mediators for the physiological DAG responses and for PE-induced tumorigenesis may aid our understanding of signal integration and can also help to design new strategies for therapeutic cancer intervention.

555

BERBERINE INHIBITS N-ACETYLTRANSFERASE ACTIVITY AND GENE EXPRESSION IN *SALMONELLA TYPHI*

Lii-Tzu Wu[1], Mei-Fen Tsou[2], Chin-Chin Ho[3], Hsiu-Maan Kuo[4] and Jing-Gung Chung[1]

Departments of [1]Microbiology and [4]Parasitology, China Medical University, Taichung;
[2]Department of Internal Medicine, China Medical University Hospital, Taichung;
[3]Department of Nursing, Chungtai Institute of Health Sciences and Technology, 11, Pro-Tze Lane, 40605, Takun, Taichung, Taiwan, R.O.C.

Arylamine carcinogens need to be activated by N-acetyltransferase (NAT) to form active metabolites that lead to induction of cancer. Berberine has been reported to induce cell death (apoptosis) and to inhibit NAT activity in human cancer cell lines (Bladder, colon and brain tumor cells). Therefore, our objective was to investigate the effect of berberine on growth, NAT activity and gene expression in *Salmonella typhi*. The growth inhibition of *S. typhi* was determined by measuring absorbance by optical density (OD at 650 nm) using a spectrophotometer. The NAT activity was determined by high performance liquid chromatography, measuring the levels of 2-aminofluorene and N-acetyl-2-aminofluorene. The results demonstrated that a 24-hour berberine treatment decreased the % of bacterial growth and levels of N-acetyl-2-aminofluorene in *S. typhi*. Polymerase chain reaction (PCR) was used to examine the gene expression of NAT (mRNAT NAT) and it indicated that berberine affects mRNA NAT expression in *S. typhi*.

556

3D-QSAR LEAD OPTIMIZATION ANALYSIS OF SOME NOVEL EUKARYOTIC TOPOISOMERASE II INHIBITORS

Ismail Yalcin, Esin Aki-Sener and Ilkay Yildiz

Pharmaceutical Chemistry Department, Faculty of Pharmacy, Ankara University, Tandogan 06100 Ankara, Turkey

Topoisomerase II (Topo II) is a nuclear enzyme in mammalian cells that interconverts stopological isomers of DNA in the presence of an energetic cofactor ATP (1). A number of anticancer drugs have been described that specifically inhibit eukaryotic Topo II and their antitumor activity is related to the formation of protein-concealed DNA strand breaks, resulting in the stabilization by the drug of an intermediary complex of the Topo II reaction (2). These drug-induced cleavable complexes have been proposed to be the primary action responsible for the antitumor activity.

In our previous studies, the *in vitro* eukaryotic Topo II inhibitor activity of some novel fused heterocyclic compounds was investigated by assaying electrophoretically after incubating the enzyme, plasmid and ATP mixture with or without inhibitors (3).

In this study, we applied the CoMFA (Comparative Molecular Field Analysis) (4) as the 3D-QSAR application using the Sybyl 6.8 Software in SGI workstation for the lead optimization to the training set of compounds having the eukaryotic Topo II inhibitory activities as pIC_{50} values.

1 Wang JP :Biochim Biophys Acta *989*: 1-9, 1989.
2 D'Arpa P and Liu LF:Biochim Biophys Acta *989*: 163-177, 1989.
3 Pinar A, Yurdakul P, Yildiz I, Temiz-Arpaci O, Acan NL, Aki-Sener E and Yalcin I: Biochemical and Biophysical Research Commun *317*: 670-674, 2004,
4 Crammer, RD, III Patterson DE and Bunce JD: J Am Chem *110*: 5959-5967, 1988,
5 Klebe G, Abraham U and Mietzner T, J Med Chem *37*: 4130-4146, 1994.

557

EXPRESSION OF GLIAL CELL LINE-DERIVED NEUROTROPHIC FACTOR FAMILY IN PERIPHERAL NERVE SHEATH TUMORS

Tetsuji Yamamoto, Toshihiro Akisue, Takuya Fujimoto, Kenta Kishimoto, Teruya Kawamoto, Toshiaki Hitora, Takashi Marui Ikuo Fujita and Masahiro Kurosaka

Department of Orthopaedic Surgery, Kobe University Graduate School of Medicine, 7-5-1 Kusunoki-cho, Chuo-ku, Kobe 650-0017, Japan

Background: Little information is available regarding the expression of the glial cell line-derived neurotrophic factor (GDNF) family ligands in peripheral nerve sheath tumors. Objective: To investigate the expression of GDNF, neurturin, persephin and Ret in tissue specimens of schwannoma, neurofibroma and malignant fibrous peripheral nerve sheath tumor (MPNST), using immunohistochemical techniques. Materials and Methods: Formalin-fixed and paraffin-embedded tissue specimens of 42 schwannomas, 6 neurofibromas and 7 MPNSTs were analyzed. All the specimens were obtained from biopsies