Joseph G. Gall

The year 2003 marks the 75th birthday of Joseph G. Gall, a founder of the field of cell biology who has contributed to the field for the past 50 or so years. Currently a staff member at the Carnegie Institution of Washington, Joe is a scientist's scientist – a researcher who embodies the positive qualities attributed to scientists: objective, logical, thoughtful in his remarks, and of impeccable integrity. As students, we noticed that Joe had a remarkable insight into the problems of cell biology, which included a broad knowledge of different organisms and their natural history – newts, frogs, *Tetrahymena*, *Drosophila*, water beetles and *Sciara*, to name a few – and chose the organism best suited for the particular biological question under study. Later we discovered through analysis of his methods, and then by his own admission, that he was an avid reader of E. B. Wilson's classic book *The Cell in Development and Heredity* and, in many cases, applied molecular or modern cytological methods to the problems Wilson had described earlier. According to Don Brown, a noted cell biologist at the Carnegie Institution and a friend, colleague and contemporary of his, Joe worked his way through *The Cell*, checking off problems as he went. It is most fitting that Joe was awarded the E. B. Wilson Award in 1983, the highest scientific honor given by the American Society for Cell Biology (ASCB).

Joe's many scientific contributions have touched nearly every component of the nucleus. His early work included analysis of lampbrush chromosome structure and function, showing that the giant lampbrush chromosomes of amphibian oocytes, which are the paired meiotic chromosomes, consist of four very long strands or chromatids with different degrees of coiling or folding. By treating the lampbrush chromosomes with DNase and following the kinetics of digestion, Joe provided evidence for the unineme model of chromosome structure – the hypothesis that a chromatid consists of a single DNA double helix. This organization, he postulated, was the same as that of chromosomes in general. He and others also showed that the giant loops of the lampbrush chromosomes consist of transcribing genes, which provide the maternal RNAs for early embryogenesis.

Joe's research also demonstrated that the nuclear pore complex has eightfold symmetry, delineated histone gene organization in the newt *Notophthalmus*, provided detailed information about snurposome composition, and (with Mary Lou Pardue) led to development of the in situ hybridization method for cytological localization of DNA and RNA – the first method capable of localizing nucleic acids to specific regions of chromosomes or the cell. This method to map genes on chromosomes paved the way for sequence analysis of genomes three decades later.

Another important discovery was Joe's finding that the 18S and 28S ribosomal RNA genes in amphibian oocytes can exist in an extrachromosomal form and undergo amplification (which was independently discovered by Don Brown and Igor Dawid, and by Joe's former postdoc Oscar Miller, Jr). This was the first demonstration that not all nuclear genes in eukaryotes are present in chromosomal DNA and constant in number. This finding also explained the existence of multiple nucleoli, which had been observed in the germinal vesicles of amphibia as early as the late 19th century. Joe went on to show that rDNA amplification occurs not only in oocytes of many amphibia but also in the oocytes of the water beetle, *Dytiscus marginalis*, and the macronuclei of the protozoan *Tetrahymena*.

Joe's interest in chromosome structure led to his analysis of the highly repeated satellite DNAs of eukaryotic cells. Biophysical studies had shown that a significant fraction of the DNA of the mouse, *Drosophila* and other organisms could be separated from the bulk of the chromosomal DNA by equilibrium centrifugation on CsCl gradients (hence the term satellite DNA). Using the newly developed technique of in situ hybridization, he and his students demonstrated that the satellite DNAs localize to the centromeric heterochromatin of the mouse and *Drosophila* chromosomes. Subsequent studies by others showed that this is a general feature of chromosome organization in both animals and plants. Joe also carried out sequence analysis of the three major satellite DNAs of *D. virilis* and showed that they consist of short, highly repeated seven-nucleotide sequences that are related to each other by single base-pair changes. The relatedness of the sequences provided evidence that the satellite DNAs are evolutionarily related to one another and may have arisen by sudden replication events followed by mutation.

Joe's studies on the rDNA of *Tetrahymena* led to another important

finding about chromosome structure. He and Elizabeth Blackburn, a postdoctoral fellow, found that the extrachromosomal rDNA molecules of *Tetrahymena* terminate in multiple repeats of a six-nucleotide sequence, 5′-TTGGGG-3′. Subsequent studies by Blackburn and others revealed that, remarkably, chromosomes of nearly all eukaryotes have this or similar six-nucleotide repeats at their telomeres. The telomeric repeats have subsequently been found to be required for maintenance of chromosome stability.

More recently, Joe has returned to the amphibian oocyte nucleus to study the structure and function of Cajal bodies, the small spherical organelles distributed throughout the nucleus that contain coilin and a constellation of RNAs, RNA polymerases and splicing factors. Although neglected for most of the 100 years since their original discovery, Cajal bodies have now been found in a variety of cells from different organisms and have excited renewed interest because of their probable role in assembly and modification of the RNA transcription and processing machinery of the nucleus.

These studies on many diverse problems in cell biology in many different organisms have revealed fundamental properties of chromosomes and the nucleus. They span half a century and reflect Joe's hands-on work at the lab bench, as well as the work of his many students.

Besides his research contributions, Joe has made significant contributions to the development of the field of cell biology. He was one of the first members of the ASCB, which was founded in 1960, and served as President in 1967-1968. His continued service to the ASCB over several decades has included significant service as an Editor for the society's journal, *Molecular Biology of the Cell*, and activities on several committees. The ASCB has grown enormously during the latter part of the 20th century and has wielded both scientific and political influence to support research in the field. It is significant that three of Joe's former students have also served as President: Mary Lou Pardue, Susan Gerbi and Elizabeth Blackburn.

Joe is probably best known as a pre-eminent microscopist, whose knowledge of microscopy is surpassed by few. He and his uncle built the microscope that he used for his PhD work, and his work throughout his career has continued to emphasize microscopy as a major technique. Joe's hobbies include collecting rare books on the history of biology and microscopy, which he carefully and lovingly peruses, valuing them for the insights of earlier scientists. The photograph shows him at the Mendel Museum in Brno, looking through Mendel's copy of Darwin's *Origin of Species*.

Joe's many former students include an extraordinarily large number of women, many of whom are now successful scientists at universities and research institutions across the United States and Europe. In recognition of his superlative training record, Joe received the AAAS Lifetime Mentor Award in 1996. Joe's deep love of science continues to be inspirational to his students. He exemplifies the tenet that the pursuit of knowledge itself is the most worthy goal, rather than personal gain or ego fulfillment. Despite his numerous accomplishments and awards, including membership in the National Academy of Sciences, the highest honor in the US, Joe is well known for his modesty. We as students always greatly appreciated the objective, reasoned discussions of scientific data (often Joe's own) that continue today, long after our departure from his laboratory, through gatherings at the annual meetings of the ASCB and other encounters. The frequent scientific discoveries that were made during our stays as students in his laboratory were accompanied by excitement and discussion by all – memories that are still vivid and remind us why we chose to follow Joe's example and become scientists.

On behalf of Joe's many students, colleagues, friends and associates, we celebrate Joe's science, his contributions to the practice of cell biology, and our good fortune at being a part of his legacy. May it continue to grow.

Sharyn A. Endow
Duke University, Durham, North Carolina, USA

Susan A. Gerbi
Brown University, Providence, Rhode Island, USA

Journal of Cell Science 116, 3849-3850

doi:10.1242/jcs.00737

Letters

JCS welcomes correspondence provoked by articles in all sections of the journal. Responses to articles in the Sticky Wicket section should be sent directly to Caveman (email: caveman@biologists.com). Correspondence relating to Research Articles, Commentaries and Cell Science at a Glance should be addressed to the Executive Editor and sent to *Journal of Cell Science*, 140 Cowley Rd, Cambridge, CB4 0DL, UK.