Basic biology of cell proliferation in cultured medium

The cells in artificial cultured medium do not express the correct in vivo phenotype because the cell's microenvironment has changed. Cell to cell and cell-matrix interaction are reduced because the cells lack the heterogeneity and three-dimensional architecture found in vivo, and many hormonal and nutritional stimuli are absent.

Cell adhesion

Most cells form solid tissue grow as adherent monolayters. So, first of all the cells in artificial culture need to attach and spread on the substrate before they will start to proliferate. The cell would attach to and spread on some plastic such as polystyrene, if the plastic was appropriately treated with an electric ion discharge or high energy ionizing radiation. The cell adhesion is mediated by specific specific cell surface receptors for molecules in the extracellular matrix, so, it seems likely that spreading may be preceded by the secretion of extracellular matrix proteins and proteoglycan by the cells. The matrix adheres to the charged substrate , and the cell then bind to the matrix via specific receptors.

Cell adhesion molecules

Three classes of transmembrane proteins have been shown to be involved in cell to cell and cell to substrate adhesion.

Class I: Cell to cell adhesion molecules: CAMs (calcium independent) and Cadherins (Calcium dependent). These are involved in interaction between homologous cells and helpful in cell-cell recognition. The cell to cell recognition helps modulating cell behavior.

Class II: These molecules are involved in cell to substrate interaction. This primarily mediated by integrins, fibronectin, laminin and callogen.

Class III: these cell adhesion molecules is the transmembrane proteoglycans, also interacting with matrix constituents such as other proteoglycans or collagen. They possess growth factor receptors that is bound by any growth factor that would stimulate growth of the cells. The growth factors recognized by these include epidermal growth factor (EGF), Fibroblast growth factors (FGFs), or platelet derived growth factor (PDGF).

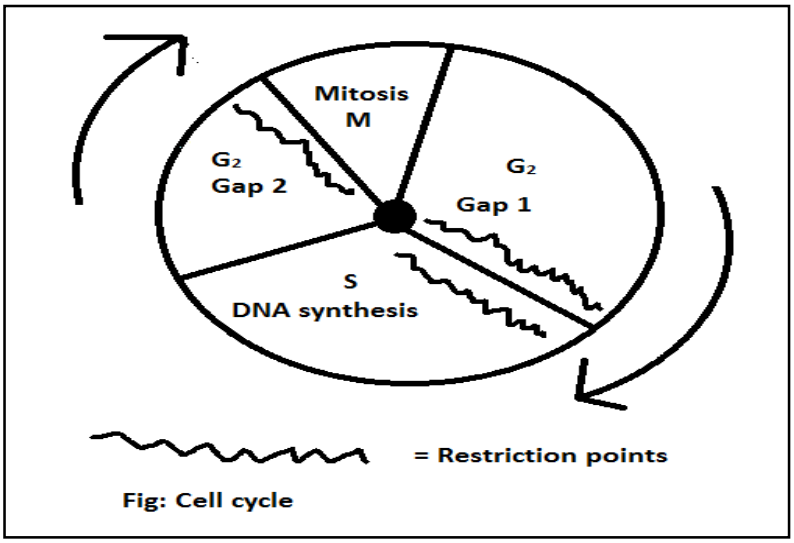

Fig: Cell cycle

Control of cell proliferation

The cell cycle is made up of four phases viz. M phase

(mitosis), G1 phase (Gap 1), S phase (DNA replication), and G2 phase (Gap 2).
The cell cycle is controlled in three stages viz. G1, S and G2 phases as shown in figure.

There are some cellular inhibitors of cell cycle, these are Rb (restricts cell cycle at G1) and P53 restricts cell cycle at (S phase and G2 phases).
The cell cycle is activated by cellular cell cycle activator molecules such as cyclins and cyclin dependent kinases (CDKs).

When there is increase in density of cells there is contact inhibition in the cells causing activation of cell cycle inhibitors and inactivation of cell cycle activators. In cancerous cell lines the cell surface molecules are lost so, there is destruction of contact inhibition hence the cell lines go on multiplying even irrespective cell density.