Fall 2024

Biochemistry and Molecular Biology Brown Bag Series

Mike Kemp, Ph.D.

"Monitoring and pharmacologically modulating circadian gene expression and responses to UV radiation in human skin"

Tuesday, September 3, 2024

11:00 AM

Location 105 Biological Sciences Building

Lab: Mike Kemp, Ph.D.

Boonshoft School of Medicine
WRIGHT STATE UNIVERSITY

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https://science-math.wright.edu/biochemistry-and-molecular-biology

Abstract

Studies in mice found that the rate of removal of UV photoproducts from DNA varies over the 24-hr day and is correlated with the expression of the DNA repair protein XPA, erythema, and skin carcinogenesis. Experimental work in human subjects similarly showed that the timing of UV exposure impacts erythema. Given that small molecule compounds that target core components of the circadian transcriptional machinery are being developed to improve different disease states, we used human skin discarded during routine surgeries to examine the effect of a combination of the cryptochrome inhibitor KS15 and REV-ERB antagonist SR8278 on the expression of circadian clock and genotoxic stress response genes such as XPA. Though significant inter-individual variability in core clock gene oscillations and responses to treatment were observed in the skin explants, increased expression of XPA and other DNA damage response genes could be observed in a subset of samples. Moreover, topical treatment of skin explants with KS15 and SR8278 partially reduced UVB-induced sunburn cell formation. However, in vitro studies showed that these compounds directly absorb UVB wavelengths to limit UV photoproduct generation. Nonetheless, our work here lays the foundation for further studies of circadian modulating compounds in human skin.