Expression of Cyclooxygenase-2 via NF-κB in Cultured Human Breast Epithelial Cells

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The inducible form of cyclooxygenase-2 (COX-2) has been often observed in various types of cancerous and transformed cells. In this study, we examined molecular mechanism underlying regulation of COX-2 expression through of the eukaryotic transcription factor NF-κB. Cyclooxygenase expression induced by 12-O-tetradecanoylphorbol-13-actate (TPA) in human breast epithelial cells (MCF10A) were inhibited by specific mitogen-activated protein kinase (MAPK) inhibitors, such as SB 203580 (p38 MAPK inhibitor) and PD 98059 (ERK inhibitor) and also by dominant negative (DN) MAP kinase expressing vectors (pCMV5-p38 MAPK DN mutant or pCEP4-pERK2 DN mutant vector). In the luciferase reporter gene assay, NF-κB transcriptional activities were suppressed by dominant negative MAPKs mutant vectors. In anther study, we assessed the COX-2 expression and NF-κB activation in activated H-ras oncogene transformed MCF10A cells, but we did not found any distinct differences between MCF10-H-ras and its parental cell line in terms of COX-2 and NF-κB activation.
These result suggest that ras activation alone is not sufficient to induce COX-2 expression in human breast epithelial cells and activation of other pathways including p38 MAPK may be required for up-regulation of COX-2 in these cells.

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Synthesis and Characterization of DDT Immunogens

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For development of the immunodetection method of DDT family (4,4'-dichlorodipheny-2,2,2-trichloroethane, a persistent and broad toxic organochlorine pesticide), various DDT derivatives were synthesized and characterized for the use of immunogen and the coating ligand of the antibody evaluation. The appropriate lengths of linkers were introduced to investigate more efficient DDT derivatives. Carboxylic acid group was chosen as a functional group for coupling with carrier protein at the terminal position of linker. DDA was readily obtained from the oxidation reation of DDT. DDHP having three carbon linker was directly prepared from the reaction of glutaric anhydride with 4-chlorophenylmagnesium bromide, subsequently chlorination of hydroxyl group at C-1 position gave DDCP. Other derivatives with long chain linker and amide group in linker were prepared through similar reaction. The detail synthetic method for DDA, DDAAP, DDHP DDCP, DDHH, DDCH, DDHHAP, DDCHAP will be discussed.
Among these hapten derivatives, DDA, DDHP and DDCP were conjugated with keyhole limpet hemocyanin for the use of immunogen to produce antibodies. The BSA conjugates of these derivatives were prepared as a coating ligand for the antibody screening. Several monoclonal antibody clones were screened using these probes.

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Effects of endocrine disruptors in whole-organ culture of mouse mammary glands

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