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EDITORIAL

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Histochemistry in gene technology

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No one would contest the notion that we are living in the era of the genome. Of several species the whole genome has been sequenced and concerning the human genome we have come pretty close. Some regard this as a major triumph of mankind, others as merely the logical endpoint of a large scale, almost industrial, analytical effort. The importance of this achievement can hardly be overestimated but, however as crucial it might be, it is only the beginning of a major new effort aiming at identifying the genes hidden in this immense collection of data and understanding the function of the proteins encoded by these genes. Functional genomics will remain hot for many years to come and is paralleled by a similar, almost industrial, development in protein analysis: functional proteomics.

Histochemists might become a little timid in this sophisticated arena. Their scientific goal, the development of methods for specific visualisation of molecules at tissue, cell or subcellular level, chemistry of the individual cell as Van Duijn, one of the eminent Dutch histochemists used to call this branch of biomedical science, is no longer recognised as a separate discipline, although every cell-, molecular- and developmental biologist and every pathologist lives with histochemistry on a day by day basis. Histochemists might be a little timid but histochemistry is more alive than ever, even though the focus of histochemistry has changed significantly. Rather than torturing and killing cells, they are now carefully kept alive and up-to-date imaging tools allow four-dimensional imaging: dynamic analysis over time of cell function at a (sub)microscopic level. In this approach, the development of genetically encoded fluorescent tags has been a major step forward. It is to this exciting new field in molecular cell biology that this special issue of Histochemistry and Cell Biology is dedicated. This topic was the focus of the 42nd annual symposium of the Society for Histochemistry, held in Les Diablerets, Switzerland. Exciting science in a spectacular setting.

Four domains of scientific development were covered. First of all the methodology. New markers, new microscopes, new approaches, towards computer-assisted analysis of the images obtained from live cells. Two contributions highlight the developments in this domain and recent results from the application of the new techniques. Adriaan Houtsmuller reports exciting new results on nuclear protein dynamics and Roeland Dirks on the visualisation of RNA in living cells. These papers also clearly illustrate the need for methodology oriented scientists: new methods do not come easy.

The second topic addressed the use of fluorescence-labelled novel or engineered genes for the study of cell function. The review by Rainer Pepperkok and his group shows the enormous impact this technology has and will continue to have to study the subcellular localisation of products of novel genes as a first step toward their further characterisation. Ken Tucker's paper is an elegant demonstration of how functional histology of the nervous system can be achieved using fluorescent proteins. Zellmer et al. demonstrate in their paper expression of foreign genes in keratinocytes.

The third topic focused on the use of fluorescent transgenes in developmental biology but also in the study of in vivo behaviour of cancer cells. How fluorescent transgenes might be used in developmental biology is elegantly demonstrated in the paper by Hadjantonakis and Nagy.

The final topic concerned the use of fluorescent tags in gene therapy. Crucial questions in this domain are what happens to the introduced vector, where it spreads and how the construct is expressed. Wahlfors et al. dem-

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onstrate how fluorescent constructs can be used to answer these questions. As Kuppen et al. discuss in their paper, histochemical detection of the vector construct is essential in order to overcome problems in this exciting new area. Testing new vectors using histochemistry is discussed by Lundstrom et al. and assessment of the efficacy of new routes of administration of therapeutic constructs by Christensen et al.

Histochemistry is as dynamic as ever. There is no doubt that visualisation of their expression at tissue, cell and subcellular level will contribute crucial data to our knowledge of the function of new genes.