神戸大学グローバルCOEプログラム
「次世代シグナル伝達医学の教育研究国際拠点」特別セミナー

第45回シグナル伝達医学グローバルCOE学術講演会

日時：2011年8月2日(火)17:00～

場所：臨床研究棟　5F　B講義室

Dr. David Mitchell

Professor,
Department of Molecular Carcinogenesis,
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Gender-bias and the acute UVB response in a *Xiphophorus* hybrid fish melanoma model

Our experiments unequivocally show that damage caused by the direct absorption of UVB by DNA and the specific types of DNA damage induced by UVB are required for melanomagenesis. Collateral to this finding we show that UVB-induced melanoma is significantly higher in males and that early life and young adult exposure to acute UV produce comparable CMM frequencies. When background levels are subtracted, 60% of males develop melanomas compared to 18% for females. The frequency of melanomas in animals not exposed to UVB is not significantly different in males and females, indicating that gender-specific pathways interact with the DNA damage response pathway to enhance susceptibility to melanoma. Unlike breast and prostate cancers, the significance of hormones in melanoma etiology is controversial due in part to clinical and *in vitro* studies frequently yielding contradictory results. In response to a tumorigenic dose of UVB we observe a general depression in circulating hormones, including dihydrotestosterone, 11-ketotestosterone (11-KT), 17β-estradiol (E_2) and cortisol, between 1.5 and 6 h post-UVB with little additional change by 24 h. Conjugated (receptor-bound) 11-KT levels drop in males and females soon after UV but by 24 h show >2-fold increase compared to baseline in males but not in females. We do not as yet understand the relationship between these events but it is evident that (1) hormones respond to UVB stress and (2) the male and female hormone responses are different. To further our understanding of the hormone response to UVB we developed quantitative real-time PCR (qPCR) for the hormone receptor genes ARα, ARβ, ERα and ERβ.

For more information
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