In Memoriam Jan-Erik Edström (1931–2013)

JAN-ERIK Edström, an innovative pioneer in micromanipulation methods to study gene expression, died on August 30, 2013, in his home in Lomma, Sweden, after a long illness. He was born on April 21, 1931, in Gothenburg, Sweden. He studied medicine at the Medical School of Gothenburg's Technical University and received the grade of M.D. in 1953. Initially, he was a lecturer of histology at his home university, starting in 1954, but later joined the faculty of the Karolinska Institutet in Stockholm as a full professor of histology in 1965. In 1979, he moved to Heidelberg and spent 6 years there as a Senior Scientist at the European Molecular Biology Laboratory (EMBL). In 1985, he was appointed professor of molecular genetics at the University of Lund, Sweden, but, as a professor emeritus, he moved back to the Karolinska Institutet in 2000.

Jan-Erik was "devilishly good at small things." This expression of surprise and deep admiration, coined by the 17th-century author Edward Norgate, was originally applied to the painter Adam Elsheimer (1578–1610), who created minute oil paintings of mythological and biblical scenes in front of wonderful tiny landscapes. It applies equally well to Edström's widely admired ability to create and use novel micromethods in cell and molecular genetics. While Elsheimer painted on small copper plates with the help of a magnifying glass, Edström performed microelectrophoresis and microcloning on small quartz plates with the help of a microscope. Elsheimer presumably used very fine hair brushes. Edström's tools were pneumatic micromanipulators, a microforge for making glass instruments of microscopic dimensions, and a microdensitometer. For the determination of RNA base ratios on a subcellular level, he isolated small samples of nuclei, nucleoli, and cytoplasm by hand under microscopic control. RNA was extracted and degraded in tiny droplets under oil, and the RNA bases were separated on silk fibers of $\sim 10\ \mu$ diameter in highly viscous buffer at $\sim 5000\ \text{V/cm}$. Base ratios in RNA samples of differ-

ent origin were then determined by measuring UV absorption in a microscope. To allow precise quantification, the original procedure involved photographing the fibers in the light from a spark gap generated between rotating cadmium electrodes and to include on each negative the image of a series of rotating sectors in the light path that produced linear steps of gray. The negatives were then scanned in a microdensitometer within the linear range of the photographic blackening curve indicated by the blackening of the linear sector images. The geometry of the sectors implied that there was even a correction for stray light.

Working on spider oocytes, Jan-Erik showed by this method for the first time that the base composition of cytoplasmic RNA is very different from that of chromosomal RNA but corresponds to that of nucleolar RNA. This finding, together with later results of other authors, led to the insight that the bulk of cytoplasmic RNA is of nucleolar origin.

This work, published in 1960 in the *Journal of Biophysical and Biochemical Cytology*, induced collaborations with Joseph G. Gall on newt oocytes and Wolfgang Beermann on salivary gland cells of the midge *Chironomus*. In both cell types, the correspondence of base compositions of RNA from cytoplasm and microisolated nucleoli was confirmed. The latter work, published in the *Journal of Cell Biology* in 1962, induced Jan-Erik's interest in using giant chromosomes as tools in molecular genetics and encouraged him to select *Chironomus* as his main experimental system. Most of his future work was based on *Chironomus* and much of that work involved micromethods. Edström and Beermann had extracted and analyzed RNA from small groups of specific chromosome segments, two of which contained cell-specific puffs, from the salivary glands of *Chironomus* larvae. Then, Jan-Erik and his students identified and characterized a cell-specific cytoplasmic RNA with messenger-like properties that hybridized to one of the puffs. Its transport from the specific chromosome region via the nuclear sap to the cytoplasm and its processing were later investigated in detail by Jan-Erik's former student, Bertil Daneholt. This cell-specific cytoplasmic RNA is now known to encode one of the major proteins of the silk-like thread that the glands produce.

Interestingly, the first results on this specific messenger RNA (mRNA) in Jan-Erik's lab were achieved at the same time as Suzuki's and Brown's elegant isolation and characterization of silk fibroin mRNA. These authors were able to rule out contamination and RNA degradation during the isolation process because the simple repetitive structure of fibroin enabled them to predict the pattern of oligonucleotides that its mRNA would yield upon RNase treatment. Jan-Erik and his associates avoided the dangers of degradation and contamination by microdissection of fixed-cell organelles and RNA extraction under conditions that avoided exposition to nuclease.

A very important achievement in molecular genetics during Jan-Erik's years in Heidelberg was the method of microcloning on the level of $10 \times 10 \mu\mu$ of DNA that he developed together with Vincent Pirotta. Before the arrival of the polymerase chain reaction, this method was welcomed and rapidly adopted by several labs, giving rise to collaborations with a number of other labs on genes in other systems, including mammalian cells. It was also taught in a number of lab courses at the EMBL. For Jan-Erik and his associates, it

provided the basis of a thorough and extended analysis of DNA sequences at the individual telomeres in the chromosome complement of *Chironomus*. These turned out to differ remarkably from the simple base repeats characteristic of most other organisms and to contain a series of different repetitive units with sizes between 150 and 400 nucleotides.

Jan Erik's genuine enthusiasm for experimental research, his ability to create novel methods for molecular genetics and to apply them to central problems, as well as his friendly, open, and altruistic mind attracted many brilliant students and guest researchers from all over the world. Many of his graduate students have made their ways into different fields of molecular genetics with great success. He will be remembered fondly by many. One image that stays with me is of Jan Erik sitting at his micromanipulator, watching under the microscope the micropipette's movements into a tiny droplet of some picograms of DNA undergoing the process of recombination.

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