occludin. Treatment of rat Ang-1 in conditionally immortalized rat brain capillary endothelial cell line TR-BBB13 for 48h induced approximately three-fold higher expression and phosphorylation of occludin in comparison with control. The upward band shift of occludin reveals the phosphorylation of occludin. Occludin phosphorylation has been implicated in the regulation of TJs function.
We show here that this is the first report of cloning and expressing the rat Ang-1 in the Bac-to-Bac baculovirus expression system. The rat Ang-1 induces the expression and phosphorylation of occludin in TR-BBB13 in vitro. Therefore, we suggest that Ang-1 regulates BBB permeability by formation of TJs.

Poster Presentations - Field D1. Medicinal Chemistry

[PD1-1] [04/19/2002 (Fri) 10:00 - 13:00 / Hall E]

Tumor Specific Prodrugs of O6-Benzylguanine as Inactivators of O6-Alkylguanine-DNA Alkyltransferase in Antibody-Directed Enzyme Prodrug Therapy

Moon Ki-Young°

Department of Clinical Pathology, Bioindustry and Technology Research Institute, Kwangju Health College, Kwangju, 506-701, Korea

In order to enhance the therapeutic effectiveness of chloroethylating anticancer drugs, O^6-benzyl-N^2-[glutamyl(carbamoyl)]guanine (1) and O^6-benzyl-9-[glutamyl(carbamoyl)]guanine (2) were synthesized and examined as tumor specific adjuvant prodrugs of O^6-benzylguanine (BG) for inactivation of O^6-alkylguanine-DNA alkyltransferase (AGT) in antibody-directed enzyme prodrug therapy (ADEPT). These compound were designed to undergo hydrolysis by carboxypeptidase G2 for the generation of BG at the tumor site, leading to improve oncotoxic selectivity in ADEPT. While compound 1 was chemically very stable under physiological aqueous buffer (pH 7.4, 37 ^{O}C), compound 2 was chemically instable. Incubation of 1 in the presence of carboxypeptidase G2, however, indicates that no BG was released. Unfortuneately, compound 1 and 2 cannot serve as prodrugs of BG.

[PD1-2] [04/19/2002 (Fri) 10:00 - 13:00 / Hall E]

Synthesis of benzothiazolyl compounds through cyclization of thiourea

Yoon JuHee°, Park HeaYoung

College of Pharmacy, Ewha Womans University

Benzothiazolyl moiety is a structural element of compounds having various biological activities such as potent and selective antitumor activity.
A new synthetic route for benzothiazole ring has been developed and a solid-phase synthetic procedure for construction of benzothiazole ring was investigated based on this method.
o-Aminophenol or o-hydroxyaminopyridine was reacted with phenyl isothiocyanate to yield the thiourea, which was cyclized to benzothiazolyl or pyridinothiazolyl compounds using trifluoroacetic acid. This route was simple and employable for the synthesis of substituted benzothiazoles.
This procedure was also applied to solid-phase synthesis of 5-aminomethyl-2-phenyl aminobenzothiazole. The chloroformate functionalized Wang resin was reacted with 4-aminomethyl-2-aminophenol, followed by the reaction with phenyl isothiocyanate and trifluoroacetic acid, to give the desired compound.

[PD1-3] [04/19/2002 (Fri) 10:00 - 13:00 / Hall E]