

Resistant Mutants to DW-286a, a Novel Quinolone Antibiotic, in *Streptococcus pneumoniae*

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Quinolone resistance in *Streptococcus pneumoniae* is related to mutations in the DNA gyrase and topoisomerase IV genes. DW-286a displayed potent activity against *S. pneumoniae* C9211 (MIC, 0.015 µg/ml) compared with gemifloxacin (MIC, 0.06 µg/ml). This study was performed to analyze the ability of DW-286a to cause resistance development in *S. pneumoniae* and to establish whether DNA gyrase or topoisomerase IV is primary target. DW-286a resistant mutants of *S. pneumoniae* C9211 were generated by stepwise selection at increasing drug concentration. Sequence analysis of PCR products from the mutant strains was used to examine the quinolone resistance-determining regions (QRDR) of GyrA and GyrB proteins of DNA gyrase and the analogous regions of ParC and ParE subunits of the DNA topoisomerase IV. First-step mutants exhibiting low-level resistance had an alteration in GyrA at Ser-83, with Ser-83 to Tyr or Phe being observed. Second-step mutants had mutations in GyrA at Ser-83 to Tyr and in ParC at Ser-79 to Tyr at the same time. Third-step mutants displaying more high-level resistance were found to have additional change in GyrA at Glu-87 to Lys. Moreover, fourth-step mutants had additional mutations in ParC at Asp-83 to Asn, together with other mutations. No changes in GyrB, and ParE were observed in these mutants. Complementary genetic and biochemical studies revealed that GyrA and ParC are dual targets for DW-286a in *S. pneumoniae*, and resistance to DW-286a in *S. pneumoniae* occurs in vitro at a low frequency. To determine the level of expression of PmrA, a putative efflux pump of *S. pneumoniae*, we performed the analysis of QC-RT PCR. There were distinguishable increases in the expression of efflux pump (PmrA), so this phenotype indicated the presence of efflux mechanism of resistance in these mutant strains.

[OC3-1] [2003-10-11 11:00 - 11:15 / ASEM Hall Meeting Room 208]

Caspase-3-mediated cleavage of Cdc6 induces nuclear localization of truncated Cdc6 and apoptosis

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We show that Cdc6, an essential initiation factor for DNA replication, undergoes caspase-3-mediated cleavage in the early stages of apoptosis in HeLa cells and SK-HEP-1 cells induced by etoposide, paclitaxel, ginsenoside Rh2, or TRAIL. The cleavage occurs at the SEVD⁴⁴²/G motif and generates an N-terminal truncated Cdc6 fragment (p49-tCdc6) that lacks the carboxy-terminal nuclear export sequence (NES). Cdc6 is known to be phosphorylated by cyclin A-Cyclin A-dependent kinase 2 (Cdk2), an event that promotes its exit from the nucleus and probably blocks it from initiating inappropriate DNA replication. In contrast, p49-tCdc6 translocation to the cytoplasm is markedly reduced under the up-regulated conditions of Cdk2 activity which is possibly due to the loss of NES. Thus, truncation of Cdc6 results in an increased nuclear retention of p49-tCdc6 that could act as a dominant negative inhibitor of DNA replication and its accumulation in the nucleus could promote apoptosis. Supporting this is that the ectopic expression of p49-tCdc6 not only promotes apoptosis of etoposide-induced HeLa cells but also induces apoptosis in untreated cells. Thus, the caspase-mediated cleavage of Cdc6 creates a truncated Cdc6 fragment that is retained in the nucleus and induces apoptosis.

[OG-1] [10/11/2003(Sat) 11:15-11:45/ Asem Hall 203]

Patient counseling of over-the-counter drugs to enhance the pharmacist's role

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This presentation is to enhance the pharmacist's role in Over-The-Counter(OTC) drug selection and patient counseling for diversification of pharmacy management after the separation of prescribing and dispensing practice in Korea. Self-medication by OTC drugs may be viewed as one element of the broader self-care treatment. The patient may use a OTC drug to manage a minor ailment, a process that may be supported by counseling from a pharmacist. Pharmacists involved in self-medication decisions have a greater involvement with patients and an

enhanced professional role. The success of OTC patient counseling depends on overcoming a variety of communication barriers due to environmental, administrative, economic, and pharmacist factors. The pharmacist has several key functions during the OTC patient encounter. First, the pharmacist should assess, by interview and observation, the patient's physical complaint, symptoms and medical condition. Second, the pharmacist must differentiate self-treatable conditions from those requiring the attention of the patient's health care provider. Third, the pharmacist must advise and counsel the patient on the proper course of action. The pharmacist should explain about providing assistance with OTC drug selection and explain how to use the OTC drug. The role of the pharmacist in optimizing the selection and ever growing use of OTC drugs is critical to the self-care treatment. Pharmacists need to practice their communication skills to make sure they can at least mentally "SOAP" out the patient's problems and achieve the proper product recommendation, often under less than ideal conditions and with limited time. By taking into account the important elements of the OTC patient counseling session and using the communication techniques described, the pharmacist will be able to reach a new level of pharmaceutical care to help the self-medicating patient.

[OG-2] [10/11/2003(Sat) 11:45-12:15/ Asem Hall 203]

The Necessity of Auxiliary Labeling

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The use of auxiliary labels in many advanced countries has shown that patients and caregivers understanding, safety and compliance with proper administration of medication is significantly increased. Although in Korea we give required information orally and written on the packaging when we dispense medication, many international studies have demonstrated a marked increase in full compliance when auxiliary labels were used. The pharmacist must insure that the patients understand how to take correctly in order to get the maximum effect of treatment.

It is common knowledge that human's memory is affected by forgetfulness and the standard labeling or handwritten instructions do not always get the attention of those taking or administering medications. Warnings about drug interactions, side effects, or how to store and administer medication can easily be over looked. Studies show that recall of information on dispensing medications from auxiliary labels was as high as 72.7% and the degree of being noticeable was 84%. Patient compliance was greatly improved and fewer mistakes were made by patients and caregivers.

Auxiliary labeling draws attention to important information using the techniques of advertising. Bright colors, symbols, easy to read and understand messages give patients and caregivers an added advantage. Korean pharmacists must consider the effectiveness of auxiliary labeling. It is crucially important to prevent misuse of medication or improper interaction with other drugs or alcohol by any methods that improve patients' and caregivers understanding and safe use of medications.

[OG-3] [10/11/2003(Sat) 12:15-12:45/ Asem Hall 208]

HbA1C value and Pre-diabetes Early Detection in the Independent Community Pharmacy

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Lifestyle change in the world is spawning an epidemic of Global Obesity.

(Newsweek August 11, 2003)

People with overweight are at great risk of developing Type II diabetes.

The A1C value provides an objective assessment of glucose control over the previous six to eight weeks. The American Diabetes Association recommended values for blood glucose and A1C appear in TABLE 4.

In case one who was found to have >7% HbA1C, he/she may be a patient with pre-DM or DM II.

The United Kingdom Prospective Diabetes Study(UKPADS) established that exerting tight control over blood glucose levels in patients with type 2 diabetes resulted in a 25% decrease in the overall microvascular complication rate, and every 1% decrease in A1C was associated with a 25% reduction in diabetes-related deaths.

Community pharmacists are ideally situated to identify early patients with risk factors for pre-diabetes, DM II and insulin resistance.