Department of Biological Sciences

JOB TALK

Speaker: Dr. Sanjay Premi, PhD

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Date/Time: Monday, September 4th, 2017 at 10:15 am
Venue: L3, LHC

Title: UV-signature DNA damage without UV and its implications in skin cancer

Skin cancer is one of the most prevalent forms of cancer and it is etiologically attributed to C→T mutations in DNA. These mutations arise from cyclobutane pyrimidine dimers (CPDs) which are created instantaneously as the energy of sunlight's ultraviolet (UV) radiation is absorbed by DNA. Melanin, produced by specialized cells called melanocytes, acts as shield for sunlight's UV. However, UV irradiated mice develop skin cancer only if their melanocytes contain melanin. To investigate this paradox, we studied the repair of UV induced CPDs in human and mouse melanocytes, and in a humanized mouse model. Surprisingly, we discovered that in addition to their instantaneous creation, CPDs were being created in melanin-containing melanocytes for hours after an initial UV exposure ended. These "delayed" or "dark" CPD also included cytosine-containing-CPD which initiate UV-signature, carcinogenic C□T mutations. We identified a novel pathway called "melanin-chemiexcitation" whereby reactive oxygen and nitrogen species oxidize melanin and generate a melanin-carbonyl in a triplet quantum state. This melanin-carbonyl contains energy equivalent to a UV photon and creates CPDs in the DNA without any exogenous UV exposure. This study made a paradigm shift in photobiology suggesting that melanin can be carcinogenic in addition to being a potent sunshield. It also validated the importance of chemically excited species in mammalian biology. We are now mapping the human genome for CPD hotspots/repair-slowspots, and investigating the role of melanin-chemiexcitation in skin cancer initiation / drug-resistance. In addition, we are screening for novel triplet energy quenchers that could potentially prevent the carcinogenic events transpiring in skin hours after sun-exposure ended.