CENTER FOR DERMAL RESEARCH

CDR SEMINAR SERIES

Linda D. Rhein, M.S., Ph.D.

Bayer Health Care Pharmaceuticals

August 4th, 2014

"Mechanisms of Photodamage and Protection with Sunscreens"

BIOGRAPHY:

Dr. Linda Rhein received her B.S. in Chemistry and her M.S. and Ph.D. in membrane and lipid biochemistry from the University of Maryland and conducted postdoctoral research at University of Pennsylvania in the area of mechanisms of sensory reception. She is currently employed at Bayer HealthCare in global drug safety focusing on dermatologics and on Rx to OTC switches.

Her most recent past positions included Novartis where she conducted research on antifungals and stretch marks, L'Oreal where she studied aging skin and secured approval of new mexoryl sunscreen NDAs, GlaxoSmithKline where her research focused on milder acne treatments, sebum macromolecular structure and use of PPARs for barrier repair and at Colgate Palmolive where she led advanced technology and clinical research in areas of surfactant irritation and skin lipids. She also is an adjunct professor at Fairleigh Dickinson University.

She has published over 50 scientific papers in skin research and is the editor of several books, most recently Aging Skin - Current and Future Therapeutic Strategies published by Allured in 2009. Dr. Linda Rhein is past President of the Society of Cosmetic Chemists, is past editor of the Journal of Cosmetic Science, and has received numerous awards from that society, the most notable was the Literature Award for excellence in publications relevant to cosmetic science. She is noted for her research in skin lipids, mechanisms of moisturization and surfactant irritation.

ABSTRACT:

Photodamage leads to mutations in the DNA and to destruction of skin matrix. Persistent UV exposure can result in rhytides, lentigines and in some instances skin cancers. UV exposure leads to dimerization of pyrimidine bases, cyclobutane pyrimidine dimers and, to a lesser extent, the pyrimidine (6– 4) pyrimidone photoproduct and their Dewar isomers and to mechanisms involving oxidized DNA bases. Replication of damaged DNA leads to an error-prone incorporation of nucleotides at the site of a photolesion, giving rise to mutations.

The tumor suppressor gene - p53 plays a major role in the protection of cells from DNA damage. In response to a genotoxic stress, the p53 nucleoprotein accumulates and specifically binds to DNA and activates transcription. The p53 protein gene product is a central component of the mechanisms that protect skin cells from malignant transformation. It regulates cell cycle progression by arresting in late G1allowing time for excision and repair processes or triggers apoptosis. The upregulation of p53 protein in response to UV is now well documented. Also p53 is the most commonly mutated gene found in human cancers, especially non-melanoma skin cancers. The determination of p53 status in normal human skin cells is a sensitive marker for the detection of UV-induced cell damage.

UV damage to skin matrix results from upregulation of expression of matrix degradation enzymes coined matrix metalloproteinases (MMP's). Removal of matrix components by MMPs is seen as a wound and requires replacement and the processes for fibrogenesis must occur for neocollagen formation. TGF-β is the master switch regulating fibrosis and exists in at least 3 isoforms TGF-β1, -β2 and -β3, secreted by platelets, fibroblasts and macrophages within the damaged site. The switch from matrix degradation to fibrogenesis is controlled by SMADs. TGF-β1 is the lead isoform stimulating fibrosis. However persistent presence of TGF-β1 potentiates excessive fibrosis ultimately resulting in scarring of skin or internal organs. Scarring of internal organs (e.g., post surgical scars, liver cirrhosis and lung fibrosis) results in a loss of organ function. Scarring due to chronic damage from persistent UV radiation exposure of skin presumably results in fine lines and wrinkles (rhytides). Therefore the balance between the 3 isoforms is critical for minimizing scarring and presumably wrinkle formation.

Protection from UV damage as first line therapy is use of sunscreens or simply staying out of the sun which is not practical. Sunscreens must provide protection across the UV spectrum 290 to 400 nm. In the US few sunscreens actually provide full protection across the UV spectrum. Such full spectrum protection requires several sunscreens preferably with high extinction coefficients capable of absorbing both UVB and UVA I and II radiation. The most recent sunscreen product approved through the NDA process is L'Oreal's Anthelios which contains octocrylene for UVB protection and also avobenzone for long wave UVA protection along with the new chemical entity ecamsule for short UVA II protection. Mineral sunscreens in the form of nanoparticles are also more effective at delivering broad spectrum protection.

LOCATION: Life Sciences Building Rutgers - The State University of New Jersey, 145 Bevier Road, Piscataway, New Jersey 08854, New Jersey Center for Biomaterials Suite - Conference Room 102

TIME: 5:30 PM

HOST: Bozena B. Michniak-Kohn, Ph.D., M.R.Pharm.S. Director, Center for Dermal Rsearch, Professor of Pharmaceutics, Ernest Mario School of Pharmacy