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Improved Detection Rate of Cytogenetic Abnormalities in Low-Grade B-Cell Lymphoma Using CpG-Oligonucleotide DSP30 and Interleukin 2 Mitogenic Stimulation
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Cytogenetic analysis is a useful tool for diagnosis and prognosis of low-grade B-cell lymphoma but is hampered by low mitotic index of mature B cells in culture. B-cell mitogens traditionally used to stimulate division of cells for chromosome analysis, including pokeweed (PWM), TPS, and lipopolysaccharide, have had limited success. Data from our clinical cytogenetics laboratory supports significantly improved abnormality detection by a combined use of CpG-oligonucleotide and interleukin 2 (OL/IL-2). Bone marrow or peripheral blood samples from 158 low-grade B-cell lymphomas, including 82 chronic lymphocytic leukemia/lymphoma (CLL) and 76 non-CLL cases, were cultured under the following 3 conditions for cytogenetic analysis: 24-hour unstimulated (ONC), 72 hours with PWM, and 72 hours with OL/IL-2. Interphase FISH (iFISH) with a CLL panel assessing trisomy 12 and deletions of 13q14.3, ATM, and TP53 was performed on 72 CLL cases. Comparing abnormality rate by study of cultured metaphase cells, the increase in detection rate for OL/IL-2 over the other 2 culture modalities was statistically significant ($P < .05$) with detection of at least 1 abnormal clone in 84 of 158 (51%) of OL/IL-2, 59 of 158 (37%) of PWM, and 17 of 158 (11%) in ONC cultures. An additional 37 (23%) cases (17 CLL and 20 non-CLL) had 1 or more clonal abnormalities (subclones) uniquely detected with OL/IL-2. iFISH was less sensitive than OL/IL-2 for cytogenetically visible aberration, and OL/IL-2 detected more abnormalities not covered by specific iFISH panels, especially balanced translocation. Use of the OL/IL-2 has significantly improved the abnormality detection rate compared with PWM as a mitogen in cultures for low-grade B-cell lymphoma and is more sensitive than iFISH for detecting cytogenetically visible aberration. Last, it revealed new abnormalities that may offer further prognostic information in the future.

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