

**Disparity Between Morphological Evidence of Apoptosis and Internucleosomal DNA Fragmentation in Hematologic Malignancies (Meeting abstract).**
**Sub-category:** [Leukemia/Lymphoma \(Adult\)](#)
**Category:** [Leukemia/Lymphoma \(Adult\)](#)
**Meeting:** [1999 ASCO Annual Meeting](#)
**Abstract No:** 114

**Author(s):** V Kravtsov, D Martincic, J Whitlock, J Greer, M Koury

**Abstract:** Induction of apoptosis in tumor cells is a key mechanism by which chemotherapeutic agents cause tumor regression. In vitro measurement of drug induced apoptosis may provide a means to predict drug responses for individual patients. A majority of apoptosis assays is based on the detection of products of internucleosomal DNA cleavage. We studied drug-induced apoptosis in promyelocytic HL60 and lymphoblastic CEM cells and in primary cultures of tumor cells from 8 AML, 5 ALL, and 4 non-Hodgkin lymphoma patients. Apoptosis was induced in myeloid cells with etoposide (E, 1--80mM), idarubicin (I, 0.5--10mM), cytarabine (C, 1--80mM) and in lymphoid cells with prednisone (P, 0.1--10mM), vincristine (V, 0.01--1mM), and daunorubicin (D, 0.1--10mM). To detect apoptosis, the microculture kinetic (MiCK) assay (Blood, 1998;92:968), DNA fragmentation and morphological tests were used. The MiCK assay monitored apoptosis over 24h and reported times of maximum apoptotic response which were specific for each drug and drug concentration. At these times, a maximum proportion of apoptotic cells could always be detected in Giemsa-stained preparations. Considering that DNA fragmentation is a late event in apoptosis, DNA was isolated and separated electrophoretically 5h after the maximum of apoptosis in the MiCK assay and morphological test. In 4 AML samples, DNA was isolated after 4, 6, 12 and 24h of drug exposure, i.e. Multiple times before and after the maximum apoptosis. Apoptosis in HL60 and CEM cells was revealed by the MiCK assay and confirmed morphologically (10 to 80% of cells were apoptotic, depending on inducers). However, "ladder" pattern of DNA fragmentation was seen only in samples from HL60 but not CEM cells. In patients' samples with morphologically confirmed apoptosis, a DNA "ladder" was revealed in 4 of 8 AMLs, 2 of 5 ALLs and 1 of 4 lymphomas. In "ladder"-positive samples, internucleosomal DNA cleavage was seen upon exposure of the cells to some drugs but not to others. For example, in two of 4 "ladder"-positive AML samples, DNA cleavage was detected in I- and C-treated cells but was not in E-treated cells. The data indicate that internucleosomal DNA cleavage is not a consistent marker of drug-induced apoptosis in human leukemia and lymphoma cells. This conclusion is in agreement with a body of studies demonstrating that DNA fragmentation is neither an exclusive nor obligatory prerequisite of apoptosis. Morphological modifications, such as changes in the cell size, plasma membrane blebbing and nuclear fragmentation, are the most consistent and reliable markers of apoptotic cell death.

**Other Abstracts in this Sub-Category**

1. High-Dose Therapy (HDT) Followed by Hematopoietic Stem Cell Transplantation (HSCT) for Relapsed Chemosensitive Hodgkin's Disease (HD): Final Results of a Randomized GHSG and EBMT Trial (HD-R1). (Meeting abstract).

**Meeting:** [1999 ASCO Annual Meeting](#) Abstract No: 5 First Author: [N Schmitz](#)
**Category:** [Leukemia/Lymphoma \(Adult\)](#)

2. Consolidation ABMT After Standard Chemotherapy Vs CHVmP/BV Alone for Primary Intermediate and High Grade NHL: A Randomized Phase III EORTC Study (Meeting abstract).