# Nuclear histochemistry: Its history in fifty volumes

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The fiftieth anniversary of the double helix was marked two years ago. The elucidation of the structure of DNA by Watson and Crick can rightfully be considered to be "the" milestone in modern biology because it has conditioned the explosive growth in our understanding of the molecular mechanisms regulating the structural and functional organization of single cells and multicellular organisms.

It is interesting to note how early on histochemical research reflected an awareness of the key role of DNA in the expression of hereditary characters. Ever since Boivin et al. (1948) and Vendrely and Vendrely (1948) established this concept on biochemical bases, there began to appear over time other papers (e.g. Ris and Mirsky, 1949; Swift., 1950; Leuchtemberger et al., 1951 or the largely comparative review article by Vialli, 1957) that established by quantitative cytochemical means that the content of DNA was an important evolutionary parameter in comparing animal and plant taxa. In fact, during those years, the quality of research had also undergone major changes, moving from qualitative analysis *in situ* to quantitative cytochemical measurements, thanks to the introduction of the more sensitive morphophotometric assays, with the first two-way or more-way handmade photometers coming from Belgium (Lison, 1950a,b, who was the author of the first technical text on quantitative histochemistry: Lison, 1960), Italy (Vialli and Perugini, 1954), and later England (Deeley, 1955). In these studies, it becomes clear that the relative nuclear DNA content is not only a species-specific constant (i.e. found in all cells and all tissues of every individual of a given species) but assumes the significance of an evolutionary parameter because its changes are interpreted to reflect chromosomal or gene mutations, and thus, genetic changes.

The principle that the nuclear DNA content is a constant was in itself a great discovery from the viewpoint of histochemistry because relative quantitative data are used (the intensity of the Feulgen reaction product in the nucleus relative to the area of the nucleus), relating a chemical colorimetric datum with a morphological one (i.e. the measurement of the size of the nucleus). It was both easy and at the same time biologically correct to use *in situ* techniques to determine the function of single cells, correlating histochemical findings with morphological measurements.

On this basis, in the second half of the last century, with the introduction of flourescent dyes which permitted the determination of DNA with greater sensitivity, not only quantitative changes in nuclear DNA during the life cycle of the cell, but also alterations in chromatin structure and organization related to the cell metabolic changes in response to different environmental stimuli, could be described. This approach was enormously successful in the analysis of cancerous tissue and is now routinely used in cytodiagnosis.

This copy of the European Journal of Histochemistry is the first issue of volume 50. Beginning as the Rivista di Istochimica Normale e Patologica (Journal of Normal and Pathological Histochemistry), the European Journal of Histochemistry has contributed with its publications to codify the science of histochemistry and has certainly had its impact on the birth and development of the histochemistry of the cell nucleus.

Starting from the front page of the first volume (Figure 1), in fact, the roster of Editors, among them Maffo Vialli, expresses how transversal is the subject matter covered by histochemistry, e.g. basic biology, human and comparative anatomy, and especially microscopic anatomy and pathological and clinical histology. And, at the same time the importance not only of histological methods, but also of physical, physico-chemical, and biochemical methods applied *in situ* are stressed.

The Indices of the first issues purposely listed purely technical papers and more biological articles in which pathological tissues or the changes in normal tissue following pathological stimuli were

VOLUME I°
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(Riv. Istoch. norm. pat.)

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1954

# RIVISTA DI ISTOCHIMICA

## NORMALE E PATOLOGICA

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**Figure 1. Front page of the first issue of the journal *Rivista di Istochimica Normale e Patologica*, 1954.**

described. In fact, as early as the second issue, there has appeared an account of a meeting dedicated to histochemistry with particular reference to tumors with some important presentations such as that by Vialli on *histochemical and morphological problems*, by the anatomo-pathologist Sirtori on the use of histochemistry in *the study and diagnosis of tumors* and by the clinician Villa on *nucleic acids in leukemic cells* (Ceriotti , 1954)

In these 50 volumes, in which the history of the European Journal of Histochemistry is written, qualitative and quantitative histochemistry of the nucleus has been an ample and constant factor. More than 230 articles have treated this topic both from basic bio-cellular aspects and from the implied applications to human pathology. This attitude has become especially apparent during the last few years, when several papers have been published which deserve high interest from the viewpoint of both the improvement of methodology (Mazzini *et al.*, 2003; Bottiroli *et al.*, 2004; Cremer *et al*, 2004; Pederson, 2004; Marziliano ey al. 2005; Sheval *et al.*, 2005) and the application to clinical research (Alexandrakis *et al.*, 2005; Fukuda *et al.*, 2005; Hirose *et al.*, 2005; Soldani *et al.*, 2005).

The Maffo Vialli International Award for Histochemistry, established by the Italian Society Histochemistry and the European Journal of Histochemistry, now in its fifth edition, has previously been assigned to three outstanding scientists

for their distinguished research on the biology of the nucleus: Mels van der Ploeg, in 1999 (Van der Ploeg, 2000), Stan Fakan, in 2003 (Fakan, 2004), and Thomas Cremer, in 2005. Their work demonstrates how histochemical studies cannot but result from the articulated integration of enzymo-histochemical, immunohistochemical and *in situ* hybridization data, more often than not associated with three dimensional computer aided reconstruction of the functional distribution of a particular chemical activity.

Nuclear histochemistry is now therefore a real molecular biology *in situ* applied to research on dynamic processes in the nucleus; and this renders the microscopic and histochemical approach absolutely irreplaceable for the progress in our understanding of cell biology.

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