Unlike the mouse models that use randomly integrated transgenes under transcriptional control of GATA-1 or β-globin gene fragments,9,10 our ErGFP-Cre model uses a defined knock-in strategy to direct fluorescent protein expression to the erythroid lineage. The defined knock-in of a GFP-Cre—encoding transgene into the endogenous erythropoietin receptor (EpoR) gene locus ensures reliable EpoR promoter–controlled transgene expression and, in addition, allows the generation of EpoR knock-out mice that accumulate green fluorescent protein (GFP)—positive erythroid progenitor cells of probably erythroid colony-forming unit (CFU-E) stage.11

In all models, including ours, tissue specificity was analyzed by flow cytometry and fluorescence microscopy, leading to a snapshot analysis of fluorescent protein expression at a distinct time point of mouse development. We examined GFP-Cre expression in different hematopoietic subpopulations of adult and embryonic ErGFP-Cre mice by flow cytometry, using an antibody cocktail staining nonerythroid hematopoietic cells11 or, in a more precise analysis, using single antibodies, and we observed a strictly erythroid-specific expression pattern of GFP-Cre.

To claim strict tissue specificity, the analysis of the transgene expression should also include tissue-specific expression over time and embryogenesis. An advantage of our ErGFP-Cre mouse model is that by crossing the mice with R26R-reporter mice, GFP-Cre–mediated LacZ expression can be induced and used as an indicator for previous or persistent GFP-Cre expression. The spatial and temporal analysis revealed that nonhematopoietic expression of GFP-Cre is restricted to the vascular system and confirmed that within the hematopoietic system GFP-Cre expression is limited to the erythroid lineage.

To the editor:
The WHO classification of mature T-cell leukemias

We read with interest the comprehensive review of mature T-cell leukemias from Herling et al.1 If anything, this study, despite the authors’ conclusions, supports the robustness of the World Health Organization (WHO) classification. Their clinical and laboratory data, which mimic our own observations, confirm that the disease entities included can be clearly defined on clinico-pathologic criteria. Herling et al1 contribute further by demonstrating TCL1 expression, as well as at Xq28, the loci (TCR) which underscores TCL1 expression, as well as at Xq28, the loci (TCR) for MTCP1. It is, in fact, our original identification of T-PLL as a disease entity with its associated karyotype2 that led scientists to identify the TCL1 gene. Even the additional cytogenetic changes in T-PLL, such as iso(8q), are rather unique to this disease.3 The 2 leukemias included in the WHO classification—T-PLL and T-large granular lymphocyte (T-LGL) leukemia—are well defined on morphology, immunophenotype, histology, and, in T-PLL, cytogenetics. These disease features continue to be refined with characteristic immunophenotypes4,5 and bone marrow histology6 more recently described in T-LGL leukemia. Use of an extended panel of antibodies including CD57 and CD16 may reduce the overlap described by Herling et al between T-LGL leukemia and other T-cell disorders. Other clinical and laboratory features outlined in that report,1 such as rising lymphocyte counts in T-PLL and cytopenias in T-LGL leukemia, are useful additions but not defining criteria. Although we have recognized a degree of morphologic heterogeneity in T-PLL,7 the consistent chromosomal abnormalities and clinical course helped to recognize 2 morphologic variants: with small cells and with cerebriform-like cells. Even in the latter, the question of Sézary syndrome should not arise because of the absence of epidermotropism when skin lesions are present in T-PLL.8

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References
Tumor biology should drive classification efforts

We readily acknowledge the many contributions of Professor Daniel Catovsky’s group to the current understanding of T-cell leukemias. However, we fundamentally disagree with the philosophy expressed by them in their present letter and elsewhere. In our opinion, tumor categorization follows understanding and does not precede it. Such classifications are always provisional and subject to improvement based on new knowledge. The current World Health Organization (WHO) scheme is no exception.

Our paper was intended to provide an overview of the types of mature T-cell leukemias encountered at a large referral center and how they relate to the WHO entities. The relative rarity of these tumors means that the unambiguous classification of T-cell tumors remains a difficult task for many hospitals, including our own. We touch on these areas, we fully expect that future versions will incorporate data on risk stratification, pattern of disease progression, and underlying pathogenesis to help guide the optimal selection and timing of therapy. Although the current WHO scheme touches on these areas, we fully expect that future versions will continue the progress in that direction.

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References


Best therapy for primary amyloidosis, a not-yet-solved question

We read with interest the paper from Dispenzieri et al in the May 15, 2004, issue of Blood on a case-match-control study comparing overall survival of 63 primary amyloidosis (AL) patients undergoing transplantation with 63 patients not undergoing transplantation. In contrast, we do not agree with J. Mehta when he wrote, in the accompanying editorial, that “The data from the Mayo Clinic and Boston University are impressive enough to make a prospective, randomised study of high-versus conventional-dose therapy in amyloidosis scientifically unattractive and practically impossible.”

In their paper, Dispenzieri et al compared the survival of amyloidosis patients who received high-dose therapy in the Mayo Clinic in the late 1980s and early 1990s with the survival of matched control patients who were treated by various therapeutic regimens, mainly melphalan and prednisone (MP), but also colchicine and vitamin E, in the early 1980s. From our point of view this study only supports the fact that for selected AL patients, in a center with a great experience, intensive treatment with stem cell support is better that treatments used in the control group. The authors themselves are much more careful than Mehta in their conclusions.

We considered 4 years ago that a prospective randomized comparison of intensive and conventional treatment was needed to solve the issue of the respective merits of both therapeutic strategies in the different risk-groups of AL patients. We thought at this time, as Mehta does, that to compare intensive treatment with MP was unattractive and we choose, as conventional treatment, an association of melphalan and high-dose dexamethasone (M-Dex: melphalan 10 mg/m² and dexamethasone 40 mg for 4 days each month up to 18 months), hypothesizing that this regimen could
The WHO classification of mature T-cell leukemias

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