Personal Statement**

Throughout my career I have been interested in the cell nucleus, particularly the structure and function of chromosomes and nuclear organelles. At various times I have concentrated on transcription, gene structure, telomeres, heterochromatin, and nuclear bodies, as outlined below. I have always been interested in developing new techniques to further these interests, the most notable of which was the development of in situ hybridization. From the beginning I have been fascinated by the giant lambbrush chromosomes found in oocytes of amphibians and many other species. Surprisingly, the advantages of these chromosomes for detailed studies of gene structure and transcription have been overlooked in recent years. My current aim is to combine the latest molecular techniques for genomic analysis with the ability to image individual genes on the lambbrush chromosomes by conventional light microscopy.

**B. Positions and Honors**

**Positions and Employment**

- **1952-1964** Instructor, Assistant Professor, Associate Professor, Professor of Zoology, University of Minnesota, Minneapolis, MN.
- **1964-1983** Ross Granville Harrison Professor of Biology, Professor of Molecular Biophysics and Biochemistry, Yale University, New Haven, CT.
- **1983-** Staff Member, Carnegie Institution for Science, Department of Embryology, Baltimore, MD.
- **1984-** Professor of Developmental Genetics, American Cancer Society.
Other Experience and Professional Memberships

- Member, NIH Cell Biology Study Section 1964-1968; Chairman, 1972-1974.
- Board of Scientific Advisors, Jane Coffin Childs Memorial Fund for Medical Research, 1986-94; 1997-98.
- Member of Corporation (Trustee), Yale University, 1989-1995.

Honors

- 1967-68 President, American Society for Cell Biology
- 1968- Member, American Academy of Arts and Sciences
- 1972- Member, National Academy of Sciences
- 1988- Member, Accademia Nazionale dei Lincei, Rome
- 1988 Recipient, Wilbur Cross Medal, Yale University
- 1989 Recipient, V. D. Mattia Award, Roche Institute of Molecular Biology
- 1989- Member, American Philosophical Society
- 1996 Recipient, AAAS Mentor Award for Lifetime Achievement
- 2002 Honorary Doctor of Medicine, The Charles University, Prague, Czech Republic
- 2004 Recipient, Lifetime Achievement Award, Society for Developmental Biology
- 2006 Recipient, Albert Lasker Special Achievement Award in Medical Research
- 2007 Recipient, Louisa Gross Horwitz Prize

C. Contribution to Science

1. Structure and function of chromosomes.

Beginning with my Ph.D. studies I have been interested in the giant lampbrush chromosomes found in the oocytes of amphibians and many other organisms. In a study of the kinetics of DNase cleavage I showed that each chromatid of these chromosomes consists of a single, extraordinarily long DNA molecule (centimeters). At that time it was almost universally believed that chromosomes of higher organisms are multi-stranded. In later studies I showed that the loops of lampbrush chromosomes actively synthesize RNA and, in fact, correspond to one or a few transcription units. My current studies focus on RNAseq of the transcripts made during the lampbrush chromosome stage of oogenesis. In addition to defining the transcriptome of the oocyte, we have discovered that both the nucleus and the cytoplasm contain stable transcripts derived from introns. All of the introns in the cytoplasm and many in the nucleus are circular RNA molecules (lariats). Most of my current effort (described in this application) is directed toward an understanding of the synthesis, processing, and storage of transcripts derived from the lampbrush chromosomes.

When I began my studies on chromosomes in the 1950s, immunofluorescence as a means of detecting specific proteins at the cellular level was in its infancy and there was no method to identify specific DNA or RNA sequences. In 1968, in collaboration with my student Mary Lou Pardue, I developed the technique of in situ hybridization, using the amplified ribosomal DNA of *Xenopus* oocytes as the target. The original technique relied on radioactive probes (3H-labeled) and autoradiography as the method of detection. Within a few years other investigators introduced fluorescent nucleic acids as probes (FISH), greatly expanding both the sensitivity and the ease of detection by fluorescence microscopy. More recently, improvements in signal amplification allow detection of single molecules of RNA and DNA in cells and tissues. In situ hybridization has now become one of the most widely used techniques in cell biology.


3. Heterochromatin.

It has been known for over 100 years that certain chromosomes or parts of chromosomes are more condensed than others during interphase and therefore appear more darkly stained. These regions of “constitutive heterochromatin” were shown to be “gene-free” in *Drosophila* and a few other organisms, despite the fact that their dense staining was due to a high concentration of DNA. My students and I used in situ hybridization to resolve this apparent paradox by showing that the DNA in these regions consists of simple sequence or “satellite” DNA. Satellite sequences are both simple and repetitive, and thus incapable of coding for proteins. We showed this first for the satellite DNA of the mouse. We then showed that *Drosophila* also contains simple sequence DNA and that these sequences are localized in the heterochromatin. Our studies reinforced the idea that there are, broadly speaking, two types heterochromatin: constitutive heterochromatin that represents gene-poor regions (the ones we studied) and facultative heterochromatin that represents a repressed state of normal chromatin.


4. Telomeres

Telomeres were first defined in the 1930s as genetic elements at the ends of chromosomes that prevented fusion of “normal” ends, as opposed to newly formed ends, which readily fused with
each other (H. Muller and B. McClintock). The nature of these ends remained a mystery until they were shown to consist of multiple repeats of a short DNA sequence, usually a hexanucleotide. The first hexanucleotide was discovered by Elizabeth Blackburn, at that time a postdoctoral student in my laboratory at Yale. My lab had been studying the rDNA of the ciliated protozoan *Tetrahymena* for some time. We had shown that the rDNA was a palindromic molecule that contained two copies each of the 18S and 28S rDNA. We were interested in the nature of the ends of the molecule, which we knew could join to form circles. Blackburn was able to sequence these ends, having just come from Fred Sanger’s lab in Cambridge, where she had learned to sequence DNA. The telomere sequence of *Tetrahymena* turned out to be \((\text{TTGGGG})_n\). Telomere sequences were soon shown to be highly conserved throughout all organisms; for instance, the telomere repeat of humans and other vertebrates is \((\text{TTAGGG})_n\).


5. Nuclear bodies

In addition to chromosomes, nuclei of plant and animal cells contain a wide variety of “nuclear bodies,” the function(s) of which are still poorly understood. In recent years my lab has focused on two nuclear bodies: the Cajal body and the histone locus body. The Cajal body was first described in the early 1900s by the neuroanatomist Ramon y Cajal, but received little attention until the 1990’s. Studies since then show that the Cajal body is involved in the assembly and modification of splicing factors. In 1999 I suggested the now accepted name “Cajal body” in honor of its discoverer. Later I identified the Cajal body in *Drosophila* as well as its signature protein coilin. Our studies on Cajal bodies in *Drosophila* and in the frog *Xenopus* led us to realize that we and others had confused two completely different nuclear bodies: the Cajal body and a body I named the histone locus body, because of its association with the histone gene loci. The confusion arose because both bodies contain the protein coilin. Just as the Cajal body is involved in the assembly and modification of splicing factors, the histone locus body is involved in assembly of the U7 snRNP and other factors required for histone mRNA maturation.


Complete List of Published Work in MyBibliography:

**D. Research Support**

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The Organization of Animal Cell Nuclei

The overall goal of this study is to understand the functional organization of the cell nucleus, in particular the structure and function of chromosomes and other nuclear organelles, with special emphasis on transcription and splicing.
CURRICULUM VITAE

JOSEPH GRAFTON GALL

PERSONAL DATA

Married September 1955 to Dolores M. Hogge.
Children: Lawrence Frederick born 1956; Barbara Grafton born 1958.
Married July 1982 to Diane M. Dwyer.

EDUCATION

Yale University, B.S., 1949, major in Zoology.

Yale University, Ph.D., 1952, major in Zoology, Ph.D. advisor: Donald F. Poulson. Title of thesis: the Lampbrush Chromosomes of the newt Triturus viridescens.

APPOINTMENTS AND PROFESSIONAL EXPERIENCE

Instructor, Assistant Professor, Associate of Zoology, University of Minnesota, Minneapolis, MN. 1952-1964.

Professor, then Ross Granville Harrison Professor of Biology, Professor of Molecular Biophysics and Biochemistry, Yale University, New Haven, CT. 1964-1983.

Staff Member, Department of Embryology, Carnegie Institution for Science, Baltimore, MD. 1983-2020.

Staff Member Emeritus, Department of Embryology, Carnegie Institution for Science, Baltimore, MD. 2020-present.

Adjunct Professor of Biology, Johns Hopkins University, Baltimore, MD. 1984-present.

American Cancer Society Professor of Developmental Genetics 1984-(lifetime).

PROFESSIONAL SOCIETIES, ORGANIZATIONS, SERVICE

American Society for Cell Biology (President, 1967-68)
Society for Developmental Biology (President 1984-85)
Genetics Society of America
American Society for the Advancement of Science
German Society for Cell Biology
Royal Microscopical Society
Member, NIH Cell Biology Study Section 1964-68; Chairman, 1972-74
Member, American Cancer Society Advisory Committee on Virology and Cell Biology (later
Cell and Developmental Biology) 1976-78; Chairman 1978-80

Chairman, Board of Scientific Counselors, National Institute of Child Health and Human Development, NIH 1986-1991


Member of Corporation (Trustee), Yale University, 1989-1995


**PROFESSIONAL HONORS:**

Member, American Academy of Arts and Sciences (1968)

Member, National Academy of Sciences (1972)

Foreign Member, Accademia Nazionale dei Lincei, Rome (1988)

Member, American Philosophical Society (1989).

President, American Society for Cell Biology (1967-68)

President, Society for Developmental Biology (1984-85)


Honorary Doctor of Science, University of Maryland, Baltimore County (1987)

Wilbur Cross Medal, Yale University (1988)

J. E. Purkynje Medal, Academy of Sciences of the Czech Republic (1999)

Honorary Member, German Society for Cell Biology (2001)

Honorary Degree, Charles University, Prague (2002)

Recipient, Lifetime Achievement Award, Society for Developmental Biology (2004)

Recipient, Albert Lasker Special Achievement Award in Medical Research (2006)

Recipient, Louisa Gross Horwitz Prize (2007)
Bibliography
Joseph G. Gall


81. Yao, M.-C., Blackburn, E., and Gall, J. (1981). Tandemly repeated C-C-C-C-A-A hexanucleotide of Tetrahymena rDNA is present elsewhere in the genome and may be related to the alteration of the somatic genome. J. Cell Biol. 90, 515-520.


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