EDITORIAL

We have projected this issue of volume 44 of the European Journal of Histochemistry, the first issue of the third millennium, to celebrate the achievements of the just-ended twentieth century, quite agreed upon as the century of histochemistry.

The issue opens with a review by van der Ploeg entitled "Cytochemical nucleic acid research during the twentieth century". This is the text of a lecture he presented in Camerino to the 1999 Congress of Histochemistry on the occasion of his receiving the 1st International Histochemical Award. The award, in memory of the founder of our Society, Maffo Vialli, was instituted for the express purpose of linking more closely our Society with other European histochemical centers, and more generally with their cell biology activities.

Prof. van der Ploeg in his article traces a very analytical history of the last century's research on nucleic acids and, through this, how our knowledge about cell biology and about how life is regulated, progressed. He begins right from the discovery at the end of the seventeenth century of a simple microscope, "insensitive to optical aberration", which permitted Van Leeuwenhoek to observe unicellular organisms for the first time. From this follows, clearly and compellingly, the evolution of biological thought about the nucleus and cell life, closely correlating it with the development of the instruments of observation and measurement, and the techniques of imaging and quantification of nucleic acids.

Since the 1950's, with Watson and Crick's discovery of the structure of DNA, and the introduction of the Jacob and Monod gene concept, molecular techniques have become increasingly sophisticated. The advent of restriction enzymes, the use of plasmid and cosmid vectors to clone DNA fragments, and the polymerase chain reaction concurred to the biological/molecular approach to study DNA. Later, the value of the histochemical approach to the problem came to be appreciated when the use of in situ PCR, and more recently, the multicolour FISH procedures, permitted the simultaneous karyotyping of all the human chromosomes, and have shown the chromosomal aberrations to be detectable on interphase cell nuclei, thus paving the way for genomic mapping. Furthermore, have been introduced methods that can reveal specific sequences of DNA (some of them being specific genes) at the level of various nuclear microdomains both in normal cells and pathologic ones.

The positioning of gene sequences and the detection of specific messenger RNA's within the nucleus, the nuclear compartmentalization of some transcription and/or processing factors have, over the last twenty years, given a clearer and more dynamic picture of the nucleus.

Prof. van der Ploeg also makes an interesting analysis of the trafficking of functionally active factors from the nucleus to the cytoplasm and vice-versa.

In his text, van der Ploeg accomplishes very well the ambitious task of placing the results from the recently introduced in situ molecular biology method within the framework of classical histochemistry; the finer localization that this approach offers provides van der Ploeg with more material to ponder over how the nucleus functions.

The achievements of histochemistry in the twentieth century described by van der Ploeg, cannot be complete without our giving due reverence to the names of the great pioneers of quantitative histochemistry, Lison and Verne, Eranko, Lillie, Glick,Vialli and coworkers who in those early years made quantitative measurements of DNA for comparative purposes among species and found, in an applied field, the first signals of the quantitative aberrations of DNA in tumor cells (Perugini and Vialli, Romanini and Pisani, etc.).

One cannot forget the many editions of the monumental work of A.G.E. Pearce "Histochemistry, theoretical and applied", which was the reference for many generations of researchers throughout the world.

In the second part of this issue are presented the Proceedings of a Symposium on the nuclear lipid signalling system. Prof. Antonio Manzoli recalls the events of research about this other parameter of cell function which began in the 1950's and has characterized the second half of the last century (this field was essentially influenced by the papers of Manzoli and his coworkers). The chapters of the Symposium, contributed by Manzoli, Maraldi *et al.*, Capitani, Cocco, Santos and Divecha, Ruben and Baldassarre, cover various aspects of the problem and the new approaches that are still in progress. As can be seen in the series of overviews, this signalling system not only complicates, but also helps to integrate and deepen the system of the nucleic acids described by van der Ploeg. It is interesting to underline how much

an important role is played in either system by the *in situ* techniques in strenghthening "the concept of a localized specific function".

One can see here the so called "new cytochemistry" with which some years ago (EJH, 41,5 1997) we dealt in an editorial, saying that the integration of different approaches and different methods would have made it possible to identify in the intracellular universe an ordered body of microdomains. This would form a base from which to go on to an ever more complete understanding of the integration between the various signalling systems.

Manzoli in the introduction to his chapter, notes that from the different reviews collected here "it could happen that sometimes more questions than answers will be provided". And he concludes that, in his opinion, "in a specific field in continuous progress, this is the most exciting news".

The third part of the issue is dedicated to the work of Grossi *et al.*, presented at the Camerino meeting on "Cell and molecular organization of immune system", with respect to " molecules that inhibit T cell functions". Herein is treated an analysis of molecular shuttling involving resting and activated T cells in the immune system which reveals the presence of some molecules at endosomal cytoplasmic localizations and parallely, corresponding molecules at the plasma membrane, at the site of cell-to-cell contact. These apparently contrasting situations are thoroughly discussed in the light of the diverse categories of lymphocytes that function as intermediaries during the negative control of lymphoproliferation and of its activation, in relation to the different phases of the immune response.

He defines the function of these molecules mainly in relation to the localization in so far as he is able to attribute to them. And this is the classical histochemical way to interpret data.

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IN MEMORIAM

With sadness we report that DAVID GLICK, honorary member of our Society, died inJanuary 2000