Methods of Determining Apoptosis in Neuro-Oncology

Review of the Literature

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SUMMARY

Tumor growth depends not only on the rate of cell proliferation but also on the rate of programmed cell death (apoptosis). Thus, treatments focusing either on the restoration of apoptosis or on triggering the apoptotic pathways may provide new treatment targets. Therefore, the ability to detect apoptosis in experimental studies is vital in our assessment of treatment success. Apoptosis detection is important in assessing treatment outcomes in both the experimental and clinical settings. Furthermore, the analysis of surgically removed specimens for apoptosis provides patient-specific data, allowing for tailored treatment plans. Many techniques are currently used to detect apoptosis, including identifying those cells exhibiting the pathognomonic morphological characteristics of apoptosis, identifying DNA breaks by the terminal deoxynucleotidyl transferase-mediated dUTP nick-end labeling assay, labeling externalized phosphatidylserine, flow cytometry techniques, laser scanning cytometry, poly(ADP-ribose) polymerase cleavage, detection of caspase activation, membrane permeability changes, mitochondrial failure, identifying denatured DNA, as well as a recent noninvasive technique for measuring apoptosis with a novel fluorescence reporter. This chapter provides an overview of these various apoptosis detection methods used in experimental studies with an emphasis on glioma research.

Key Words: Apoptosis; glioma; programmed cell death.

1. INTRODUCTION

Gliomas are among the most difficult tumors to treat. Despite advances in surgery, radiation, and chemotherapy, the prognosis for patients with malignant gliomas remains poor (1,2). Patients with the most aggressive grade of glioma, glioblastoma multiforme (GBM), have a median survival of 1 yr (1,3,4). Tumor growth depends not only on the rate of cell proliferation but also on the rate of programmed cell death (apoptosis) (5,6). Furthermore, genomic alterations affecting apoptotic pathways have been implicated in tumorigenesis (7–11). Thus, glioma treatments focusing either on the restoration of apoptosis or on triggering the apoptotic pathways may provide new treatment targets. Therefore, the ability to detect apoptosis in experimental studies is vital in our assessment of treatment success. This chapter provides an overview of the various apoptosis detection methods used in experimental studies with an emphasis on glioma research. Although we have focused on these methods in glioma research, the methods described are more broadly applicable to other nervous system tumors as well.
Fig. 1.