Taiwanese American Association of Pharmaceutical Sciences

台美藥劑學會

2019 TAAP Symposium

Speaker Introduction

Bio:

Assistant Research Professor, Ernest Mario School of Pharmacy, Rutgers UniversitySenior Councilor, Dermal Toxicology Specialty Section, Society of Toxicology Dr. Chang is currently serving as an Assistant Research Professor in the Department of Pharmacology and Toxicology, Ernest Mario School of Pharmacy (EMSOP), Rutgers University, Piscataway, NJ 08854. Her research, as Investigator of the Rutgers University CounterACT Research Center of Excellence, mainly focuses on the study of mustard toxicity (sulfur mustard and nitrogen mustard) with emphasis on the mechanism of action of these vesicants in an induced dermal injury model. She received her doctorate in Food Science from Rutgers University; later, she received her toxicology training as a postdoctoral fellow at the Joint Toxicology Graduate Program, UMDNJ/Rutgers University. She has presented her work at regional and annual meetings including COUNTERACT, Society of Toxicology (SOT) and Experimental Biology. She has been invited to speak at several national and international symposiums. She is author/co-author of 36 published abstracts, 18 peer-reviewed articles and two book chapters, and currently has four more manuscripts in progress. Her most recent publication was selected as the recipient of the 2019 DTSS best paper of the year award. Dr. Chang currently also serves as the Senior Councilor in the Dermal Toxicology Specialty Section, the executive officer committee of SOT. Dr. Chang has mentored a number of toxicology graduate students and pharmacy doctoral

students. Students have presented their works at regional and annual meetings and won poster competition awards.

Abstract:

Sulfur Mustard-Induced Cutaneous Injuries and Therapeutic ApproachesSulfur mustard (bis-2-chloroethylsulfide, SM), a highly reactive alkylating agent, produces stronginflammation, edema, and vesication in exposed skin and mucous membranes, and constitutes a potentially serious threat to military and civilian populations. While its mechanisms of toxic action are yet poorly defined, animal models demonstrate disruption of the skin architecture at the dermal-epidermal junction (DEJ). In this regard, SM exposure resembles the blistering diseases, epidermolysis bullosa (EB), in which ECM components in the lamina lucida region of the basement membrane zone (BMZ) are implicated. Disruption of the α3, ß2, or γ2 chains of laminin 332 (formerly laminin 5), a key adhesion glycoprotein of the DEJ, results in vesication that may be further enhanced by the actions of matrix metalloproteinases (MMPs). Therapeutic approaches may target molecules involved in SM-induced injuries, including the initial alkylation, protease activation, prolonged inflammation, and delayed wound repairs. A novel, bifunctional anti-inflammatory prodrug (NDH 4338) designed to target cyclooxygenase 2 (COX2), an enzyme that generates inflammatory eicosanoids, and acetylcholinesterase, an enzyme mediating activation of cholinergic inflammatory pathways in a model of SM-induced skin injury. Adult SKH-1 hairless male mice were exposed to SM using a dorsal skin vapor cup model. NDH 4338 was applied topically to the skin 24, 48, and 72 hr post-SM exposure. After 96 hr, SM was found to induce skin injury characterized by edema, epidermal hyperplasia, loss of the differentiation marker, keratin 10 (K10), upregulation of the skin wound marker keratin 6 (K6), disruption of the basement membrane anchoring protein laminin 322, and increased expression of epidermal COX2. NDH 4338 post-treatment reduced SM-induced dermal edema and enhanced skin re-epithelialization. This was associated with a reduction in COX2 expression, increased K10 expression in the suprabasal epidermis, and reduced expression of K6. NDH 4338 also restored basement membrane integrity, as evidenced by continuous expression of laminin 332 at the DEJ. Taken together, these data indicate that a bifunctional anti-inflammatory prodrug stimulates repair of SM induced skin injury and may be useful as a medical countermeasure.