

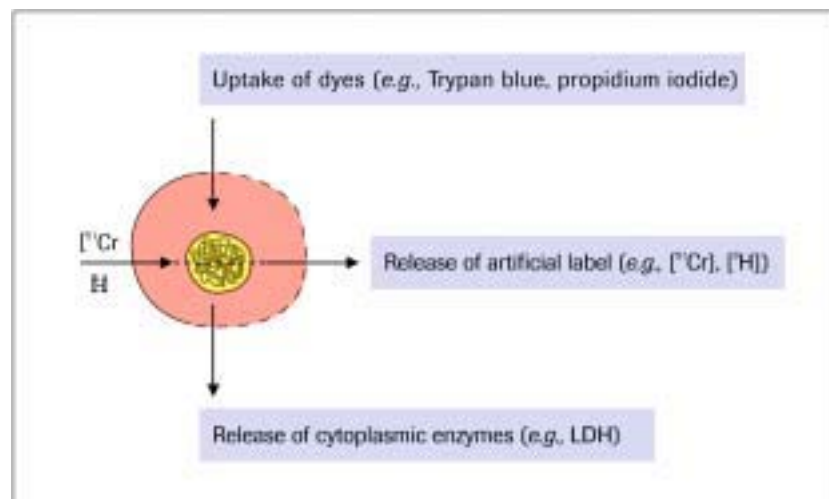
3. Cytotoxicity Assay Methods

3.1 Relationship between cytotoxicity, apoptosis and necrosis

As discussed in Section A 1.1 of this guide, there are two experimentally distinguishable mechanisms of cell death: necrosis, the “accidental” cell death that occurs when cells are exposed to a serious physical or chemical insult, and apoptosis, the “normal” cell death that removes unwanted or useless cells.

In contrast to these two cell death processes, cytotoxicity does not define a specific cellular death mechanism. Rather, cytotoxicity is simply the cell-killing property of a chemical compound (such as a food, cosmetic, or pharmaceutical) or a mediator cell (such as a cytotoxic T cell), independent from the mechanisms of death.

Note: Cytotoxicity may also be used, as it is in this guide, to denote a laboratory method for detecting dead cells, regardless of the mechanism of their death.



▲ Figure 41: Schematic illustration of the three basic principles to assess plasma membrane leakage.

Example of cytotoxicity

A common example of cytotoxicity is cell-mediated cytotoxicity. Cells of the immunessystem [such as cytotoxic T cells, natural killer (NK) cells, and lymphokine-activated (LAK) cells] can recognize and destroy damaged, infected and mutated target cells. Although the recognition machinery used by these cells is very different, their mechanism of target cell destruction may be very similar.

Two possible cytotoxic mechanisms have been proposed for cell-mediated cytotoxicity: (i) the apoptotic mechanism, in which the effector cell triggers an autolytic cascade in the target cell and the genomic DNA fragments before cell lysis; and (ii) the lytic mechanism, in which lytic molecules, notably perforin, are secreted by the effector cell into the intercellular space and polymerize to form pores in the target cell membrane, leading to cell lysis^{3, 47}. These two mechanisms are not mutually exclusive and, quite possibly, are complementary.