MCF10A Human Breast Epithelial Cells

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The matrix metalloproteases (MMPs) play important roles in invasion, metastasis and angiogenesis in various cell types. Tissue inhibitor of metalloprotease (TIMP)-2, an endogenopus inhibitor of MMP-2, has been shown to inhibit invasion and metastasis. We have previously shown that MMP-2 is responsible for the H-ras-induced invasive and migrative phenotypes in MCF10A human breast epithelial cells. Here, we investigated the effect of TIMP-2 overexpression on invasion and migration in H-ras MCF10A cells. Human TIMP-2 gene was effectively introduced into H-ras MCF10A cells by retrovirus-mediated gene delivery. TIMP-2 overexpression mediated by retrovirus significantly inhibited invasiveness and migration of H-ras MCF10A cells in a dose-dependent manner. We also show the antiangiogenic effect of TIMP-2 gene delivery. Taken together, our study shows that retrovirus-mediated delivery of TIMP-2 efficiently inhibits metastatic progression of ras-trnasformed human breast epithelial cells, suggesting a potential use of the TIMP-2 gene therapy for the treatment of breast cancer.
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[PC3-14] [2003-10-10 09:00 - 13:00 / Grand Ballroom Pre-function]

Novel Cell-based Protease Assay System for Molecular Cell Biology and Drug Discovery

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Recently development of cell-based assay systems which are useful in molecular cell biology and drug discovery attracts significant attention. Here, we introduce a new technologies for monitoring enzyme activity and its inhibition inside living cells. Among various enzymes, proteases are important targets for studying various biological and disease-related processes such as viral infections, apoptosis and Alzheimer's disease. In this study, a sensitive cell-based protease detection system that enables direct fluorescence detection of a target protease and its inhibition inside living cells is introduced. The CellPA^{TM} system provides a fluorescent molecular beacon protein comprising an intracellular translocation signal sequence(s), a protease-specific cleavage sequence(s) and a fluorescent marker sequence(s). The molecular beacon protein is designed to change its intracellular translocation upon cleavage by a target protease, e.g., from cytosol to a subcellular organelle, or from a subcellular organelle to cytosol or another subcellular organelle. Details of the mechanism and level of the protease action can be monitored at a single cell level, and accordingly the cell population in terms of the level of the protease activity can be accurately enumerated. The clear change in the fluorescence image of the cell makes the CellPA^{TM} system as an ideal tool for various life science and drug discovery researches including the HTS&HCS applications. Various formats of the CellPA^{TM} system for monitoring HCV NS3 protease, caspase-3, caspase-8, β-secretase etc. will be presented.

[PC3-15] [2003-10-10 09:00 - 13:00 / Grand Ballroom Pre-function]

Erythropoietin increases neuronal cell differentiation : association of transcriptional factors AP-1 and NF-κB activation

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Erythropietin (EPO), a hematopoietic factor is also required for normal brain development, and its receptor is localized in brain. Therefore, it is possible that EPO could act as a neurotropic factor inducing differentiation of neurons. The present study, we therefore investigated whether EPO can increase differentiation of undifferentiated cortical neuron isolated from postneonatal (Day 1) rat brains and PC12 cell, undifferentiated dopaminagic cell line. EPO dose (1-100 U/ml) dependently increased cell differentiation and expression of differentiation marker gene (neurofilament and tyrosine hydroxylase) in both cells. Since our previous study (Jung et al., 2003, Mol.