USE OF HUMAN LYMPHOBLASTOID CELL LINES TO DETERMINE CELLULAR HYPERSENSITIVITY TO PHYSICAL AND CHEMICAL AGENTS

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INTRODUCTION

During the past decade, human lymphoblastoid cell lines have become recognized as providing a convenient source of material for studies of human genetic diseases [1-7]. Lymphocytes may be transformed with Epstein-Barr (EB) virus to produce immortal cell lines [8-10]. They are termed lymphoblastoid because of their morphological similarities to the immature lymphocytes called lymphoblasts.

USE OF LYMPHOBLASTOID CELL LINES

Table 1 lists some of the advantages and disadvantages of lymphoblastoid cell lines for use in laboratory studies. Using EB virus for transformation only a small volume of blood, usually less than 10 ml is commonly sufficient to establish a line, making the procedure usable for children as well as adults [8, 9].

The lymphoblastoid cell lines appear to be immortal in that they can be passed (subcultured) indefinitely. They thus avoid the problems of senescence found in fibroblast cultures. Further, passing the lymphoblastoid cell lines does not involve trypsinization which is time consuming and may alter cell properties.

Lymphoblastoid cell lines may be grown rapidly in suspension culture in RPMI 1640 medium supplemented with 10-20% fetal calf serum. They grow exponentially to a plateau concentration of 1-3 × 10^6 cells/ml with a doubling time of 15-30 h. Refeeding may be easily accomplished by removing a portion of the culture and adding fresh medium.
Table 1. Advantages and Disadvantages of Human Lymphoblastoid Cell Lines for Laboratory Investigations

A. Advantages
Small volume of blood to initiate line
Immortal
Suspension culture
Rapid doubling time
High concentration
Suitable for cellular and biochemical studies
Retain characteristic sensitivities

B. Disadvantages
Theoretical EB virus risk to workers
Cells from some patients difficult to transform
Possible alteration of cellular properties due to transformation or to presence of viral antigens

Large numbers of lymphoblastoid cells are much easier to obtain for biochemical studies than are adherent fibroblasts. Most established lines are B lymphocytes and may produce antibodies. Lymphoblastoid lines retain many of the characteristic genetic hypersensitivities found in fibroblasts or lymphocytes [1-7].

The disadvantages of the lymphoblastoid cell lines mainly relate to the presence of EB virus. This virus has been associated with infectious mononucleosis, African Burkett's lymphoma and nasopharyngeal carcinoma [11]. The transformed cells express certain viral antigens but typically do not produce infectious virus. Low levels of infectious virus have been induced by treatment of lymphoblastoid cells with agents such as bromodeoxyuridine [12, 13] or TPA [14]. Thus these cells should be handled carefully using conditions appropriate for low risk oncogenic viruses including vertical laminar flow hoods, gloves, mechanical pipettes and decontamination of all waste material. We routinely inactivate liquid waste with povodine iodine (Wescodyne), autoclave all disposable waste and decontaminate reusable materials such as hemocytometers with dilute sodium hypochlorite, soap and 95% ethanol.

A proportion of adults have serum antibodies to EB virus indicating that they probably had clinical infectious mononucleosis or sub-clinical exposure to EB virus [11]. These people are presumably immune to re-infection with EB virus. Those laboratory workers without EB virus serum antibodies are followed with periodic antibody testing. However, I am not aware of any EB virus infection of laboratory workers which has been shown to be caused by exposure to lymphoblastoid cell lines.