Annals of Oncology **8** *(Suppl. 2)*: S1–S2, 1997.

Introduction

The Sixth Lugano Conference: Basic science papers

S. T. Ong,[1] R. Stupp[2] & J. E. Ultmann[1]

[1]*Section of Hematology/Oncology, Department of Medicine, University of Chicago, Chicago, IL, USA;* [2]*Center for Oncology, University Hospital, Lausanne, Switzerland*

The Lugano conferences have in the past stressed both clinical and basic science research in the study of lymphomas. This year has been no exception, and we witnessed an obvious increase both in the number and scientific content of the presentations and abstracts in the meeting. Herein we include some of the interesting presentations in the basic sciences and pathological classification of lymphomas.

Since the last meeting in 1993, an important new classification of lymphomas has emerged. Originally published in *Blood* in 1994, the REAL classification is an attempt by the International Lymphoma Study Group to develop a consensus list of currently recognizable lymphoid neoplasms that can be diagnosed with available morphologic, immunologic, and genetic techniques, and which have distinct clinical features. Certainly, the REAL classification is an excellent review of the known lymphoma entities and, significantly, directs our thinking toward treating each lymphoma as a different disease, with its own distinctive genotype and biologic behavior, each of which may require a specific therapy. However, as the authors pointed out in their original article, this is only an interim classification, and remains as imperfect as our knowledge of lymphomas. Ongoing efforts are being made to improve the clinical relevance of biologically based classifications by consensus meetings between pathologists and clinicians. With better understanding of the underlying causes of malignancy, and the additional genetic 'hits' that confer more aggressive behavior and resistance to chemotherapy, we may actually find ourselves adopting even more detailed classifications in the future. The explosion of research in molecular oncology is the force driving us in this direction. The question at present is to determine if such a classification better serves the patient in terms of improved assessment of risk factors and improved treatment. Such questions are being answered with retrospective analyses, such as those that were presented by Fisher and Armitage at the 1996 conference, and ongoing prospective trials.

One distinctive entity, MALT lymphoma, is a particularly instructive example. The recognition of this lymphoma by Isaacson in the 1980s and its association with *H. pylori* infections paved the way for the astounding regressions that are seen when the associated *H. pylori* infections are treated. A number of papers confirmed that early-stage and low-grade disease can be effectively treated in 90% of cases with a combination of antibiotics and anti-ulcer therapy. The relapse and long-term survival rates have yet to be described. The recognition of MALT lymphoma as a distinct clinicopathologic entity, its association with *H. pylori*, and the disease-specific therapy have been a remarkable advance encouraged by careful pathologic and epidemiologic studies. A special issue of *Annals of Oncology* that includes many of the presentations at the 1996 conference on MALT lymphomas has been published recently.

Since the last conference yet another infectious agent, Kaposi's sarcoma-associated herpes virus, or human herpes virus 8, has been strongly associated with a rare but clinicopathologically distinct lymphoma: the primary effusion lymphomas. The studies by Knowles, in which Southern blotting or PCR-based techniques were used to look for KSHV, demonstrated the specificity of this virus in body cavity-based lymphomas but not in AIDS- and non-AIDS-related lymphomas or Hodgkin's lymphoma. These findings are obviously important, describing a new infectious agent and its possible role in the etiology of these rare lymphomas. Ultimately they may also herald a cause-directed therapeutic approach that combines antiviral therapy and conventional chemotherapy.

The 1996 conference also witnessed the more careful characterization of known proto-oncogenes in lymphoma: *bcl*-1, *bcl*-2, *bcl*-3, and *bcl*-6. The recognition of mantle-cell lymphomas (within the REAL classification) and the realization that these lymphomas overexpress the cyclin D1 gene, at the *bcl*-1 locus, in the majority of cases, further justifies its recognition as a distinct biologic entity. We also learned that the transformation to diffuse large-cell lymphoma by follicular lymphoma is associated with somatic mutations of the *bcl*-2 gene. Whether this is responsible for the more aggressive behavior of the large-cell lymphomas has yet to be shown. Falini and others showed us using immunohistochemical techniques that normal germinal centers express *bcl*-6, as well as follicular, large-cell, and Burkitt's lymphomas. Interestingly, it was also demonstrated that the protein is also expressed in L & H cells of lymphocyte-predominant Hodgkin's disease.

Two presentations suggested answers to long-standing questions regarding the biology of Hodgkin's disease: the cell of origin of the Reed–Sternberg cell and the role,

if any, of eosinophils in the pathogenesis of Hodgkin's disease. Rajewksy et al. presented data for the B-cell origin of the Reed–Sternberg cell. These elegant data were derived from single-cell PCR studies in which they showed VH gene rearrangements in Reed–Sternberg cells from 12 out of 13 patients with classical Hodgkin's disease. Furthermore, these cells demonstrated a high level of somatic mutations, suggesting an origin from the germinal center cell. A paper by Pinto et al., investigating the role of eosinophils in Hodgkin's disease, suggested that they were capable of promoting Reed–Sternberg cell proliferation by way of its CD30 ligand. This paper suggests a role for the eosinophil in the pathogenesis of Hodgkin's disease, and suggests another potential therapeutic target in this disease.

As evidenced by the following selection of papers, the quality of the science presented at the Lugano conferences continues to be of the highest standards. The interactions between basic scientists and clinicians are one of the most valuable aspects of these conferences, and will in future ensure both the success of the meetings and their important role in the battle against lymphoma.