CENTER FOR DERMAL RESEARCH

CDR SEMINAR SERIES

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Johnson & Johnson
Consumer & Personal Products Worldwide (CPPW)

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"Paradoxical anti-inflammatory activity from Sertaconazole Nitrate Through Induction of Pro-inflammatory Signaling Cascades"

BIOGRAPHY:

Dr. Michael Southall is a Research Director & Fellow of the Global Skin Biology & Pharmacology and Skin Care Innovation Platforms, Research & Development for Consumer & Personal Products Worldwide (CPPW), a unit of Johnson & Johnson Consumer Companies, Inc. In his position, Dr. Southall strives to develop a pipeline of technologies that are scientifically proven to provide safe and clinically effective skincare benefits. He received his Ph.D. in Pharmacology at Indiana University School of Medicine in Indianapolis, where he also completed his Post Doctoral Fellowship in Dermatology.

During his professional career, Dr. Southall has twice been awarded the Johnson Medal, the highest scientific recognition at Johnson and Johnson for excellence in research. He also received a grant from the Dermatology Foundation to study skin inflammation. He currently serves on the editorial board for the Journal of Pharmacology and Experimental Therapeutics, is a member of the scientific advisory board for The Institute for In Vitro Sciences and the WG4 working group of the International Standards Organization (ISO). He has published over 40 peer-reviewed papers and book chapters on inflammation, oxidative stress and natural products and is an inventor on 14 granted patents and 60 patent applications.

ABSTRACT:

Sertaconazole nitrate is a topical antifungal agent that exhibits anti-inflammatory activity; however, the mechanism for this action was unknown. We investigated the cellular mechanisms by which sertaconazole exerts its anti-inflammatory activity in keratinocytes and human peripheral blood mononuclear cells (PBMCs). Paradoxically, sertaconazole was found to activate the proinflammatory p38 mitogen-activated protein kinase. Treatment with sertaconazole also resulted in the induction of cyclooxygenase-2 (COX-2) and the subsequent release of prostaglandin E2 (PGE2). Knocking down p38 in keratinocytes using small interfering RNA resulted in an inhibition of sertaconazole-induced PGE2 release confirming that activation of p38 was required for PGE2 production.

Additionally, in stimulated keratinocytes and human PBMCs, sertaconazole was found to suppress the release of cytokines. Treatment with anti-PGE2 antiserum or the COX-2 inhibitor NS398 reversed the inhibitory effects of sertaconazole on the release of proinflammatory cytokines, linking endogenous PGE2 with the anti-inflammatory effects. Finally, in an in vivo mouse model of tetradecanoyl phorbol acetate (TPA)-induced dermatitis, the sertaconazole-mediated inhibition of TPA-induced ear edema was reversed by NS398. Biochemical analysis of tissue biopsies revealed increase in PGE2 levels in sertaconazole-treated mice. Thus, activation of the p38-COX-2-PGE2 pathway by agents such as sertaconazole provides anti-inflammatory therapeutic benefits

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