 Cytometry Part A 58A:53–54 (2004)

Clinical Cytometry Perspective

A Look at Where We Came From and Where We Are Going

This issue of *Cytometry* celebrates the 25th anniversary of the founding of the Society of Analytical Cytology, now the International Society of Analytical Cytology (ISAC). This period has seen cytometry grow from its humble beginnings some 40 years ago to a technology that is used in a wide range of scientific disciplines in human, animal, plant, and material science studies. As illustrated by the articles contained in this issue, it should be stressed that cytometry is more than just a technology; it encompasses studies based on the science of quantitative cells to understand the regulation and behavior of cells.

To this growth on the side of basic sciences, a parallel explosion in the use of cytometry in the clinical sciences has occurred over the past 25 years. The next set of seven articles highlights this growth in clinical cytometry. The contributions vary in their depth and focus, but all point to the evolution of clinical cytometry from the fringes of diagnostic pathology some 25 years ago to what is now an integral and key component of laboratory medicine. It begins with a poignant commentary from Frank Mandy on the rapid proliferation of flow cytometers in a clinical setting in response to the emergence of one of the worst infectious diseases in the 20th century, the human immunodeficiency virus, and the critical need for this testing in resource-poor countries with the now widespread availability of antiretroviral therapy for a disease that continues to haunt the world. We then take a walk through the major areas of clinical cytometry with the authors of each article (Raul Braylan, Alberto Orfao, Mike Keeney, Bruce Bagwell and their colleagues) to provide a historical perspective and a peek at what is to come in an exciting future. A vignette by Jan Gratama and associates then looks at the exciting and rapidly developing arena of detection of antigen-specific T cells representing an example of how a productive synergy between cytometry and immunology continues to provide scientists with a better understanding of the complex immune response.

We end this volume with an article by George Janossy highlighting the extremely exciting role that cytometry will play in the genomics and proteomics era. His contribution highlights the developing, intimate connection between genomics, proteomics, cytometry, and clinical science; a synergistic interaction that will be key if we are to understand how newly discovered genes and proteins function in the regulatory environment of the cell, and how their deregulation leads to disease. All of this is happening in the background of what, for myself, having been involved in clinical cytometry for some 20 years, is the most exciting time yet. We have seen an evolution of the instrumentation to the point when virtually all clinical laboratories have equipment capable of three- to four-color analyses, with the leading clinical laboratories quickly moving to five-, six-, seven-color or more analyses. This level of analysis assessing a large number of parameters simultaneously is necessary to facilitate specific selection of cell subpopulations along with analysis of therapeutic targets and therapeutic response in the abnormal cells (and their heterogeneous subpopulations) and normal cell components. This will continue to fuel what is a relatively recent and fundamental change in how flow cytometric data are used. Initially, flow cytometric data in the setting of leukemia and lymphoma analyses was used primarily as an adjunct to diagnosis, and it remains a key adjunctive component of the primary diagnostic workup in hematopoietic malignancies. However, there is now an explosive expansion in the use of these data in making patient-specific therapeutic decisions and in therapeutic monitoring. This began with the emergence of antigen- and ligand-driven therapies such as Rituximab and Campath (watch for an upcoming review article on antibody and ligand therapies in the near future in *Communications in Clinical Cytometry*), an area that continues to grow. However, key roles for cytometric analyses are also evolving, with the new generation of targeted therapies that are even more highly targeted at the malignant cells. Many of these early and successful targeted therapies, such as the bcr:abl kinase inhibitor therapy, to mention only one, are kinase inhibitors. Cytometric assays to monitor kinase activity are rapidly being developed (1–3) and are a part of most clinical trials of these new generations of targeted therapies as key analyses to help understand drug action, emergence of drug resistance, and interactions with other therapies used in combination with these targeted therapies. It is clear that these cell-based cytometric assays are going to move to the clinical laboratory in the near future, thus ensuring a growing role of clinical cytometry in patient therapeutic decisions and monitoring. This is fortuitously timed with a wealth of now readily available, highly specific, antibodies directed against phosphorylated epitopes of a wide variety of proteins involved in signaling pathways regulating cell behavior. It is also fortu-

Published online in Wiley InterScience (www.interscience.wiley.com).
DOI: 10.1002/cyto.a.20010

nate that the emergence of a wide range of dyes to couple with these reagents to routinely facilitate complex multiparameter analyses in a clinical setting has occurred in the recent past. Thus, although challenges remain in a number of areas including regulatory, economic, and training issues, in my opinion, like no other in the past, a bright, growing, and exciting future awaits clinical cytometry.

Charles Goolsby
Editor-in-Chief

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